Shire 2016 Investor Day

November 10, 2016

Opening Remarks

Jeff Poulton, CFO

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

Forward-Looking Statements

Statements included herein that are not historical facts, including without limitation statements concerning future strategy, plans, objectives, expectations and intentions, 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 conducts its own manufacturing operations for certain of its products and is reliant on third party contract manufacturers to manufacture other products and to provide goods and services. Some of Shire’s products or ingredients are only available from a single approved source for manufacture. 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 significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- certain of Shire’s therapies involve lengthy and complex processes, which 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;
- Shire’s products and product candidates face substantial competition in the product markets in which it operates, including 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 the combined company’s revenues, financial condition or results of operations;
- inability to successfully compete for highly qualified personnel from other companies and organizations;
- failure to achieve the strategic objectives with respect to Shire’s acquisition of NPS Pharmaceuticals, Inc., Dyax Corp. (“Dyax”) or Baxalta Inc. (“Baxalta”) 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, as well as changes in foreign currency exchange rates and interest rates, that adversely impact the availability and cost of credit and customer purchasing and payment patterns, including the collectability of customer accounts receivable;
- failure of a marketed product to work effectively or if such a product is the cause of adverse side effects could result in damage to the Shire’s reputation, the withdrawal of the product and legal action against Shire;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to Shire’s activities in the highly regulated markets in which it operates may result in significant legal costs and the payment of substantial compensation or fines;
- 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 incurred substantial additional indebtedness to finance the Baxalta acquisition, which may decrease its business flexibility and increase borrowing costs;
- difficulties in integrating Dyax or Baxalta into Shire may lead to the combined company not being able to realize the expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits at the time anticipated or at all; and

Other risks and uncertainties detailed from time to time in Shire’s filings with the Securities and Exchange Commission, including those risks outlined in “ITEM 1A: Risk Factors” in Shire’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2016.

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.

Shire is at a key inflection point in its history…

Context for Today

- Momentum towards our long-term strategic aspirations
- Recently completed largest acquisition ever
- Significant new opportunity with leading hematology and immunology franchises
- Numerous near-term catalysts for our exciting late-stage clinical pipeline

The “New” Shire

- THE leading global biotechnology company focused on rare diseases and other highly specialized conditions
- Enhanced profile, with leadership in multiple high-value franchises and industry-leading capabilities
- Strong track-record of commercial excellence and an expanded global footprint
- Commitment to innovation and strong execution driving our robust clinical pipeline of next-generation therapies
- Experienced and disciplined management team with a nimble, performance-driven organization

Shire

Investor Day agenda

TIME	TOPIC	SPEAKER
8:00-8:30am	*Registration/Breakfast*	
8:30-8:35am	Introduction to 2016 Shire Investor Day	Jeff Poulton
8:35-9:00am	Shire's Approach to Innovation	Flemming Ornskov, M.D., MPH
9:00-9:20am	R&D Strategy and Pipeline Transformation	Phil Vickers, Ph.D.
9:20-10:20am	Leadership in Rare Hematology	Kim Stratton Guest Speaker: Michael D. Tarantino, MD
10:20-10:45am	*Morning Break*	
10:45-11:15am	Leadership in Immunology	Perry Sternberg
11:15-11:45pm	Morning Q&A	Shire Team
11:45-12:30pm	*Lunch*	
12:30-12:50pm	Pipeline Update: GI programs SHP621 for EoE and SHP647 for IBD	Howard Mayer, M.D.
12:50-1:10pm	Pipeline Update: SHP607 for Complications of Prematurity	Norman Barton, M.D.
1:10-1:30pm	Pipeline Update: SHP620 for CMV in Transplant Patients	Howard Mayer, M.D.
1:30-1:40pm	Pipeline Update: SHP465 for ADHD	Howard Mayer, M.D.
1:40-2:00pm	Pipeline Update: SHP643 for Hereditary Angioedema (HAE)	Wolfram Nothaft, M.D
2:00-2:30pm	Closing Remarks and Afternoon Q&A	Flemming Ornskov and Shire Team
2:30-3:00pm	*Reception*	

Shire’s Approach to Innovation

Flemming Ornskov, M.D., MPH, Chief Executive Officer

Shire is creating a unique leadership platform

The leading rare disease-focused biotech

Sharp focus leads to high impact

Focused patient communities

Rare diseases
Highly specialized conditions

- Precision innovation and technologies
- Culture of collaboration and execution
- Global resource and expertise

High patient impact
Breakthrough therapies for patients with significant unmet needs

High societal value
Improved patient outcomes and value for customers

Sustained growth
Sustainable rare disease market serving multiple patient communities with high unmet need

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Strategic rationale

The unmet need in rare diseases and highly specialized conditions creates an opportunity for innovation

Life-altering conditions with significant unmet needs

- Debilitating, often life-threatening conditions with substantial impact on patients and their caregivers
- Significant demands on healthcare systems: chronic treatment, repeated hospital visits, supportive care
- Societal economic burden due to patient and caregiver leave and loss of productivity

Opportunity for innovation

- Over 7,000 diseases, of which only 5% have treatments
- Increasing share of regulatory approvals in US, EU and Japan
- Often accelerated development due to priority review and phase-skipping
- R&D incentives, and lower overall R&D costs

High sector growth
+12% CAGR for rare diseases,
vs 6% projected for pharma overall through 2020[1]

Extraordinary patient impact
Breakthrough therapies and improved patient outcomes

(1) EvaluatePharma Orphan Drug Report, 2015.

Shire brings a focused, stepwise approach to innovation that meets the needs of patients across therapeutic areas

Patients' clinical needs

Medical	Go-to-Market	Diagnostics	Delivery	Patient Support
• Targeted approach to addressing unmet need • Deep medical & scientific expertise • Balance Business Dev. & Research	• Customer-facing innovations • New ways to approach markets • Access • Pioneering manufacturing improvements	• Patient screening • Patient finding • Personalized solutions *(e.g., myPKfit)*	• Adminstration and dosing improvements *(e.g., Cuvitru, Adynovate, SHP643)* • Smart devices	• Patient advocacy • Patient services

MEDICAL

GO-TO-MARKET

DIAGNOSTICS

DELIVERY

PATIENT SUPPORT

Consistent approach

Shire builds therapeutic strategies with first in class, best in class and differentiated products

* Subject to regulatory approval

Shire's innovation engine streamlines the development, regulatory and value demonstration process…

Research

Development

Regulatory

Health Economics

Agnostic to internal or external sourcing of innovation

Shire's Research capability is a:

Source of NCEs & NBEs

Enabler of access to best compounds for internalization

Clinical development is a core capability of Shire

Track record of developing acquired assets

Trials completed ahead of schedule

Right path

2 recent Breakthrough Status designations

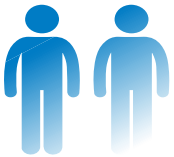
Right label

Value creation through differentiation

Right value

Working with payers to create compelling value dossier

…and leverages our partnerships with patients and healthcare providers to bring our medicines to a global audience



Patients & Partners

100+
relationships with patient advocacy groups

44K+
patients helped with access and affordability

Cincinnati Children's

Boston Children's Hospital
Until every child is well

WFH
WORLD FEDERATION OF HEMOPHILIA

NORD
National Organization for Rare Disorders

Critical Mass

22K+
employees in offices across

68 countries

90+
plasma collection centers

17 high quality manufacturing sites

Shire's Culture

Delivered Outcomes

Millions of patients
treated in the past 10 years[1]

Products available in **100+** countries

30+
planned product launches by 2020

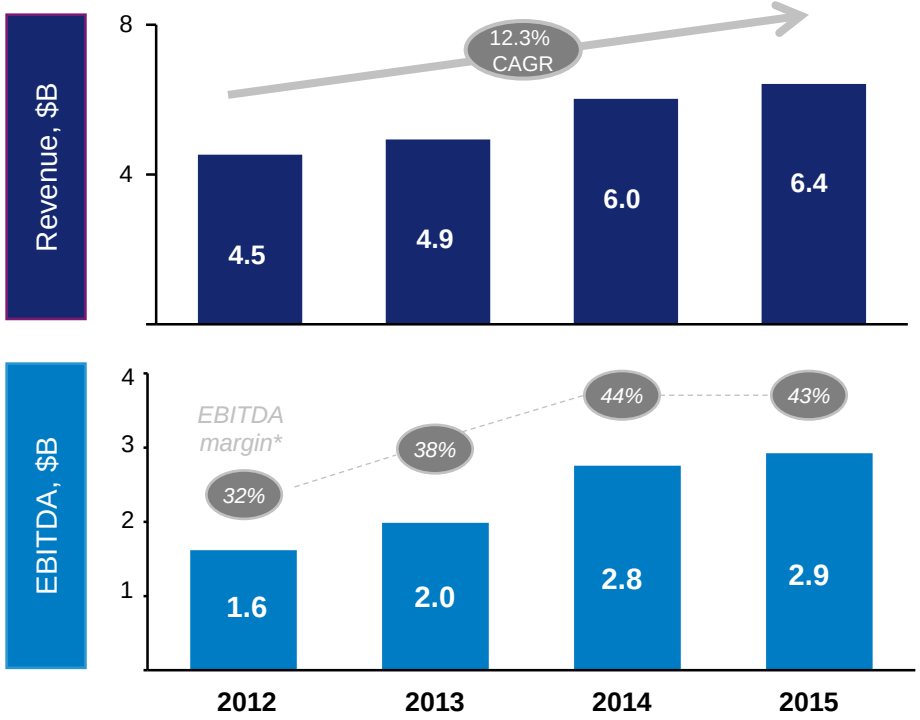
40+
clinical programs in pipeline

Source: Company financial disclosures, management projections
(1) IMS Health, management estimates, data since 2006

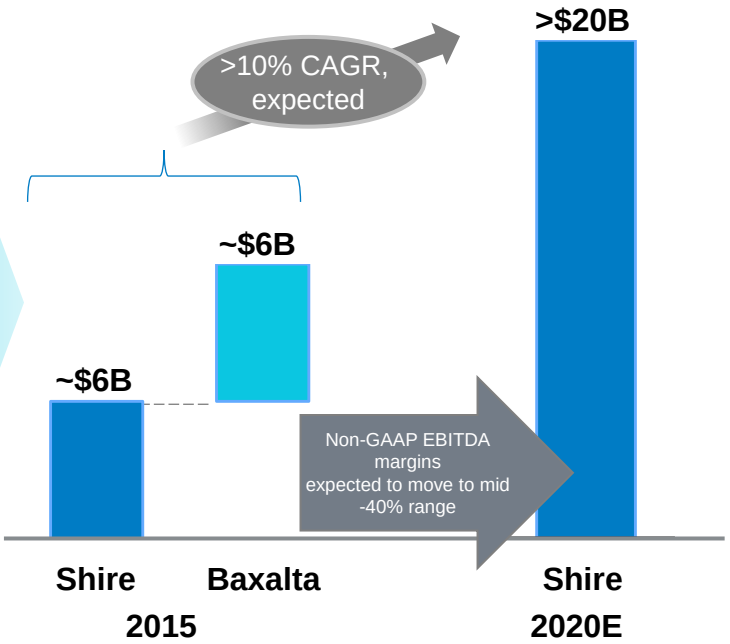
Consistent results

Delivered consistent historical revenue and profitability growth, with the right strategy for continuing this trend

Strong growth over the last several years



Addition of Baxalta expected to fuel continued revenue growth toward our stated "20 x 20" goal



Net debt / EBITDA anticipated to reach 2-3X by end of 2017

Source: Company financial disclosures, management projections
* Non GAAP EBITDA as a % of product sales, excluding royalties and other revenues

Looking ahead

Several key growth drivers that should play an important role in helping us achieve our $20B by 2020 aspirations

Significant pent-up demand
- ~16M diagnosed patients in US with limited treatment options

Strong launch
- In 2+ mos since launch, >75K Rxs; 17%TRx & 45%NBRx market share

Hemophilia

Increased diagnosis, prophylaxis rates and personalization
- Expected drivers of continued growth, especially in ex-US markets
- Decades of clinical experience and data generation

Recent and upcoming launches
- Adynovate, Vonvendi, Obizur expected to contribute meaningfully to revenue by 2020

ADHD / BED

Few signs of adult market saturation
- Adult market continues to outpace total ADHD market

Expected approval and launch of SHP465 in 2017
- Provides further revenue driver for franchise

International markets
- BED and adult ADHD international roll-out

Phase III Pipeline*

20+ registered / Phase III programs, most expected to launch by end of 2020

6 new molecular / biologic entities to be highlighted today

SHP607 (neonatology complications)
SHP620 (CMV infection)
SHP621 (eosinophilic esophagitis)
SHP643 (hereditary angioedema)
SHP647 (inflammatory bowel disease)
SHP465 (ADHD)

* Subject to regulatory approval

We run our business in a responsible and ethical way and are accountable for our social, economic and environmental impacts

Our Leadership

Most Sustainable Corporations in the World GLOBAL100

Newsweek GREEN RANKINGS 2016

GLOBAL DAY OF SERVICE 2016 #SHIREGDS

seriousfun children's network founded by paul newman

FTSE4Good

ACMG Foundation for Genetic and Genomic Medicine Better Health Through Genetics™

Our Culture

- Working with global humanitarian aid organizations to improve access to Shire's rare disease medicines
- Supporting the next generation of medical geneticists
- Enabling children with serious illnesses to participate in camp experiences
- Organizing Shire's annual Global Day of Service where employees volunteer and get involved with community projects around the world
- Recently recognized by AllTrials as the #1 pharmaceutical company for our clinical trial transparency record

Shire

Conducting a STEM experiment at a school for children with special needs at Shire's most recent Global Day of Service

Shire's profile as we approach 2017

- We have built the leading biotech focused on rare disease and highly specialized conditions
- Deepest and most innovative pipeline in our history
- Expected to deliver double digit top-line growth
- Anticipated expanding Non GAAP EBITDA margins
- Cash generation allows near-term debt servicing
- Stated goal of $20B in revenues by 2020
- Strategic focus → Proven approach → High impact

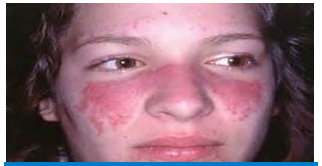
R&D Strategy and Pipeline Transformation

Philip Vickers, Ph.D.
Global Head of Research & Development

Shire

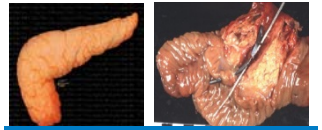
Through growth and transformation, patients at the very heart of our thinking

HEMOPHILIA



SLE

HUNTER



Pancreatic Cancer

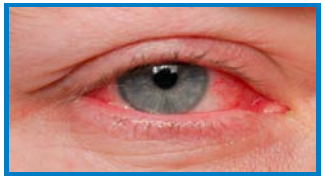
ALL

HAE

ADHD

MLD

Complications of Prematurity



CONJUNCTIVITIS

DRY EYE

adRP

Type 1 Gaucher Disease

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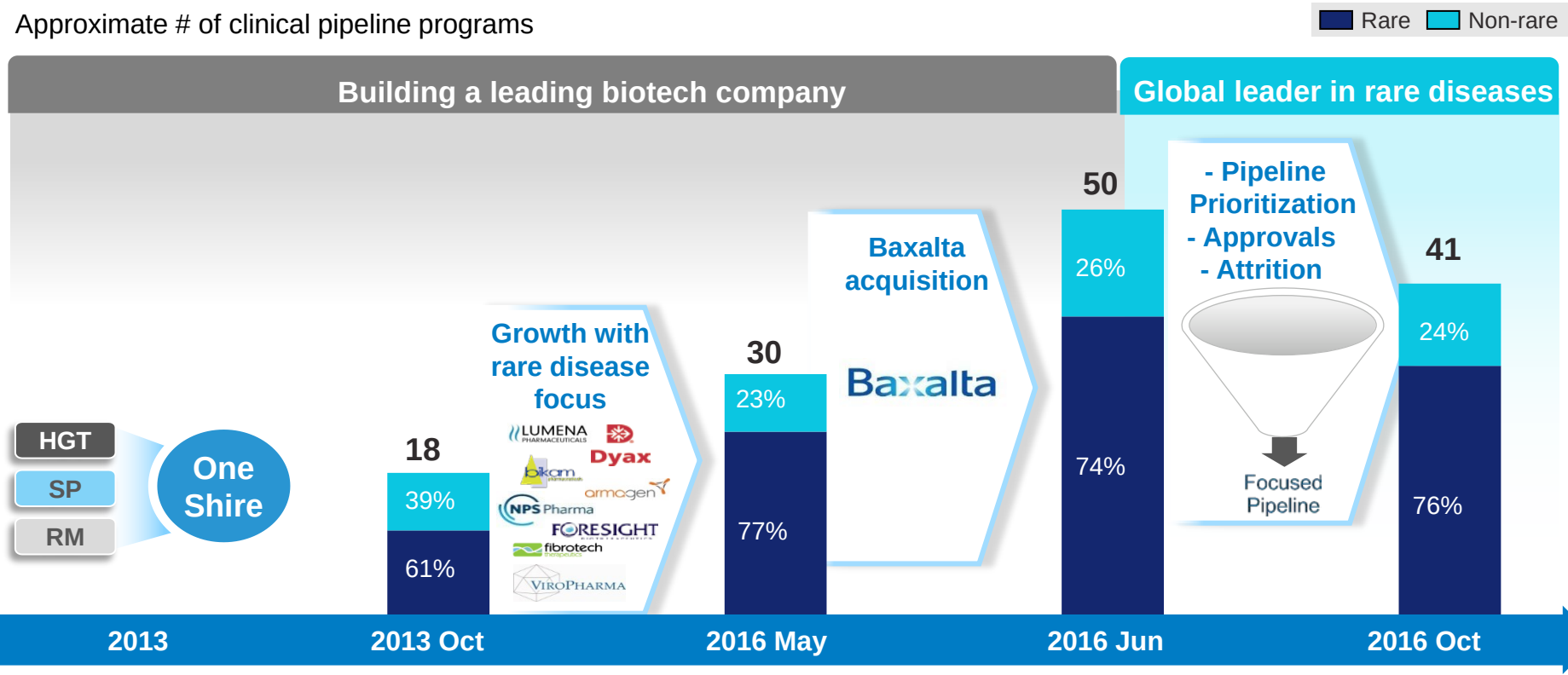
Over three years Shire has built an industry-leading rare disease pipeline

Approximate # of clinical pipeline programs



Sharp focus has lead to industry-leading rare disease pipeline

Focus and invest in areas of domain expertise

- Therapeutic area focus
- Rare Disease focus

Expand areas of domain expertise

- Targeted licensing and acquisition
- Expand into Ophthalmology
- Increase value of acquired assets (e.g., ViroPharma)

Innovation focused on the needs of patients

- Balance internal and external programs
- External partnerships

Operational excellence

- Clinical trial design, trial recruitment
- Engagement with regulatory authorities

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Pipeline transformation since 2013

Progression of in-house programs

- E.g. Vyvanse for BED, Intrathecal Programs
- 'One Shire' consolidated Shire business units

Vyvanse® (lisdexamfetamine dimesylate)
10 • 20 • 30 • 40 • 50 • 60 • 70 mg capsules

ONE INTEGRATED R&D ORG
ONE
Structure | Culture | Purpose

Access to external innovation

- Multiple partnerships with world leading technology providers

ethris ENABLING THERAPIES
ARMAGEN TECHNOLOGIES Biotechnology for the Brain
arGEN-X
SOPHYSA
Nimbus Discovery

Acquisition of external assets and companies

- Baxalta (Hematology, Immunology, Oncology)
- Dyax (HAE)
- Premacure (complications of prematurity)
- NPS (SBS and hypoparathyroidism)
- SARCode (Dry eye)
- ViroPharma (HAE)
- Lumena (cholestatic liver disease)

Baxalta
Dyax
NPS Pharma
SARCode bioscience
premacure
LUMENA PHARMACEUTICALS

Increase value of acquired assets*

- Investigation of potential new uses of Cinryze
- Eosinophilic esophagitis
- CMV infection

CINRYZE® C1 esterase inhibitor (human)
ViroPharma Incorporated

Shire

* Subject to regulatory approval

Resulting pipeline is robust with rare disease indications at all stages of development

Research and Preclinical	Phase 1	Phase 2		Phase 3		Registration	Recent approvals
35+ programs • Internally developed and via partnership • Both rare disease and specialty conditions • Multiple modalities including NCEs, MAbs, proteins, and gene therapy	**SHP611** (MLD)	**Onivyde** (Pancreatic Cancer, 1st line)	**SHP620**[5] (CMV infection in transplant patients)	**SHP609** (Hunter IT) Ph 2/3	**Obizur** (CHAWI surgery)	**Natpar - EU** (Hypoparathyroidism)	**Cuvitru** (PID)
	SHP622 (Friedreich's Ataxia)	**Onivyde - Japan**[2] (Pancreatic Cancer, post gemcitabine)	**SHP625**[4] (PFIC)	**SHP621**[4] (EoE)	**Calaspargase Pegol** (ALL)	**Adynovate** (Hemophilia A)	**Xiidra** (Dry eye)
	SHP623[1] **(rC1-INH)** (NMO)	**SHP607**[3] (BPD and IVH)	**SHP625** (ALGS)	**SHP643**[4] (HAE Prophylaxis)	**10% Hyqvia+Kiovig** (CIDP)	**Intuniv - Japan** (ADHD)	**Onivyde - EU** (Pancreatic Cancer, Line 2)
	SHP631 (Hunter CNS)		**SHP626** (NASH)	**Firazyr - Japan** (Acute HAE) Ph 2/3	**Obizur** (CHAWI on demand)		
	SHP655[5] **(BAX930)** (hTTP)		**SHP640**[5] (Infectious Conjunctivitis)	**Cinryze - Japan** (HAE Prophylaxis)	**Alpha-1 Antitrypsin** (Acute GvHD)		
	SHP656 (BAX826) (Hemophilia A)		**SHP647**[5] (CD)	**Cinryze SC** (HAE Prophylaxis)	**SHP465**[6] (ADHD)		
			SHP647[5] (UC)	**Cinryze** (AMR)	**SHP555 - US** (Chronic Constipation)		
			SHP652 (SM101) (SLE)	**Gattex - Japan** (Adult SBS)	**Vyvanse - Japan** (ADHD) Ph2/3		
			SHP653 (imalumab) (mCRC)	**Vonvendi**[7] (VWD)			

Rare indication

Non-rare indication

Pipeline excludes: Oncaspar lyophilized, Alpha-1 prophylaxis, and Buccolam

(1) rC1-INH previously being developed as SHP623 for HAE prophy; After Ph1 completion will be developed for NMO; (2). Registrational study; (3). SHP607 originally developed for ROP

(4) Granted breakthrough designation by FDA; (5). Phase 3 ready study; (6). SHP465 received positive Ph3 data in April (child./Ado), June (Adults) 2016;

(7) Approved in US for on-demand in adults, in phase 3 for surgery, peds/prophylaxis Ph3 study to begin in 4Q16, and in EU is registration-ready for On-demand in adults

Note: Phase 2/3 programs shown as Phase 3

Innovation mindset matches rare disease terrain

- **Little understanding of the diseases** – very little information
- **No precedent** for clinical study design & endpoints
- **Regulatory path is untrodden**
- **Few and hard-to-find patients**, geographically dispersed for study and clinical trial enrollment
- Increased focus on **payers' perspective, real world evidence, value demonstration**
- **Intense need for education** of patients, caregivers and physicians
- Extremely high medical need – pressure for **early access**
- **Clinical trial transparency**

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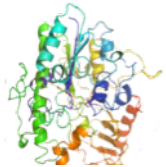
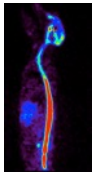
Serial innovation in areas of strategic focus:
Hunter Syndrome and HAE

Hunter Syndrome



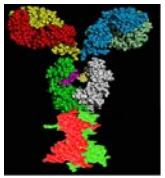
elaprase (idursulfase)

- Novel Enzyme Replacement Therapy (ERT)
- IV administration



Hunter IT program*

- Novel CNS delivery device for ERT
- Novel formulation
- Combination product



'Trojan Horse' program*

- Novel delivery approach for ERT
- IV delivery

HAE

CINRYZE (C1 esterase inhibitor (human)) firazyr (icatibant injection) KALBITOR ecallantide

- Ability to address both prophylactic and acute HAE needs
- Prophylaxis requires IV administration

SHP616* (CINRYZE) HAE Prophylaxis

- Novel delivery method
- Subcutaneous formulation to allow patient-administered prophylaxis

Dyax

- Novel antibody therapy
- Subcutaneous administration

Shire

* Under investigation

Shire's approach to fostering a culture of innovation

Leaders role-modeling behaviors that support innovation	• Engagement of leaders with colleagues across organization
Set expectations around innovation and risk, support with resources	• Define risks and objectively manage to crisp go/no-go decision points • Balance risk across portfolio • Clear decision-making, minimize layers
Recognize innovation	• Clearly build into rewards and recognition
Acceptance that with risk comes some failures	• Remove fear of failure • Promote learning from failures
Drive innovation across organization, not just Research	• Clinical, Regulatory, Medical Affairs, Business Development, Finance, HR, Manufacturing, Commercial

Operational excellence in clinical development has been critical to our recent success

Critical Success Factors

- Innovative clinical trial design
- Frequent regulatory engagement
- Clinical Operations excellence
- Targeted recruitment strategy

Recent Example

Xiidra for Dry Eye Disease

- Before Xiidra, no agent approved for signs and symptoms of dry eye disease
- Xiidra clinical program was largest in dry eye disease (>2500 patients)
- Second Phase 3 symptom study (OPUS-3) complemented data from OPUS-2 and recruited with speed
- Early and frequent engagement with FDA
- Very high quality submission

Shire

Making major progress while successfully integrating

Major Approvals & Launches

Approval of CUVITRU
for Primary Immune Deficiency in Europe and the US

FDA Approval of XIIDRA (Lifitegrast)
for Dry Eye Disease

EMA Approval of ONIVYDE for 2nd Line Metastatic Pancreatic Cancer

Approval of Vyvanse in Canada for BED in adults

Approval of Lialda in adults in Japan for UC

Launch of VONVENDI in adults in the US for vWD

Development Progress & Acquisitions

2 Breakthrough Therapy Designations
- SHP621, SHP625

1 Fast Track FDA Designation
- SHP626 for NASH

Completed Enrollment for Phase 3 Studies
- SHP609: Hunter Syndrome (IT Program)
- SHP643: HAE

Completion of Phase 2 study
- SHP607: complications of prematurity

Acquisition
- SHP647 integrin antagonist for IBD

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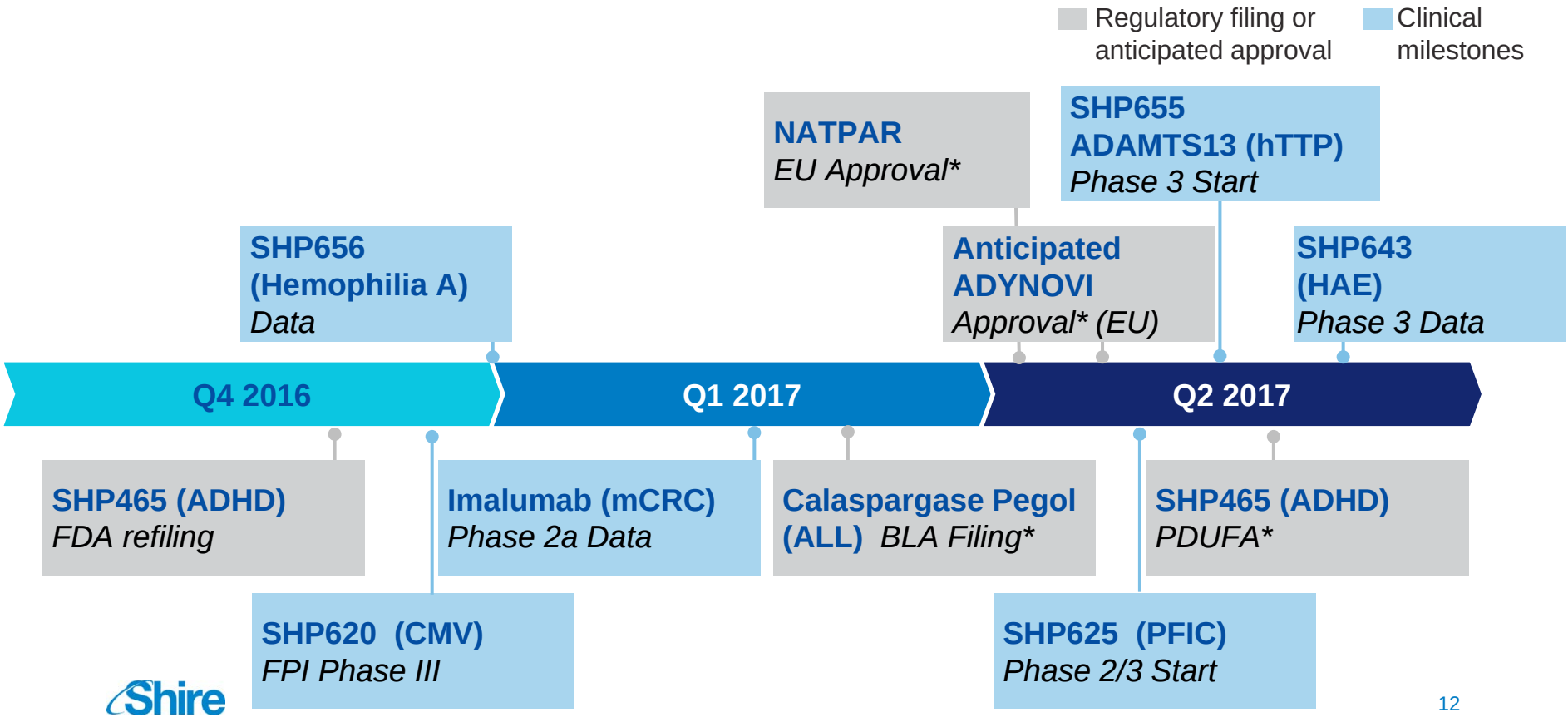
Looking forward – Anticipated near-term milestones



