Solidifying our Leadership in Rare and Highly Specialized Diseases

Flemming Ornskov, MD, MPH **CEO**
Jeff Poulton **CFO**

Q3 Results 2016
November 1, 2016

Tyler
HAE

Shire

“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.

Agenda

1. Business update **Delivering, Integrating, Upgrading and Innovating**		**Flemming Ornskov, MD, MPH**
2. Financial review		**Jeff Poulton**
3. Summary		**Flemming Ornskov, MD, MPH**
4. Q & A		**All**

Shire

Solidifying our leadership in rare and highly specialized diseases

Delivering

- Record product sales performance
- Strong growth from legacy Shire products, including XIIDRA launch
- Remain on target and on track to deliver our non GAAP full year 2016 guidance

Integrating

- Integration proceeding ahead of relevant benchmarks
- Ahead of synergy target YTD, and on-track for Year 3 guidance
- Manufacturing network optimization underway

Upgrading

- Upgrading execution of Baxalta franchises using the Shire commercial platform
- Combined approach for commercial ops, market access, patient services
- Expanding geographic reach of our product portfolio and services

Innovating

- New product approvals (CUVITRU & ONIVYDE) and key product launches (XIIDRA & VONVENDI) since Q2 results
- Driving late stage, global assets such as SHP643 (HAE) and SHP647 (IBD)
- Innovative clinical pipeline with promising late-stage programs

Delivering: Record product sales and Non-GAAP earnings with Baxalta acquisition and supported by performance of legacy Shire franchises

Financial highlights

- Addition of first full quarter of Baxalta franchises has led to record product sales of $3.3B
- As expected, pro forma sales growth was at the mid single digit level against a strong comparative period;
- Legacy Shire franchises delivered 12% growth, while legacy Baxalta franchise growth of -1% was impacted by the timing of large orders
- Non GAAP diluted earnings per ADS decreased year on year, primarily due to higher Non GAAP operating income being more than offset by the impact of a higher number of shares issued as consideration for the Baxalta transaction.
- We remain on target and track to deliver our full year 2016 guidance, which was recently upgraded at Q2 earnings

Product Sales

Non GAAP Diluted Earnings per ADS(2)(3)

(1) Growth rates are at Constant exchange rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2016 performance (restated using 2015 exchange rates for the relevant period) to actual 2015 reported performance.
(2) See slide 36 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q3 2016: -$1.29, Q3 2015: $2.29).

Delivering: Multiple growth drivers across the portfolio

Hematology sales $884m; -6%(1)(2)	FEIBA [anti-inhibitor coagulant complex] ADYNOVATE [Antihemophilic Factor (Recombinant), PEGylated] ADVATE [Antihemophilic Factor (Recombinant)]	• Growth in hematology held back by the timing of large orders in international markets compared to strong prior year period • Underlying trends in demand are in line with overall market growth
Genetic diseases sales $676m; +6%(1)	REPLAGAL agalsidase alfa elaprase (idursulfase) firazyr (icatibant injection)	• Growth driven by FIRAZYR and LSD portfolio primarily due to an increase in number of patients • Increase to the number of patients on therapy with CINRYZE was more than offset by the impact of US supply constraints
Neuroscience sales $616m; +16%(1)	Vyvanse ADDERALL XR intuniv (guanfacine)	• VYVANSE continues to perform strongly, with growth driven by increased use in adults in the US, pricing, and continued growth in international markets • SHP465 for the treatment of ADHD to be filed by end of 2016
Immunology sales $606m; +5%(1)(2)	HyQvia [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] GAMMAGARD LIQUID [Immune Globulin Infusion (Human)] 10% Cuvitru [Immune Globulin Subcutaneous (Human)] 20%	• Immunoglobulin sales grew at 9%, driven by a strong performance by GAMMAGARD and increased adoption of HYQVIA • CUVITRU launches to take place in the US from November, with European launches to follow in 2017
Internal medicine sales $463m; +16%(1)	Lialda (mesalamine) 2g Gattex [Recombinant DNA origin] for injection Natpara (parathyroid hormone) for injection	• LIALDA sales benefiting from continued market share growth • Growth from new patient adds on GATTEX and NATPARA
Oncology sales $55m; +64%(1)(2)	oncaspar pegaspargase onivyde pegylated liposomal irinotecan hydrochloride trihydrate	• ONCASPAR continues to perform well in the US; further growth expected internationally, as commercial launches are initiated across EU • European approval for ONIVYDE granted - the first and only approved treatment option for adult patients with metastatic adenocarcinoma of the pancreas, in combination with 5-fluorouracil and leucovorin who have progressed following gemcitabine-based therapy
Ophthalmics sales $14m; N/A	xiidra (lifitegrast ophthalmic solution) 5%	• Positive contribution from XIIDRA, with strong early prescription trends and market share data, as well as increasing levels of managed care access • Regulatory submission made in Canada

