Q3 2017 Results

October 27, 2017

Flemming Ornskov, MD, MPH – CEO

Jeff Poulton – CFO

Matt Walker – Head of Technical Operations

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

Statements included herein that are not historical facts, including without limitation statements concerning future strategy, plans, objectives, expectations and intentions, 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, among other things, significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- 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 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, including expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits at the time anticipated or at all with respect to Shire’s acquisitions, including NPS Pharmaceuticals Inc., Dyax Corp. or Baxalta Incorporated 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 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 has increased its borrowing costs and may decrease its business flexibility; and

a further list and description of risks, uncertainties and other matters can be found in Shire’s most recent Annual Report on Form 10-K and in Shire’s subsequent Quarterly Reports on Form 10-Q, in each case including those risks outlined in “ITEM 1A: Risk Factors”, and in subsequent reports on Form 8-K and other Securities and Exchange Commission filings, all of which are available on Shire’s website.

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

Agenda

1. Quarterly business update		Flemming Ornskov, MD, MPH
2. Financial review		Jeff Poulton
3. Manufacturing network review		Matt Walker
4. Summary and Q & A		Flemming Ornskov, MD, MPH

Shire

Shire is the leading global biotech focused on rare diseases

Clear Biotech Profile

with 65% of 2017 sales expected to come from biologic drugs

1 Rare Disease Leader	Innovative, rare disease-focused biotech committed to differentiated and high patient-impact medicines
2 Strong Immunology Franchise	With the addition of Baxalta, Immunology is now the fastest growing franchise
3 Robust R&D Pipeline	~40 programs in clinical development including 17 currently in Phase 3 trials; expected to be key drivers for future growth

Shire

Strong business performance continued in Q3

GROWTH

- Achieved quarterly product sales of $3.5B
  - An increase of 7% from Q3 2016
- Delivered Non GAAP diluted earnings per ADS of $3.81[1][3]
  - An increase of 20% from Q3 2016
- Continued advancement of our innovative late-stage clinical portfolio (e.g., MYDAYIS, SHP643, SHP555)

EFFICIENCY

- Baxalta integration continues to track ahead of plan
- Non GAAP EBITDA margin of 44%[2][3]
- Manufacturing network review has identified >$100MM in expected additional annual savings beginning in 2019 and expected to increase to $300MM annually by 2023

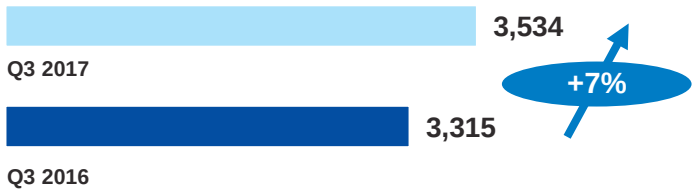
CAPITAL ALLOCATION

- $920MM reduction in Non GAAP net debt[3] in Q3 2017
- On track to meet our 2-3x Non GAAP net debt / Non GAAP EBITDA target by end of 2017[3]
- Strategic review of Neuroscience franchise on track to read-out by year-end

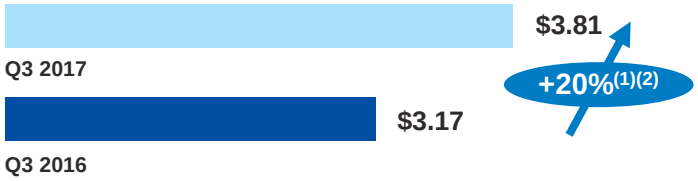
(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Diluted EPS-ADS (Q3 2017: $1.81).
(2) This is a Non GAAP financial measure as a percentage of total revenue. The most directly comparable measure under US GAAP is Net Income Margin (Q3 2017: 15%).
(3) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Robust product sales and Non GAAP earnings growth

PRODUCT SALES ($MM)



NON GAAP DILUTED EARNINGS PER ADS[1][2]

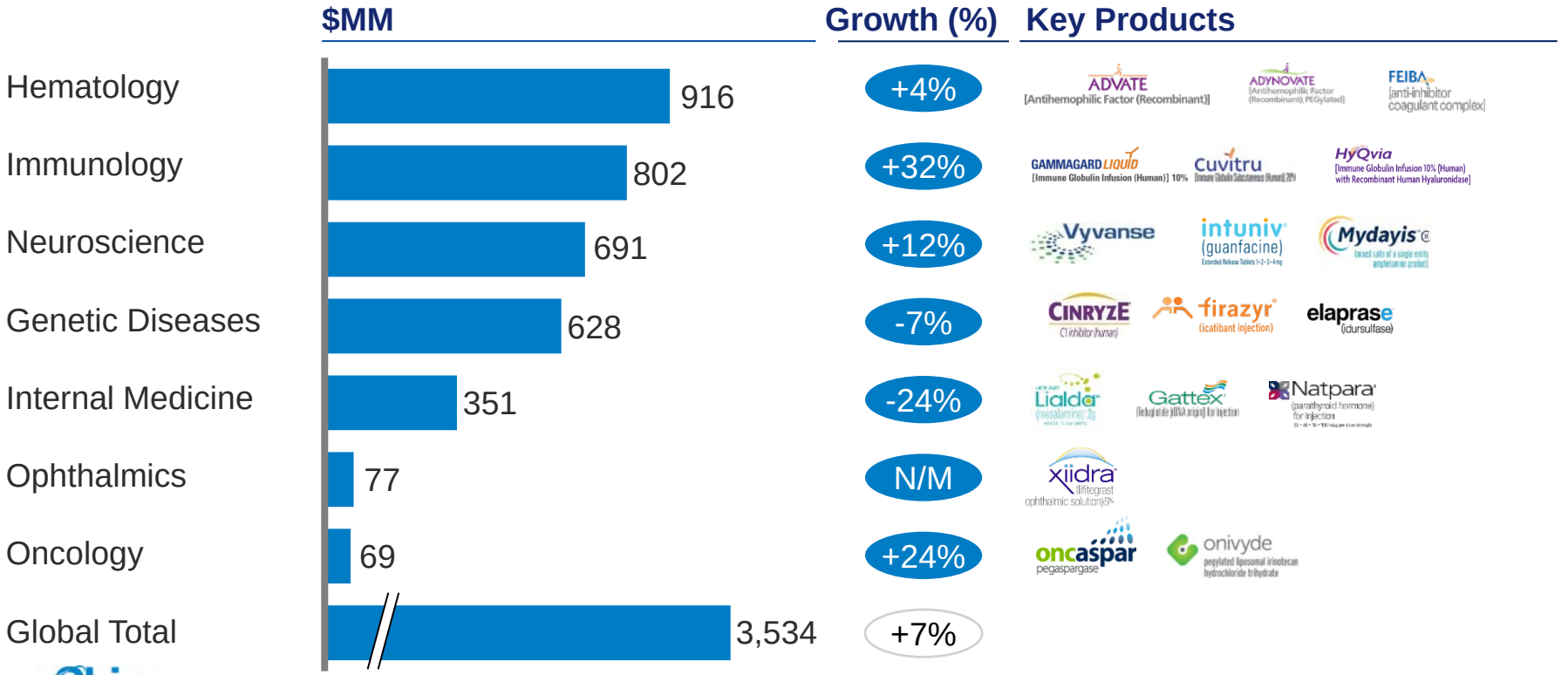


FINANCIAL HIGHLIGHTS

- Product sales of $3.5B and 7% growth
- Total revenues of $3.7B and 7% growth
- Non GAAP diluted earnings per ADS growth of 20%[2]
- Net cash provided by operating activities grew 101% to $1,055MM