* Subject to regulatory approval

Afternoon session: Six late-stage programs

Rare Disease Leadership

Gastroenterology
SHP621 – (Eosinophilic Esophagitis)

Transplant Medicine
SHP620 – (CMV Infections)

Neonatology
SHP607 – (Complications of Prematurity)

Genetic Diseases
SHP643 – (Hereditary Angioedema)

Specialty Condition Leadership

Gastroenterology
SHP647 – (Inflammatory Bowel Disease)

Neuroscience
SHP465 – (ADHD)

Shire

Shire's Leadership in Rare Hematology

Kim Stratton
Head International Commercial

International Region has strong expertise in Rare Diseases and a strong focus on Hematology

All countries **outside of USA**

Present in 68 countries and bringing products to patients in 100+ markets

Old Shire

~70% Rare Diseases

Largest Franchise: Genetics (LSD/ HAE)

New Shire

~90% Rare Diseases

Largest Franchise: Hematology > 40% of sales

Shire

Shire leading Rare Hematology

Shire leads this dynamic market

- **Large global dynamic market** with **growth of 3-5%**
- Shire is the leader with **longest heritage, broadest portfolio & leading market share of 36%**

Shire has 3 key growth drivers

- **Drive diagnosis & prophylaxis** in developing markets
- **Drive prophylaxis & personalization** in developed markets
- Geographic & portfolio expansion **with +100 launches across +40 countries**

Shire has best in class portfolio

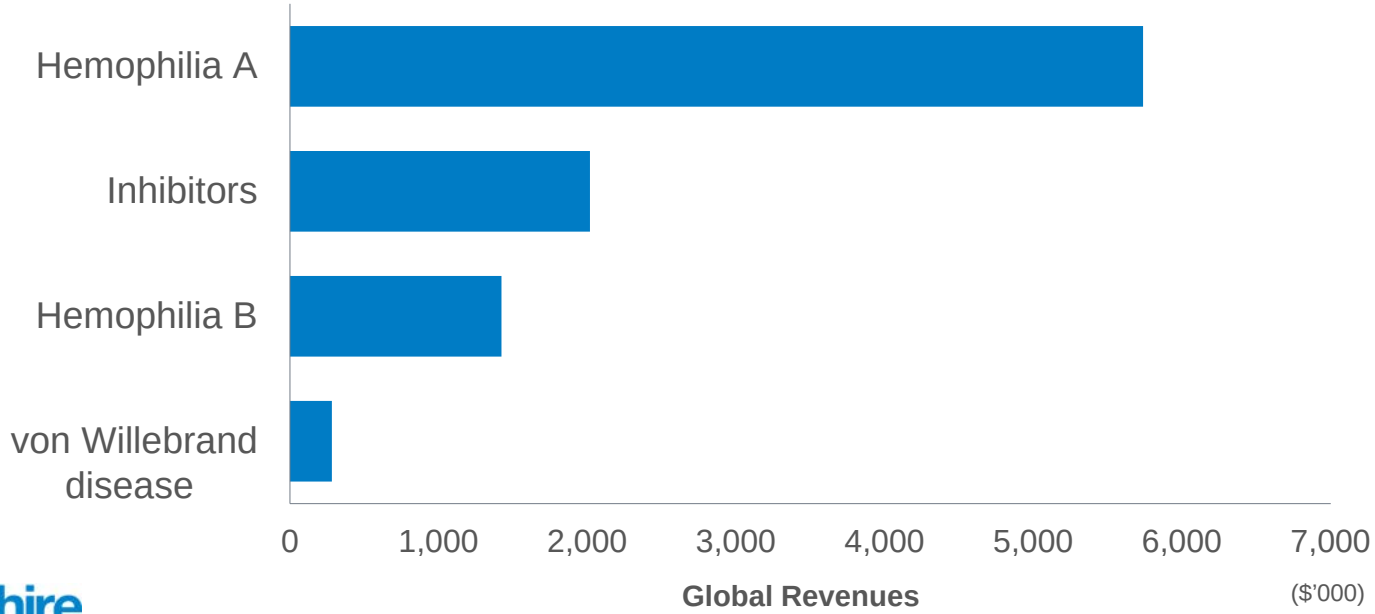
- **ADVATE** family **remains the gold standard** therapy for Hemophilia A
- **FEIBA and Immune Tolerance Induction** (ITI) will continue to be the treatment of choice for vast majority of inhibitor patients

Shire is a serial innovator

- **Upgrade** current brands
- **Drive personalization** with Shire medical devices & trough studies
- **Develop transformational therapies,** e.g. gene therapies

Globally, the Rare Hematology market is large and growing, led by Hemophilia A

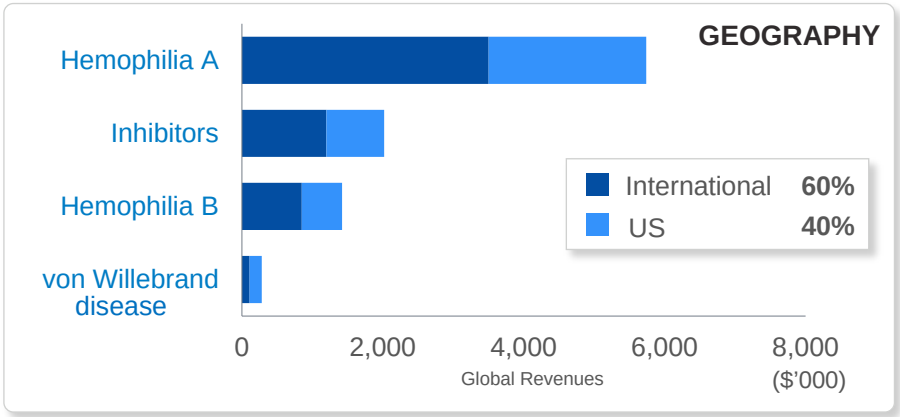
$10B market today continues to grow,
expected to reach $13B by 2020

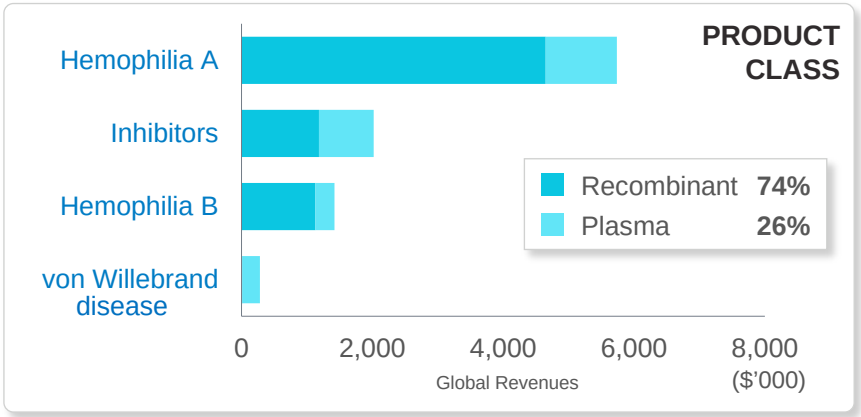


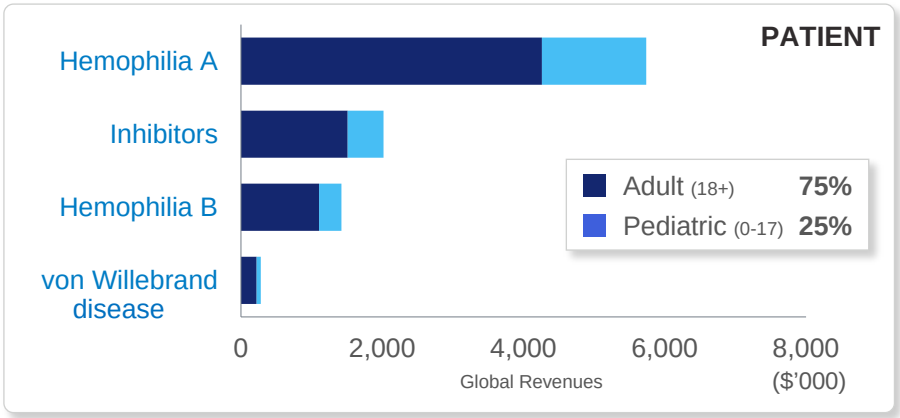
Shire

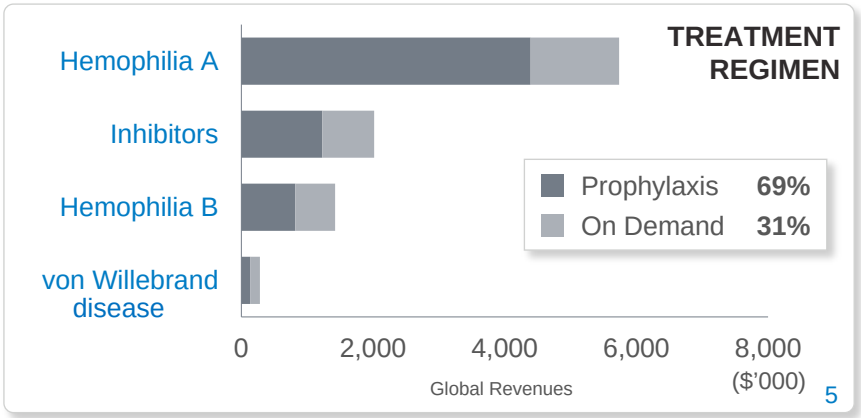
2015, Shire Proprietary Data on File

The Rare Hematology market is heterogeneous, dynamic and increasingly complex







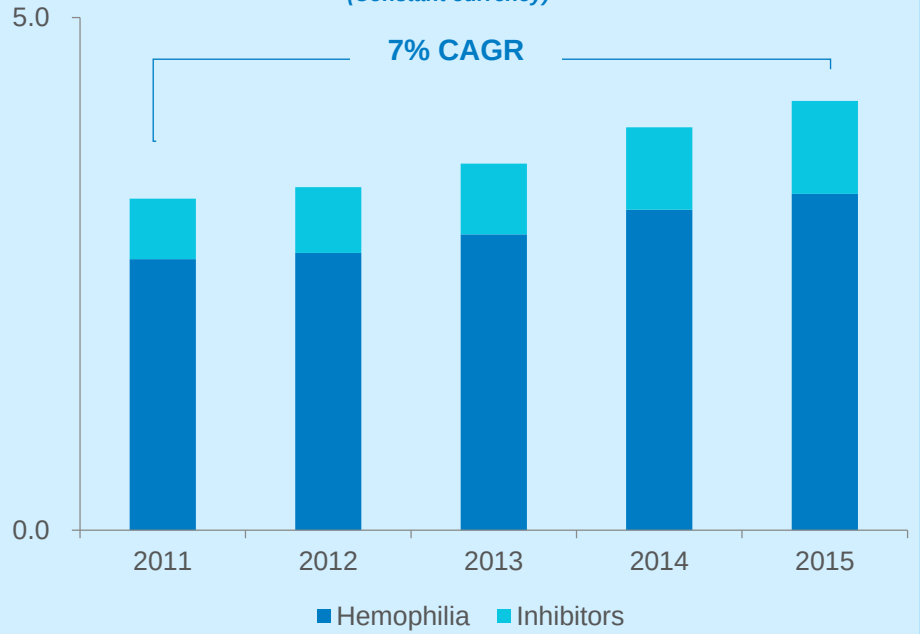


2015, Shire Proprietary Data on File

Shire has deep expertise and established leadership with an industry-leading, comprehensive portfolio in Rare Hematology

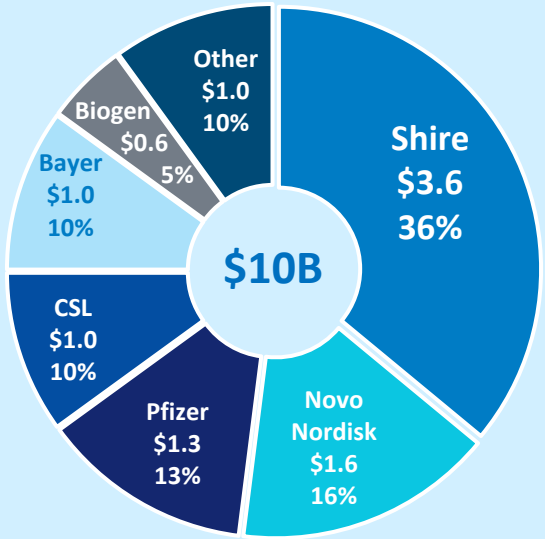
Annual Global Sales ($B)

(Constant currency)



Global 2015 revenue ($B)*

(Actual rates)



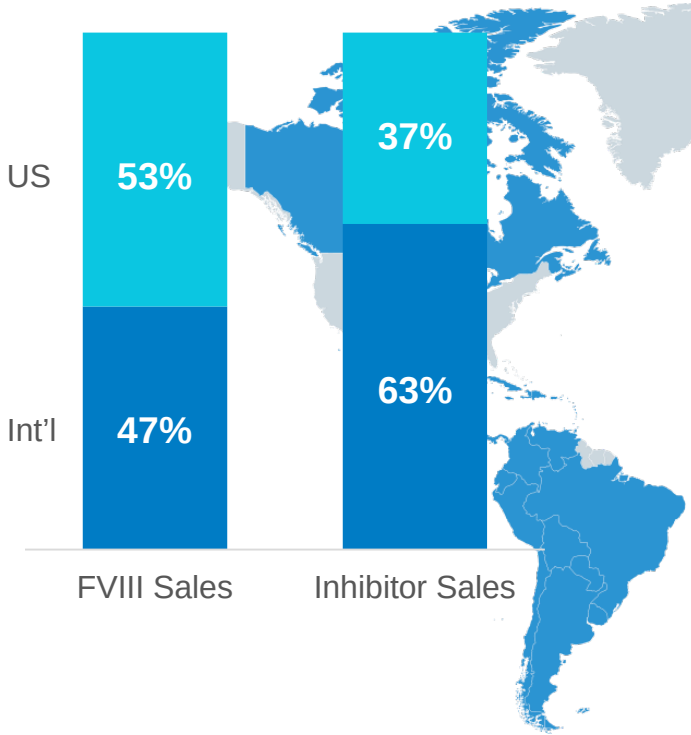
3-5% projected CAGR through 2020 despite increasing competition^

*Global market revenues shown at 2015 actual rates, sourced through competitive disclosure. ^Actual rates, previously disclosed by legacy Baxalta

Only Shire's unrivalled, best-in-class portfolio offers personalized care

		Shire	Biogen	Novo	Bayer	CSL	Pfizer	Octa-pharma
Indications	Hemophilia A	ADVATE ADYNOVATE	✓	✓	✓	✓	✓	✓
	Hemophilia w/ Inhibitors	FEIBA		✓				
	Hemophilia B	RIXUBIS	✓			✓	✓	✓
	Acquired Hemophilia A	Obizur		✓				
	Von Willebrand disease	vonvendi				✓		✓
Technologies	Plasma derived factors	✓				✓		✓
	Recombinant factors	✓	✓	✓	✓	✓	✓	✓
	Extended Half Life (EHL)	✓	✓					
	Personalized treatment	my PK FiT						

Shire's global Rare Hematology footprint continues to grow



Products available today in **100+ countries**

100+ Launches (products and new indications) **40+ countries** through 2018

ESTABLISHED

ADVATE
FEIBA
RECOMBINATE
IMMUNATE
HEMOFIL M
IMMUNINE

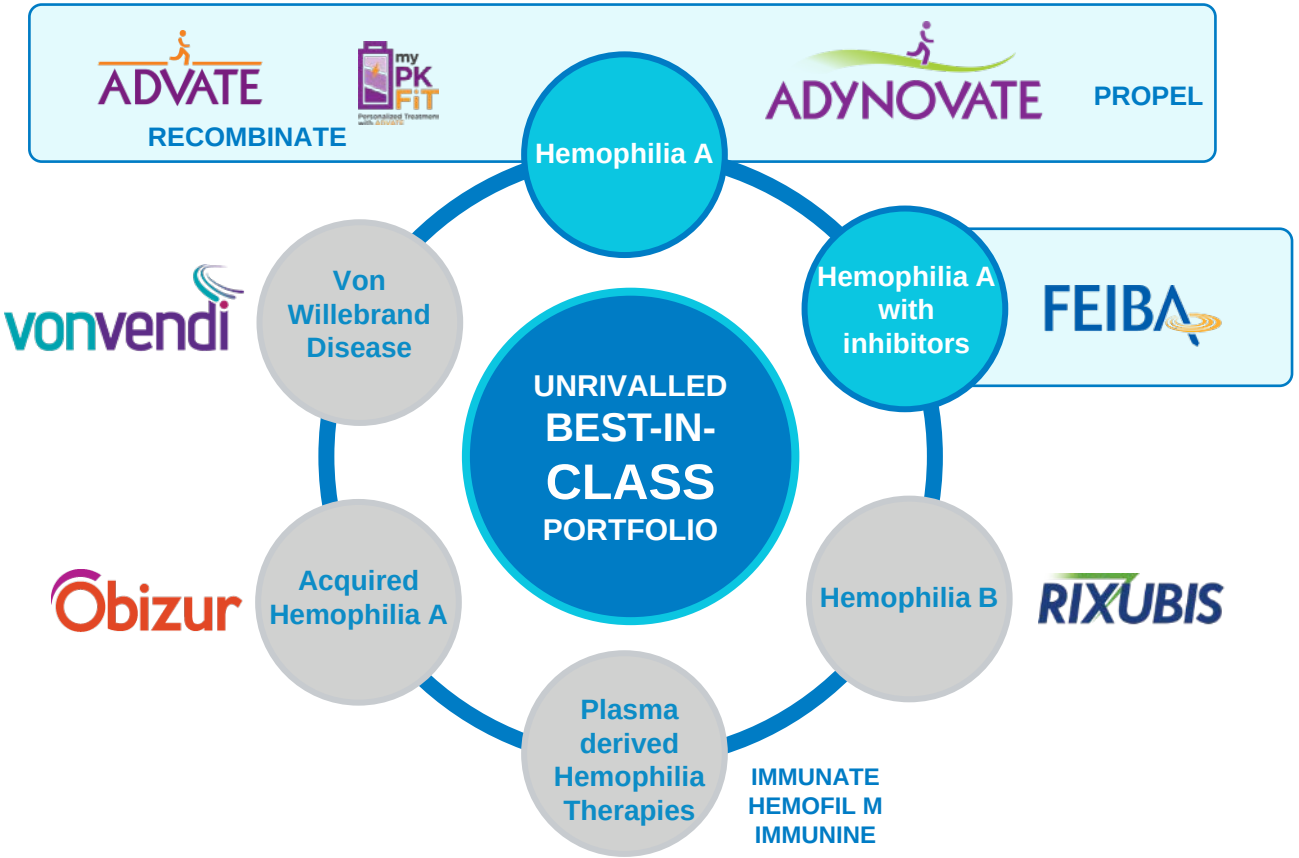
LAUNCHING

ADVATE my PK FiT
ADYNOVATE
RIXUBIS
Obizur
vonvendi

Shire

Shire analysis

Shire's world-class leadership in Rare Hematology



The 3 key unmet medical needs in Hemophilia A

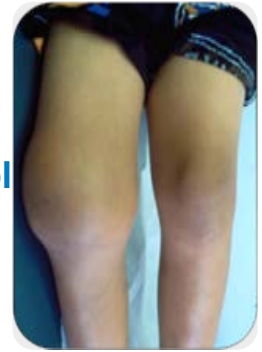
Early diagnosis for all

- High Annual Bleed Rate (ABR): >40[1]
- Disability
- Life expectancy early teens[2] for undiagnosed patients

Diagnosis from Birth

Early prophylaxis for all

- Moderate ABR: 2-10[3]
- Loss of work/ school
- Reduced joint / bone health



Prophylaxis

Personalized for one

- Everyone is unique
- Low ABR: <2[4]
- "Normal life" experience and expectancy

Personalized Care

1. Hua 2014. 2. Mejia, et al. Jrnl Thromb Haem. 2006.
3. Valentino et al. Haemophilia. 2012. 4. Gringeri et al. WFH Poster 2016

Shire, raising global standards of care and minimizing annual bleed rates, driving best patient outcomes

Early diagnosis for all

only 25% → 100%
of patients are diagnosed[1]

On Treatment
e.g. India, China, Vietnam
HEMOFIL M IMMUNATE RECOMBINATE ADVATE

Early prophylaxis for all

only 8% → 60%
of patients receive prophylaxis[1]

Prophylaxis
e.g. Russia, Brazil, Argentina
ADVATE

Personalized for one

<3% → 100%
of prophylaxis patients receive personalized care[2]

Personalized Care
e.g. US, Japan, Europe*
ADVATE, my PK FiT, ADYNOVATE PROPEL

Shire

1. World Federation of Hemophilia Annual survey
2. Shire analysis

* myPKFiT is not approved in the United States

Parents and patients are loyal to established treatments and not willing to compromise efficacy and safety

Decisions largely driven by **efficacy, safety and personalization**

49% of patients have never switched treatment or have switched only once[1]

Patients prefer **product enhancements** within a trusted portfolio rather than switch to an entirely new product

1. Shire analysis

ADVATE is the proven gold standard Factor VIII therapy

Worldwide leader approved in 50+ countries

More than 13 years of real world experience

Clinicians rate ADVATE as the Trusted Standard of Care[1]

1

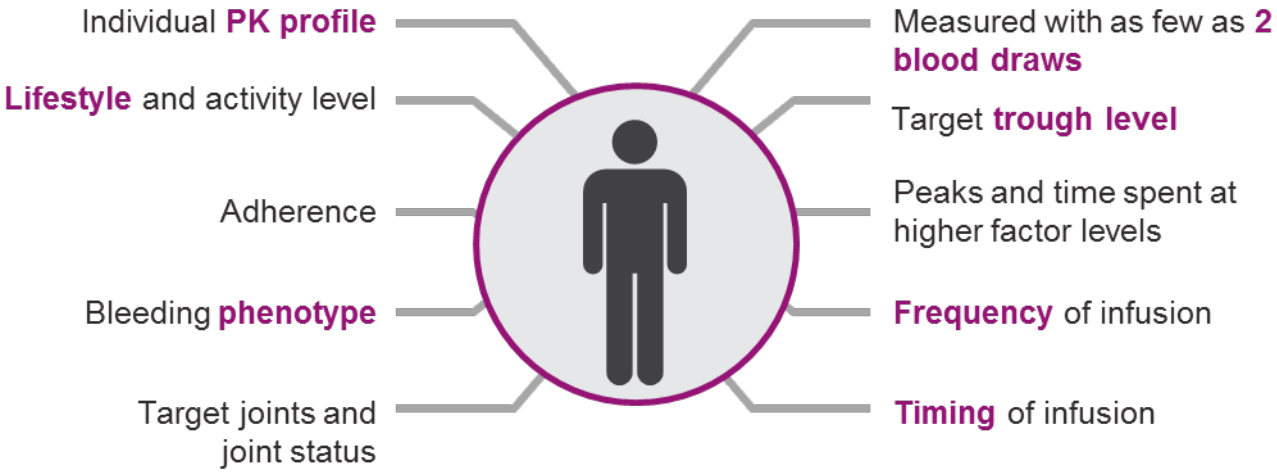
- solid clinical data
- effective prophylaxis
- trusted by patients

42%	**Proven bleed prevention** of patients on ADVATE prophylaxis bleed free
1.66	**Proven effectiveness in the real world** Annual Bleed Rate (ABR)
0.15%	**Proven safety in the real world** Inhibitor rate in severe previously treated patients

1. Shire analysis

ADVATE + myPKFiT: the only registered software based medical device for personalized Hemophilia dosing

Considering the uniqueness of each patient → **Personalized prophylaxis tailored for each patient**



ADVATE

myPKFiT
Personalized Treatment with ADVATE

Trough levels >1% = more patients reach ZERO bleeds

Filed in the US

~3X Physicians **more likely to prescribe ADVATE** after using myPKFiT

Shire

ADYNOVATE: expanding personalization of care, building on the success of ADVATE

ADYNOVATE

PROVEN ADVATE BLEED PREVENTION

SIMPLE, TWICE-WEEKLY INFUSION

STRONG COMMERCIAL MOMENTUM

- **Launched in US in Q4 2015 and in Japan in Q2 2016**
- **European Launch 2017**
- **Pediatric and Surgery indications 2017 (US, JP)**

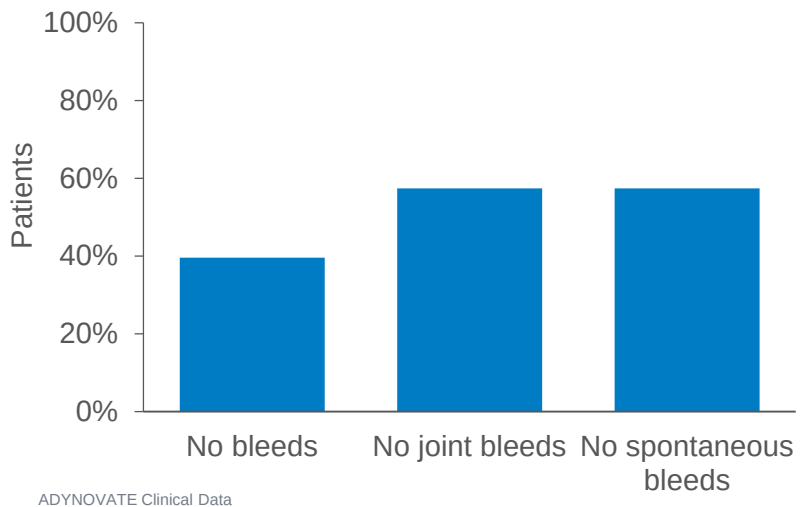
Momentum with new patients from across portfolio and competition

Launch on track

Shire

ADYNOVATE + PROPEL: Continuing research to optimize outcomes with personalized approach

40% of patients achieve zero bleeds on prophylaxis[1,2]

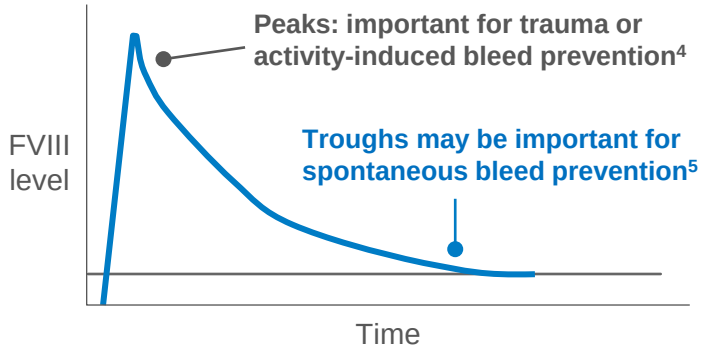


ADYNOVATE Clinical Data

Per-protocol Analysis Set (PPAS): N=101.

PROPEL Study

Can a threshold of FVIII trough level of 10-12% further reduce annual bleed rate to zero[3]?



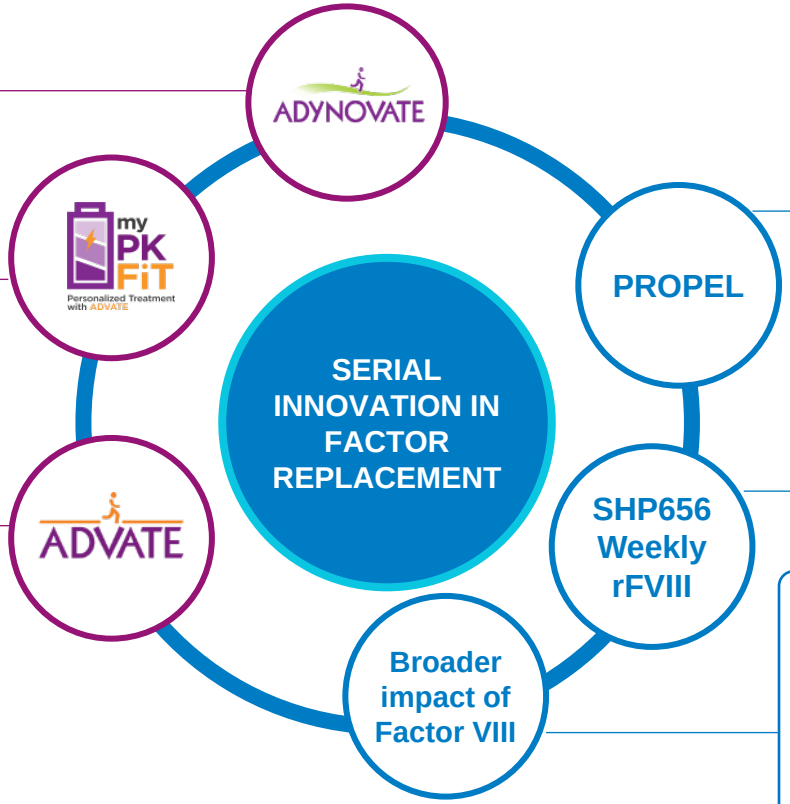
1. Konkle, EAHAD 2015 Poster 2. Konkle, Blood. 2015. 3. Den Uijl Haemophilia, 2011.
4. Valentino WFH 2014. 5. Collins PW. J Thromb and Haemost. 2012

Shire's Hemophilia A portfolio: Leadership based on proven factor therapy & serial innovation

ADYNOVATE:
Personalized care with proven ADVATE bleed prevention with twice-weekly infusion

ADVATE+myPKFiT:
Personalized PK-based dosing

ADVATE: Proven efficacy and safety
profile with +13 years of real world experience



PROPEL Study:
Can a threshold of FVIII trough level of 10-12% further reduce annual bleed rate to zero?