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(2) Growth rates represent the Q3 pro forma results compared to recast Q3 2015 results as previously disclosed by Baxalta following the separation from Baxter.

Delivering: The XIIDRA launch provides a template for Shire's brand-centric approach to commercial excellence

Shire approach to asset

xiidra (lifitegrast ophthalmic solution)5%

- Launch planning started **>2 years in advance of approval**
- Developed **specified targeting** and **clear messaging**
- **Adequately resourced** with innovative approach to building the market
- **Coordinated global approach** across functions, like Commercial, R&D, and Tech Ops

Early results

- Ready for **early approval** July 11 with **product available** for rapid distribution
- Major **launch meeting** and **disease state awareness** campaign launched in August
- Over **12,000 eye care providers have prescribed XIIDRA** as of October 14
- **69%** of **top prescribers** have written XIIDRA as of October 14
- **Very positive** early physician and patient feedback
- **International roll out** on track; regulatory submission made in Canada

Shire

Delivering: Shire has launched the eyelove™ campaign to increase disease awareness

Disease state awareness campaign started end of August

"Station domination" in NYC, Boston, Chicago

Positive feedback from both optometrists and ophthalmologists

"Definitely increasing the awareness of dry eyes. A lot of people asking dry eye questions. A lot like the eye love website due to good info.

– Optometrist

"I definitely agree that the marketing campaign has increased the awareness of DED for all patients.

– Ophthalmologist

Shire

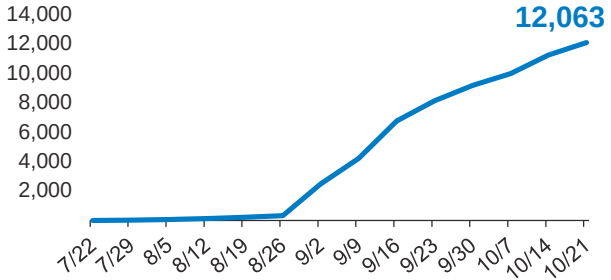
Delivering: Early awareness coupled with commercial excellence has delivered strong initial XIIDRA prescription growth