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Diluted EPS-ADS (Q3 2017: $1.81, Q3 2016: -$1.29).
(2) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

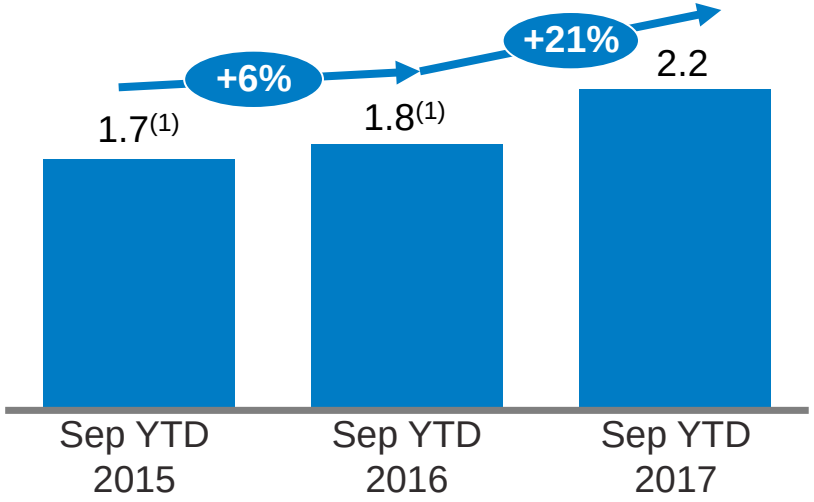
Q3 2017 sales growth generated across our broad portfolio



Shire

Immunology continues to be a core growth driver – a key franchise acquired with Baxalta

Global Immunology Revenues, $B



Key Shire Brands

GAMMAGARD LIQUID Cuvitru HyQvia Flexbumin

Key Growth Drivers

- **Market penetration**
  - Growing diagnosis rate
  - Rising standard of care
- **Geographic expansion**
- **Play-to-win strategy**
  - Improved contracting strategy – hospital contracting focused on broader portfolio
  - Tenders – reentering countries with full portfolio
- **Demand for subcutaneous delivery**
  - HYQVIA and CUVITRU, combined, grew ~75% in Q3 2017 YoY
- **Strong long-term fundamentals**
  - Generally not subject to typical pharmaceutical sales erosion following patent expiry
  - Strong plasma collection and fractionation capabilities

Shire

(1) Recast pro forma revenues following Shire's acquisition of Baxalta on June 3, 2016.

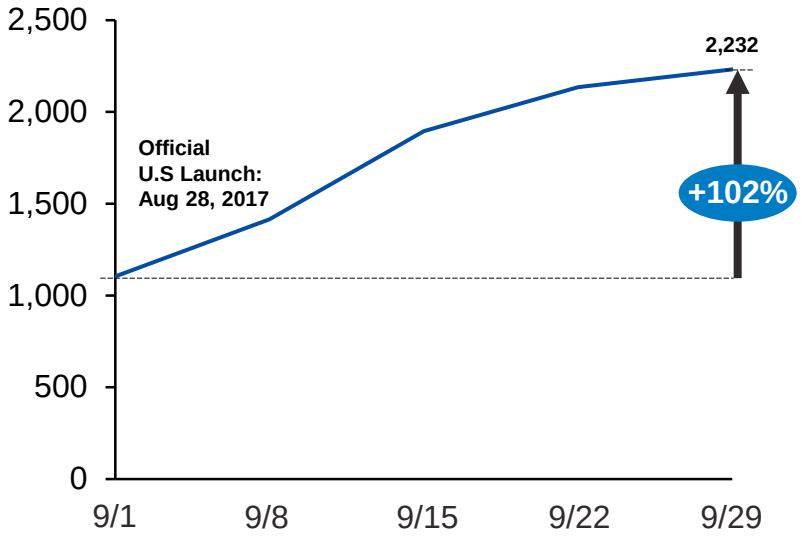
MYDAYIS is off to a strong start

>3,000
Unique prescribers(1)

>11,000
Unique patients(1)

>19,000
Total prescriptions(1)

Launch curve(1) (Total RXs)



Positive community feedback(2)

~80% of Early Experience Program Prescribers would recommend / prescribe MYDAYIS to appropriate patients

~70% of Early Experience Program patients indicated high satisfaction scores related to product efficacy

(1) IMS PlanTrak* and Connective Rx redemption data from approval to October 17, 2017.
(2) Shire market research Sept 2017. Early Experience Program included ~5,000 patients and ~3,000 physicians with access to MYDAYIS prior to its official launch on August 28, 2017.
* IMS data: IMS information is an estimate derived from the use of information under license from the following IMS Health Information service: IMS PlanTrak. IMS expressly reserves all rights including rights of copying, distribution and republication.

CINRYZE manufacturing interruption and resolution

Context:

- Sole 3rd party manufacturer with historic difficulties producing enough product to meet patient demand
- Further manufacturing interruption led to product shortages, starting in August 2017

Resolution:

- 3rd party manufacturer has addressed the issue and resumed production in September 2017
- Due to timing of FDA release of previously produced CINRYZE, planned Q3 US supply of~$100MM was shipped in October instead of September
- FDA has accepted an application to enable a second source of production at Shire's in-house manufacturing facilities
  - Subject to FDA approval, we expect production to begin in early Q1 2018
- CINRYZE supply could be tight until a second source has been approved and we can build inventory

Pipeline activities continue to advance

REGULATORY ACTIONS AND COMMERCIAL LAUNCHES

- MYDAYIS (ADHD) launch in U.S.
- Lifitegrast (Dry Eye Disease) submission for approval in Europe (Decentralized Procedure validated by UK as Reference Member State)
- New Formulation of ONCASPAR (acute lymphoblastic leukemia) positive CHMP opinion in Europe
- SHP654 (Hemophilia A) awarded Orphan Drug Designation by FDA

Remain on target to file for FDA approval for both SHP555 (chronic constipation) in late 2017 and SHP643 (HAE) in late 2017 – early 2018

CLINICAL UPDATES

- SHP616 (HAE – subcutaneous) positive Phase 3 results
- INTUNIV (ADHD) positive Phase 3 results in adult patients with ADHD in Japan
- SHP607 (prevention of chronic lung disease in extremely premature infants) granted Fast Track Designation by FDA

Shire

Agenda

1. Quarterly business update		Flemming Ornskov, MD, MPH
2. Financial review		Jeff Poulton
3. Manufacturing network review		Matt Walker
4. Summary and Q & A		Flemming Ornskov, MD, MPH

Q3 2017 reported key financials summary

	Q3 2017 $MM	Q3 2016 $MM	Reported Growth	CER Growth[1][7]
Product sales	3,534	3,315	+7%	+6%
Royalties and other revenues	164	137	+20%	+19%
Total revenue	3,698	3,452	+7%	+6%
Non GAAP combined R&D and SG&A[2][7]	1,212	1,239	-2%	-3%
Non GAAP EBITDA[3][7]	1,618	1,347	+20%	+19%
Non GAAP EBITDA margin[4][7]	44%	39%	5 ppc	n/a
Non GAAP effective tax rate[5][7]	15%	13%	n/a	n/a
Non GAAP diluted EPS – ADS[6][7]	3.81	3.17	+20%	+19%
Net cash provided by operating activities	1,055	526	+101%	n/a