SHP656: Weekly EHL* based on ADVATE

- PSA technology
- Phase 1 trial underway
- **Phase 3 could start in 2017**

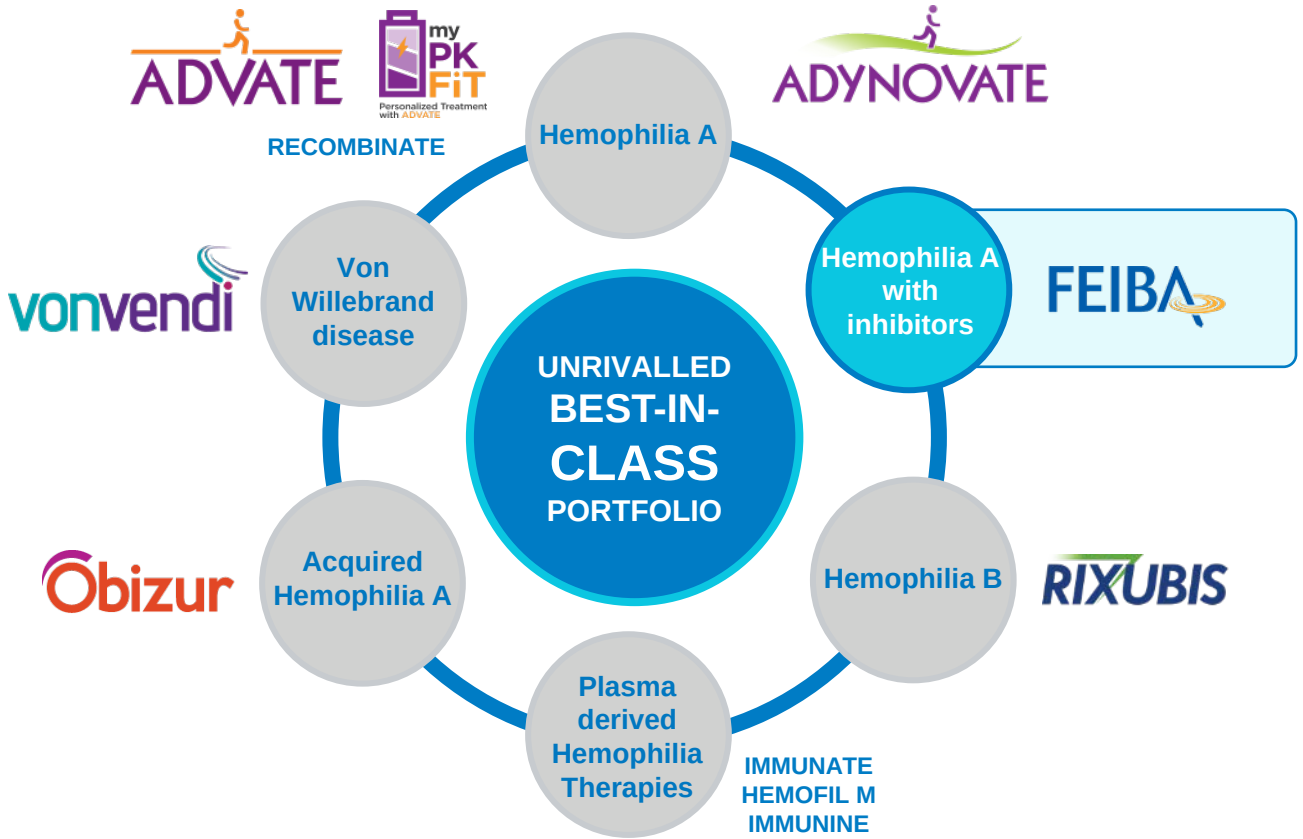
Broader impact of Factor VIII beyond coagulation cascade

- Bone and joint health
- Quality of the clot formation
- "Feel good factor"

* Extended Half Life

Shire

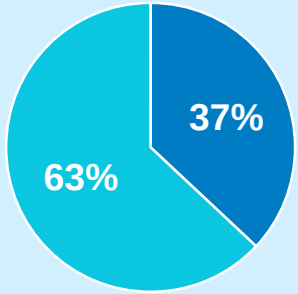
Shire's global leadership in Rare Hematology



Global inhibitor market is driven by international growth

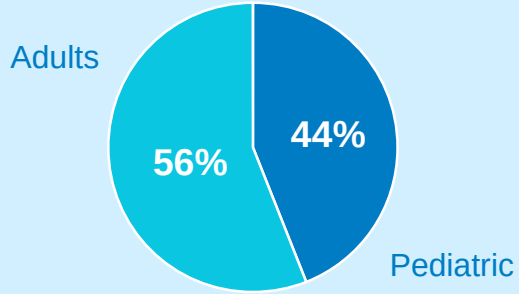
~$2B Global Market

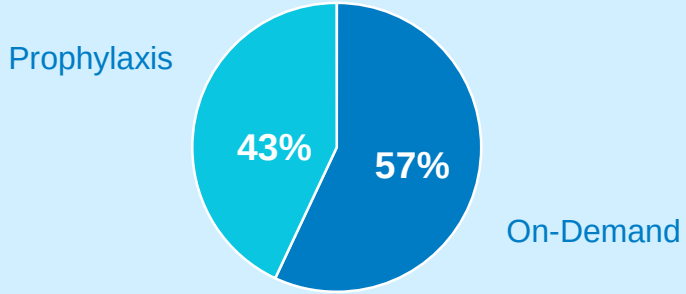
Shire Sales



Distinct Patient Segments

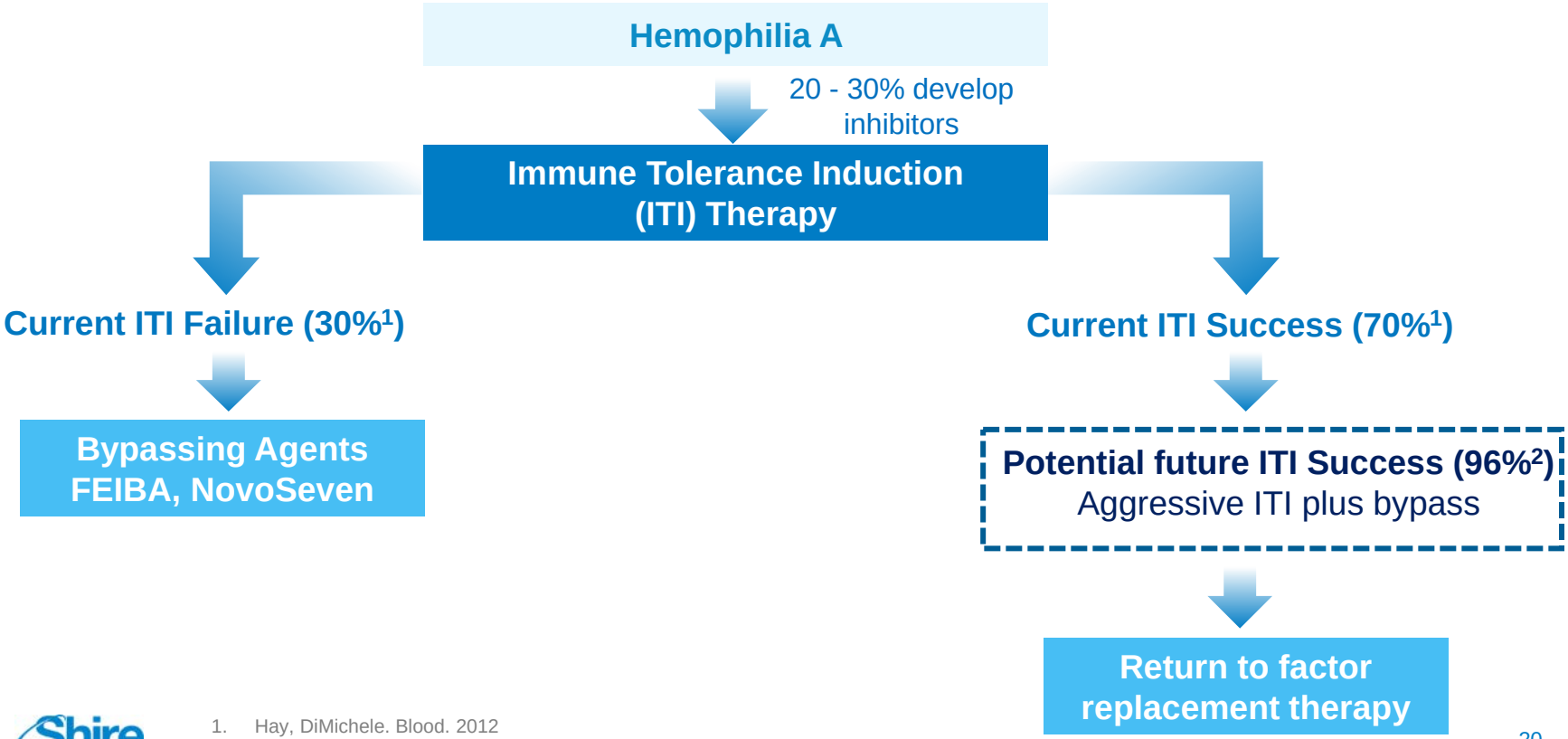
(percent of patients)





Shire analysis

Eradicating the inhibitor and returning to factor replacement therapy through ITI is the primary goal for inhibitor patients



1. Hay, DiMichele. Blood. 2012
2. Nakar et al, Hemophilia 2014

70% of physicians report being satisfied with on-demand or prophylactic bypassing therapy

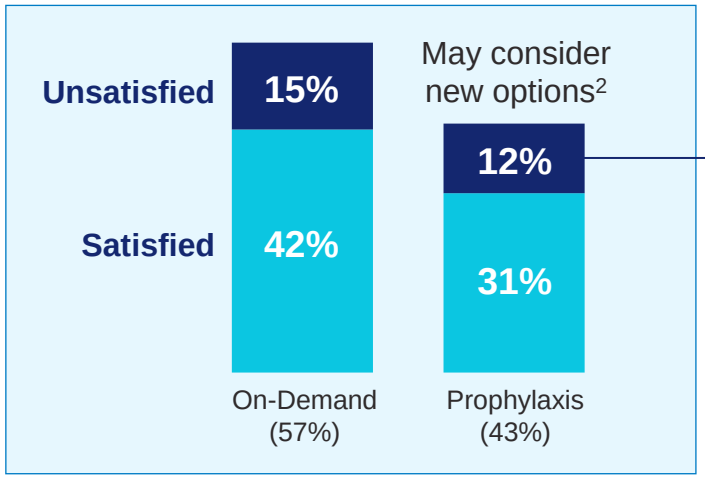
Hemophilia A

20 - 30% develop inhibitors

Immune Tolerance Induction (ITI) Therapy

Reported current ITI Failure (30%[1])

Bypassing Agents FEIBA, NovoSeven



Potentially related to:

- Non-optimal outcomes
- Treatment burden

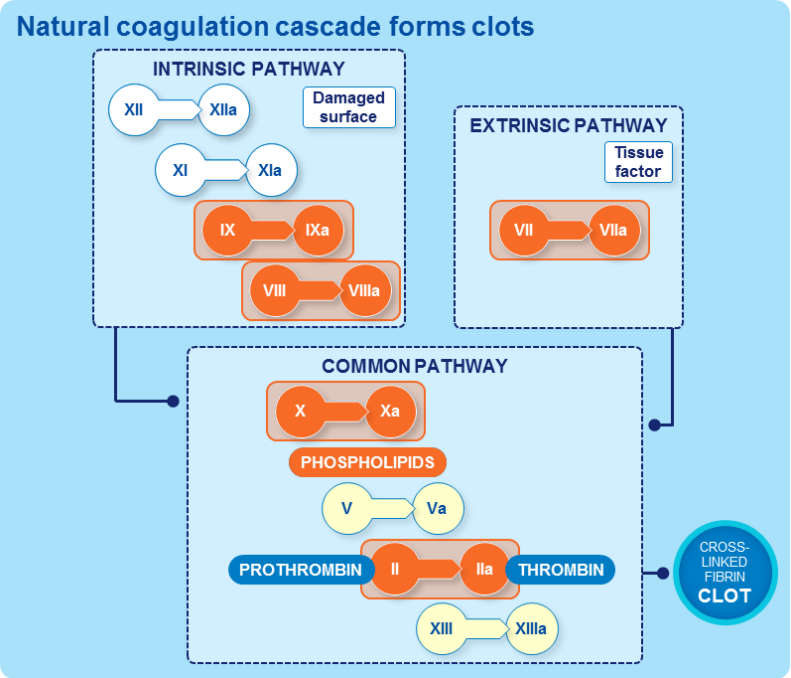
1. Hay, DiMichele. Blood. 2012.
2. Shire Data on File.

FEIBA offers a unique mechanism with 40+ years of global real world experience of bypassing therapy

Only FEIBA acts on all three pathways

FEIBA's unique multi-factor mechanism regulates coagulation cascade

Enables a clot to form as close as possible to the body's natural process in a self-regulated manner



Only bypass widely approved for both **prophylaxis and on-demand**

Continued investments to upgrade FEIBA

- Patient support programs
- Upgraded infusion experience

Shire

Future innovation for inhibitor patients will be driven by : eradication, prediction and prevention

ERADICATE

Primary Treatment Goal

- Standard of care is early ITI +/- bypassing agent
- Drive up eradication from 70% to 96%

PREDICT

Predict high risk patients

- Predictive modelling, algorithms and biomarkers to identify high-risk patients

PREVENT

Prevent inhibitor development

- Increase early prophylaxis
- Critical first 20 exposure days[1]

1. Gouw et al. Blood. 2007.

Future innovation in Rare Hematology

Non-factor Based Therapies

- Shire non-factor R&D **commenced in late 1990s,** e.g. bi-specific and anti-TFPI programs
- **15 years of know-how** and extensive IP with dozens of patents
- Understanding impact of **non-factor/factor co-administration** on patient safety
- Continuing internal and external programs with **bi-specific and other non-factor** treatments

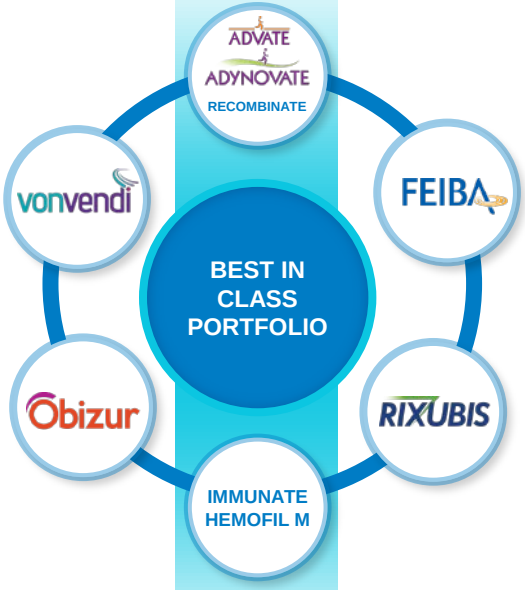
Gene Therapy

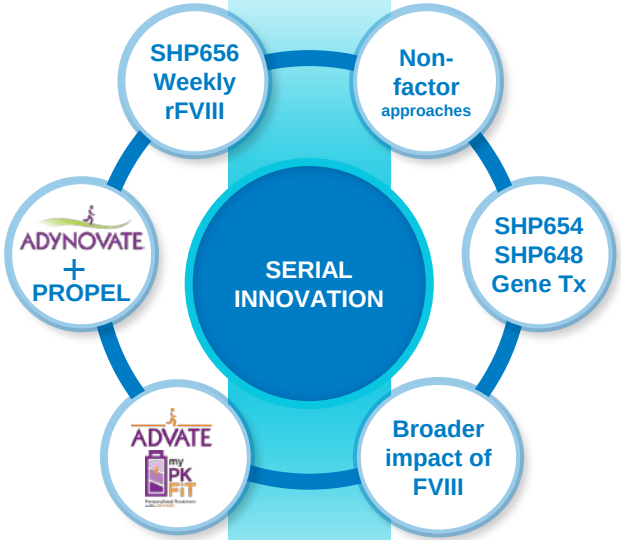
- Potential for **transformative care** as a multi-year treatment for certain patient segments
- **SHP654:** 2017 **Phase 1 clinical** studies commence for Hemophilia A
- **SHP648**: Pre-clinical for Hemophilia B

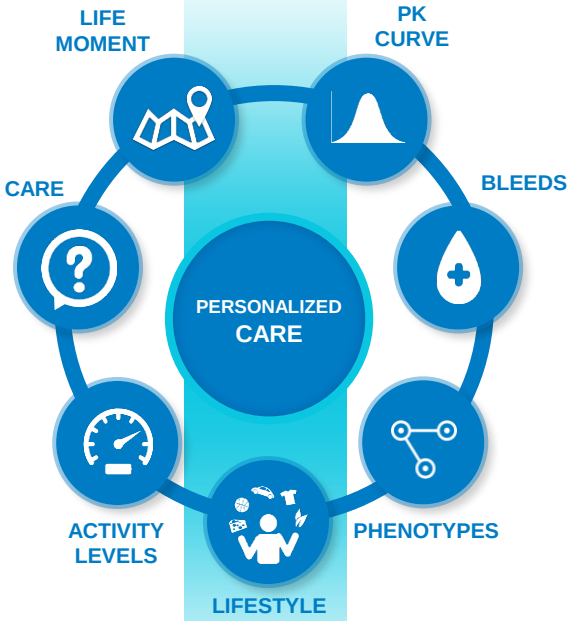
Other Therapies

- **SHP655**: **Phase 1** recombinant ADAMTS13 for hereditary TTP (thrombotic thrombocytopenic purpura)

Shire leading in Rare Hematology







Michael D. Tarantino, MD

Medical Director and President, Bleeding
& Clotting Disorders Institute, Peoria, Illinois

Professor of Pediatrics and Medicine, University of
Illinois College of Medicine at Peoria

Shire

The Physician's Perspective on Personalized Care for Hemophilia

Michael Tarantino, MD

Shire

Treating hemophilia means understanding the distinct needs of the patient community

Hemophilia care is multifactorial

- Proper diagnosis and treatment planning
- Clinical characteristics and patient-related factors
- Variability throughout life stages

Complex decision making warrants a personalized approach to optimize outcomes[1]





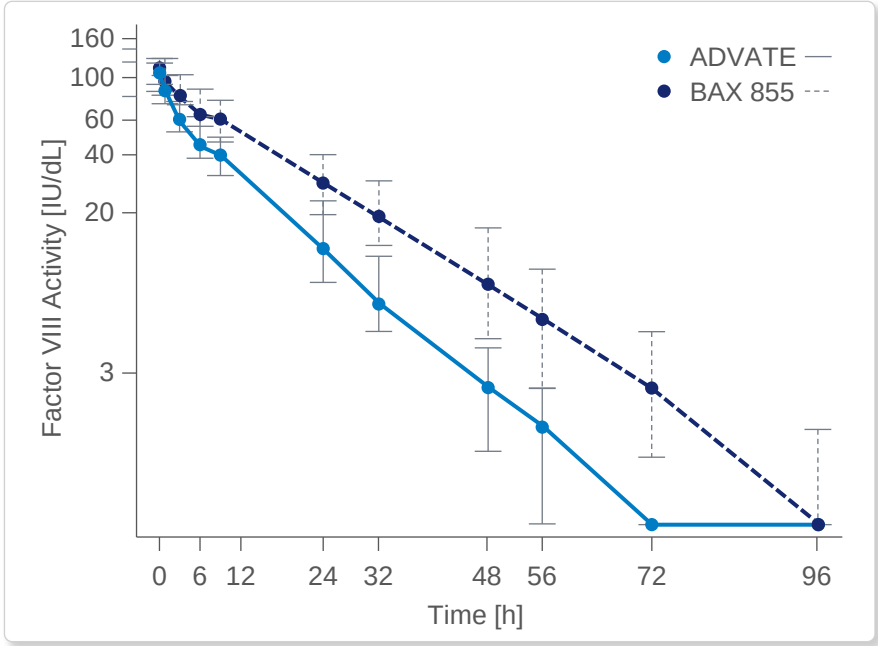
Shire

1. National Hemophilia Foundation-McMaster University Guideline on Care Models for Hemophilia Management. Haemophilia 2016.

Each patient is unique and requires a highly individualized approach

Inter-patient variability warrants an individualized approach that addresses patient activity, lifestyle, and potential acute events to properly protect against bleeds[1,2]

- PK Parameters
- Care Goals
- Activity Levels
- Bleed Phenotype
- Age
- Lifestyle
- Joint Status

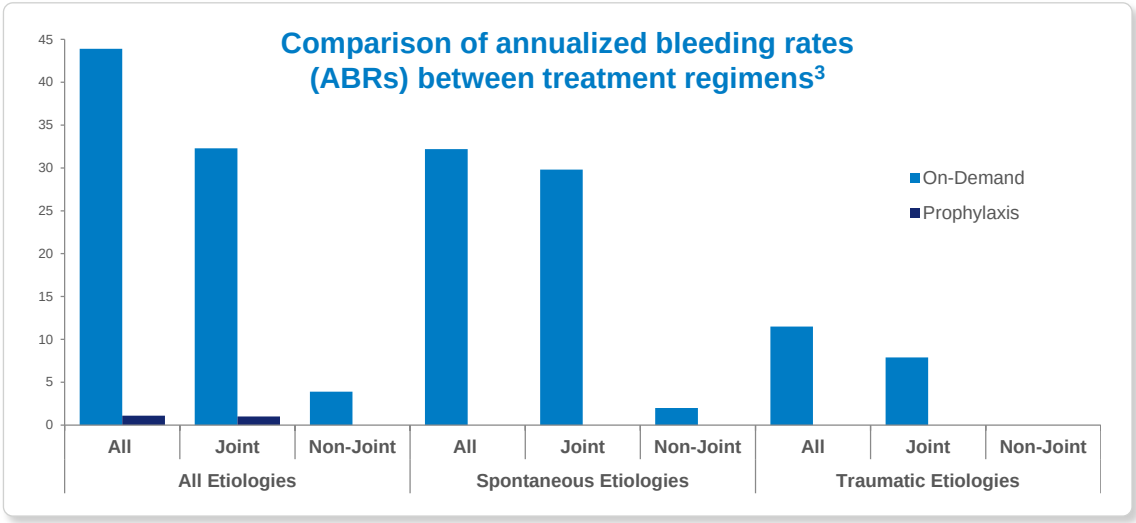


1. Valentino LA, et al. Haemophilia. 2014
2. Konkle et al. Blood 2015.

Clinicians need options that build on proven concepts, can be trusted and reliable

Factor therapy, use of prophylaxis[1] have revolutionized the treatment of hemophilia[2]

Patients have benefited from improved quality of life, decreased morbidity, and increased life expectancy[2]



Considerations for future care:

1. Opportunities remain to improve care and address persistent unmet needs
2. Innovation is important and requires reliable, sustainable solutions
3. Safety and efficacy must not be compromised by convenience or non-outcomes-related attributes

1. Srivastava A et al. Haemophilia. 2013. 2. Franchini M, Mannucci PM. Semin Thromb Hemost. 2014.
3. Valentino et al. J Thromb Haemost . 2012

New generations of care for hemophilia are reaching zero bleeds with a personalized approach

- Significant strides have been made with safe, effective regimens, but the community seeks new options that build on success of factor replacement therapy
- Hemophilia treatment parameters are complex and evolve over the course of the patient's life
- New options should build on the success of the treatment paradigm of factor replacement

Shire's Leadership in Rare Hematology

Kim Stratton
Head International Commercial

Shire leading Rare Hematology

Shire leads this dynamic market

- **Large global dynamic market** with **growth of 3-5%**
- Shire is the leader with **longest heritage, broadest portfolio & leading market share of 36%**

Shire has 3 key growth drivers

- **Drive diagnosis & prophylaxis** in developing markets
- **Drive prophylaxis & personalization** in developed markets
- Geographic & portfolio expansion **with +100 launches across +40 countries**

Shire has best in class portfolio

- **ADVATE family will remain the gold standard** therapy for Hemophilia A
- **FEIBA and Immune Tolerance Induction** (ITI) will continue to be the treatment of choice for vast majority of inhibitor patients

Shire is a serial innovator

- **Upgrade** current brands
- **Drive personalization** with Shire medical devices & trough studies
- **Develop transformational therapies,** e.g. gene therapies

Shire


ThankYou
Merci
Salamat
Kop
Hvala
Tack
Xie
Gra
kun
Dankie
Kruthagnathalu
Arigatou
Dhonnobaad
Asante
Dhanyavad
Khopjai
Dhanyavaadaalu
Dakujem
Waad
Daw
krap
Dank
Takk
Gamsahapnida
Te ekkür
Dekuju/Dekujeme
Kasih
Mamnoon
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Leadership in Immunology through Innovation, Global Execution, and Patient Support

Perry Sternberg, Head US Commercial

Summary

Shire is well positioned for further growth in Immunology

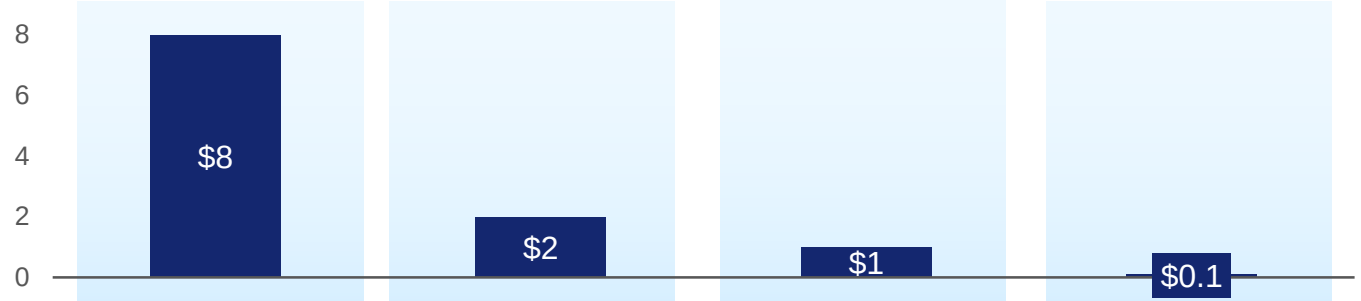
- **Global immunology market is $11B and growing at +6-8% annually**
  - Majority of the market is immunoglobulins (IG)
  - Three large global players: CSL, Grifols, and Shire, each with more than 20% market share
  - IG market growth is driven by aging population, increasing diagnosis, new products and shifts in the point of care
- **Shire's Immunology business is ~$2B and growing in line with the market**
  - Broad portfolio, particularly in fast growing subcutaneous IG (SCIG)
  - HyQvia recently launched and Cuvitru launching
- **Shire is well positioned to drive further growth**
  - Lever Shire's commercial effectiveness capabilities
  - Serially innovate, including six programs outside IG
  - Expand patient services offering

Shire

1. For all indications
Note: Market share based on MRB 2014 Source: MRB Worldwide

Immunology market is $11B and growing at 6-8%, expected to be $15B by 2020

2015 immunology market size (USD $B)



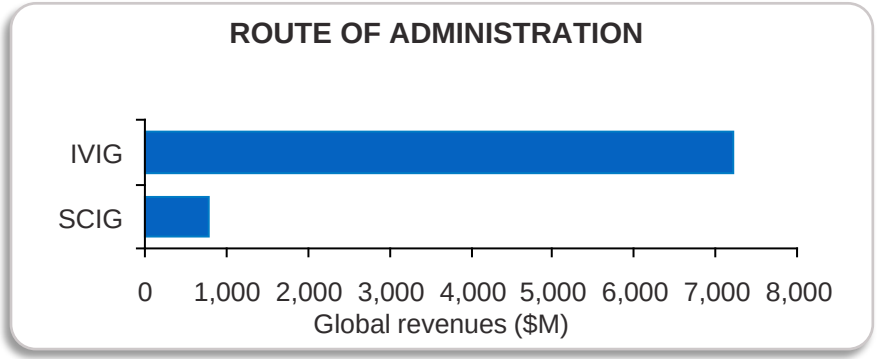
	IG	Albumin	Alpha 1	Protein C
Delivery	Intravenous (IV), subcutaneous (SC)	IV	IV (including self infusion option)	IV
Site of Care	Hospital, Home, Clinic	Hospital	Home, Clinic	Hospital, Home, Clinic
Growth	6% IV, 20% SC	5%	6%	n/a

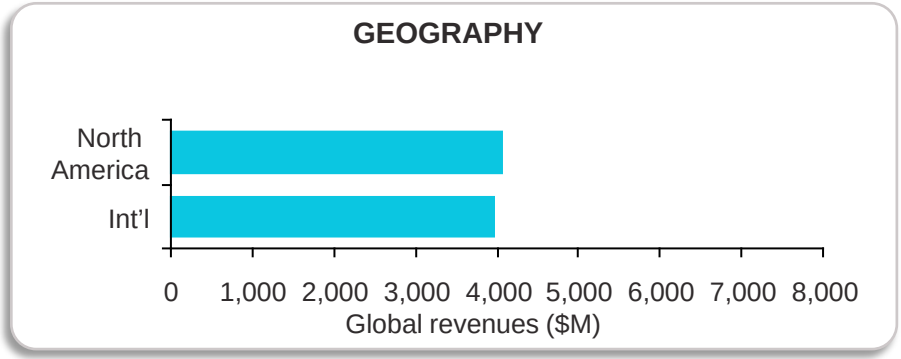
Growth drivers

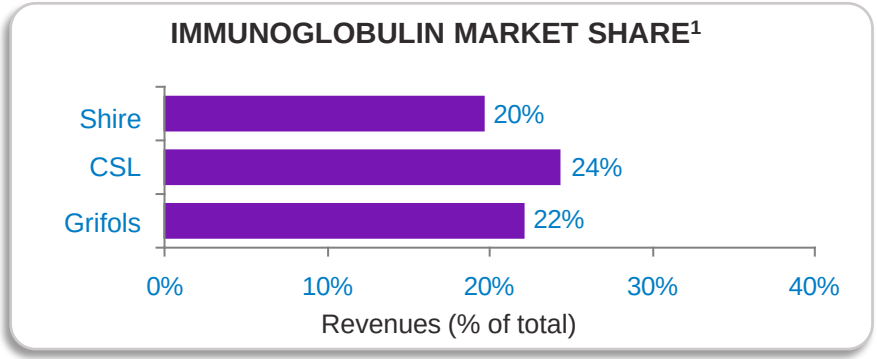
- Aging population
- Increasing diagnosis
- New product launches
- Shift in the care setting from hospital to home care