64,732*
Scripts YTD

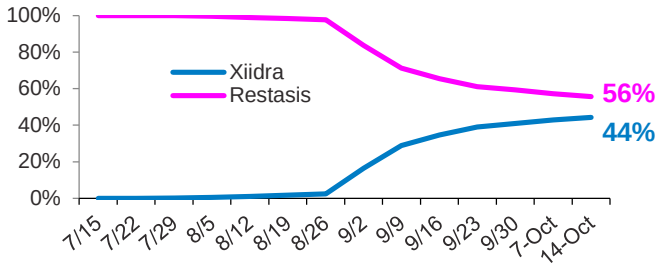
16%*
TRx market share

44%**
NBRx market share

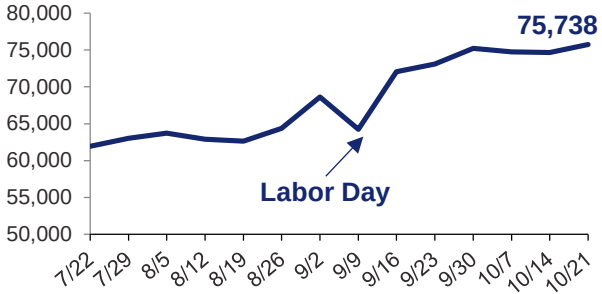
16% XIIDRA Market Share



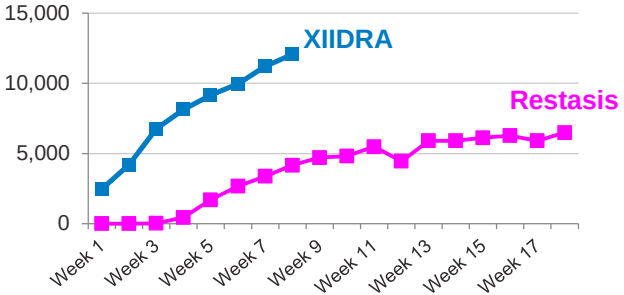
44% XIIDRA New-to-Brand Market Share



22% Overall Market Growth Since 1H2016



XIIDRA vs Restasis Launch Curves



*Through w/e 10/21
**Through w/e 10/14

Source: IMS TRx data, through October 21, 2016

Delivering: Access to over 75% of covered lives within ~8 weeks of launch provides a platform for continued patient access and growth

Commercial lives: XIIDRA has approximately 75% of lives covered in Tier 2 and Tier 3.

87% of weekly Rxs filled through commercial plans

Select Managed Care Formulary Highlights

Plan	Effective Date	Status
CVS/CareMark	October 2016	• Preferred product • Parity to Restasis • Exclusive for advanced control (smaller subset)
Express Scripts	October 2016	• Preferred product • Parity to Restasis
Aetna	November 2016	• Preferred product all Aetna/Coventry lives • Parity to Restasis
Prime Commercial Prime Part D	November 2016 November 2017	• Added to National Formulary parity to Restasis • Parity to Restasis

Integrating: The integration of Baxalta is ahead of industry benchmarks with significant accomplishments across three areas of work

Org design and placement

- ✓ **Org design and talent selection** largely complete(1)
- ✓ **Employee retention and morale** metrics are healthy
- ✓ New **organization is balanced** between legacy employees

Financing & value capture

- ✓ **Bond financing successfully completed**
- ✓ Year-to-date **synergy realization** is ahead of plan
- ✓ Initiatives to hit $700M+ in **synergies** by Year 3 on track

Business/ Functional integration

- ✓ Decision made to **exit Biosimilars**, streamline Oncology
- ✓ **Manufacturing network optimization** initiated
- ✓ First **international commercial site consolidations** completed

Shire

(1) With exception of UK, France and certain countries that have yet to transfer from Baxter International Inc. to legacy Baxalta due to, among other reasons, the need to obtain certain consents from governmental authorities

Upgrading: We are transitioning legacy Baxalta franchises to the Shire model of commercial excellence

Improved targeting

- Increased focus on **marketing and brand differentiation**
- Integrated approach to **market access**
- Improved **segmentation** and salesforce **execution**

Increased investment

- Revised approach to commercial **launches and campaigns**
- Increased **share of voice** for key products

Geographic expansion

- Applying a **coordinated approach** to our global footprint
- Accelerating ex-US **launch opportunities**
- Expanding expertise in **patient identification and services**

Shire

Innovating: Shire has a strong clinical development pipeline with near and long term potential

Phase 1	Phase 2		Phase 3		Registration	Recent approvals
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 (Friedrich'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] (IBD)	**Cinryze SC** (HAE Prophylaxis)	**SHP465**[6] (ADHD)		
		SHP652 (SM101) (SLE)	**Cinryze** (AMR)	**SHP555 - US** (Chronic Constipation)		
		SHP653 (imalumab) (mCRC)	**Gattex - Japan** (Adult SBS)	**Vyvanse - Japan** (ADHD) Ph2/3		
			Vonvendi[7] (VWD)			

Changes since Q2 2016 results:

- SHP610 in Sanfilippo A discontinued
- Biosimilar programs discontinued
- Pacritinib partnership with CTI BioPharma Corp terminated

Rare indication

Non-rare indication

Pipeline excludes: Pipeline excludes Obizur On Demand, 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

Innovating: We focus on developing first-, best-, and new-to-class assets with global opportunities, such as XIIDRA, SHP643, and SHP647

2016 Approvals and launches

- **XIIDRA** in Dry Eye Disease– US launch underway
- **VONVENDI** in Von Willibrand Disease – US launch underway
- US approval granted for **CUVITRU** in primary immunodeficiency in September 2016; launch planned for Q4 2016
- EU approval granted for **ONIVYDE** in second line treatment of pancreatic cancer in adult patients; preparations for launch underway