(1) Growth rates are at Constant Exchange Rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2017 performance (restated using 2016 exchange rates for the relevant period) to actual 2016 reported performance.
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q3 2017: $1,263m, Q3 2016: $1,387m).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income (Q3 2017: $551m, Q3 2016: -$387m).
(4) This is a Non GAAP financial measure as a percentage of total revenue. The most directly comparable measure under US GAAP is Net Income Margin (Q3 2017: 15%, Q3 2016: -11%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Effective Tax Rate (Q3 2017: 2%, Q3 2016: -38%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Diluted EPS-ADS (Q3 2017: $1.81, Q3 2016: -$1.29).
(7) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Q3 product sales performance

	Q3 2017 Sales			Growth vs. Q3 2016	
$MM	U.S.	International	Total	Reported	CER[1][2]
Hemophilia	358	368	725	+3%	+3%
Inhibitor Therapies	71	120	191	+5%	+4%
Hematology Total	**428**	**488**	**916**	**+4%**	**+3%**
Immunoglobulin Therapies	487	119	605	+28%	+28%
Bio Therapeutics	86	110	197	+47%	+45%
Immunology Total	**573**	**229**	**802**	**+32%**	**+32%**
VYVANSE	477	62	538	+5%	+5%
ADDERALL XR	99	7	106	+32%	+32%
MYDAYIS	10	-	10	N/A	N/A
Other Neuroscience	7	30	37	+56%	+53%
Neuroscience Total	**593**	**98**	**691**	**+12%**	**+12%**
FIRAZYR	174	22	196	+34%	+33%
ELAPRASE	41	112	153	+4%	+1%
REPLAGAL	-	117	117	-1%	-4%
VPRIV	38	52	90	+2%	+1%
CINRYZE	46	11	57	-66%	-66%
KALBITOR	16	-	16	+44%	+44%
Genetic Disease Total	**315**	**313**	**628**	**-7%**	**-8%**
LIALDA/MEZAVANT	61	25	87	-58%	-59%
GATTEX/REVESTIVE	73	12	85	+46%	+45%
PENTASA	72	-	72	-16%	-16%
NATPARA	39	-	39	+68%	+68%
Other Internal Medicine	12	56	68	-22%	-24%
Internal Medicine Total	**257**	**94**	**351**	**-24%**	**-25%**
Ophthalmics	77	-	77	N/M	N/M
Oncology	47	21	69	+24%	+22%
Total Product Sales	**2,291**	**1,243**	**3,534**	**+7%**	**+6%**

(1) Growth rates are at Constant exchange rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2017 performance (restated using 2016 exchange rates for the relevant period) to actual 2016 reported performance.

(2) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

YTD 2017 reported performance metrics

Year on Year Growth:	YTD 2017[1]
Product sales	45%
Non GAAP R&D[2][9]	29%
Non GAAP SG&A[3][9]	30%
Combined Non GAAP R&D and SG&A[4][9]	30%

Ratios: As % of Total Revenue	YTD 2017[1]	YTD 2016[1]
Non GAAP gross margin[5][9]	77%	79%
Non GAAP R&D[6][9]	10%	12%
Non GAAP SG&A[7][9]	23%	26%
Non GAAP EBITDA[8][9]	44%	42%

(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (YTD 2017: +29%).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (YTD 2017: +31%).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (YTD 2017: +30%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Gross Margin (YTD 2017: 69%, YTD 2016: 64%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (YTD 2017: 12%, YTD 2016: 13%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (YTD 2017: 24%, YTD 2016: 27%).
(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income Margin (YTD 2017: 11%, YTD 2016: -2%).
(9) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

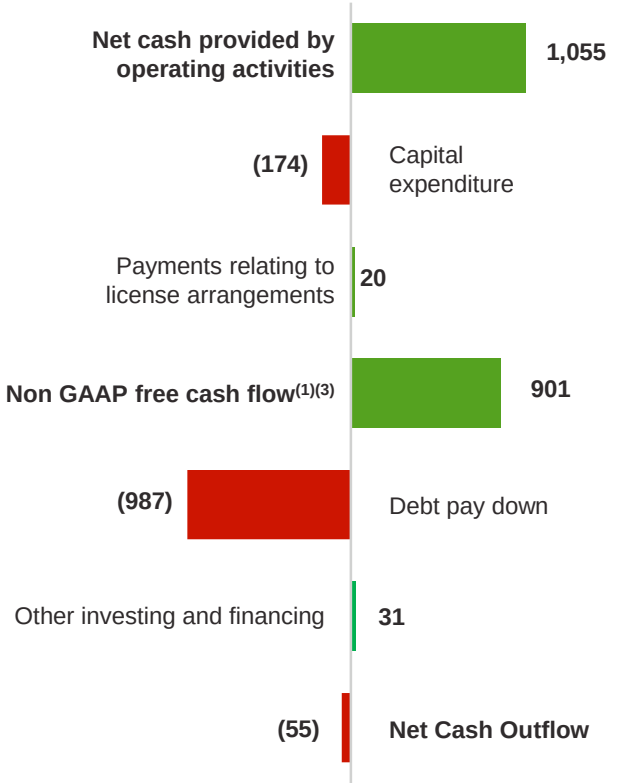
Strong Q3 operating cash flow drives $920M reduction in Non GAAP net debt

2017 Non GAAP Net Debt Progression

$MM	Jun 30, 2017	Sep 30, 2017	Q3 Change	Dec 31, 2016	YTD Change
Cash and cash equivalents	**264**	**209**	**(55)**	**529**	**(320)**
Long term borrowings	18,011	17,614		19,553	
Short term borrowings	3,198	2,622		3,062	
Capital leases	351	349		354	
Total borrowings, capital leases, and other debt	**21,560**	**20,585**	**(975)**	**22,969**	**(2,384)**
Non GAAP net debt[3]	**21,296**	**20,376**	**(920)**	**22,439**	**(2,063)**

Leverage at September 30, 2017
Non GAAP net debt / Non GAAP EBITDA ratio[2][3] 3.2x

Q3 2017 Cash Flow $MM



(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net cash provided by operating activities (Q3 2017: $1,055m).
(2) Non GAAP EBITDA on a trailing 12 month basis to September 30, 2017.
(3) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

2017 guidance reiterated

	Full year 2017 dynamics	
	Current guidance as updated at Q2	Impact of FX rates on guidance
Product Sales	$14.3 - $14.6 billion	~0%
Royalties & other revenues	$600 - $700 million	
Non GAAP gross margin(1)	74.5% - 76.5%	
Non GAAP combined R&D and SG&A(1)	$4.9 - $5.1 billion	
Non GAAP depreciation(1)	$450 - $500 million	
Non GAAP net interest/other(1)	$500 - $600 million	
Non GAAP effective tax rate(1)	16% - 17%	
Non GAAP diluted earnings per ADS(1)	$14.80 - $15.20	~0%
Capital Expenditure	$800 - $900 million	

The FX impact on guidance is based on September 18th, 2017 actual exchange rates (€:$1.19524, £:$1.34885, CHF:$1.04004, CAD:$0.81265, ¥:$0.00897). The estimated impact of a 10% appreciation in the US Dollar against the respective currency, over the remainder of the year, on our 2017 Guidance is as follows:

	Revenue	Earnings
EUR	-1.5%	-0.6%
GBP	-0.2%	-0.4%
CHF	-0.1%	0.1%
CAD	-0.2%	-0.5%
JPY	-0.2%	-0.4%
Other	-0.5%	-0.2%