Source: MRB Worldwide; Includes total market data for all the above plasma products, including competitor data. Excludes non-immunology plasma, non-profits and companies selling mainly in closed markets; growth rates from 2014 MRB report

IG market grows globally, has multiple indications and shifts towards home care







1. 2014 data
Source: Shire analysis and MRB

IG, the largest component of the market, is used to treat multiple conditions and is used across specialties

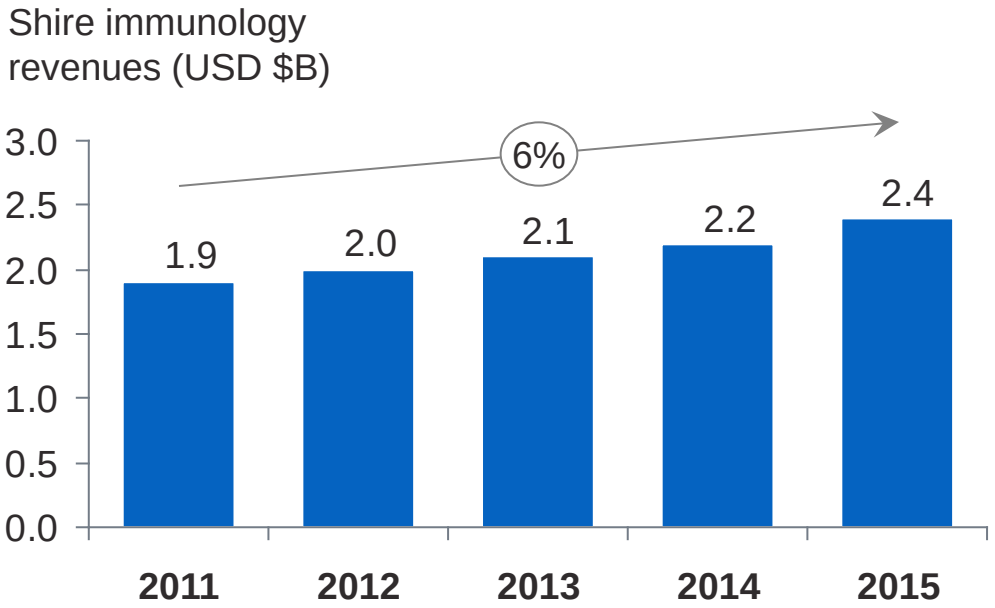
Immunoglobulin

Shire's leading indication

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
Contribution (grams)	27%	19%	4%	50%

** Select examples, approvals vary by country, see local package insert*

Our $2B immunology franchise has grown in-line with the market



Geographical split

US: ~70%

International: ~30%

Growing presence in SCIG

SCIG growth 2013-2015: >25%

Driven by launch of HyQvia

Source: Shire analysis; revenue for total immunology division, in constant currency

Shire's Portfolio

Shire has one of the broadest portfolios approved for self-infusion, allowing physicians to tailor patient treatment

Self infusion available

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

1. Includes Albumin, Protein C, pdFVIII, Hyperimmunes, other bleeding disorders, etc.

We expect to deliver our growth through three pillars

Our commercial execution is underscored by winning products and proven global success

Address needs with differentiated products

- Segmentation & targeting
- Differentiated products
- New indications
- Patient services

Build global foothold

- Clear messaging & marketing
- Reliable & high quality plasma
- State-of-the-art manufacturing
- International presence

For example: SCIG

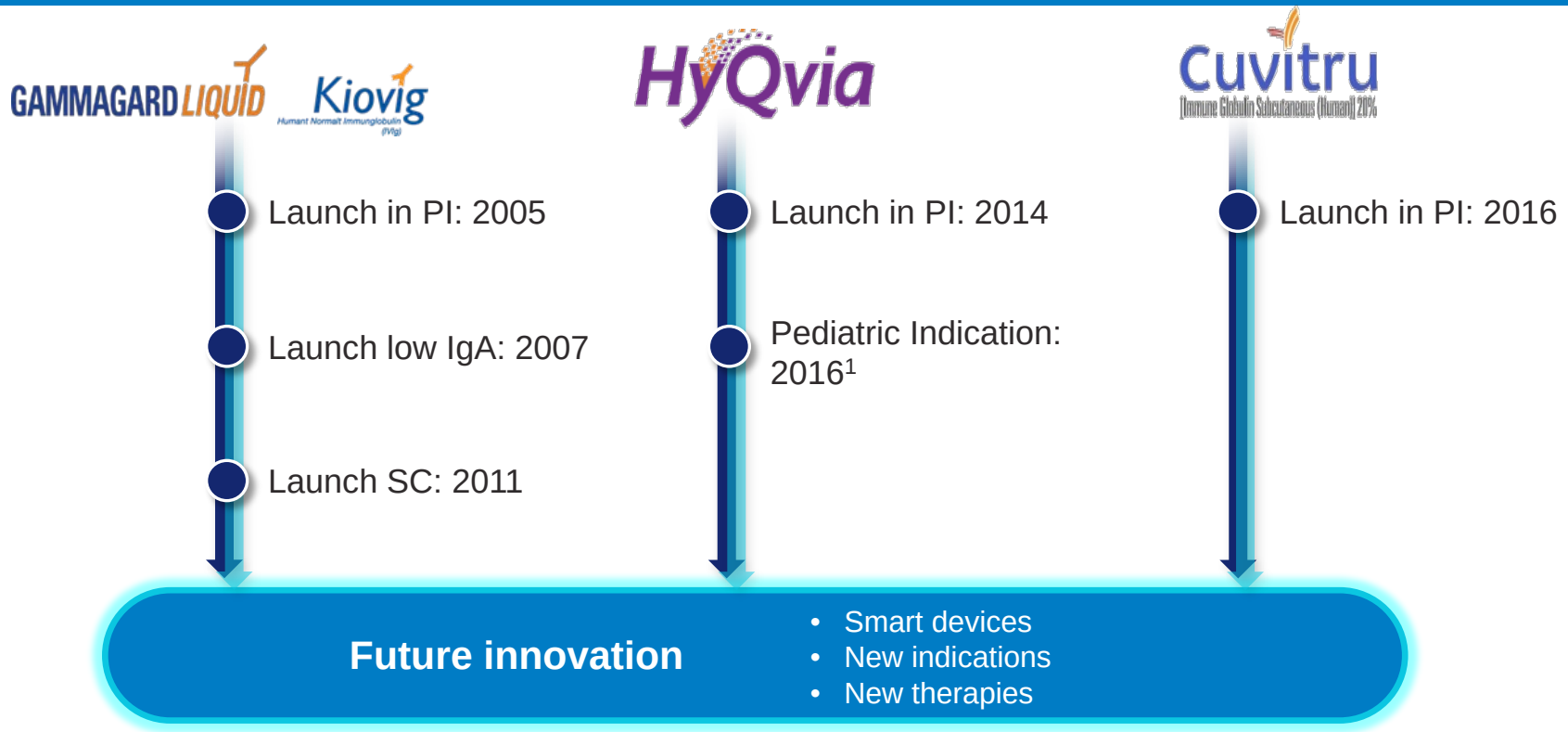
HyQvia

Only SCIG with option for monthly infusion on market

Cuvitru

Expanding our SCIG platform with 20% concentration

We have a history of serial-innovation in developing novel treatments



Select examples, not exhaustive

1. Currently only available within Europe

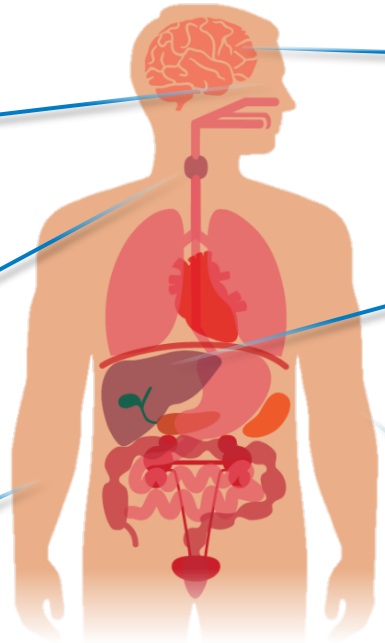
Note; Kiovig, Gammagard, and HyQvia launched in other geographies, timelines not included

Shire is positioned to lever our existing capabilities to grow this business and expand our leadership position

Ophthalmology
Leveraging expertise with Xiidra in dry eye disease

Blood disorders
Leveraging expertise with Cinryze in hereditary angioedema

Transplant
Cinryze targeting AB mediated rejection; maribavir targeting CMV infection



Neurology
IG therapies targeting new indications in CIDP

Transplant
Glassia targeting new GvHd indication

Rheumatology
SHP652 targeting Systemic Lupus Erythematosus

We are expanding beyond plasma into monoclonal antibodies (MAbs)

Understanding their journey enables us to provide better support for our patients

Example patient journey for PI

	Awareness	Diagnosis	Treatment	Management & Support
Key steps	• Patient arrives with a history of recurrent infections • Frequently treated with antibiotics • May eventually be referred to specialist	• Patient is diagnosed with PI • Patient seeks to understand diagnosis / disease • Patient considers treatment options	• Patient initiated on IVIG treatment in hospital / office • Patient / physician considers alternate treatment options (e.g., switch from IVIG to SCIG)	• Patient learn self-care with nurse assistance • Patient / physician / payer manage ongoing disease

10-15 yrs[1]

1. 12.4 years on average from the time symptoms begin. 2007 Immune Deficiency Foundation Survey

Understanding their journey enables us to provide better support for our patients

Example patient journey for PI

Key steps

Awareness
- Patient arrives with a history of recurrent infections
- Frequently treated with antibiotics
- May eventually be referred to specialist

Diagnosis
- Patient is diagnosed with PI
- Patient seeks to understand diagnosis / disease
- Patient considers treatment options

Treatment
- Patient initiated on IVIG treatment in hospital / office
- Patient / physician considers alternate treatment options (e.g., switch from IVIG to SCIG)

Management & Support
- Patient learn self-care with nurse assistance
- Patient / physician / payer manage ongoing disease

10-15 yrs[1]

Support services

- Nurse home services
- Free trials (Hello Program)
- Copay assistance (MyIgCoPayCard), Smart Start
- Educational programs
- Resources & support website (MyIgSource)
- Patient ambassadors (My Life, My Story)

1. 12.4 years on average from the time symptoms begin. 2007 Immune Deficiency Foundation Survey

Summary

Shire is well positioned for further growth in Immunology

- **Global immunology market is $11B and growing at +6-8% annually**
  - Majority of the market is immunoglobulins (IG)
  - Three large global players: CSL, Grifols, and Shire, each with more than 20% market share
  - IG market growth is driven by aging population, increasing diagnosis, new products and shifts in the point of care
- **Shire's Immunology business is ~$2B and growing in line with the market**
  - Broad portfolio, particularly in fast growing subcutaneous IG (SCIG)
  - HyQvia recently launched and Cuvitru launching
- **Shire is well positioned to drive further growth**
  - Lever Shire's commercial effectiveness capabilities
  - Serially innovate, including six programs outside IG
  - Expand patient services offering

1. For all indications
Note: Market share based on MRB 2014. Source: MRB Worldwide

Thank you!

Advancing an Exciting Late-Stage Clinical Portfolio

Philip Vickers, Ph.D.
Global Head of Research & Development

Shire

Afternoon session: Six late stage programs

Rare Disease Leadership

Gastroenterology
SHP621 – (Eosinophilic Esophagitis)

Transplant Medicine
SHP620 – (CMV Infections)

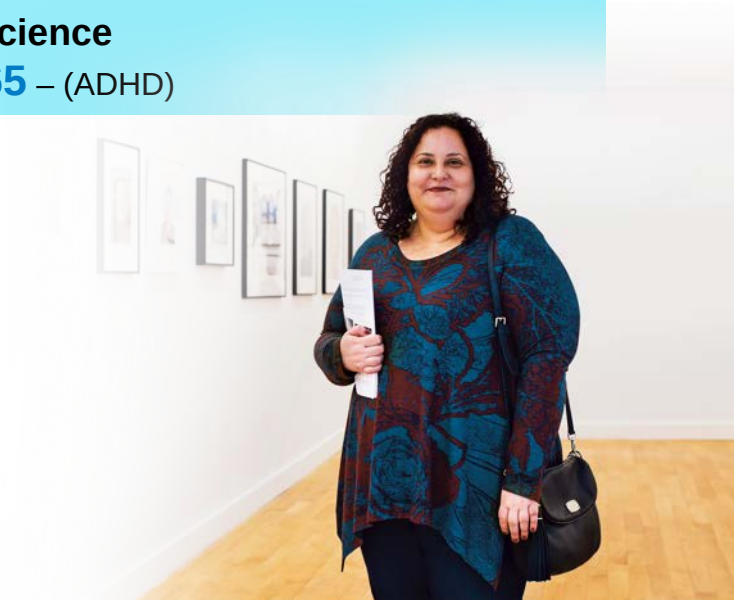
Neonatology
SHP607 – (Complications of Prematurity)

Genetic Diseases
SHP643 – (Hereditary Angioedema)

Specialty Condition Leadership

Gastroenterology
SHP647 – (Inflammatory Bowel Disease)

Neuroscience
SHP465 – (ADHD)



Shire

Today's pipeline program agenda

TOPIC	SPEAKER	TIME (ET)
GI Programs *SHP621 / SHP647*	Howard Mayer	12:30 - 12:50
Neonatology Program *SHP607*	Norman Barton	12:50 - 1:10
Transplant Program *SHP620*	Howard Mayer	1:10 - 1:30
Neuroscience Program *SHP465*	Howard Mayer	1:30 - 1:40
HAE Program *SHP643*	Wolfram Nothaft	1:40 - 2:00

SHP621 has the potential to be 1st approved agent to treat eosinophilic esophagitis

- Eosinophilic esophagitis is **characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation**
- SHP621 consists of **budesonide formulated in a viscous suspension** designed to increase the residence time on the surface of the esophagus compared to other topical steroid formulations
- SHP621 has **completed a Phase 2 trial that met co-primary endpoints** as well as an open label extension
- SHP621 **was granted Breakthrough Designation (BTD) by FDA in May 2016** for the treatment of EoE
- Shire **is conducting a Phase 3 Induction study** (SHP621-301) with **first subject screened Nov 2015** and randomized on January 8, 2016
- In addition a **Phase 3 Treatment Extension study (SHP621-302) is currently enrolling**

Overview of eosinophilic esophagitis (EoE)

Disease Description

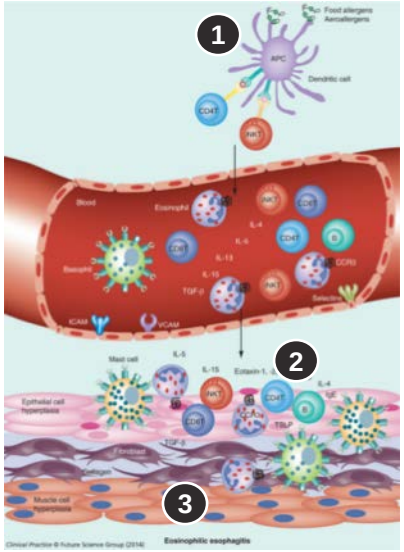
- Chronic, immune/antigen-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically ≥15 eosinophils / HPF
- Typically triggered by external allergens, most commonly food, resulting in eosinophilic infiltration into the esophagus
- Most patients with EoE also have other atopic conditions including food allergies (70%), asthma (56%), or allergic rhinitis (43%)

Epidemiology

- An estimated 150,000+ cases of EoE in US (2014), expected to increase due to greater diagnosis, incidence rates and potential treatment options

Current Treatments & Limitations

- No currently approved therapeutic agents
- Currently treated with off-label use of corticosteroids and dietary modifications
- Treatment remains suboptimal for many patients



1 **Allergen exposure**

2 **Immune activation**

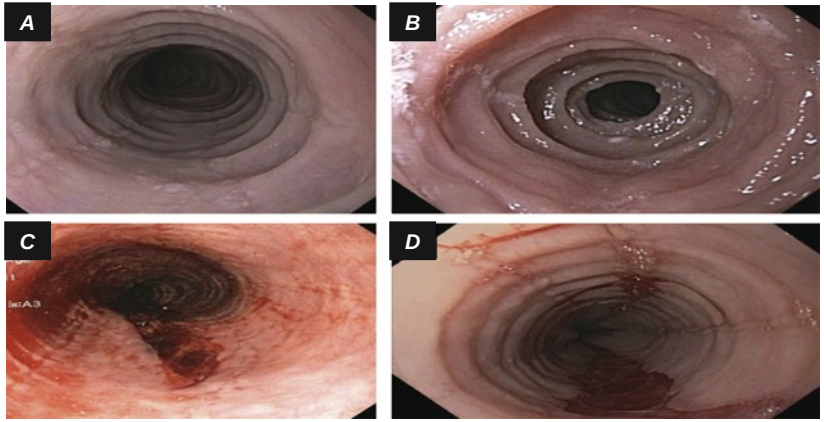
3 **Esophageal remodeling**

Source: Dellon E. *Gastroenterol Clin North Am.* 2014 June ; 43(2): 201–218

Currently no approved treatments for EoE

Symptoms vary by age and may ultimately lead to fibrosis in the esophagus

- **Children:** feeding disorders, dysphagia, vomiting, abdominal pain, heartburn
- **Adolescents and adults:** dysphagia & food impaction



A **B** *Remodeling starting to occur - increased ring formation and tightening of the esophagus causing difficulty in swallowing*

C **D** *Esophageal mural tears occurring following esophageal dilation, likely indicative of diffuse loss of esophageal elasticity*

EoE is currently treated through off-label use of corticosteroids and dietary changes

- **Topical corticosteroids** require extensive modifications before using
  - **"Puff and swallow"**: A topical corticosteroid, typically Flovent® (fluticasone), is aerosolized and swallowed to get into the esophagus
  - **Viscous coating**: A topical corticosteroid, typically Pulmicort® (budesonide), is mixed with Splenda® (sucralose) to create a viscous liquid
- **Systemic corticosteroids** effective, however chronic use presents safety concerns
- **Dietary therapy** (amino acid formulas and food elimination diets) effective but hard to maintain

No approved treatment for EoE currently exists

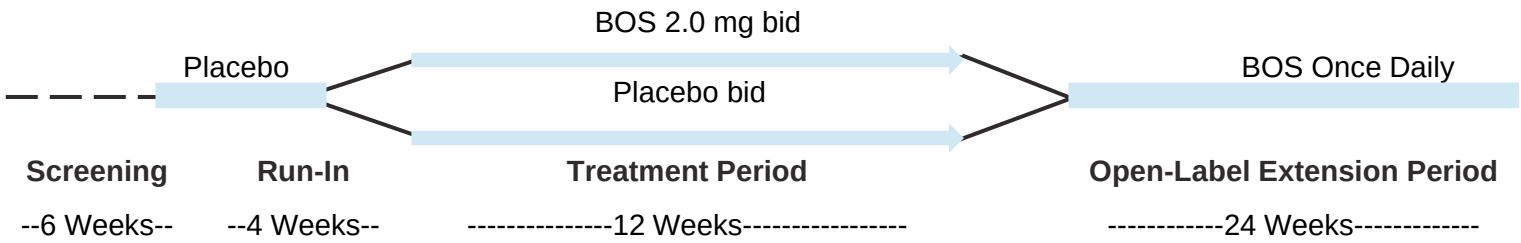
SHP621 is a novel budesonide formulation specifically to target EoE

SHP621 is a budesonide oral suspension (BOS) that is designed to improve corticosteroid delivery for the treatment of EoE

- **Budesonide is a corticosteroid that targets inflammatory pathways** through down-regulation of cytokines
- **BOS is a proprietary viscous oral formulation of budesonide** designed to coat the esophagus where the drug can act

Benefits	Description
Budesonide has demonstrated efficacy in EoE	• Topical corticosteroids already widely accepted as a “standard” therapy for EoE • BOS has demonstrated significant histologic response for treating EoE and dysphagia symptom improvement
Budesonide has an established benefit/risk profile	• Topical budesonide has a well established safety record based on approved products • Low dose and bioavailability of BOS suggests minimal expected influence on the hypothalamic-pituitary-adrenal axis
BOS can target the inflammation locally	• Available data suggests BOS can be used chronically due to ease of administration
Shire has strong capability to serve the needs of patients with EoE	• Significant experience in both GI and immunology • Strong track record in navigating both development and commercialization of rare disease drugs

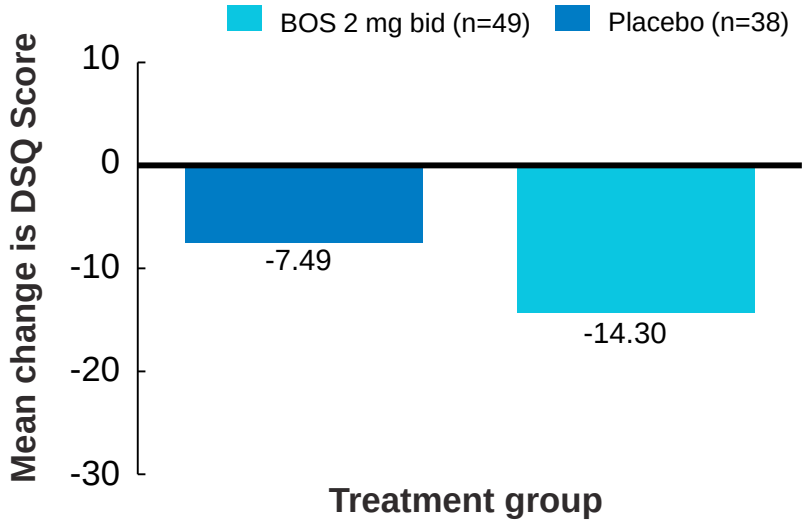
Phase 2 trial conducted to assess efficacy and safety of SHP621



Description	A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study With an Open Label Extension in Adolescent and Adult Subjects (11 - 40 Years of Age) With Eosinophilic Esophagitis
Primary Endpoints	• Histologic response rate (peak eosinophil count </=6/hpf) at week 16 • Dysphagia symptom response (change in DSQ) at week 16

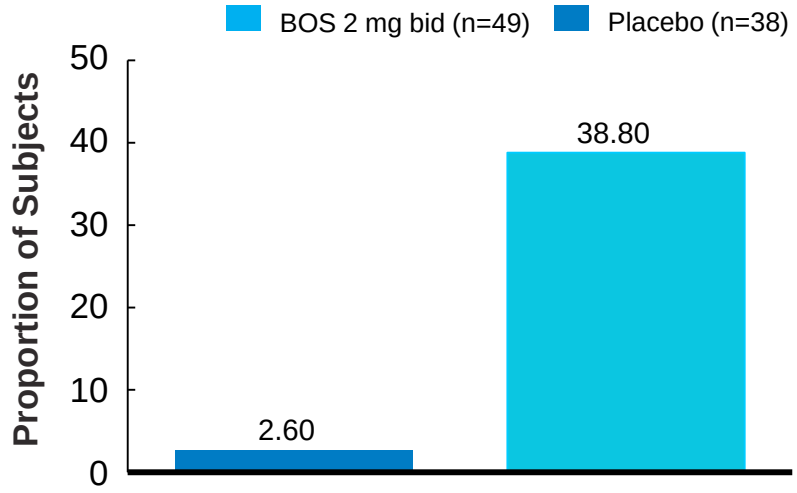
SHP621 met its co-primary endpoints (1/2)

Co-Primary Endpoint
Change from Baseline in DSQ Score at Week 16



P=0.0096
ANCOVA

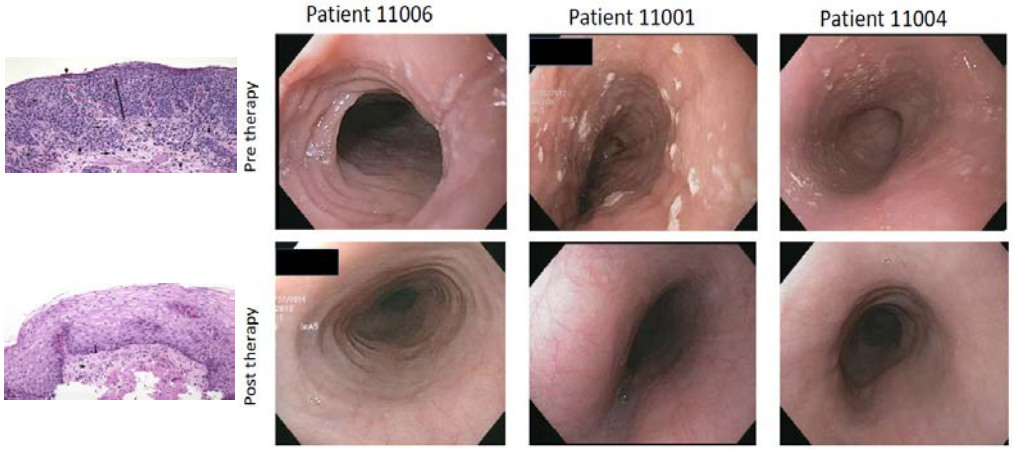
Co-Primary Endpoint
Histologic Response to Treatment at Week 16



P<0.0001
Fisher's Exact

SHP621 met both signs and symptoms endpoints (2/2)

Clinical meaningful benefit for patients …

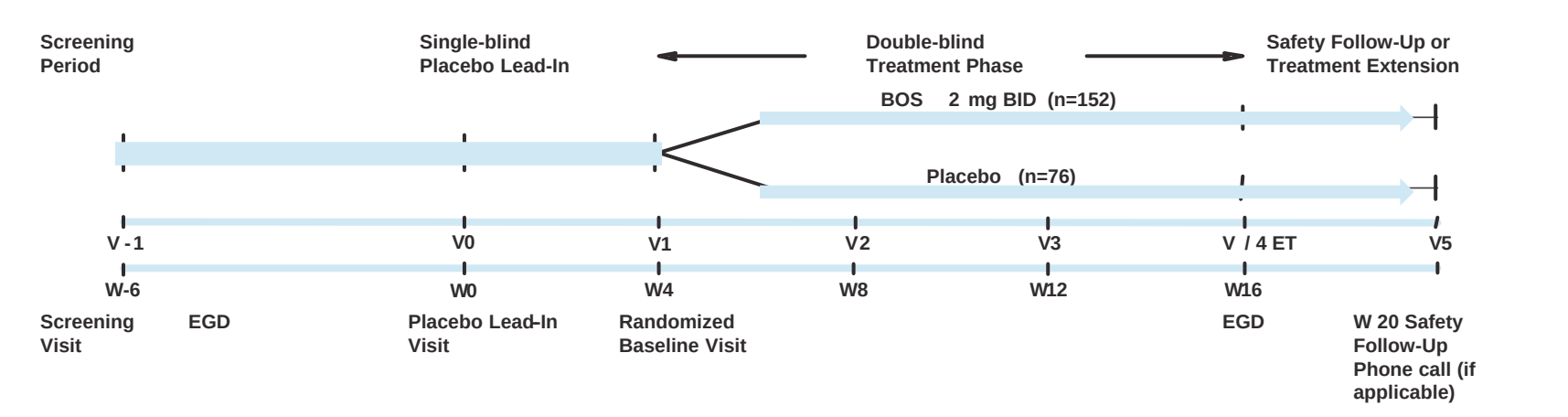


	Patient 11006	Patient 11001	Patient 11004
DSQ Change	- 8.2	-37.7	-18.7
Eosinophil Change	94 → 0	290 → 0	135 → 77

… Led to BTD for SHP621

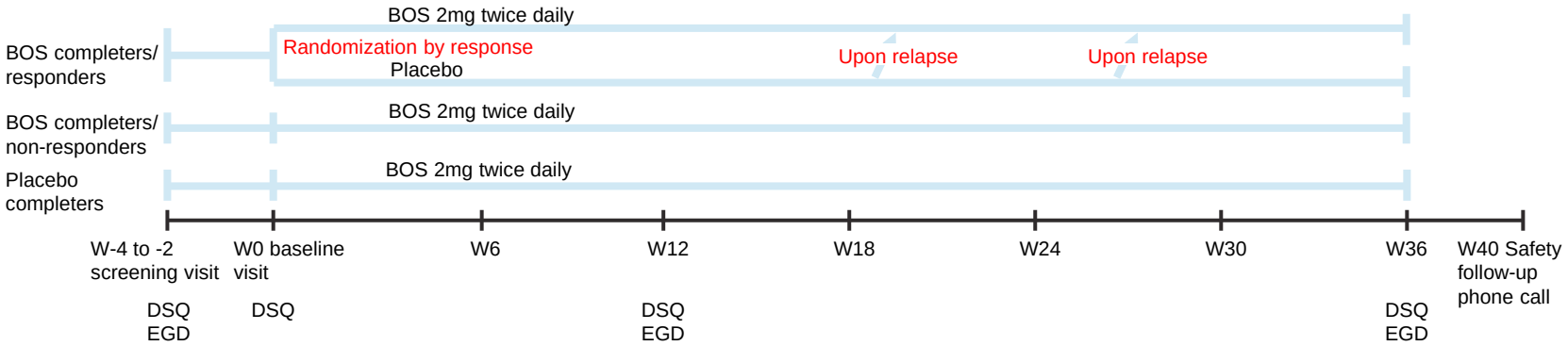
- SHP621 was granted BTD on May 31, 2016
  - EoE is a serious condition with no FDA-approved therapies
  - SHP621 demonstrated substantial improvement in clinically significant endpoints
- BTD will ensure the most efficient development pathway by
  - Ensuring more frequent conversations with senior FDA officials
  - Delineating a well-defined treatment and dosing regimen for product labeling

SHP621-301 induction study: Ongoing Phase 3 trial



Description	Budesonide Oral Suspension (BOS) in Adolescent and Adult Subjects (11 - 55 Years of Age, Inclusive) With Eosinophilic Esophagitis: A Phase 3 Randomized, Double-blind, Placebo-controlled Study
Primary Endpoints	• Dysphagia symptom response (change in DSQ) at week 16 • Peak of ≤6 eos/HPF across all available esophageal levels at week 16

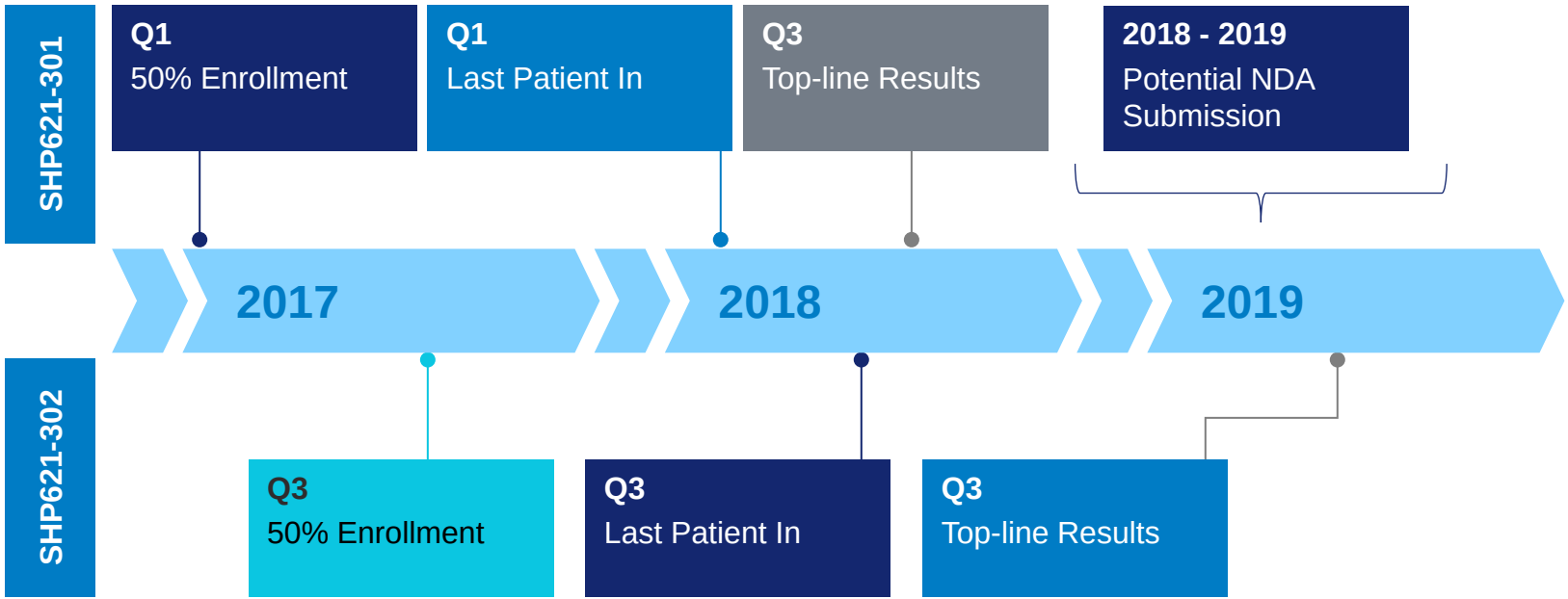
SHP621-302 extension study ongoing



Description	A Phase 3, Multicenter, Double-blind Extension Study to Evaluate Maintenance of Efficacy of Oral Budesonide Oral Suspension (BOS) and Long-term Treatment Effect of OBS in Adolescent and Adult Subjects (11 to 55 Years of Age, Inclusive) With Eosinophilic Esophagitis (EoE)
Primary Endpoint	Relapse during the double-blind randomized withdrawal period

Key dates and anticipated next steps for SHP621

SHP621
Eosinophilic Esophagitis



SHP647 has the potential to add a differentiated biologic to the treatment paradigm in IBD

- SHP647, a novel biologic for the treatment of IBD, is a **strong fit with Shire's strategic positioning and interest in select specialty markets**
- **Addresses the unmet need** for a tolerable and effective alternative to anti-TNFs **in moderate-to-severe IBD**
- **Differentiated from other anti-integrin antibodies** as SHP647 is the only anti-integrin directly targeting MAdCAM-1
- **Gut-specific activity**, with a **potentially differentiated and improved safety profile** as compared to current treatments
- Shire plans to pursue **Phase 3 development in UC and CD**

Overview of inflammatory bowel disease (IBD)

Disease Description

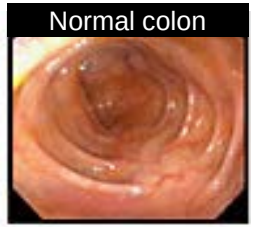
- IBD includes Crohn's disease (CD) and ulcerative colitis (UC), which are serious, chronic, inflammatory diseases of the intestine
- Both are relapsing / remitting conditions that, when active, are characterized by inflammation of the affected area
- Wide spectrum of disease exists but both typically exhibit abdominal pain, diarrhea, and can result in more severe complications including fistulas, strictures, toxic megacolon and other severe GI complications

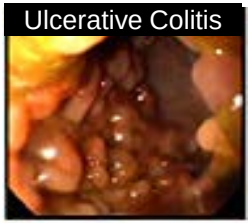
Epidemiology

- ~950K CD and 1.3M UC patients across G7 countries
- ~12-15% are pediatric patients

Current Treatments & Limitations

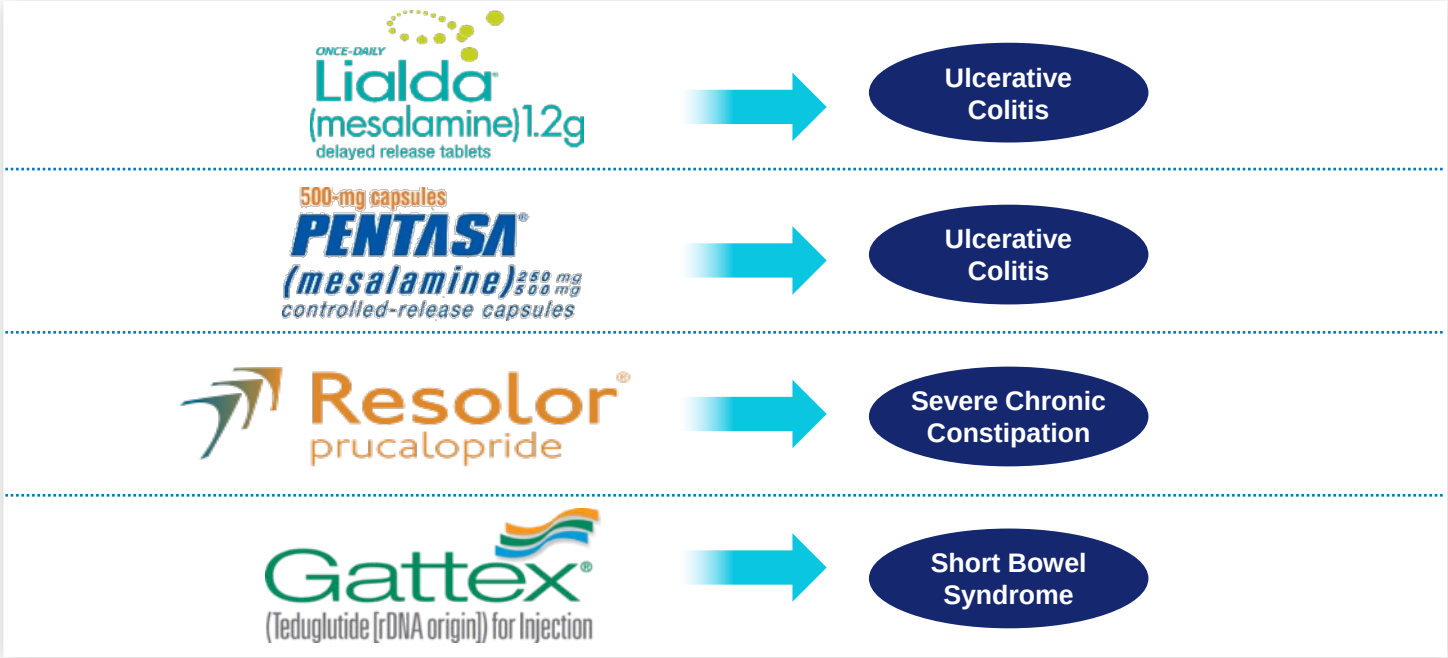
- Treatment goals include treating acute flare-ups and maintaining remission
- Treatment decisions depend on disease location and severity
- Biologics, with or without immunosuppressants, are the standard of care in steroid-refractory IBD patients
- Despite the success of anti-TNF biologics, ~1/3 do not respond to induction and ~20% lose response each year
- ~75% of CD and ~30% of UC patients eventually require surgery





Sources: Decision Resources, Crohn's and Colitis Foundation

SHP647 is a strategic addition to GI and if approved, would extend our leadership in UC and CD



SHP647 a novel biologic for the treatment of IBD, is a strong fit with Shire's strategic positioning and interest in select specialty markets

SHP647 molecule overview

Overview

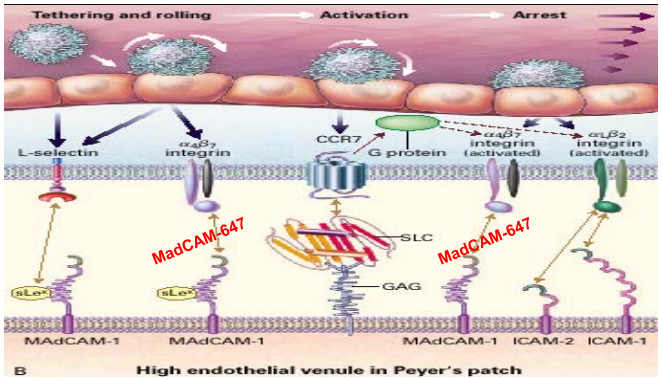
- Fully-humanized, highly potent and selective anti-MAdCAM mAb (IgG2, 150Kda)
- Administered subcutaneously every 4 weeks
- Evaluated in >700 patients in Phase 1 and 2
- Phase 3 trials expected to begin after consultation with global health authorities

Value Proposition

- Only anti-integrin directly targeting MAdCAM-1
- A potentially differentiated and improved safety profile as compared to current treatments - may eliminate the risk of PML
- Potential to move up the treatment pyramid in IBD
- Subcutaneous injection may be preferred

Mechanism of Action

- MadCAM appears to facilitate excessive lymphocyte infiltration under conditions of chronic gastrointestinal inflammation
- SHP647 binds MAdCAM-1, preventing the binding of α4β7+ lymphocytes to MadCAM expressing sites in the high endothelial venules of the GI tract
- SHP647 reduces lymphocyte homing to the gut and GI inflammation



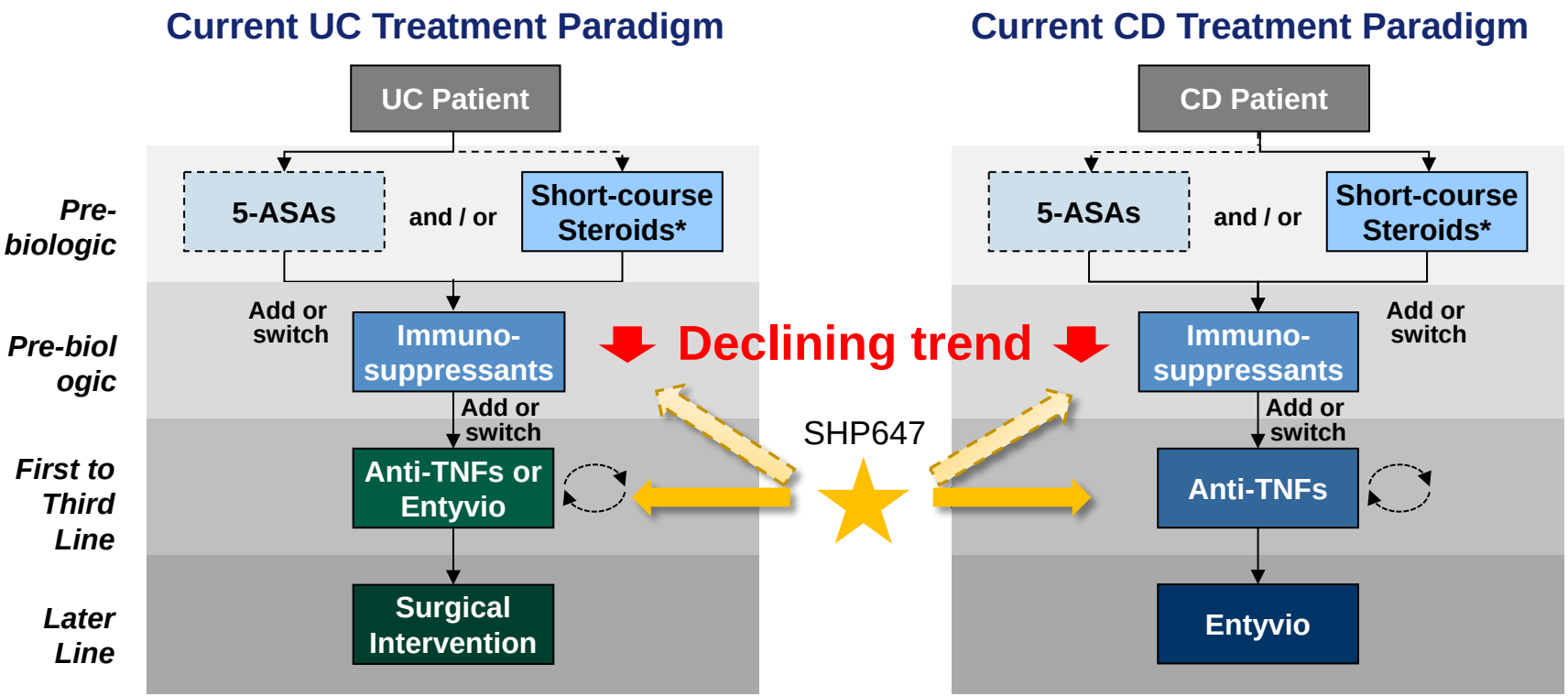
Adapted from Cheroutre and Madakamutil 2004

MAdCAM: Mucosal vascular addressin cell adhesion molecule PML: Progressive multifocal leukoencephalopathy (PML)

Summary of Phase 2 data

- Primary endpoint met in a randomized, double-blind placebo-controlled Phase 2 study (n=357) in patients with moderate to severe Ulcerative Colitis (“TURANDOT”)
  - Primary end point was week 12 remission, defined as total Mayo score ≤2 with no subscore >1
  - Remission and mucosal healing were significantly greater in the 22.5mg and 75mg dose groups vs placebo
- In a Phase 2 study in patients with active moderate to severe Crohn’s Disease (“OPERA”, n=267), the primary endpoint of CDAI-70 response showed a numerical difference between SHP647 and placebo without reaching statistical significance
  - However, remission at week 12 appeared to be substantially higher in the subjects with high baseline CRP levels
- SHP647 did not affect immune surveillance in the central nervous system of anti-TNF and immunosuppressant experienced Crohn’s Disease patients who are anti-TNF inadequate responders (TOSCA)

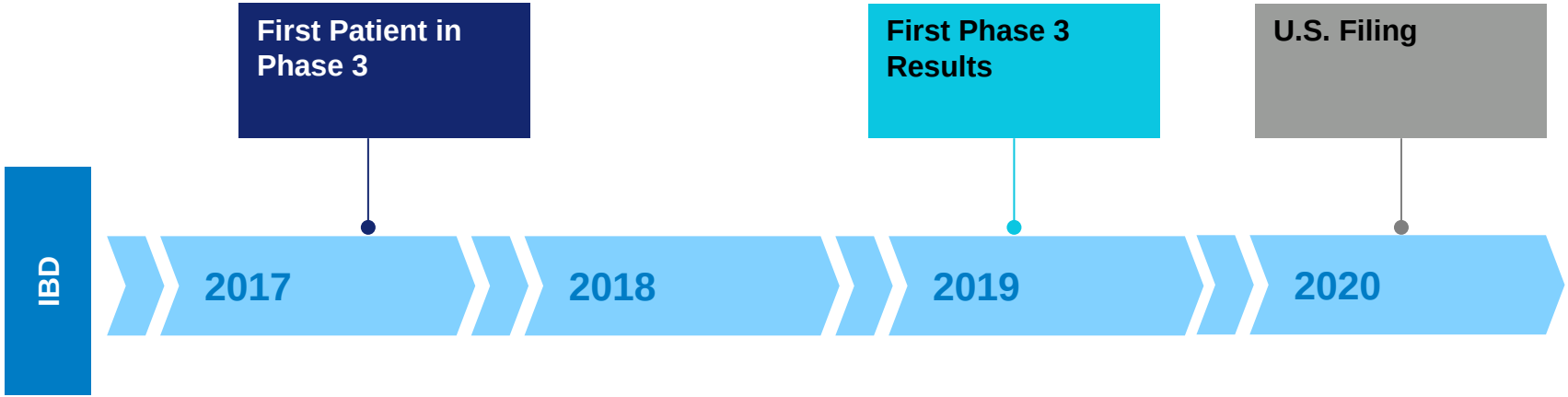
Increasing trend to move to Anti-TNFs after orals in UC; Entyvio starting to be used now prior to Anti-TNFs where plans allow



Source: UpToDate; Encuity Treatment Answers; Shire analysis; Physician Interviews; ClearView Analysis.
* Short-course steroids may be used to treat flares at any stage.

Key dates and anticipated next steps for SHP647

SHP647
IBD



Key takeaways for our two promising late-stage GI programs

Significant market opportunity	Both EoE and IBD provide significant market opportunity to augment Shire's high growth existing billion dollar+ GI franchise
Significant unmet patient need	EoE: Currently no approved therapeutic agents IBD: Need for additional treatment options before / after existing biologic therapies
Strong differentiation and innovation	SHP621: Novel delivery of well characterized drug SHP647: Novel mechanism of action
Encouraging Phase 2 data	Encouraging Phase 2 data for both SHP621 and SHP647 supports Phase 3 development
Near-term progress expected	SHP621: Phase 3 recruitment to continue in 2017 and expected complete by 2018 SHP647: Phase 3 trial to initiate in 2017

Shire

Today's pipeline program agenda

TOPIC	SPEAKER	TIME (ET)
GI Programs *SHP621 / SHP647*	Howard Mayer	12:30 - 12:50
Neonatology Program *SHP607*	Norman Barton	12:50 - 1:10
Transplant Program *SHP620*	Howard Mayer	1:10 - 1:30
Neuroscience Program *SHP465*	Howard Mayer	1:30 - 1:40
HAE Program *SHP643*	Wolfram Nothaft	1:40 - 2:00

SHP607 has the potential to prevent certain severe complications in extremely preterm infants

SHP607
Neonatal Complications Of Preterm Birth

- Preterm infants born less than 28 week gestational age (GA) commonly suffer from complications, including:
  - **Bronchopulmonary Dysplasia (BPD)**
  - **Retinopathy of Prematurity (ROP)**
  - **Intra-ventricular hemorrhage (IVH)**
  - and other serious co-morbidities
- Currently **no treatments available / approved** to prevent certain severe neonatal complications
- SHP607 is a rhIGF-1/rhIGFBP-3 complex acquired from Premacure in 2013
  - Increase of serum IGF-1 levels to the normal physiologic range for corresponding GA **may prevent certain complications of prematurity***
- Shire reported topline results from Phase 2 clinical studies in June 2016
  - Study did not meet primary endpoint: reduction in severity of retinopathy of prematurity (ROP)
  - However, study demonstrated **clinically relevant effects on secondary endpoints:** development of severe bronchopulmonary dysplasia (BPD) and intraventricular hemorrhage (IVH)
- Shire to **pursue development** with a focus on BPD and IVH

* Subject to clinical trials

Overview of severe complications in preterm infants

SHP607
Neonatal Complications Of Preterm Birth

Disease Description

- Extremely preterm infants are predisposed to pulmonary, neurological and eye disorders due to underdevelopment of lungs, brain, and eye
- BPD is a chronic lung disease caused by mechanical ventilation and oxygen supplementation (sO2) and / or infection
  - BPD patients often develop long-term respiratory symptoms and functional abnormalities
- IVH occurs when there is bleeding into the ventricles within the brain which can lead to developmental delays and problems controlling movement
- ROP occurs when there is abnormal development of blood vessels in the retina of the eye which can lead to retinal detachment and substantial or total loss of vision

Epidemiology

- ~120K premature babies are born before 28 weeks GA in US/EU/JP/ROW markets with NICU infrastructure [1]
- Neonatal morbidities in infants born 24-28 weeks gestational age occur at the following rates[2]
  - BPD: ~50%
  - IVH (severe): ~ 20%
  - ROP (≥ grade 3): ~15%

Current Treatments & Limitations

- Patients with BPD often require oxygen therapy for months and surgical intervention can be used in patients with IVH and ROP with suboptimal results
- There is no current truly effective pharmacological treatment to treat or prevent BPD, IVH, or ROP in preterm infants

1. Lancet 2012; 379: 2162–72. 2. Stoll et al, JAMA. 2015;314(10):1039-1051. doi:10.1001/jama.2015.10244

IGF-1 plays a key role in fetus development

IGF-1 plays a critical role in development in utero*

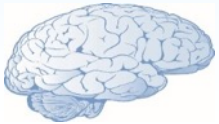
IGF-1 is a **major growth factor in the fetus**, with rising concentrations during mid-late gestation to support accelerated 3rd trimester growth

- In humans and mice, deficiencies result in growth and developmental problems both *in utero* and after preterm birth

IGF

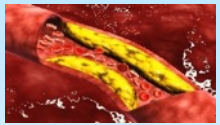
Neurologic

- Affects CNS development
- Associated with brain size/ anatomy and developmental delay

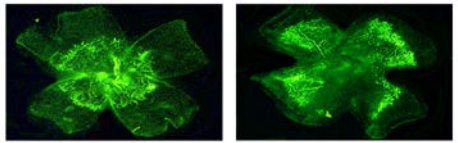


Vascular

- Associated with Retinopathy of Prematurity (ROP) and long term risks of cardiovascular disease
- Critical for neonatal retinal (eye) vascular development

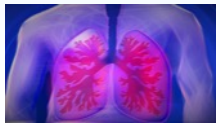


IGF-I -/- mouse **WT mouse**

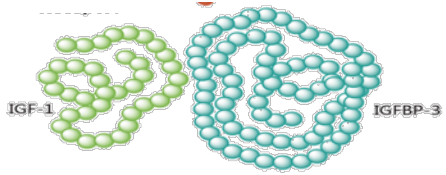


Pulmonary

- Critical for prenatal lung growth
- Associated with Broncho-pulmonary Dysplasia (BPD) in preterm infants



SHP607 is a rhIGF-1/rhIGFBP-3 complex being developed to address certain neonatal complications of preterm birth



Recombinant insulin like growth factor 1 (7.6 kDa)

Insulin-like growth factor binding protein-3 (28.7 kDa)

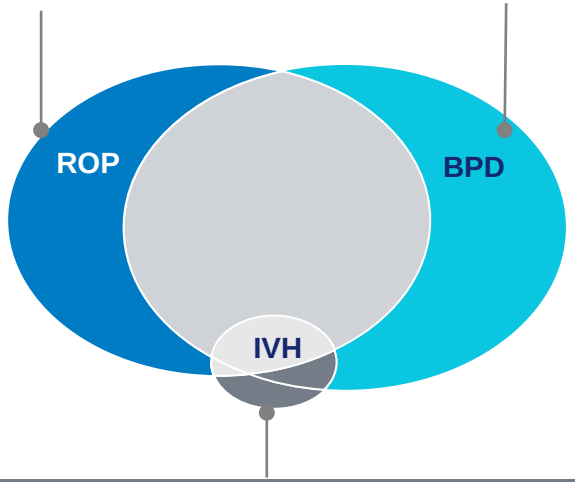
- Granted Orphan Drug Designation in the EU and US (for ROP)

*Hellstrom et al, Acta Pediatrica, Volume 105, Issue 6, 2016

Significant overlap between BPD, IVH and ROP

Any ROP
- ~50% of any ROP cases have BPD
- ~15% of any ROP cases have Severe IVH

BPD
- ~65% of BPD cases have any ROP
- ~15% of BPD cases have severe IVH



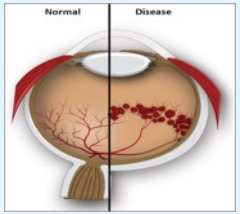
Severe IVH
- ~60% of Severe IVH cases have BPD
- ~75% of Severe IVH cases have any ROP

Source: Courtesy Ann Hellstroem, Institute of Neuroscience and Physiology, Sahlgrenska Academy, Gothenburg University, 416 85 Gothenburg, Sweden.

BPD, IVH and ROP are associated with significant morbidity and mortality

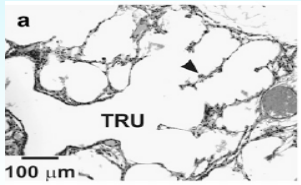
ROP– Retinopathy of Prematurity

No prescription treatment approved for prevention of ROP, current standard of care is laser therapy for severe cases of ROP; Avastin® and Lucentis® used off-label

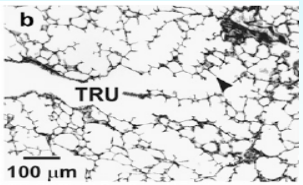


BPD – Bronchopulmonary Dysplasia

- **Form of chronic lung disease**
- ~**Significant mortality** (15-20%) and **morbidity**



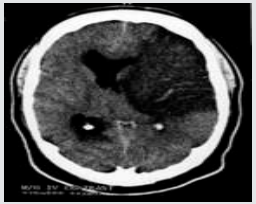
BPD (arrested alveolar growth and septation)



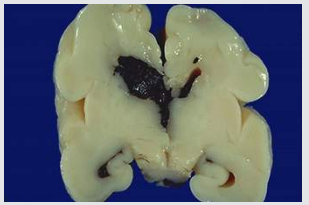
Normal Septation

IVH – Intraventricular Hemorrhage

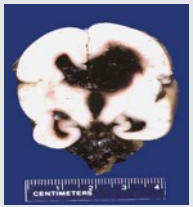
- **Bleeding in the brain's ventricular system**
- IVH can be lethal or survivable, followed often by loss of brain tissue termed **porencephaly**



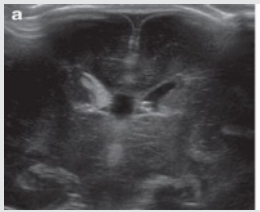
24-week Survivor
Porencephaly



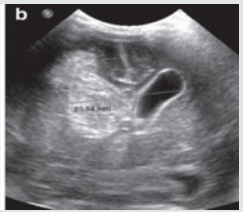
24-week, Smooth Cortex
Lethal Right Grade IV IVH



Lethal Left Grade IV
Right Grade III



28-week
Right Grade III



4-days later
Grade IV

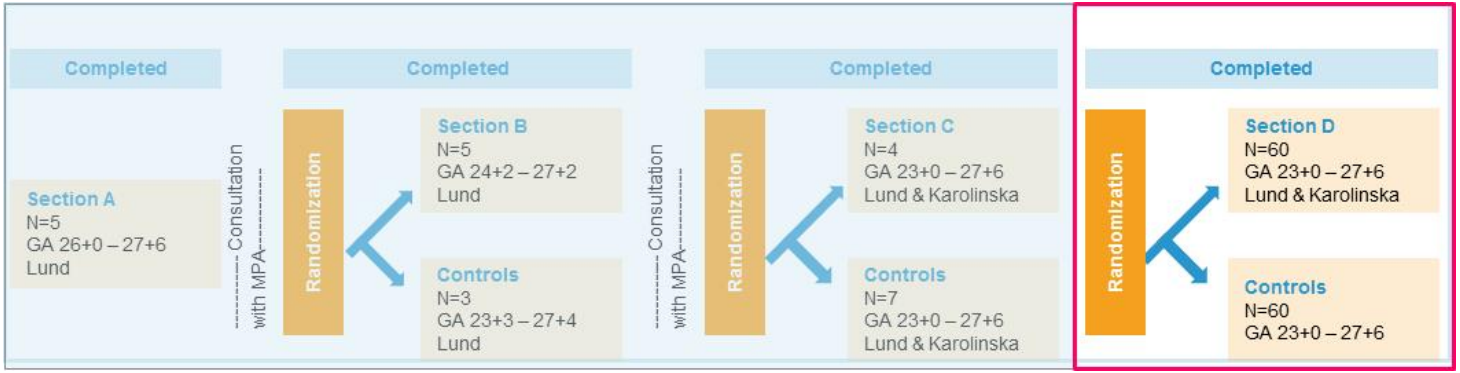
Shire

Images courtesy of Dr. Robert Ward, Professor Emeritus of Pediatrics/Neonatology, University of Utah

Phase 2 clinical design

SHP607
Neonatal Complications
Of Preterm Birth

Discussed previously



Primary Endpoint

- Maximum severity of ROP stage across all retinal examinations

Secondary Endpoint

- **Development of BPD, by severity, as diagnosed by oxygen challenge testing at PMA 36 weeks**
- **Brain development as assessed by changes in head circumference and brain volume via MRI**
- **Development of IVH at any time during the study as assessed by cerebral ultrasound**
- Time to discharge from the neonatal intensive care (TDNIC)
- Growth parameters including body weight and length
- Area under curve for max severity of ROP stage (AUC for ROP) or max severity of ROP stage ≥3

Phase 2 clinical results: Evaluable patients

SHP607
Neonatal Complications
Of Preterm Birth

Analysis sets

Enrolled 121

	rhIGF-1/rhIGFBP-3 n (%)	Standard of Care n (%)
Intent-to-Treat Set	61	60
Safety Analysis Set	61 (100.0)	60 (100.0)
Full Analysis Set	61 (100.0)	60 (100.0)
Evaluable Set	24 (39.3)	60 (100.0)

Evaluable set: All subjects in ITT Population who met at least 70% of IGF-1 levels within the target range (28-109 µg/L) and who received at least 70% duration of treatment.