(1) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Agenda

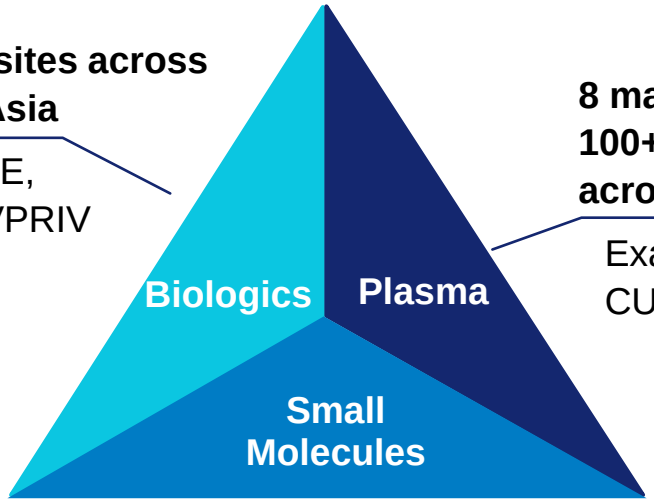
1. Quarterly business update		Flemming Ornskov, MD, MPH
2. Financial review		Jeff Poulton
3. Manufacturing network review		Matt Walker
4. Summary and Q & A		Flemming Ornskov, MD, MPH

Shire

15 manufacturing sites across the globe

7 manufacturing sites across US, Europe and Asia

Examples: ADVATE, ELAPRASE and VPRIV



8 manufacturing sites and 100+ BioLife Collection Centers across US and Europe

Examples: GAMMAGARD, CUVITRU and ALBUMIN

Outsourced manufacturing

Examples: VYVANSE and MYDAYIS

Shire

15 **Manufacturing facilities** **(17 post integration of Baxalta)**

15K **Employees**

40+ **External strategic partners**

Manufacturing initiatives to drive growth and efficiencies

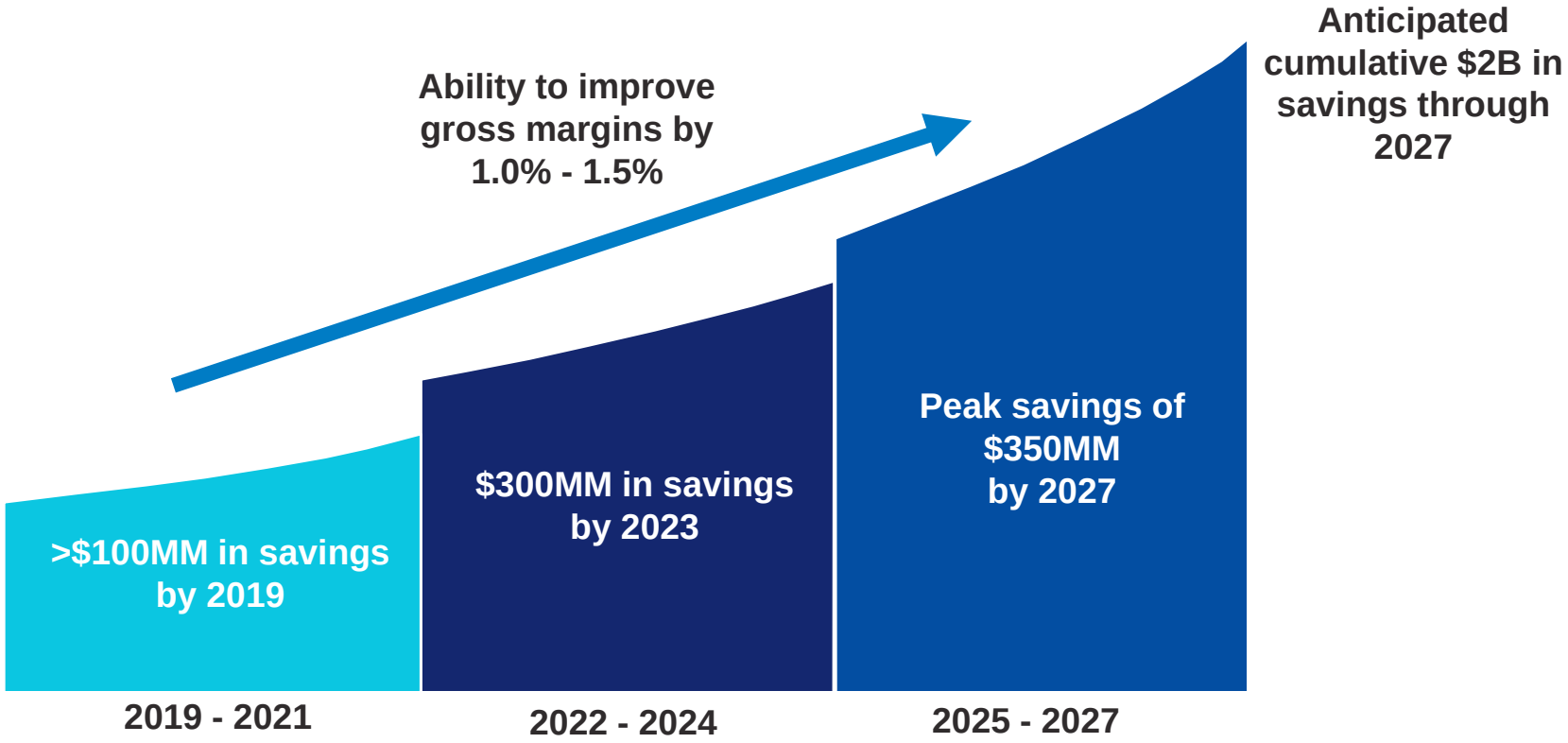
Manufacturing Network Review Objectives

- Effectively and efficiently meet future demand while improving quality and compliance
- Increase utilization and improve working capital

Initiatives

1. **Modernize**: 3 additional sites to be divested based on utilization (biologics, not plasma); new site builds continue; investment in remaining sites
2. **Position for growth**: Continue with plasma production expansion at Covington. Site adds ~30% capacity starting in 2018 and new plasma collection sites opening to meet demand
3. **Enhance capabilities**: Focus sites on clear roles to further enhance core capabilities and improve efficiencies (e.g., gene therapy, devices, launch capabilities)

Expected annual savings to COGS to exceed $100MM by 2019 and reach $300MM by 2023(1)



(1) Shire internal financial analysis, October 2017.

Agenda

1. Quarterly business update		Flemming Ornskov, MD, MPH
2. Financial review		Jeff Poulton
3. Manufacturing network review		Matt Walker
4. Summary and Q & A		Flemming Ornskov, MD, MPH

Shire

On track for continued success in 2017 and beyond

Q3 SUMMARY

- Delivered solid sales and Non GAAP EPS growth, despite CINRYZE and LIALDA headwinds, driven by rapidly growing Immunology business
- Reiterated full year 2017 financial guidance
- Executed strong launch of MYDAYIS
- Advanced late stage clinical pipeline
- Identified additional annual manufacturing network efficiencies
- Continued to pay down debt

KEY PRIORITIES FOR Q4

- Finalize FDA filings of SHP643 and SHP555
- Stabilize supply of CINRYZE
- Drive continued product sales growth across the portfolio
- Recruit for open executive leadership positions
- Read-out of Neuroscience franchise strategic review