Phase 2 results: ROP

SHP607
Neonatal Complications Of Preterm Birth

Evaluation Criteria

- The study used the ICROP classification
- Time points (Local exam and Retcam):
- 31W PMA
- Every 1-2 weeks based on evaluation of local pediatric ophthalmologist
- 40W PMA +/- 4d
- Both the local pediatric ophthalmologist and central readers were masked to treatment status

Full Analysis and Evaluable Set

Maximum Severity of ROP Stage across All Examinations by a Local Pediatric Ophthalmologist – Full Analysis Set & Evaluable Set

	Full Analysis Set		Evaluable Set	
	rhIGF-1/rhIGFBP-3 (N = 61) n (%)	Standard of Care N = 60 n (%)	rhIGF-1/rhIGFBP-3 (N = 24) n (%)	Standard of Care N = 60 n (%)
Patients with ROP Exam	49	53	22	53
Stage				
0	10 (20.4)	16 (30.2)	6 (27.3)	16 (30.2)
1	7 (14.3)	8 (15.1)	5 (22.7)	8 (15.1)
2	13 (26.5)	21 (39.6)	6 (27.3)	21 (39.6)
3	11 (22.4)	2 (3.8)	2 (9.1)	2 (3.8)
3+	7 (14.3)	6 (11.3)	2 (9.1)	6 (11.3)
4	1 (2.0)	0	1 (4.5)	0
5	0	0	0	0
Missing	12	7	2	7

- Study did not meet primary endpoint in reducing the severity of ROP
- One possible explanation could be drug delivery to retinal tissue

Phase 2 results: BPD

SHP607
Neonatal Complications Of Preterm Birth

Evaluation Criteria

- Assessment of presence/ severity of BPD was obtained via a standardized Oxygen Challenge Test performed at 36W PMA
- Definitions based upon NICHD BPD definitions for premature infants born < 32 weeks GA:
- Mild BPD: oxygen requirement for the first 28 days but in room air at PMA 36 weeks
- Moderate BPD: oxygen requirement for the first 28 days and oxygen <30% at PMA 36 weeks
- Severe BPD: oxygen requirement for the first 28 days and oxygen >30% and continuous positive airway pressure or mechanical ventilation at PMA 36 weeks

Full Analysis and Evaluable Set

	Full Analysis Set		Evaluable Set	
	rhIGF-1/rhIGFBP-3 (N = 61) n (%)	Standard of Care N = 60 n (%)	rhIGF-1/rhIGFBP-3 (N = 24) n (%)	Standard of Care N = 60 n (%)
Patients with BPD Assessment	47	49	21	49
Severity of BPD				
No BPD	4 (8.51%)	4 (8.16)	2 (9.52)	4 (8.16)
Mild	23 (48.94)	16 (32.65)	13 (61.90)	16 (32.65)
Moderate	9 (19.15)	5 (10.20)	5 (23.81)	5 (10.20)
Severe	10 (21.28)	22 (44.90)	1 (4.76)	22 (44.90)
Unable to determine	1 (2.13)	2 (4.08)	0 (0)	2 (4.08)

- Study demonstrated clinically relevant effects in the secondary endpoint related to BPD

Phase 2 results: IVH

SHP607
Neonatal Complications
Of Preterm Birth

Evaluation Criteria

- Assessment of presence/ absence and grade of IVH was obtained via cerebral ultrasounds at the following time points:
  - Day 0, 3, 7, 14, 21
  - Week 40 PMA (End of Study)
- The examination included standardized measurements of hemorrhagic lesions, periventricular leukomalacia, and cyst localization.
- Assessment of IVH was made by the centralized pediatric radiologist who was blinded to treatment status

Full Analysis and Evaluable Set

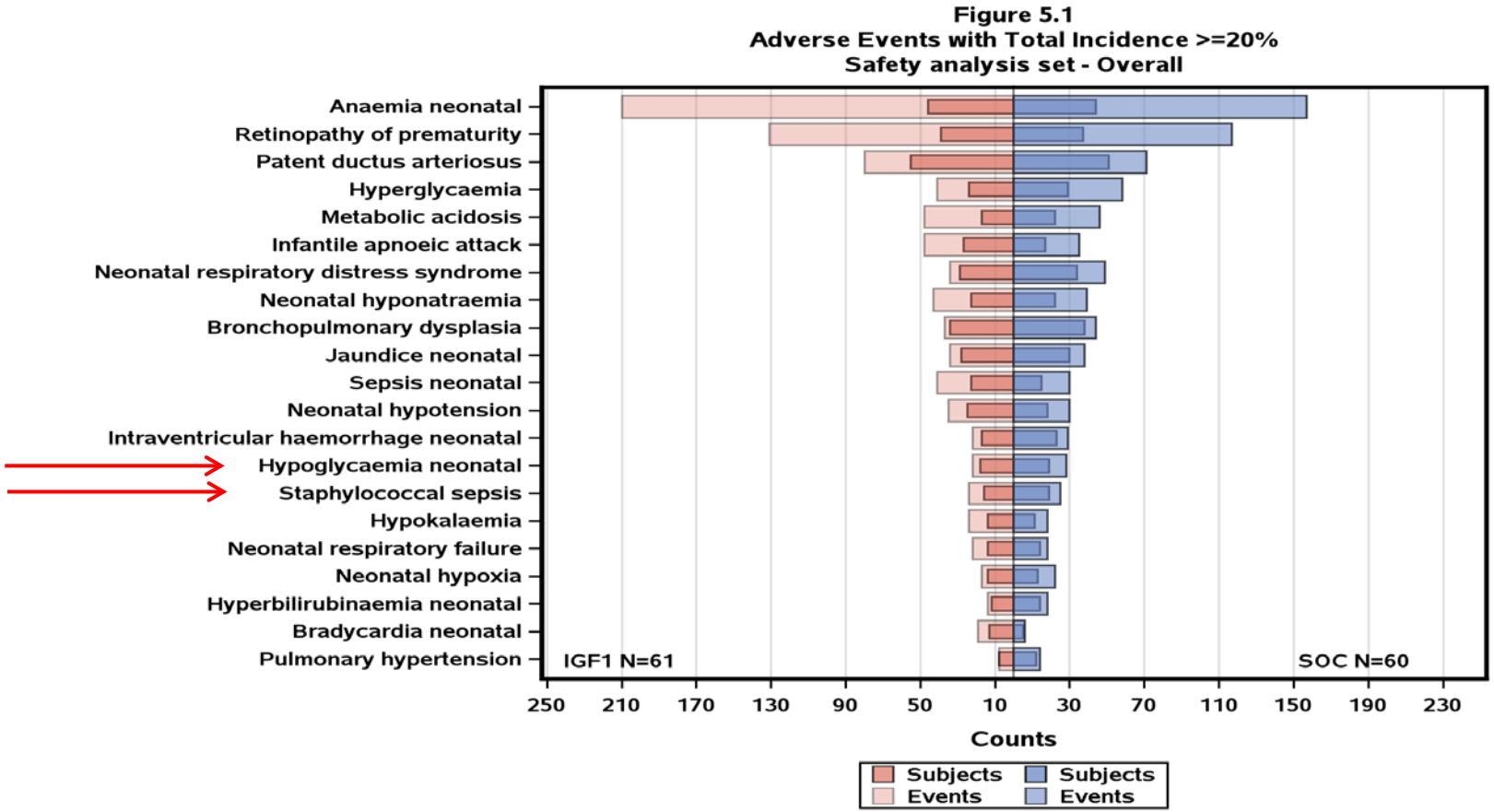
Maximum IVH Grade across All Examinations

	Full Analysis Set		Evaluable Set	
	rhIGF-1/rhIGFBP-3 (N = 61) n (%)	Standard of Care N = 60 n (%)	rhIGF-1/rhIGFBP-3 (N = 24) n (%)	Standard of Care N = 60 n (%)
IVH Grade				
0-1	49 (80.3)	42 (70.0)	20 (83.3)	42 (70.0)
2	4 (6.6)	4 (6.7)	2 (8.3)	4 (6.7)
3	6 (9.8)	9 (15.0)	2 (8.3)	9 (15.0)
4	2 (3.3)	5 (8.3)	0	5 (8.3)

- Positive trend in the secondary endpoint related to intraventricular hemorrhage (IVH)

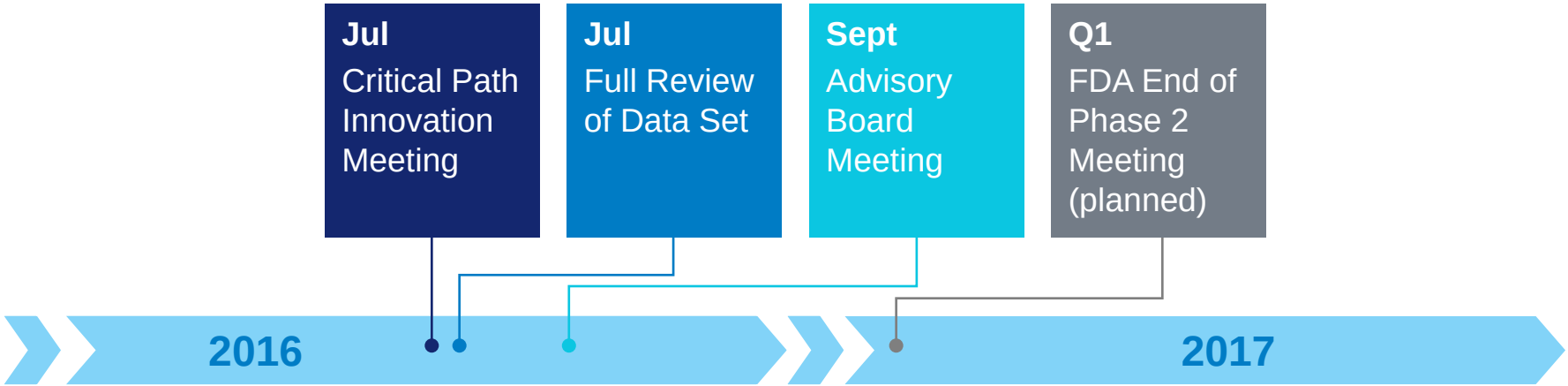
Phase 2 reported adverse events

SHP607
Neonatal Complications
Of Preterm Birth



Key dates and anticipated next steps for SHP607

SHP607
Neonatal Complications
Of Preterm Birth



Key takeaways for our promising neonatology program

SHP607
Neonatal Complications Of Preterm Birth

Significant market opportunity	~120K extremely preterm infants born each year across markets with NICU infrastructure representing a large potential market opportunity
Significant unmet patient need	Complications in extremely pre-term infants can be common and severe, particularly BPD, IVH, and ROP. Limited options to prevent these morbidities or predict their occurrence
Strong differentiation and innovation	SHP607 is the only drug in development targeting the IGF1 pathway to potentially prevent certain complications of preterm birth
Encouraging Phase 2 data	Encouraging Phase 2 data has bolstered our excitement about this program and will help inform the design of our Phase 3 program
Near-term progress expected	End of Phase 2 meeting planned for early 2017 which will further inform next steps

Shire

Today's pipeline program agenda

TOPIC	SPEAKER	TIME (ET)
GI Programs *SHP621 / SHP647*	Howard Mayer	12:30 - 12:50
Neonatology Program *SHP607*	Norman Barton	12:50 - 1:10
Transplant Program *SHP620*	Howard Mayer	1:10 - 1:30
Neuroscience Program *SHP465*	Howard Mayer	1:30 - 1:40
HAE Program *SHP643*	Wolfram Nothaft	1:40 - 2:00

SHP620 (Maribavir) has the potential to be 1st new approved anti-CMV agent in >10 years

- **Cytomegalovirus** (CMV) is a herpes virus with **potential for serious illness in transplant recipient patients** and in other patients with compromised immune systems
- There have been **no new anti-CMV agents in >10 years**, building significant demand for new therapies to meet an unmet need
- SHP620 **targets CMV UL97 protein kinase** to inhibit viral encapsidation and nuclear egress of viral particles
- SHP620 shows **potent antiviral activity,** including against strains of CMV resistant or refractory to other anti-CMV agents
- All clinical studies to date show a **reasonable safety profile** characterized by less hematologic and renal toxicity, in contrast to other anti-CMV drugs
- Currently available anti-CMV drugs are effective, however **use is limited due to toxicity,** particularly those used for the treatment of patients with resistant/refractory disease

Overview of CMV infection in transplant patients

Disease Description

- CMV infection is common but generally asymptomatic in healthy patients
- Immunocompromised patients are at greater risk for CMV disease
- Immunosuppression renders transplant recipients vulnerable[1]
- CMV disease in immunocompromised patients may result in potentially life-threatening dysfunction in multiple organ systems
  - Indirect effects of CMV infection include increased rates of other infections (and EBV-related PTLD), graft dysfunction, graft rejection (SOT), graft vs host disease (SCT), and mortality[2]

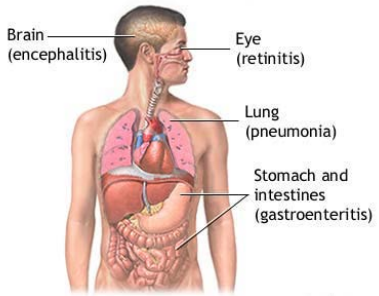
Epidemiology

- There are >100,000 solid organ transplants and >50,000 hematopoietic stem cell transplants performed per year worldwide[3,4]
- CMV infection/reactivation occurs in 50–80% SCT recipients[5–7]
- CMV disease occurs in 6-10%[8-11] of SOT recipients

Current Treatments & Limitations

- Anti viral drugs commonly used for both prophylactic and therapeutic treatment
- Neutropenic and nephrotoxic effects associated with current agents often lead to dose reductions or interruptions and significant toxicity
- Increasing drug-resistance to existing agents is becoming particularly problematic

Potential Sites of CMV Infection



SCT, stem cell transplant; SOT, solid organ transplant; EBV, Epstein–Barr virus; PTLD, post-transplant lymphoproliferative disorders

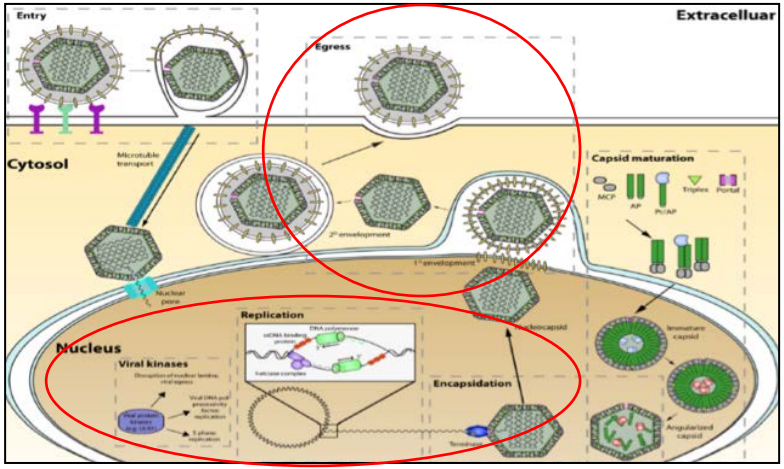
1. Kotton CN, Fishman JA. J Am Soc Nephrol 2005;16(6):1758–74; 2. Kotton CN. Am J Transplant 2013;13(Suppl 3):24–40. 3. http://www.who.int/transplantation/gkt/statistics/en/;
4. http://www.who.int/transplantation/hsctx/en/; 5. Goodrich JM, et al. N Engl J Med 1991;325:1601–07; 6. Einsele H, et al. Blood 1995;86:2815–20; 7. Zhang LF, et al. Transpl Infect Dis 2011;13(6):622–32; 8. Linares L, et al. Transplant Proc. 2011 Jul-Aug;43(6):2145-8; 9. Manuel O et al. Am J Transplant. 2013 Sep;13(9):2402-10; 10. San Juan R, et al. Clin Infect Dis. 2008 Oct 1;47(7):875-82; 11. de la Hoz RE, et al. J Clin Virol 2002;25(Suppl 2):S1–12

Molecular mechanisms of SHP620 and current treatments

SHP620 history

- Orphan designation granted in US and EU for both prevention and treatment indications
- Phase 3 prophylaxis studies in SCT and liver transplant recipients tested 100 mg BID doses: MBV failed to meet primary efficacy endpoints of preventing CMV disease vs. comparators
- Molecule acquired by Shire as part of Viropharma acquisition

SHP620 MOA



- **Chemical class:** benzimidazole riboside; SHP620 (MBV)
- **Inhibits CMV UL97 protein kinase** thereby **inhibiting CMV DNA replication, maturation, encapsidation and nuclear egress of viral capsids**

Current treatment options

Drug/MOA	Toxicity
Ganciclovir/ Nucleoside (dGTP) analog, inhibits DNA replication	Bone marrow suppression (anemia, thrombocytopenia, neutropenia), carcinogenic, teratogenic
Valganciclovir/ Ganciclovir prodrug (see above)	
Foscarnet/ Pyrophosphate analog, inhibits viral DNA polymerase	Renal toxicity, seizures
Cidofovir/ Monophosphate nucleotide analog, inhibits viral DNA polymerase	Renal toxicity, bone marrow suppression, carcinogenic, teratogenic

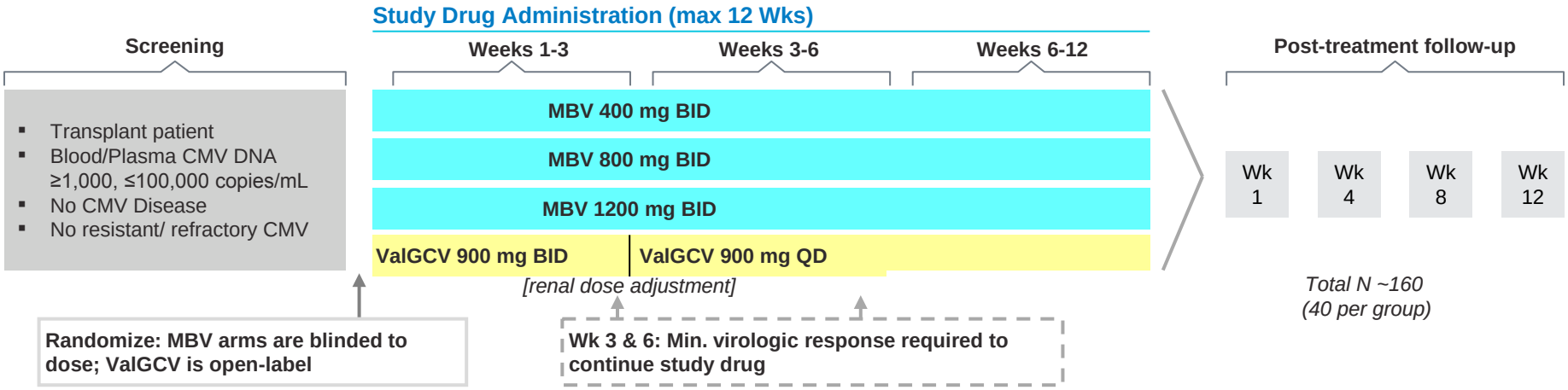
SHP620 for CMV treatment: Use outside of clinical trials at 400 mg BID

	US Emergency-IND (E-IND) [1]	EU ATU [2]
Population studied	**Resistant / Refractory CMV**	
Number with data	6	12
SCT / SOT	1 / 5	3 / 9
Known resistance mutations to GCV or FOS	4 (67%)	11 (92%)
Virologic response	CMV Undetectable: 4 (67%)	CMV ↓ ≥1.5 log or undetectable: 6/ 12 (50%)

1. Avery R et al. Tranplant Infect Dis 2010; 12:489-96. 2. Alain S, et al. Transplant Proc. 2013; 45:1603-7

Phase 2 clinical trial (620-203): Treatment of asymptomatic CMV viremia

SHP620
Transplant



Treatment Arms

- A Phase 2, randomized, dose-ranging study to assess the safety and anti-CMV activity of **SHP620 versus Valganciclovir for treatment of CMV infections** in transplant recipients who do not have CMV organ disease
- Patients were treated with MBV (400, 800, or 1200mg BID) or Valganciclovir (ValGCV, 900mg QD)
  N ~120 patients, 40 per group

Primary Endpoint

- Number of patients with confirmed undetectable plasma Cytomegalovirus (CMV) DNA within 6 weeks
- Number of patients with a Treatment Emergent Adverse Event (TEAE)

Shire

Efficacy results (SHP620-203)

Analysis of Confirmed Undetectable Plasma CMV DNA *within 6 Weeks* (ITT-S Population) (B)

Week 6	MBV 400 mg BID (N=40)	MBV 800 mg BID (N=40)	MBV 1200 mg BID (N=39)	MBV All Doses (N=119)	ValGCV 900 mg BID (N=40)
Number of subjects with missing data, n (%)	1 (2.5)	0	1 (2.6)	2 (1.7)	1 (2.5)
Undetectable Plasma CMV DNA					
No, n (%)	8 (20.0)	7 (17.5)	10 (25.6)	25 (21.0)	13 (32.5)
Yes, n (%)	31 (77.5)	33 (82.5)	28 (71.8)	92 (77.3)	26 (65.0)

Summary of Confirmed Undetectable Plasma CMV DNA (Central Laboratory) within 6 Weeks by Subgroup (ITT-S Population)

Subjects with Undetectable Plasma CMV DNA, n (%)	SHP620 400 mg BID (N=40)	SHP620 800 mg BID (N=40)	SHP620 1200 mg BID (N=39)	SHP620 All Doses (N=119)	Valganciclovir 900 mg BID (N=40)
Baseline plasma CMV DNA					
Low (<10,000 copies/mL)	24/26 (92.3)	21/24 (87.5)	23/28 (82.1)	68/78 (87.2)	20/27 (74.1)
High (≥10,000 copies/mL)	7/14 (50.0)	12/16 (75.0)	5/11 (45.5)	24/41 (58.5)	6/13 (46.2)
Transplantation type					
Stem cell transplant	16/20 (80.0)	16/21 (76.2)	14/20 (70.0)	46/61 (75.4)	10/21 (47.6)
Solid organ transplant	15/20 (75.0)	17/19 (89.5)	14/19 (73.7)	46/58 (79.3)	16/19 (84.2)

Source: Shire analysis

Select treatment-emergent adverse events by frequency (ITT-S Population)-SHP620-203

Preferred Term	MBV 400mg BID (N=40)	MBV 800mg BID (N=40)	MBV 1200mg BID (N=39)	MBV All Doses (N=119)	ValGCV 900mg BID (N=40)
Number of Subjects with Any TEAE, n (%)	**39 (97.5)**	**38 (95.0)**	**39 (100.0)**	**116 (97.5)**	**33 (82.5)**
Dysgeusia, n (%)	18 (45.0)	16 (40.0)	14 (35.9)	48 (40.3)	1 (2.5)
Nausea, n (%)	9 (22.5)	7 (17.5)	11 (28.2)	27 (22.7)	6 (15.0)
Diarrhoea, n (%)	7 (17.5)	7 (17.5)	10 (25.6)	24 (20.2)	4 (10.0)
Vomiting, n (%)	4 (10.0)	8 (20.0)	12 (30.8)	24 (20.2)	4 (10.0)
Anaemia, n (%)	2 (5.0)	7 (17.5)	3 (7.7)	12 (10.1)	1 (2.5)
Neutropenia, n (%)	1 (2.5)	3 (7.5)	1 (2.6)	5 (4.2)	2 (5.0)
Leukopenia, n (%)	2 (5.0)	2 (5.0)	0	4 (3.4)	3 (7.5)
Thrombocytopenia, n (%)	2 (5.0)	1 (2.5)	1 (2.6)	4 (3.4)	1 (2.5)
White blood cell count decreased, n (%)	0	0	1 (2.6)	1 (0.8)	1 (2.5)
Immunosuppressant drug level increased, n (%)	2 (5.0)	2 (5.0)	6 (15.4)	10 (8.4)	0
Headache, n (%)	4 (10.0)	4 (10.0)	6 (15.4)	14 (11.8)	1 (2.5)
Renal failure, n (%)	3 (7.5)	1 (2.5)	5 (12.8)	9 (7.6)	0
Blood creatinine increased, n (%)	2 (5.0)	2 (5.0)	2 (5.1)	6 (5.0)	1 (2.5)

Data Source: Table 11.3.2.4.1

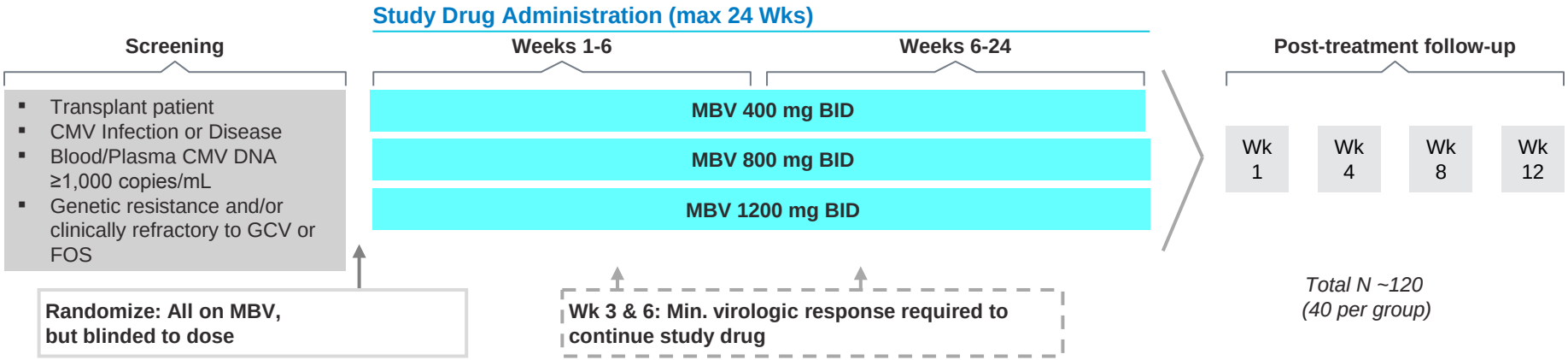
SHP620-203: Phase 2 safety results

Summary of Clinical Lab Evaluations –Treatment Emergent Neutropenia (ITT-S)

Parameter	MBV 400mg BID (N=40)	MBV 800mg BID (N=40)	MBV 1200mg BID (N=39)	MBV All Doses (N=119)	ValGCV 900mg BID (N=40)
Number of Subjects with Baseline and at least One Post-Baseline ANC, n (%)	40 (100.0)	40 (100.0)	38 (97.4)	118 (99.2)	39 (97.5)
Neutropenia - ANC Values <1000/mm^3 (1.0 x 10^9/L)					
Number of Subjects with Neutropenia at Baseline, n/N (%)	0	4/40 (10.0)	3/38 (7.9)	7/118 (5.9)	0
Number of Subjects with at least One Occurrence of Neutropenia through Week 6, n/N (%)	2/40 (5.0)	1/40 (2.5)	2/38 (5.3)	5/118 (4.2)	6/39 (15.4)
Number of Subjects with at least One Occurrence of Neutropenia through Week 12, n/N (%)	2/40 (5.0)	1/40 (2.5)	3/38 (7.9)	6/118 (5.1)	7/39 (17.9)
Neutropenia - ANC Values <500/mm^3 (0.5 x 10^9/L)					
Number of Subjects with Neutropenia at Baseline, n/N (%)	0	0	1/38 (2.6)	1/118 (0.8)	0
Number of Subjects with at least One Occurrence of Neutropenia through Week 6, n/N (%)	0	1/40 (2.5)	0	1/118 (0.8)	2/39 (5.1)
Number of Subjects with at least One Occurrence of Neutropenia through Week 12, n/N (%)	0	1/40 (2.5)	1/38 (2.6)	2/118 (1.7)	2/29 (5.1)

Source: Shire analysis

Phase 2 clinical trial (SHP620-202): Treatment of resistant/refractory CMV



Treatment Arms

- A phase 2, randomized study to assess the safety and anti-CMV activity of different doses of SHP620 for treatment of CMV infections that are **resistant or refractory** to treatment with Ganciclovir/Valganciclovir or Foscarnet in transplant recipients (EU- centers only)
- Patients were treated with MBV (400, 800, or 1200mg BID)
  N ~120 patients, 40 per group

Primary Endpoint

- Number of patients with confirmed undetectable plasma Cytomegalovirus (CMV) DNA within 6 weeks
- Number of patients with a Treatment Emergent Adverse Event (TEAE)

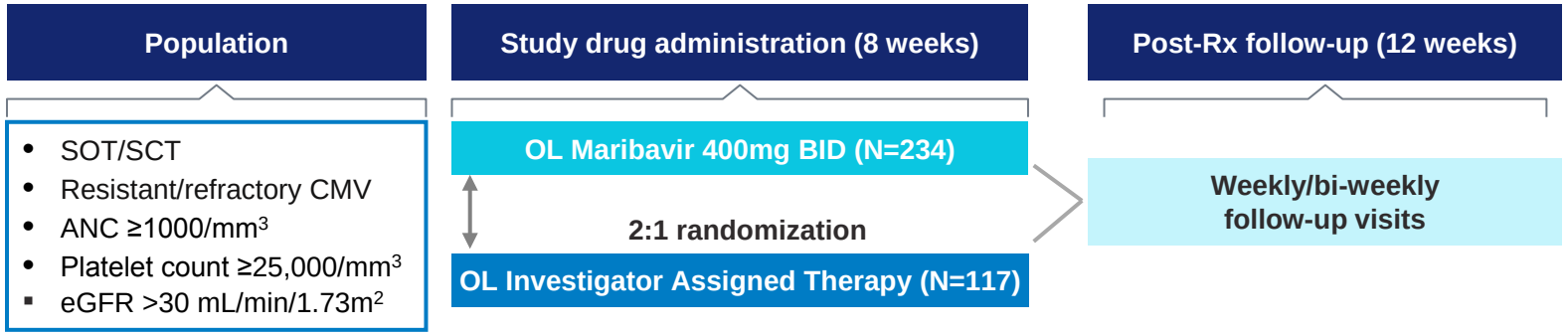
Efficacy results (SHP620-202)

	MBV 400mg BID (N=40)	MBV 800mg BID (N=40)	MBV 1200mg BID (N=40)	MBV All Doses (N=120)
Undetectable Plasma CMV DNA within 6 Weeks (ITT-S Population)				
Number of Subjects with Missing Data, n (%)	0	0	2 (5.0)	2 (1.7)
No, n (%)	12 (30.0)	15 (37.5)	11 (27.5)	38 (31.7)
Yes, n (%)	28 (70.0)	25 (62.5)	27 (67.5)	80 (66.7)
95% CI	(53.5, 83.4)	(45.8, 77.3)	(50.9, 81.4)	(57.5, 75.0)

Summary of Confirmed Undetectable Plasma CMV DNA (Central Laboratory) within 6 Weeks by Subgroup

	SHP620 400 mg BID (N=40)	SHP620 800 mg BID (N=40)	SHP620 1200 mg BID (N=40)	SHP620 All Doses (N=120)
Baseline plasma CMV DNA: n, (%)	0	0	2 (5.0)	2 (1.7)
Low (<10,000 copies/mL)	19/23 (82.6)	18/21 (85.7)	18/23 (78.3)	55/67 (82.1)
High (≥10,000 copies/mL)	8/16 (50.0)	7/19 (36.9)	8/16 (50.0)	23/51 (45.1)
CMV Genetic Mutations: n, (%)				
Yes	14/22 (63.6)	14/25 (56.0)	15/24 (62.5)	43/71 (60.6)
No	14/18 (77.8)	11/15 (73.3)	12/16 (75.0)	37/49 (75.5)

Planned Phase 3 – SHP620-303



Treatment Arms

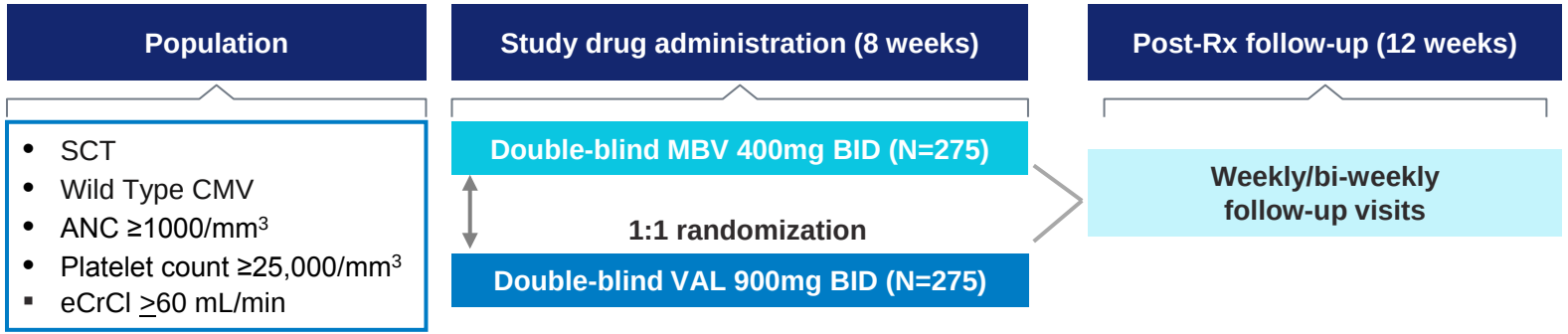
- Demonstrate efficacy of MBV versus standard Rx for R/R CMV
- R/R CMV, SOT/SCT Recipients, Open-label, Standard Therapy Comparator (investigator's choice) (N~350)

Primary Endpoint

- Confirmed clearance of plasma CMV DNA (CMV viremia clearance) at the end of 8 weeks of treatment
- Key secondary - CMV viremia clearance at the end of 8 weeks of treatment and resolution/improvement of tissue invasive CMV disease for subjects symptomatic at baseline or achievement of clearance of viremia and no symptoms of tissue invasive CMV disease for subjects asymptomatic at baseline at the end of 8 weeks of treatment, followed by maintenance of this treatment effect for an additional 8 weeks off treatment

SCT, stem cell transplant; SOT, solid organ transplant; ANC, Absolute Neutrophil Count, eGFR, Estimated Glomerular Filtration Rate; OL, Open Label

Planned Phase 3 – SHP620-302



Treatment Arms

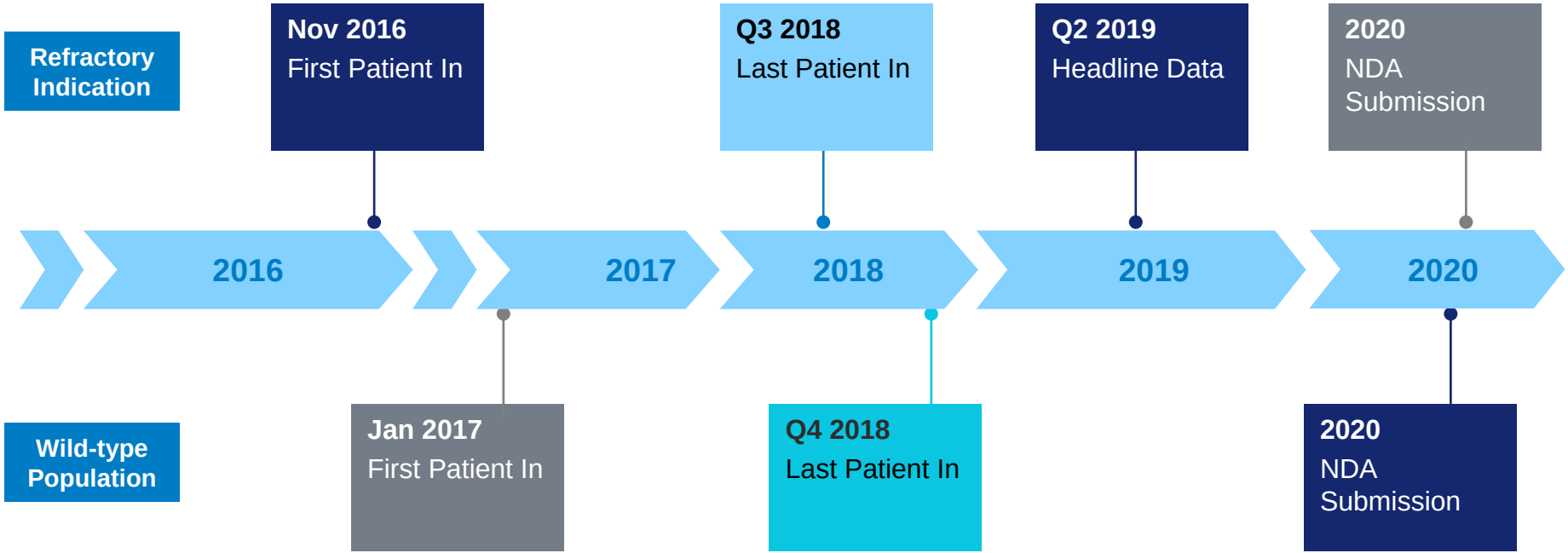
- Wild Type CMV, SCT recipients, double blinded. Patients randomized to MBV (400mg BID) or valganciclovir comparator (900mg BID) (N ~ 550)

Primary Endpoint

- Confirmed clearance of plasma CMV DNA (CMV viremia clearance) at the end of 8 weeks of treatment
- Key Secondary - Maintenance of CMV viremia clearance achieved after the end of 8 weeks of treatment through Study Week 16

SCT, stem cell transplant; ANC, Absolute Neutrophil Count; eCrCl, Estimated Creatinine Clearance; MBV, Maribavir; VAL, valganciclovir

Key dates and anticipated next steps for SHP620



Key takeaways for our promising transplant program

Significant market opportunity	> 100K solid organ and >50K hematopoietic stem cell transplants performed each year world-wide creates a large potential market opportunity
Significant unmet patient need	Transplant patients are at particular risk for CMV infection / disease Current antivirals are limited by toxicity profile and increasing drug-resistance
Strong differentiation and innovation	SHP620 has a novel mechanism of action and offers potential to be the first new anti-CMV agent in >10 years
Encouraging Phase 2 data	Encouraging Phase 2 data has bolstered our excitement about this program and has informed the design of our Phase 3 program
Near-term progress expected	Phase 3 trial in refractory population expected to initiate Q4 2016 and Phase 3 in wild-type population expected in Q1 2017

Today's pipeline program agenda

TOPIC	SPEAKER	TIME (ET)
GI Programs *SHP621 / SHP647*	Howard Mayer	12:30 - 12:50
Neonatology Program *SHP607*	Norman Barton	12:50 - 1:10
Transplant Program *SHP620*	Howard Mayer	1:10 - 1:30
Neuroscience Program *SHP465*	Howard Mayer	1:30 - 1:40
HAE Program *SHP643*	Wolfram Nothaft	1:40 - 2:00

SHP465 has the potential to provide long-acting therapeutic option to treat ADHD

- **Unmet need for long-acting therapeutic options to treat ADHD**
- SHP465 contains a **three bead formulation of mixed amphetamine salts providing ADHD symptom control** at 16 hours post dose
- Molecule has had a long development history: **SHP465 first received an FDA approvable letter in 2007** but was not pursued further until 2014
- Three studies required by FDA to support re-submission
  - Ph3 Safety and efficacy study in Peds/Adol (6-17 yr) with ADHD (SHP465-305)
  - Ph3 Safety and efficacy study in adults (18-55 yr) with ADHD (SHP465-306)
  - Open label Ph1 study PK study in Peds/Adol (6-17 yr) with ADHD (SHP465-111)
- **All of these studies successfully met their primary and key secondary endpoints**
- **Resubmission expected in Q4 2016** which would enable **launch in H2 2017***

* Subject to regulatory approval

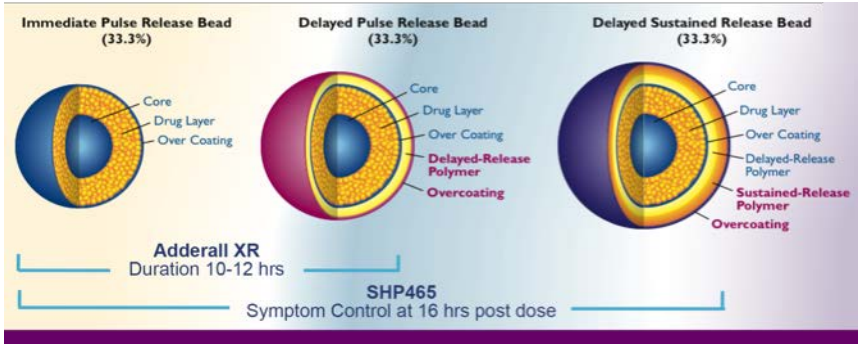
SHP465 is well-positioned to treat both the adult and pediatric populations with ADHD*

Adult ADHD is the fastest-growing segment of the overall ADHD patient population

- **Attention-deficit/hyperactivity disorder (ADHD) is a psychiatric disorder** characterized by developmentally inappropriate degrees of inattentiveness, impulsivity & hyperactivity
  - **ADHD is not just a childhood disease:** 2-6% of adults have ADHD
- **Many adult and some younger patients are taking 2 doses of various treatments** to achieve symptom control points to need for new options for long-acting therapeutics

SHP465 will provide meaningful improvement in symptom relief for the adult and pediatric ADHD populations

- **A three bead formulation** of mixed amphetamine salts is designed to provide ADHD symptom control at 16 hours post administration of a single dose



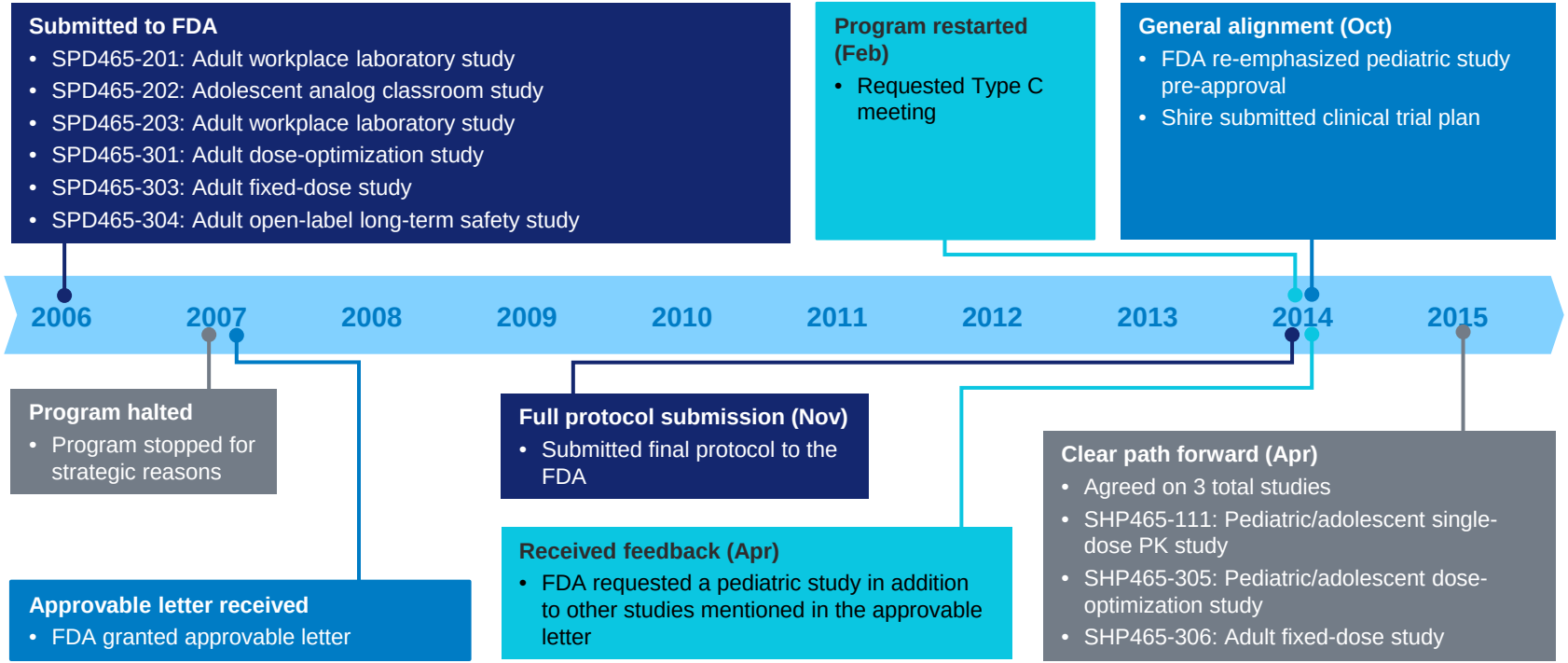
- Has been studied in a **broad patient population** and at **multiple doses**

Shire

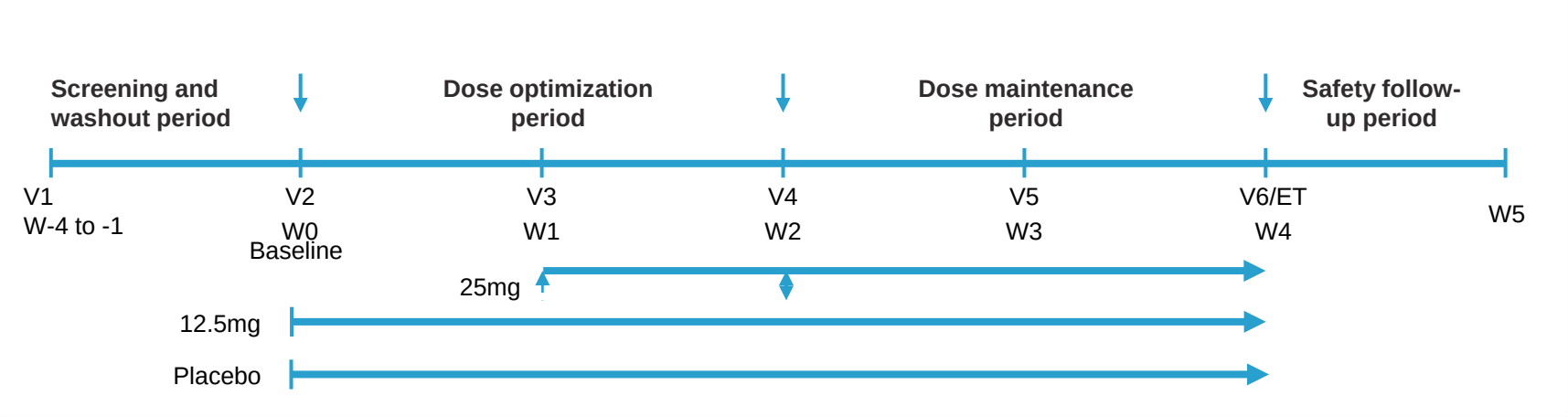
* Subject to regulatory approval

Granted an FDA approvable letter in '07, required additional studies for re-submission

SHP465
ADHD



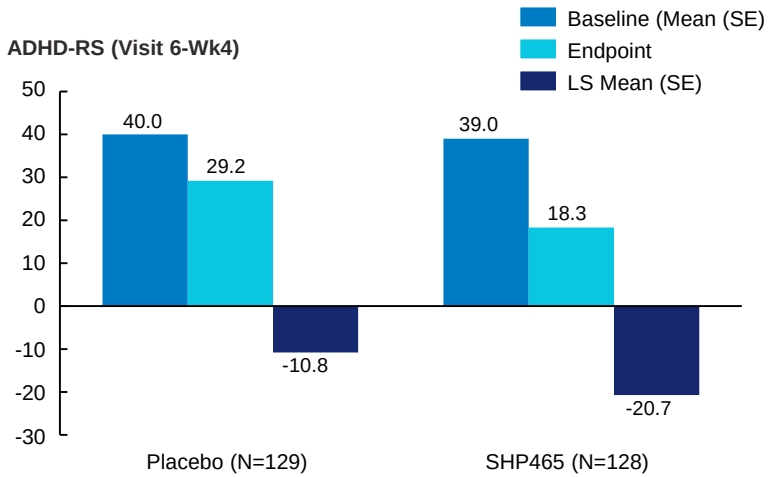
SHP465-305: Safety and efficacy study in children and adolescents aged 6 - 17 years



Description	A Phase 3, Randomized, Double-blind, Multi-center, Placebo-controlled, Dose-Optimization, Safety and Efficacy Study of SHP465 in Children and Adolescents Aged 6-17 Years with Attention-Deficit Hyperactivity Disorder (ADHD)
Primary Endpoint	Change from baseline in ADHD-RS-IV

SHP465-305 (Pediatric): Efficacy results

ADHD-RS (Primary Endpoint)



Diff in LS Mean (SE)	-9.9 (1.59)
95% CI for Diff	(-13.0, -6.8)
p-value	<0.001

CGI-I (Key Secondary Endpoint)

Visit 6 (Week 4) Change from baseline	**Placebo (N=129)**	**SHP465 (N=128)**
LS Mean (SE)	3.0 (0.11)	2.2 (0.11)
Diff in LS Mean (SE)		-0.8 (0.15)
95% CI for Diff		(-1.1, -0.5)
p-value		<0.001

Dichotomized CGI-I

	Placebo (N=129)	**SHP465 (N=128)**
Improved, n (%)	47 (36.4)	77 (60.2)
Not improved, n (%)	82 (63.6)	51 (39.8)
p-value	…	<0.001

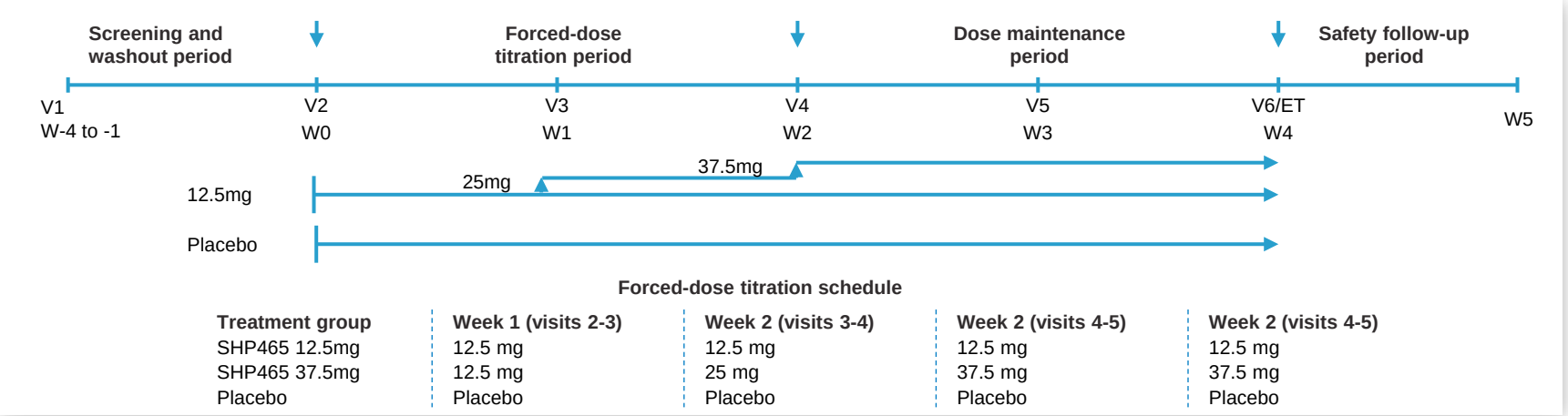
SHP465-305 (Pediatric): Safety results

Preferred Term	Placebo (N=131) n (%) m	SHP465 (N=132) n (%) m
Decreased appetite	9 (6.9) 9	40 (30.3) 44
Headache	14 (10.7) 18	16 (12.1) 18
Insomnia[1]	2 (1.5) 2	15 (11.4) 17
Irritability	2 (1.5) 2	9 (6.8) 9
Nausea	4 (3.1) 5	9 (6.8) 10
Weight decreased	1 (0.8) 1	7 (5.3) 7

Adverse events with high frequencies consistent with that observed with other stimulants

[1] Insomnia started early (1st wk) after Tx, mild/moderate in severity and recovered during Tx
SOURCE: Table 14.2.5

SHP465-306: Safety and efficacy study in adults aged 18-55 years



Forced-dose titration schedule

Treatment group	Week 1 (visits 2-3)	Week 2 (visits 3-4)	Week 2 (visits 4-5)	Week 2 (visits 4-5)
SHP465 12.5mg	12.5 mg	12.5 mg	12.5 mg	12.5 mg
SHP465 37.5mg	12.5 mg	25 mg	37.5 mg	37.5 mg
Placebo	Placebo	Placebo	Placebo	Placebo

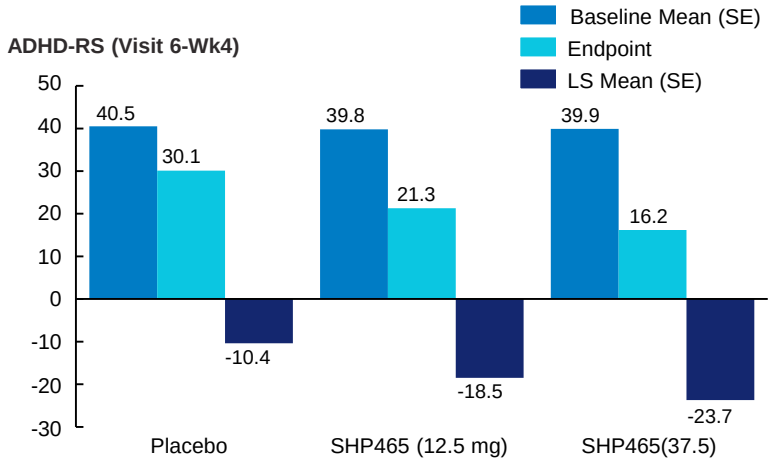
Description	A Phase 3, Randomized, Double-blind, Multicenter, Placebo-controlled, Forced-dose Titration, Safety and Efficacy Study of SHP465 in Adults Aged 18-55 Years with Attention-deficit/ Hyperactivity Disorder (ADHD)
Primary Endpoint	Change from baseline in ADHD-RS-IV

1. Least squares mean difference

ET=early termination;
V=visit; W=week

SHP465-306 (Adult): Efficacy results

ADHD-RS (Primary Endpoint)



	SHP465 12.5 mg	SHP465 37.5 mg
Diff in LS Mean (SE)	- 8.1 (1.87)	- 13.3 (1.88)
95% CI for Diff	(-11.7, -4.4)	(-17.0, -9.6)
p-value	<0.001	<0.001

CGI-I (Key Secondary Endpoint)

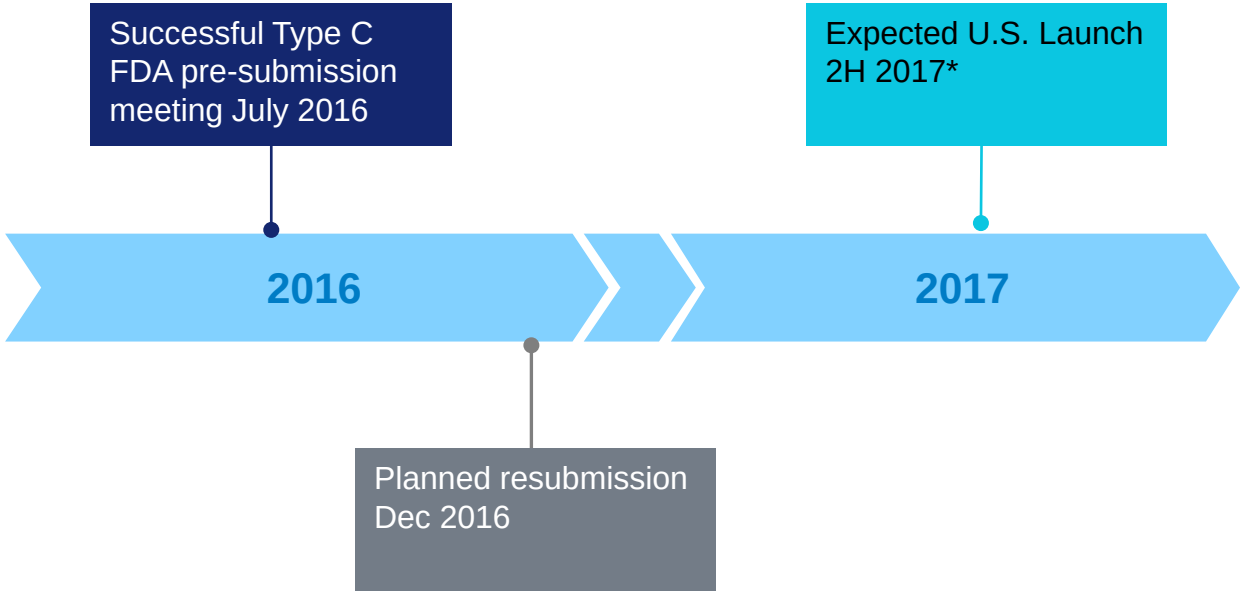
Visit 6 (Week 4) Change from baseline	Placebo (N=86)	SHP465 12.5 mg (N=89)	SHP465 37.5 mg (N=88)
LS Mean (SE)	3.1 (0.12)	2.4 (0.12)	1.9 (0.13)
Diff in LS Mean (SE)	…	-0.8 (0.17)	-1.2 (0.18)
95% CI for Diff	…	(-1.1, -0.4)	(-1.6, -0.9)
Effect Size	…	0.68	1.11
p-value	…	<0.001	<0.001

Dichotomized CGI-I

	Placebo (N=86)	SHP465 12.5 mg (N=89)	SHP465 37.5 mg (N=88)
Improved, n (%)	26 (30.2)	49 (55.1%)	66 (75.0)
Not Improved, n (%)	60 (69.8)	40 (44.9)	22 (25.0)
p-value	…	<0.001	<0.001

Key dates and anticipated next steps for SHP465

SHP465
ADHD



* Subject to regulatory approval

Key takeaways for our promising new ADHD program

Significant market opportunity	Shire has been the leader in ADHD for many years and SHP465 represents an opportunity to further extend this position and grow our multi-billion dollar franchise
Significant unmet patient need	Unmet needs exists for a growing patient population seeking a long-acting therapeutic option in ADHD
Strong differentiation and innovation	SHP465 contains a novel, three bead formulation providing additional innovation to the ADHD treatment landscape
Encouraging Phase 2 data	Phase 3 studies successfully met their primary and key secondary endpoints
Near-term progress expected	FDA resubmission expected in Q4 2016 which would enable launch in H2 2017*

Shire

* Subject to regulatory approval

Today's pipeline program agenda

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Neuroscience Program *SHP465*	Howard Mayer	1:30 - 1:40
HAE Program *SHP643*	Wolfram Nothaft	1:40 - 2:00

SHP643 has the potential to bring meaningful improvement in the treatment of hereditary angioedema (HAE)

- HAE is a rare, debilitating genetic inflammatory condition, which causes episodes of swelling in the face, extremities, and GI tract and can be life threatening
  - **~30-40% of patients afflicted by HAE** in the U.S. and EU **remain undiagnosed**
  - **Prophylactic treatment is likely underutilized** with roughly 40% of patients only treating their attacks acutely on an as-needed basis[1]
- Opportunity to improve on the efficacy, safety, and convenience of current treatment options
- Novel kallikrein inhibitor SHP643 (DX-2930) acquired as part of the Dyax deal in November 2015
- **Proof of concept** demonstrated for SHP643 in long-term prophylaxis of HAE without any apparent safety signals to date
  - SHP643 has received both an **orphan drug designation** and a **breakthrough designation**
- Shire is conducting a single pivotal trial, together with an open-label extension study; enrollment completed in Q3 2016

1. Shire market research

Overview of hereditary angioedema (HAE)

Disease Biology

- Characterized by recurrent attacks of angioedema
- Attack locations vary by episode; commonly involve extremities, GI tract or upper airway
- Due to genetic deficiency of C1-esterase inhibitor (C1-INH)
- Attacks result from uncontrolled plasma kallikrein activation