Thank you… Questions and Answers

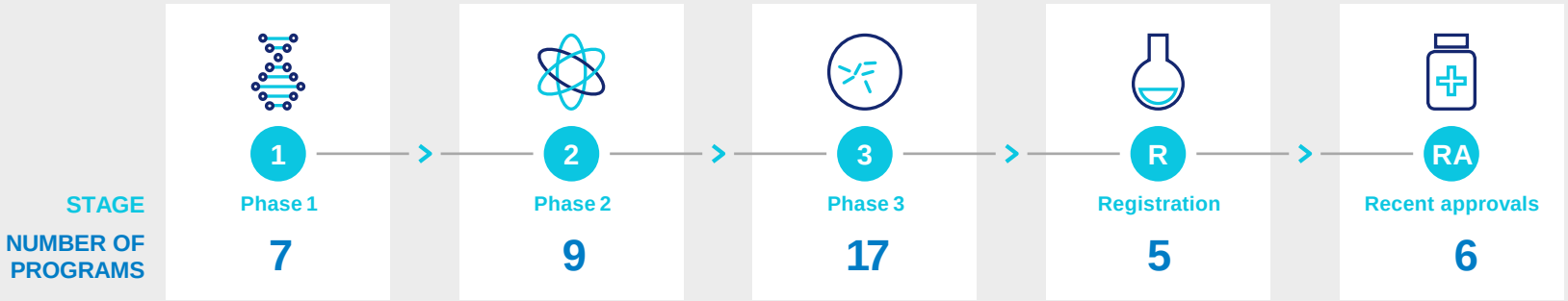
APPENDIX

Innovation is the lifeblood of our current and future success

We focus our innovation across areas with **high unmet medical need**

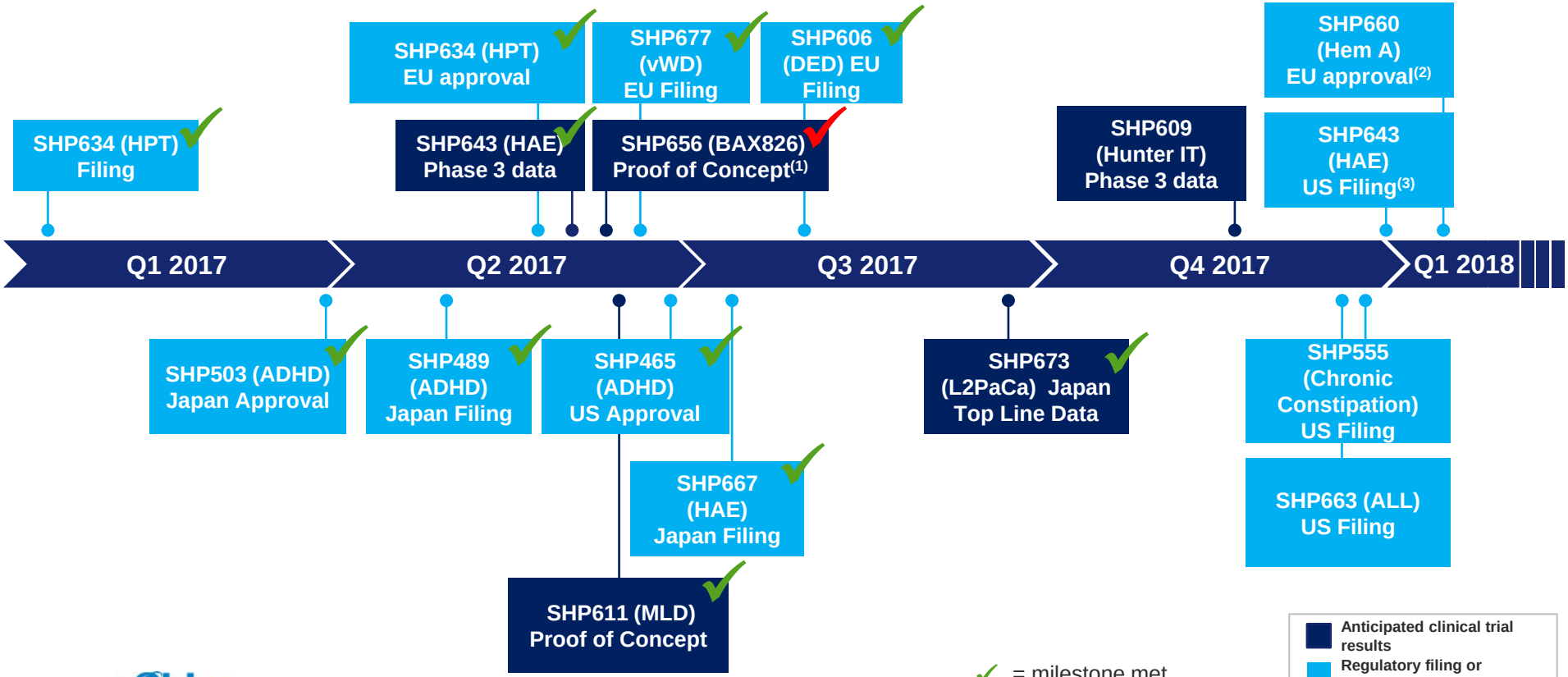
We aim to **expand our rare disease expertise** and offerings through **research and partnerships**, and to extend our existing portfolio of products to **new indications and therapeutic areas**

CLINICAL PROGRAMS IN PIPELINE



Pipeline as of October 2017.

Key anticipated events in 2017



✓ = milestone met

✓ = milestone met but not advancing

(1) Top Line Data and the results were not supportive of continued development.
(2) Anticipated date subject to ongoing discussions with EMA.
(3) Remain on target to file for FDA approval in late 2017 – early 2018.

Note: Timings are approximated to the nearest quarter and where appropriate subject to regulatory approval.

Pipeline is robust at all stages of development

RESEARCH AND PRECLINICAL

35+ programs

- Internally developed and via partnership
- Both rare disease and specialty conditions
- Multiple modalities including NCEs, MAbs, proteins, and gene therapy

PHASE 1

- **SHP611** (MLD)
- **SHP631** (Hunter CNS)
- **SHP634 – Japan** (Hypoparathyroidism) *LCM for NATPARA*
- **SHP639** (Glaucoma)
- **SHP654** (Hemophilia A, Gene Therapy)
- **SHP673** (Small Cell Lung Cancer, 1st Line) *LCM for ONIVYDE*
- **SHP680** (Neurological Conditions)

PHASE 2

- **SHP607**(2) (BPD and IVH)
- **SHP615- Japan** (Seizures) *LCM for BUCCOLAM*
- **SHP625**(3) (PFIC)
- **SHP625** (ALGS)
- **SHP626** (NASH)
- **SHP652 (SM101)**(5) (SLE)
- **SHP659** (Dry Eye)
- **SHP673 - Japan**(1) (Pancreatic Cancer, post gemcitabine) *LCM for ONIVY'DE*
- **SHP673** (Pancreatic Cancer, 1st line) *LCM for ONIVYDE*

PHASE 3

- **SHP555 – US** (Chronic Constipation)
- **SHP609** (Hunter IT) Ph 2/3
- **SHP616 – Japan** (HAE Prophylaxis) *LCM for CINRYZE*
- **SHP616 SC** (HAE Prophylaxis) *LCM for CINRYZE*
- **SHP616** (AMR) *LCM for CINRYZE*
- **SHP620** (CMV infection in transplant patients)
- **SHP621**(3) (EoE)
- **SHP633 – Japan** (Adult SBS) *LCM for GATTEX*
- **SHP640** (Infectious Conjunctivitis)
- **SHP643**(3) (HAE Prophylaxis)
- **SHP647** (UC)
- **SHP647** (CD)
- **SHP655** (cTTP)
- **SHP663** (ALL)
- **SHP671** (CIDP) *LCM for HYQVIA*
- **SHP671** (Pediatric PID) *LCM for HYQVIA*
- **SHP672** (CHAWI surgery) *LCM for OBIZUR*

REGISTRATION

- **SHP489 – Japan** (ADHD) *LCM for VYVANSE*
- **SHP660**(4) **– EU** (Hemophilia A) *LCM for ADYNOVATE*
- **SHP667** (Pediatric HAE) *LCM for FIRAZYR*
- **SHP667 - Japan** (HAE) *LCM for FIRAZYR*
- **SHP677** (VWD) *LCM for VONVENDI*

RECENT APPROVALS

- **INTUNIV – Japan** (ADHD)
- **XIIDRA – US** (Dry eye)
- **MYDAYIS– US** (ADHD)
- **NATPARA – EU** (Hypoparathyroidism)
- **CINRYZE** (Pediatric HAE Prophylaxis)
- **GATTEX** (Pediatric SBS)

Programs terminated in Q3 2017
- SHP623 NMO

Rare indication

Non-rare indication

Pipeline excludes: Oncaspar lyophilized, and Alpha-1 prophylaxis.
(1) Registrational study; (2) SHP607 originally developed for ROP; (3) Granted breakthrough designation by FDA; (4) Aproved in U.S. for on-demand, prophylaxis in adults and children and in perioperative management. (5) Working closely with the FDA to resolve their questions.
Note: Phase 2/3 programs shown as Phase 3.

Shire

Pipeline as of Oct 2017

Capital allocation priorities for 2018

CREATING SHAREHOLDER VALUE

1. **Organic growth** - Invest in innovation to support core franchises
2. **Reduce leverage** - Maintain an investment grade credit rating
3. **Dividends** - Maintain a progressive policy
4. **Surplus capital**
   - **Selective business development** - Focus on in-licensing and bolt-on opportunities
   - **Share buybacks** - To be considered

Reported regional product sales and pro forma growth analysis

Q3 2017	US	EU	LATAM	APAC[3]	Other	Total
Product Sales $MM	2,291	664	140	224	215	3,534
% of Product Sales	65%	19%	4%	6%	6%	
YoY Growth	**2%**	**9%**	**5%**	**37%**	**27%**	**7%**

YTD 2017	US	EU	LATAM	APAC[3]	Other	Total
Product Sales $MM[1]	6,950	1,874	482	623	609	10,538
% of Product Sales	66%	18%	5%	6%	6%	
Pro forma YoY Growth[2]	**7%**	**3%**	**16%**	**23%**	**13%**	**8%**

(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) Growth rates represent YTD 2017 reported sales compared to recast pro forma 2016 sales following Shire's acquisition of Baxalta on June 3, 2016.
(3) APAC region includes Japan.

Royalties and other revenues

	Q3 2017 $MM	Q3 2016 $MM	Reported Growth
SENSIPAR	43	39	+11%
3TC and ZEFFIX	16	16	-1%
FOSRENOL	14	14	+4%
ADDERALL XR	8	5	+64%
Other Royalties	31	19	+65%
Royalties	**111**	**92**	**+21%**
Other Revenues	7	6	+7%
Contract Manufacturing Revenue	46	39	+18%
Total Royalties & Other Revenues	**164**	**137**	**+20%**

Income statement growth analysis

$MM	2016 Q1[1]	2016 Q2[1]	2016 Q3[1]	2016 Q4[1]	2016 FY[1]	2017 Q1[1]	2017 Q2[1]	2017 Q3[1]
Total Product Sales	$1,627	$2,322	$3,315	$3,621	$10,886	$3,412	$3,592	$3,534
versus prior year	*+14%*	*+57%*	*+110%*	*+123%*	*+78%*	*+110%*	*+55%*	*+7%*
Royalties & Other Revenues	$82	$107	$137	$185	$511	$160	$154	$164
versus prior year	*+26%*	*+31%*	*+75%*	*+101%*	*+61%*	*+95%*	*+44%*	*+20%*
Total Revenue	$1,709	$2,429	$3,452	$3,806	$11,397	$3,572	$3,746	$3,698
versus prior year	*+15%*	*+57%*	*+109%*	*+122%*	*+78%*	*+109%*	*+54%*	*+7%*
Non GAAP Gross Margin[2][7]	86.7%	80.4%	74.9%	75.3%	78.0%	78.3%	76.1%	76.5%
Combined Non GAAP R&D and SG&A[3][7]	$651	$934	$1,239	$1,354	$4,178	$1,221	$1,237	$1,212
versus prior year	*+14%*	*+34%*	*+90%*	*+97%*	*+60%*	*+88%*	*+32%*	*-2%*
Non GAAP EBITDA Margin[4][7]	49%	42%	39%	40%	41%	44%	43%	44%
Non GAAP Tax Rate[5][7]	18%	16%	13%	17%	16%	16%	16%	15%
Non GAAP diluted Earnings per ADS[6][7]	$3.19	$3.38	$3.17	$3.37	$13.10	$3.63	$3.73	$3.81
versus prior year	*+12%*	*+29%*	*-2%*	*+13%*	*+12%*	*+14%*	*+10%*	*+20%*

(1) Results from continuing operations including Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) This is a Non GAAP financial measure as a percentage of total revenue. The most directly comparable measure under US GAAP is Gross Margin (Q3 2017: 72.9%, Q3 2016: 49.7%).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q3 2017: -9%, Q3 2016: +103%).
(4) This is a Non GAAP financial measure as a percentage of total revenue. The most directly comparable measure under US GAAP is Net Income Margin (Q3 2017: 15%, Q3 2016: -11%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Effective Tax rate (Q3 2017: 2%, Q3 2016: -38%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Diluted EPS-ADS (Q3 2017: $1.81, Q3 2016: -$1.29).
(7) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Non GAAP free cash flow measures

Net cash provided by operating activities and Non GAAP free cash flow reconciliation	Q3 2017 $MM	Q3 2016 $MM	Reported Growth
Net cash provided by operating activities	**1,055**	**526**	**+101%**
Capital expenditure	(174)	(221)	
Payments relating to license arrangements	20	90	
Non GAAP free cash flow[(1)(2)]	**901**	**395**	**+128%**

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net cash provided by operating activities (see details above).
(2) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Q3 2017 – operating income US GAAP and Non GAAP

	Q3 2017 $MM	Q3 2016 $MM	Reported Growth
Non GAAP Operating Income[1][2] from continuing operations	**1,498**	**1,254**	**+19%**
Integration and acquisition costs	(300)	(1,198)	
Amortization and asset impairment	(482)	(355)	
Divestments and reorganization costs	(6)	(107)	
Legal and litigation costs	(1)	1	
US GAAP Operating Income from continuing operations	**709**	**(406)**	**N/M**

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is US GAAP Operating Income (see details above).
(2) See slide 39 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 33 to 38 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