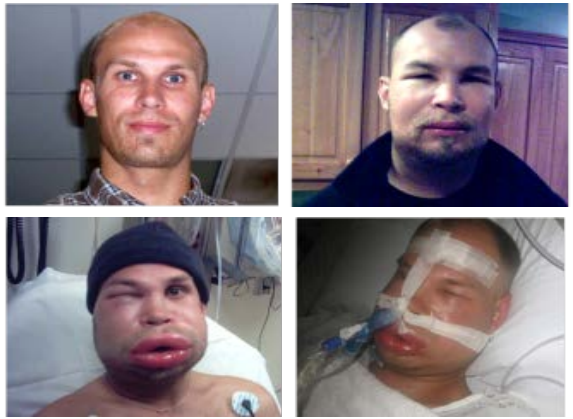
Epidemiology

- Prevalence estimated to be 1 per 50,000
- Affects ~ 42,000 people globally
- 60% of global HAE patients undiagnosed; 30-40% in U.S./EU
- 30% mortality in patients with laryngeal attacks
- Prophylactic treatment likely underutilized (up to 40% of U.S./ EU treated patients still on acute treatment only)

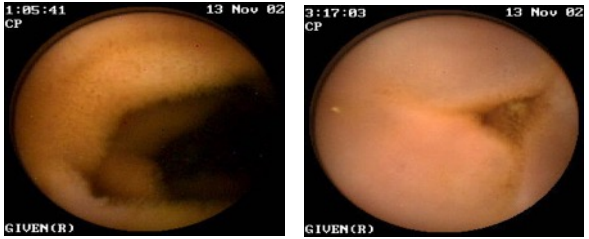
Current Treatments & Limitations

- Acute therapies – icatibant, ecallantide, C1-INH
- Prophylactic therapies – C1-INH, androgens, tranexamic acid
- Opportunities to improve efficacy, safety, and convenience of existing treatment options

Progression of a single HAE attack

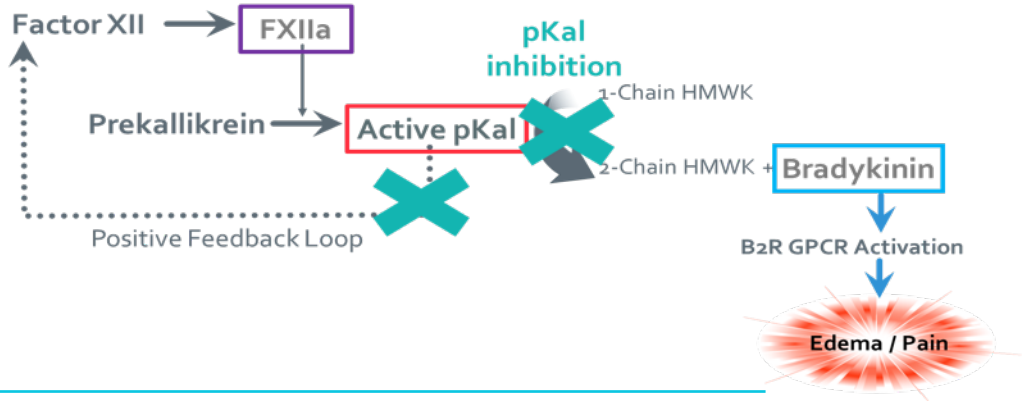


Submucosal edema in the gastrointestinal (GI) tract



Source: Zuraw BL. Clinical practice. Hereditary Angioedema.N Engl J Med. 2008;359(10):1027-1036)

Mechanism of action of SHP643 in HAE



Molecule & MOA

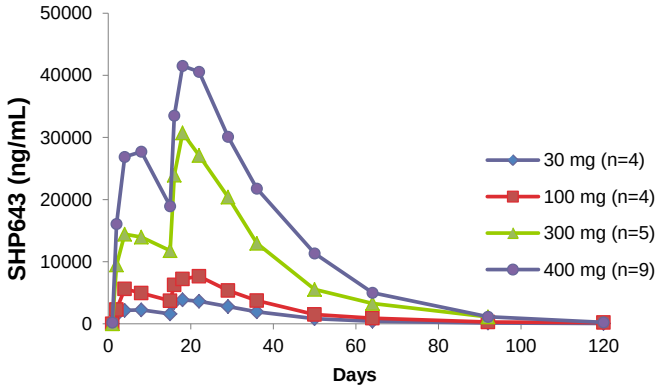
- Recombinant, fully human IgG1, kappa light chain monoclonal antibody
- Highly potent and specific inhibitor of plasma kallikrein (ki = 125 pM)

Potential Attributes / Disease Impact

- Potential for improved efficacy and convenience
- No relevant safety signals and dose-limiting toxicity observed, to date
- Convenient administration (subcutaneous, low injection volume)
- Long half-life enables infrequent dosing
- Long-acting injectable profile viewed favorably by physicians
- Received orphan drug designation in 2013 and breakthrough designation in 2015

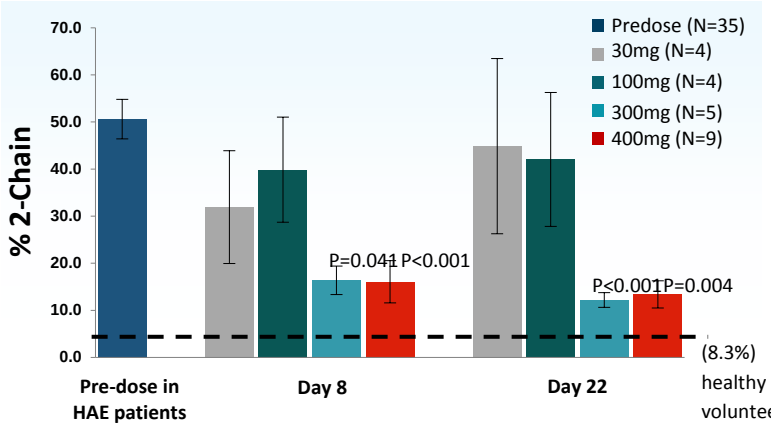
Phase 1b Study: PK/PD Results

Pharmacokinetics[1]



Dose proportional increase in SHP643 concentrations; mean elimination half-life ~ 2 weeks

Pharmacodynamics



300mg and 400mg doses of SHP643 reduced cleaved kininogen in HAE plasma to levels approaching that of healthy subjects

- Low incidence of anti-drug antibodies which were determined to be non-neutralizing

Note: 400 mg PK analysis excludes 2 patients. One patient who received only 1 dose of DX-2930 and one patient who did not have Type I or II HAE

Phase 1b study: Trial results

Efficacy and safety

	SHP643 300mg (N=4)	SHP643 400mg (N=11)	SHP643 300+ 400mg (N=15)
% reduction vs. placebo	100	88	91
P-value vs. Placebo*	<0.0001	0.005	0.0012

*Mixed Model repeated measurements with analysis of variance (baseline attack frequency as covariate) and assuming Poisson distribution

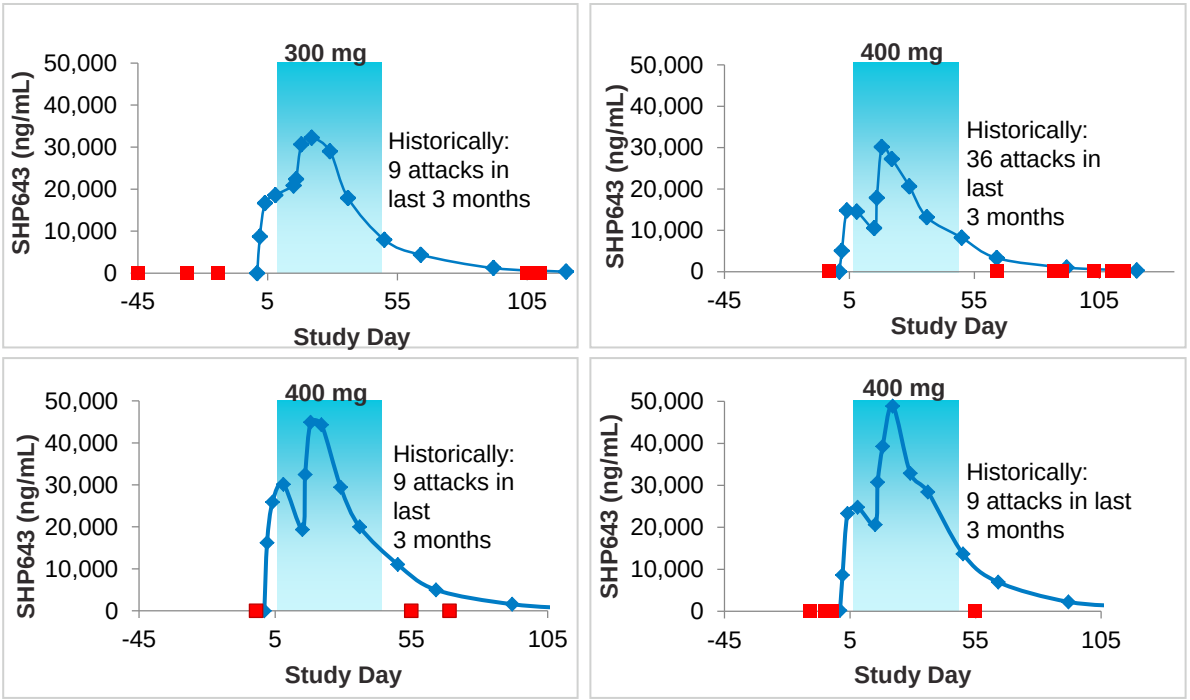
	SHP643 300mg (N=4)	SHP643 400mg (N=11)	SHP643 300 + 400mg (N=15)	Placebo (N=11)
Attack-free subjects (Day 8 to 50)	4/4 (100%) p=0.026	9/11 (82%) p=0.030	13/15 (87%) p=0.004	3/11 (27%)

Fisher exact best for each treatment arm vs. placebo

Note: These pre-specified analysis only evaluated HAE patients with baseline rate of ≥ 2 attacks in last 3 months. Day 8 to 50 attack rates were adjusted for baseline rates

There were no deaths, serious adverse events, discontinuations due to an adverse event, or relevant safety signals following SHP643 treatment

Relationship of efficacy and drug exposure in patients with multiple attacks

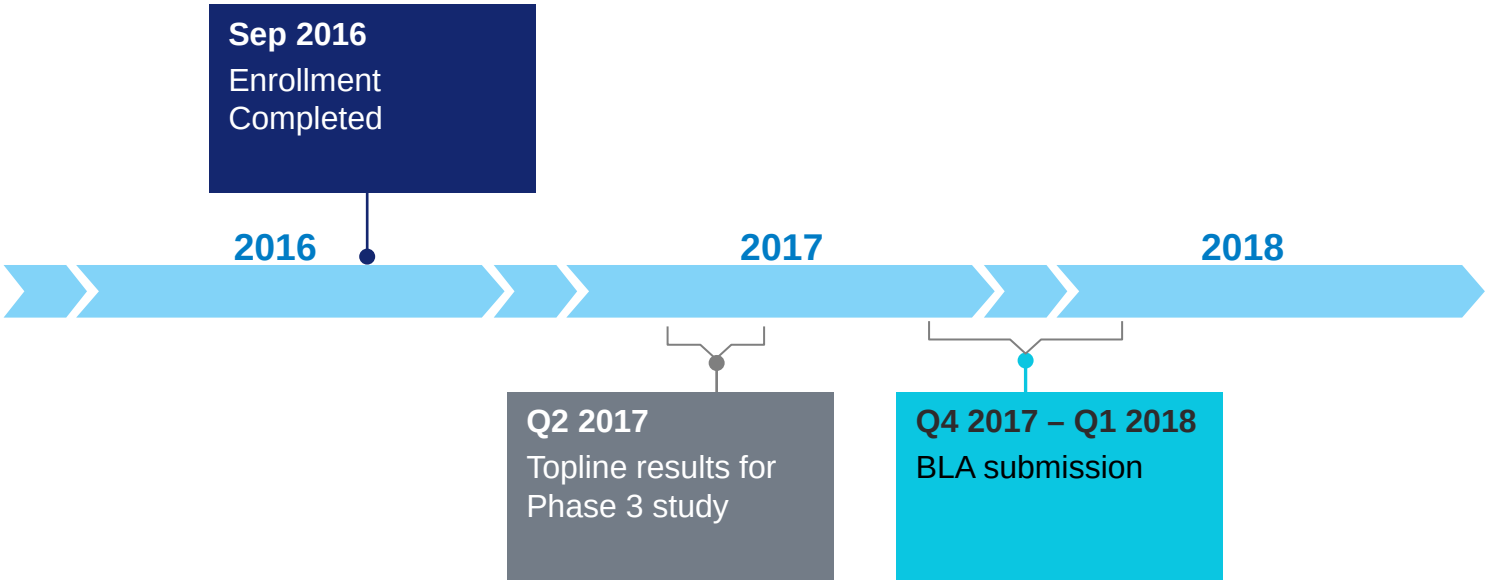


Phase 3 clinical plans (HELP Phase 3 study)

SHP643
HAE

Treatment Arms	• Randomized, double-blind, placebo-controlled, parallel arm, multi-center study • Goal: enroll 120 subjects • Minimum required baseline attack rate of > 1 investigator-confirmed HAE attack per 4 weeks as confirmed during the run-in period • SHP643 (3 different dosing arms) vs. placebo in 2:1 ratio
Primary Endpoint	• Efficacy of SHP643 in preventing HAE attacks (number of HAE attacks/week)

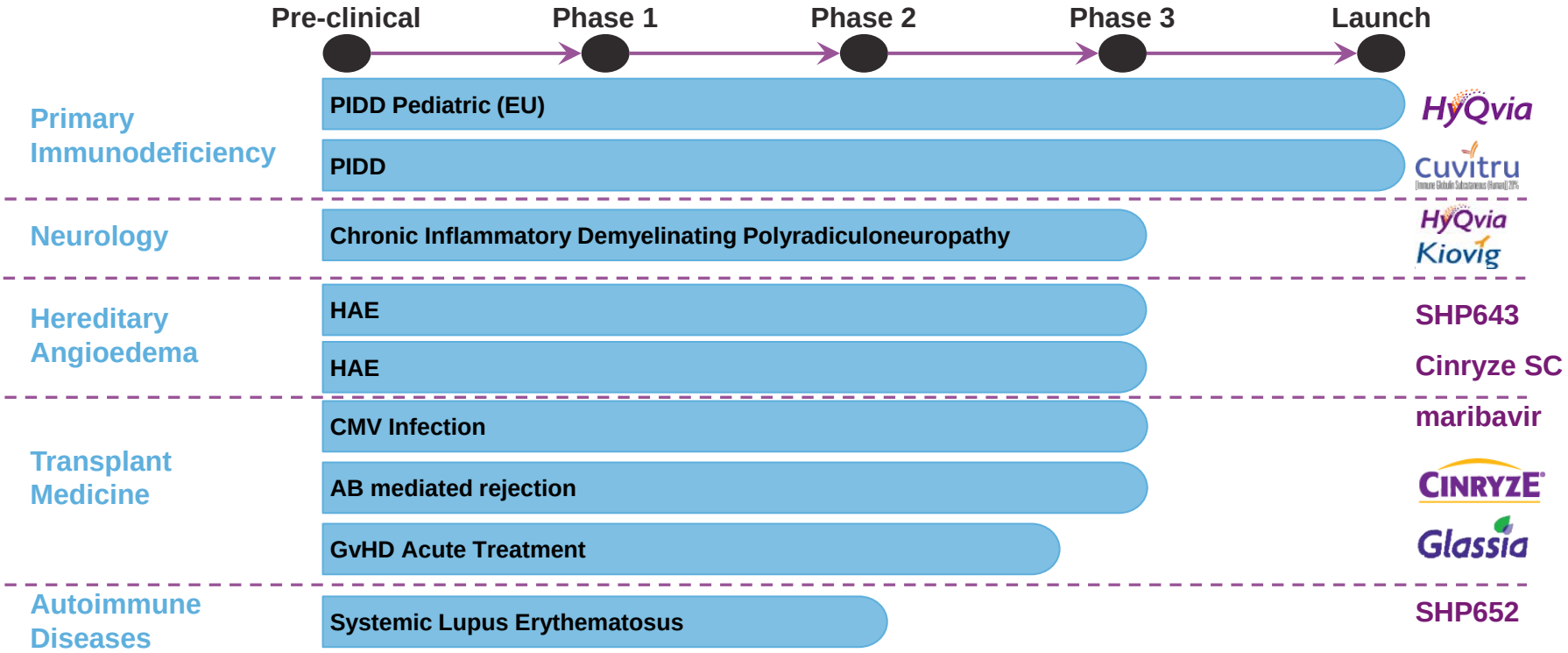
Key dates and anticipated next steps for SHP643



Key takeaways for our new HAE program

Significant market opportunity	SHP643 represents a significant opportunity to expand Shire's leadership position in the treatment of HAE
Unmet patient need	Opportunity to improve upon the efficacy, safety, and convenience of current treatment options - a large segment of the HAE population currently receiving on-demand treatment only, but could benefit from improved prophylaxis options
Strong differentiation and innovation	SHP643 represents a novel, monoclonal antibody approach to address unmet need in HAE
Encouraging Phase 2 data	Strong clinical proof of concept has been established
Near-term progress expected	Phase 3 study fully enrolled with top-line data expected in Q2 2017

Expanding leadership in Immunology through a novel pipeline



Shire

Closing Remarks

Flemming Ornskov, M.D., MPH, Chief Executive Officer

Shire is creating a unique leadership platform

The leading rare disease-focused biotech

Sharp focus leads to high impact

Focused patient communities

Rare diseases
Highly specialized conditions

- Precision innovation and technologies
- Culture of collaboration and execution
- Global resource and expertise

High patient impact
Breakthrough therapies for patients with significant unmet needs

High societal value
Improved patient outcomes and value for customers

Sustained growth
Sustainable rare disease market serving multiple patient communities with high unmet need

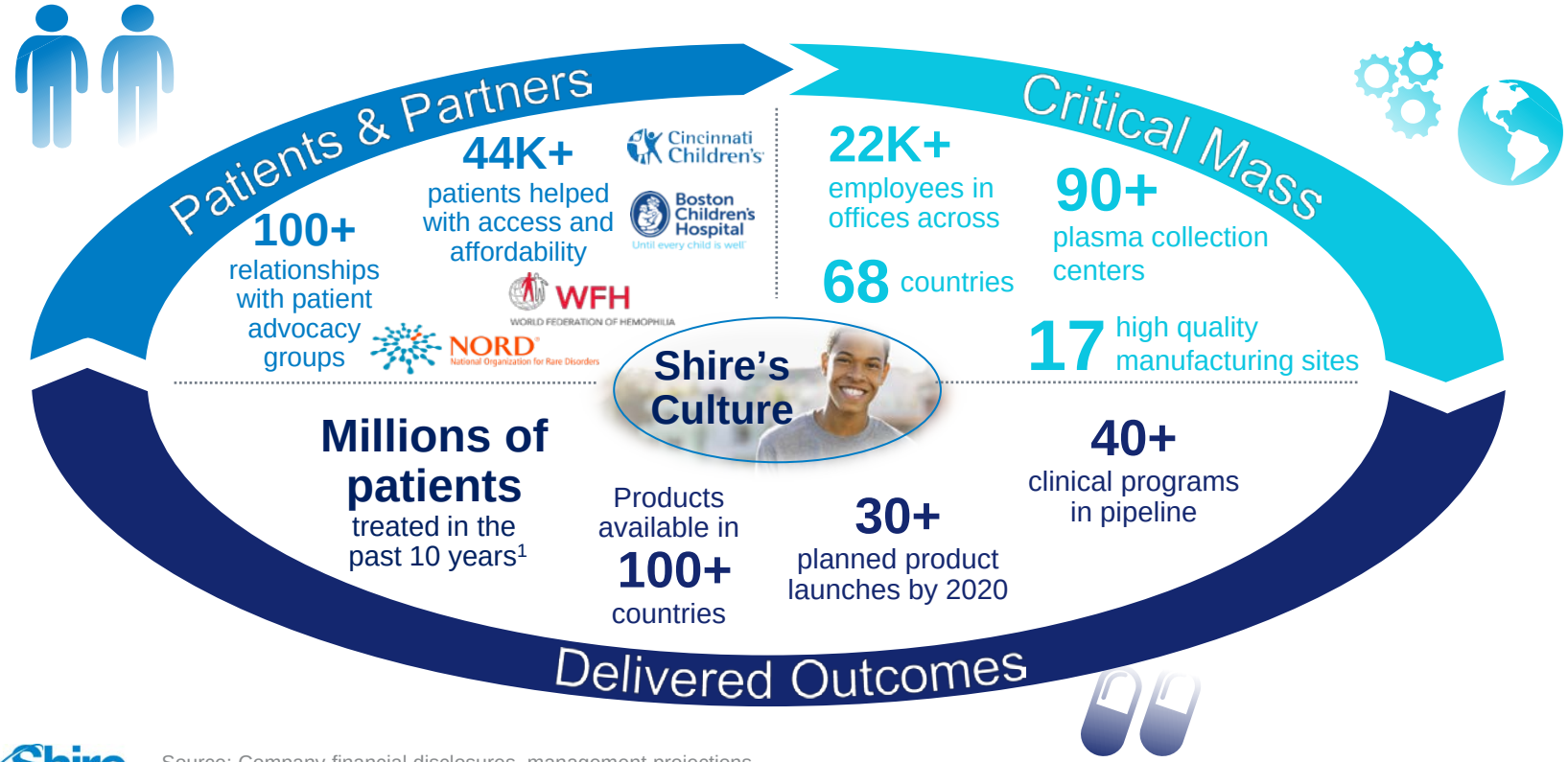
Shire

Consistent approach

Shire builds therapeutic strategies with first in class, best in class and differentiated products

* Subject to regulatory approval

…and leverages our partnerships with patients and healthcare providers to bring our medicines to a global audience



Source: Company financial disclosures, management projections

(1) IMS Health, management estimates, data since 2006

Six new programs highlighted today demonstrate the breadth and depth of innovation at Shire

SHP621*
(eosinophilic esophagitis)
Breakthrough therapy
Orphan drug (US)

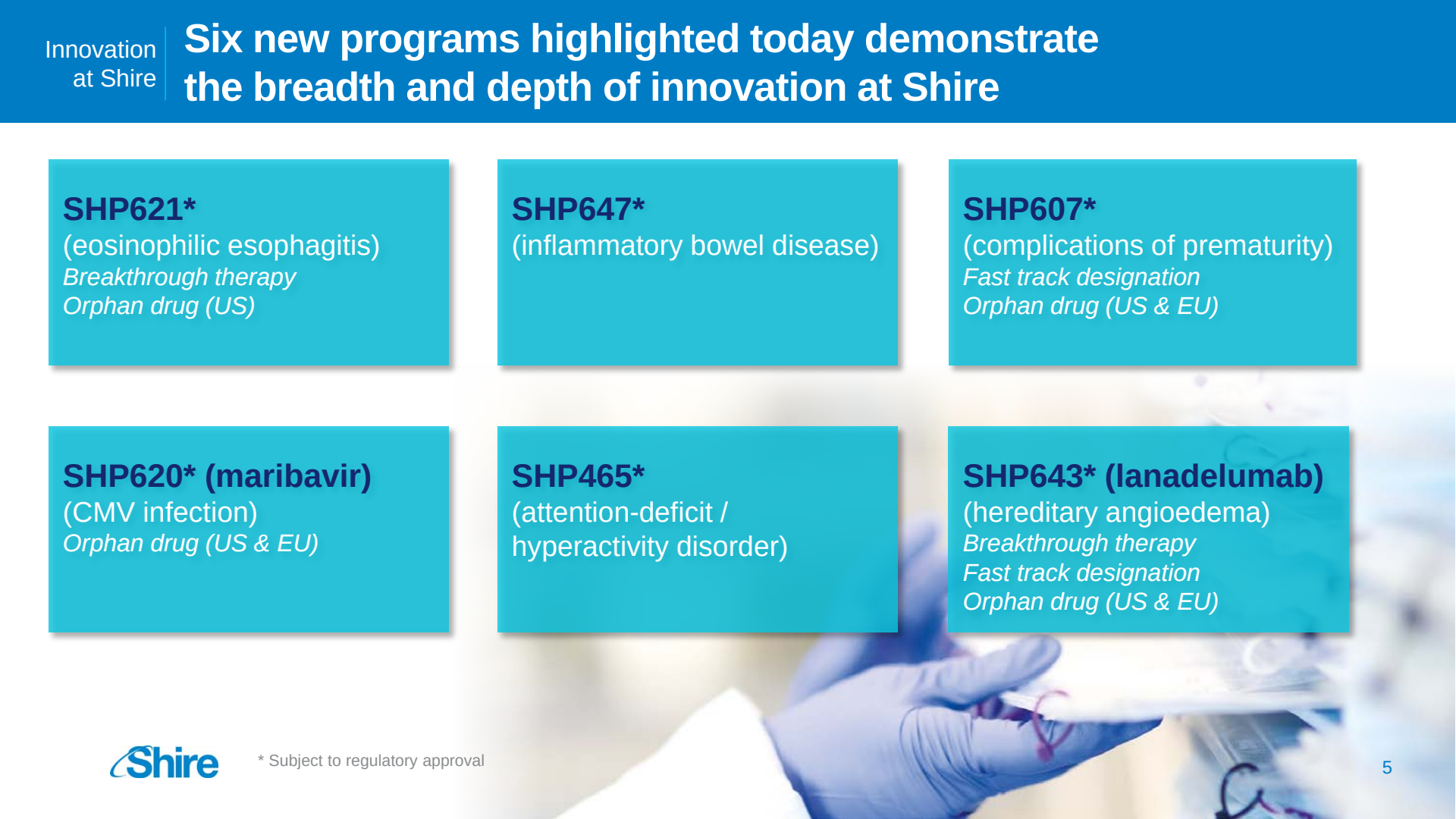
SHP647*
(inflammatory bowel disease)

SHP607*
(complications of prematurity)
Fast track designation
Orphan drug (US & EU)

SHP620* (maribavir)
(CMV infection)
Orphan drug (US & EU)

SHP465*
(attention-deficit / hyperactivity disorder)

SHP643* (lanadelumab)
(hereditary angioedema)
Breakthrough therapy
Fast track designation
Orphan drug (US & EU)

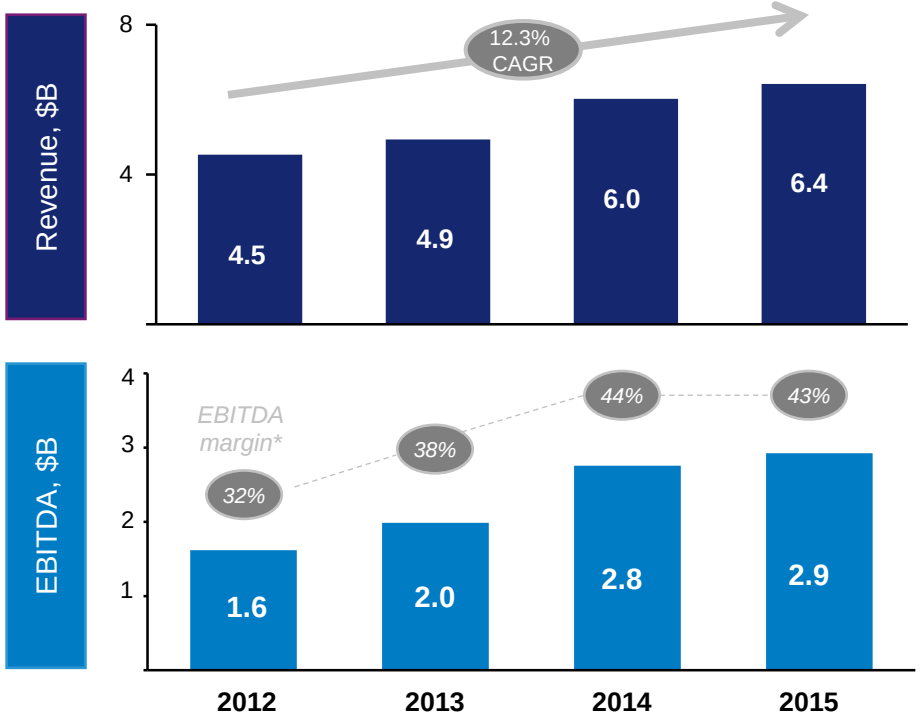


* Subject to regulatory approval

Consistent results

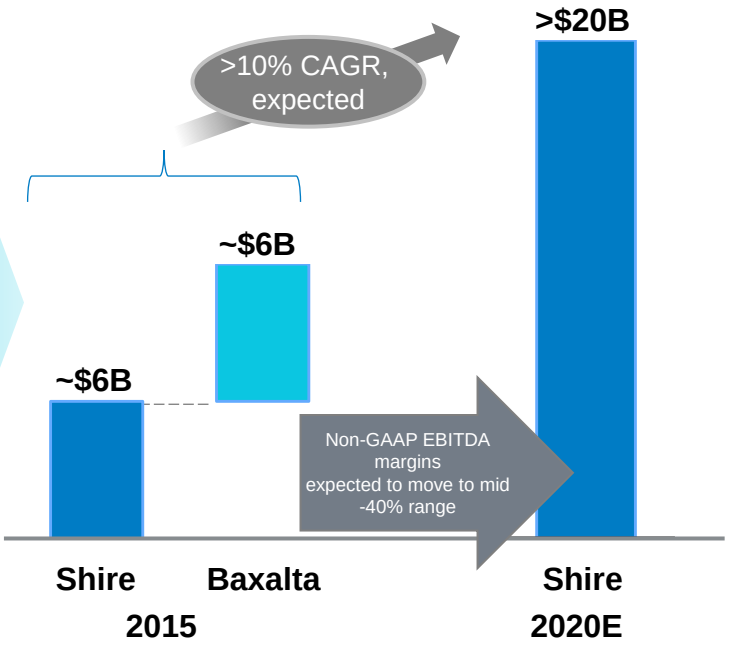
Delivered consistent historical revenue and profitability growth, with the right strategy for continuing this trend

Strong growth over the last several years



Source: Company financial disclosures, management projections
* Non GAAP EBITDA as a % of product sales, excluding royalties and other revenues

Addition of Baxalta expected to fuel continued revenue growth toward our stated "20 x 20" goal



Net debt / EBITDA anticipated to reach 2-3X by end of 2017