US GAAP to Non GAAP reconciliation
For the three months ended September 30, 2017

$MM	US GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**3,697.6**	**-**	**-**	**-**	**-**	**-**	**-**	**3,697.6**
Costs and expenses:								
Cost of product sales	1,001.4	-	(63.3)	-	-	-	(70.1)	868.0
R&D	402.8	-	-	-	-	-	(10.8)	392.0
SG&A	859.7	-	-	-	(1.0)	-	(39.0)	819.7
Amortization of acquired intangible assets	482.4	(482.4)	-	-	-	-	-	-
Integration and acquisition costs	237.0	-	(237.0)	-	-	-	-	-
Reorganization costs	5.4	-	-	(5.4)	-	-	-	-
Loss on sale of product rights	0.3	-	-	(0.3)	-	-	-	-
Depreciation	-	-	-	-	-	-	119.9	119.9
Total operating expenses	2,989.0	(482.4)	(300.3)	(5.7)	(1.0)	-	-	2,199.6
Operating Income	**708.6**	**482.4**	**300.3**	**5.7**	**1.0**	**-**	**-**	**1,498.0**
Total other expense, net	(140.5)	-	1.9	4.3	-	-	-	(134.3)
Income from continuing operations before income								
taxes and equity losses of equity method investees	568.1	482.4	302.2	10.0	1.0	-	-	1,363.7
Income taxes	(13.5)	(108.4)	(66.8)	(2.6)	(0.1)	(11.1)	-	(202.5)
Equity in losses of equity method investees, net of taxes	(3.4)	-	-	-	-	-	-	(3.4)
Income from continuing operations	**551.2**	**374.0**	**235.4**	**7.4**	**0.9**	**(11.1)**	**-**	**1,157.8**
Loss from discontinued operations, net of tax	(0.4)	-	-	0.4	-	-	-	-
Net income	**550.8**	**374.0**	**235.4**	**7.8**	**0.9**	**(11.1)**	**-**	**1,157.8**
No. of Shares	911.6							911.6
Diluted earnings per ADS	**$1.81**	**$1.24**	**$0.77**	**$0.03**	**-**	**($0.04)**	**-**	**$3.81**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired ($482.4 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Baxalta ($63.3 million), acquisition and integration costs primarily associated with Baxalta ($240.4 million), net credit related to the change in the fair value of contingent consideration liabilities ($3.4 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($1.9 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Reorganization costs primarily relating to facility consolidations ($5.4 million), net loss on sale of product rights ($0.3 million), gains on sale of long-term investments ($4.3 million), tax effect of adjustments and loss from discontinued operations, net of tax ($0.4 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($1.0 million), and tax effect of adjustments;

(e) Other: One-time income tax adjustment on subsidiary move from Zurich to Zug ($11.1 million); and

(f) Depreciation reclassification: Depreciation of $119.9 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

US GAAP to Non GAAP reconciliation
For the three months ended September 30, 2016

$MM	US GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**3,452.1**	**-**	**-**	**-**	**-**	**-**	**-**	**3,452.1**
Costs and expenses:								
Cost of product sales	1,736.2	-	(803.8)	(11.6)	-	-	(54.5)	866.3
R&D	511.1	-	(110.0)	-	-	-	(9.0)	392.1
SG&A	875.6	-	-	-	0.5	-	(29.6)	846.5
Amortization of acquired intangible assets	354.9	(354.9)	-	-	-	-	-	-
Integration and acquisition costs	284.5	-	(284.5)	-	-	-	-	-
Reorganization costs	101.4	-	-	(101.4)	-	-	-	-
Gain on sale of product rights	(5.7)	-	-	5.7	-	-	-	-
Depreciation	-	-	-	-	-	-	93.1	93.1
Total operating expenses	3,858.0	(354.9)	(1,198.3)	(107.3)	0.5	-	-	2,198.0
Operating income	**(405.9)**	**354.9**	**1,198.3**	**107.3**	**(0.5)**	**-**	**-**	**1,254.1**
Total other expense, net	(191.3)	-	47.4	-	-	-	-	(143.9)
(Loss)/income from continuing operations before income taxes and equity losses of equity method investees	(597.2)	354.9	1,245.7	107.3	(0.5)	-	-	1,110.2
Income taxes	229.6	(88.9)	(244.1)	(44.6)	0.3	-	-	(147.7)
Equity in losses of equity method investees, net of taxes	(0.9)	-	-	-	-	-	-	(0.9)
(Loss)/income from continuing operations	**(368.5)**	**266.0**	**1,001.6**	**62.7**	**(0.2)**	**-**	**-**	**961.6**
Loss from discontinued operations, net of tax	(18.3)	-	-	18.3	-	-	-	-
Net (loss)/income	**(386.8)**	**266.0**	**1,001.6**	**81.0**	**(0.2)**	**-**	**-**	**961.6**
No. of Shares	900.2					10.4		910.6
Diluted (losses)/earnings per ADS	**($1.29)**	**$0.88**	**$3.31**	**$0.27**	**-**	**-**	**-**	**$3.17**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired ($354.9 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Baxalta ($803.8 million), costs relating to license arrangements ($110.0 million), acquisition and integration costs primarily associated with Baxalta and Dyax ($274.3 million), net charge related to the change in the fair value of contingent consideration liabilities ($10.2 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($47.4 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Inventory write-off relating to the closure of a U.S. facility ($11.6 million), reorganization costs primarily relating to facility closure and consolidation ($101.4 million), net gain on sale of product rights ($5.7 million), tax effect of adjustments and loss from discontinued operations, net of tax ($18.3 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($0.5 million), and tax effect of adjustments;

(e) Other: Impact of dilutive shares; and

(f) Depreciation reclassification: Depreciation of $93.1 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

US GAAP to Non GAAP reconciliation
For the nine months ended September 30, 2017

$MM	US GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**11,015.7**	**-**	**-**	**-**	**-**	**-**	**-**	**11,015.7**
Costs and expenses:								
Cost of product sales	3,437.3	-	(688.7)	-	-	-	(209.2)	2,539.4
R&D	1,324.5	(20.0)	(123.7)	-	-	-	(37.0)	1,143.8
SG&A	2,647.7	-	-	-	(8.6)	4.0	(117.3)	2,525.8
Amortization of acquired intangible assets	1,280.5	(1,280.5)	-	-	-	-	-	-
Integration and acquisition costs	696.7	-	(696.7)	-	-	-	-	-
Reorganization costs	24.5	-	-	(24.5)	-	-	-	-
Gain on sale of product rights	(0.4)	-	-	0.4	-	-	-	-
Depreciation	-	-	-	-	-	-	363.5	363.5
Total operating expenses	9,410.8	(1,300.5)	(1,509.1)	(24.1)	(8.6)	4.0	-	6,572.5
Operating income	**1,604.9**	**1,300.5**	**1,509.1**	**24.1**	**8.6**	**(4.0)**	**-**	**4,443.2**
Total other expense, net	(412.9)	-	5.4	(8.9)	-	-	-	(416.4)
Income from continuing operations before income								
taxes and equity earnings of equity method investees	1,192.0	1,300.5	1,514.5	15.2	8.6	(4.0)	-	4,026.8
Income taxes	(44.6)	(305.2)	(260.6)	(7.6)	(3.1)	(11.0)	-	(632.1)
Equity in earnings of equity method investees, net of taxes	0.1	-	-	-	-	-	-	0.1
Income from continuing operations	**1,147.5**	**995.3**	**1,253.9**	**7.6**	**5.5**	**(15.0)**	**-**	**3,394.8**
Gain from discontinued operations, net of tax	18.6	-	-	(18.6)	-	-	-	-
Net income	**1,166.1**	**995.3**	**1,253.9**	**(11.0)**	**5.5**	**(15.0)**	**-**	**3,394.8**
No. of Shares	912.1							912.1
Diluted earnings per ADS	**$3.84**	**$3.27**	**$4.13**	**($0.04)**	**$0.02**	**($0.05)**	**-**	**$11.17**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Impairment of IPR&D intangible asset ($20.0 million), amortization of intangible assets relating to intellectual property rights acquired ($1,280.5 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Baxalta ($688.7 million), costs relating to license arrangements ($123.7 million), acquisition and integration costs primarily associated with Baxalta ($552.4 million), net charge related to the change in the fair value of contingent consideration liabilities primarily related to SHP643 ($144.3 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($5.4 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Reorganization costs primarily relating to facility consolidations ($24.5 million), net gain on sale of product rights ($0.4 million), gains on sale of long-term investments ($8.9 million), tax effect of adjustments and gain from discontinued operations, net of tax ($18.6 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($8.6 million), and tax effect of adjustments;

(e) Other: One-time adjustment to pension expense ($4.0 million), income tax adjustment on subsidiary move from Zurich to Zug ($11.1 million), and tax effect of adjustments; and

(f) Depreciation reclassification: Depreciation of $363.5 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

US GAAP to Non GAAP reconciliation
For the nine months ended September 30, 2016

$MM	US GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**7,590.5**	**-**	**-**	**-**	**-**	**-**	**-**	**7,590.5**
Costs and expenses:								
Cost of product sales	2,762.9	-	(1,097.3)	(11.6)	-	-	(85.2)	1,568.8
R&D	1,023.0	(8.9)	(110.0)	-	-	-	(20.7)	883.4
SG&A	2,025.8	-	-	-	(16.1)	-	(69.4)	1,940.3
Amortization of acquired intangible assets	702.5	(702.5)	-	-	-	-	-	-
Integration and acquisition costs	738.6	-	(738.6)	-	-	-	-	-
Reorganization costs	115.7	-	-	(115.7)	-	-	-	-
Gain on sale of product rights	(12.2)	-	-	12.2	-	-	-	-
Depreciation	-	-	-	-	-	-	175.3	175.3
Total operating expenses	7,356.3	(711.4)	(1,945.9)	(115.1)	(16.1)	-	-	4,567.8
Operating Income	**234.2**	**711.4**	**1,945.9**	**115.1**	**16.1**	**-**	**-**	**3,022.7**
Total other expense, net	(323.1)	-	91.5	6.0	-	-	-	(225.6)
(Loss)/income from continuing operations before income taxes and equity losses of equity method investees	(88.9)	711.4	2,037.4	121.1	16.1	-	-	2,797.1
Income taxes	218.4	(184.9)	(408.2)	(48.7)	(5.8)	-	-	(429.2)
Equity in losses of equity method investees, net of taxes	(1.9)	-	-	-	-	-	-	(1.9)
Income from continuing operations	**127.6**	**526.5**	**1,629.2**	**72.4**	**10.3**	**-**	**-**	**2,366.0**
Loss from discontinued operations, net of tax	(257.5)	-	-	257.5	-	-	-	-
Net (loss)/income	**(129.9)**	**526.5**	**1,629.2**	**329.9**	**10.3**	**-**	**-**	**2,366.0**
No. of Shares	725.5					5.4		730.9
Diluted (losses)/earnings per ADS	**($0.54)**	**$2.16**	**$6.70**	**$1.35**	**$0.04**	**-**	**-**	**$9.71**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Impairment of IPR&D intangible asset ($8.9 million), amortization of intangible assets relating to intellectual property rights acquired ($702.5 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Baxalta ($1,097.3 million), costs relating to license arrangements ($110.0 million), acquisition and integration costs primarily associated with Baxalta and Dyax ($773.4 million), net credit related to the change in the fair value of contingent consideration liabilities ($34.8 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($91.5 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Inventory write-off relating to the closure of a U.S. facility ($11.6 million), reorganization costs primarily relating to facility closure and consolidation ($115.7 million), net gain on sale of product rights ($12.2 million), loss on divestment of non-core subsidiary ($6.0 million), tax effect of adjustments and loss from discontinued operations, net of tax ($257.5 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($16.1 million), and tax effect of adjustments;

(e) Other: Impact of dilutive shares; and

(f) Depreciation reclassification: Depreciation of $175.3 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

Non GAAP measures

This presentation contains financial measures not prepared in accordance with US GAAP. These measures are referred to as “Non GAAP” measures and include: Non GAAP operating income; Non GAAP net income; Non GAAP diluted earnings per ADS; effective tax rate on Non GAAP income before income taxes and (losses/earnings) of equity method investees (effective tax rate on Non GAAP income); Non GAAP CER; Non GAAP cost of sales; Non GAAP gross margin; Non GAAP R&D; Non GAAP SG&A; Non GAAP other expense; Non GAAP free cash flow, Non GAAP net debt, Non GAAP EBITDA and Non GAAP EBITDA margin.

The Non GAAP measures exclude the impact of certain specified items that are highly variable, difficult to predict, and of a size that may substantially impact Shire’s operations. Upfront and milestone payments related to in-licensing and acquired products that have been expensed as R&D are also excluded as specified items as they are generally uncertain and often result in a different payment and expense recognition pattern than ongoing internal R&D activities. Intangible asset amortization has been excluded from certain measures to facilitate an evaluation of current and past operating performance, particularly in terms of cash returns, and is similar to how management internally assesses performance. The Non GAAP financial measures are presented in this press release as Shire’s management believes that they will provide investors with an additional analysis of Shire’s results of operations, particularly in evaluating performance from one period to another.

Shire’s management uses Non GAAP financial measures to make operating decisions as they facilitate additional internal comparisons of Shire’s performance to historical results and to competitor’s results, and provides them to investors as a supplement to Shire’s reported results to provide additional insight into Shire’s operating performance. Shire’s Remuneration Committee uses certain key Non GAAP measures when assessing the performance and compensation of employees, including Shire’s executive directors.

The Non GAAP financial measures used by Shire may be calculated different from, and therefore may not be comparable to, similarly titled measures used by other companies - refer to the section “Non GAAP Financial Measure Descriptions” below for additional information. In addition, these Non GAAP financial measures should not be considered in isolation as a substitute for, or as superior to, financial measures calculated in accordance with US GAAP, and Shire’s financial results calculated in accordance with US GAAP and reconciliations to those financial statements should be carefully evaluated.

Non GAAP Financial Measure Descriptions

Where applicable the following items, including their tax effect, have been excluded when calculating Non GAAP earnings and from our Non GAAP outlook:

Amortization and asset impairments:
- Intangible asset amortization and impairment charges; and
- Other than temporary impairment of investments.

Acquisitions and integration activities:
- Up-front payments and milestones in respect of in-licensed and acquired products;
- Costs associated with acquisitions, including transaction costs, fair value adjustments on contingent consideration and acquired inventory;
- Costs associated with the integration of companies; and
- Noncontrolling interests in consolidated variable interest entities.

Divestments, reorganizations and discontinued operations:
- Gains and losses on the sale of non-core assets;
- Costs associated with restructuring and reorganization activities;
- Termination costs; and
- Income/(losses) from discontinued operations.

Legal and litigation costs:
- Net legal costs related to the settlement of litigation, government investigations and other disputes (excluding internal legal team costs).

Additionally, in any given period Shire may have significant, unusual or non-recurring gains or losses which it may exclude from its Non GAAP earnings for that period. When applicable, these items would be fully disclosed and incorporated into the required reconciliations from US GAAP to Non GAAP measures.

Depreciation, which is included in Cost of sales, R&D and SG&A costs in our US GAAP results, has been separately disclosed for presentational purposes.

Free cash flow represents net cash provided by operating activities, excluding up-front and milestone payments for in-licensed and acquired products, but including capital expenditure in the ordinary course of business.

Non GAAP net debt represents cash and cash equivalents less short and long term borrowings, capital leases and other debt.

A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented on pages 33 to 38.

Non GAAP CER growth is computed by restating 2017 results using average 2016 foreign exchange rates for the relevant period.

Average exchange rates used by Shire for the three months ended September 30, 2017 were $1.31:£1.00 and $1.17:€1.00 (2016: $1.32:£1.00 and $1.11:€1.00). Average exchange rates used by Shire for the nine months ended September 30, 2017 were $1.28:£1.00 and $1.11:€1.00 (2016: $1.40:£1.00 and $1.11:€1.00).