Clinical program updates

- FDA resubmission for **SHP465 (ADHD)** expected by year end
- **SHP643 (HAE)** Phase 3 study fully enrolled; top line data expected Q2 2017
- **SHP647 (IBD)** Phase 3 initiation expected 1H2017
- **SHP609 (Hunter IT)** Phase 2/3 study fully enrolled; top line data expected Q4 2017
- Phase 3 study for **SHP620/maribavir (resistant/refractory CMV viremia)** expected to start before year end
- Phase 2 studies for **SHP626 (NASH)** have initiated, with first patients screened\aq

Financial Review

Jeff Poulton
Chief Financial Officer

Q3 2016 reported key financials summary

	Q3 2016 $m[1]	Q3 2015 $m	Reported Growth	CER Growth[2][10]
Product sales	3,315	1,577	+110%	+111%
Royalties and other revenues	137	78	+75%	+72%
Total revenue	3,452	1,655	+109%	+109%
Non GAAP combined R&D and SG&A[3][10]	1,239	652	+90%	+91%
Non GAAP EBITDA[4][10]	1,347	758	+78%	+76%
Non GAAP EBITDA margin[5][6][10]	38%	43%	-5% ppc	-6% ppc
Non GAAP effective tax rate[7][10]	13%	10%	n/a	n/a
Non GAAP diluted EPS – ADS[8][10]	3.17	3.24	-2%	-3%
Non GAAP cash generation[9][10]	830	588	+41%	n/a

(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) This is a Non GAAP financial measure. constant exchange rate ("CER") performance is determined by comparing 2016 performance (restated using average 2015 foreign exchange rates for the relevant period) to actual 2015 reported performance.
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q3 2016: $1,387m, Q3 2015: $684m).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net loss/income (Q3 2016: -$387m, Q3 2015: $453m).
(5) Non GAAP earnings before interest, tax, depreciation and amortization ("EBITDA") as a percentage of product sales, excluding royalties and other revenues and cost of sales related to contract manufacturing revenue.
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income Margin (Q3 2016: -11%, Q3 2015: 27%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Tax Rate (Q3 2016: 38%, Q3 2015: -5%).
(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q3 2016: -$1.29, Q3 2015: $2.29).
(9) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Cash provided by operating activities (Q3 2016: $526m, Q3 2015: $561m).
(10) See slide 36 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Q3 2016 pro forma (1) product sales performance

	Q3 2016 Sales			Pro forma Growth vs. Q3 2015	
$ in Millions	**US**	**Int.**	**Total**	**Reported**	**CER(2)**
Hemophilia	355	348	702	-5%	-5%
Inhibitor Therapies	73	108	182	-13%	-13%
Hematology Total	**428**	**456**	**884**	**-6%**	**-6%**
Cinryze	152	14	165	-12%	-12%
Firazyr	129	17	146	+19%	+19%
Kalbitor	11	-	11	n/a	n/a
Elaprase	38	109	147	+9%	+11%
Replagal	-	119	119	+7%	+7%
Vpriv	40	48	88	+3%	+4%
Genetic Disease Total	**370**	**307**	**676**	**+5%**	**+6%**
Vyvanse	468	45	513	+20%	+20%
Adderall XR	75	5	81	+3%	+3%
Other Neuroscience	3	20	23	-21%	-18%
Neuroscience Total	**546**	**70**	**616**	**+15%**	**+16%**
Immunoglobulin Therapies	381	91	472	+8%	+9%
Bio Therapeutics	72	62	134	-6%	-5%
Immunology Total	**453**	**154**	**606**	**+5%**	**+5%**
Lialda	188	20	209	+18%	+18%
Pentasa	85	-	85	-3%	-3%
Gattex	50	9	58	+35%	+36%
Natpara	23	-	23	+238%	+238%
Other Internal Medicine	35	52	87	+0%	+1%
Internal Medicine Total	**382**	**81**	**463**	**+15%**	**+16%**
Ophthalmology Total	**14**	**0**	**14**	**n/a**	**n/a**
Oncology	**45**	**11**	**55**	**+64%**	**+64%**
Total Product Sales	**2,238**	**1,078**	**3,315**	**+6%**	**+6%**

(1) Growth rates represent the Q3 pro forma sales compared to recast Q3 2015 pro forma sales as previously disclosed by Baxalta following its separation from Baxter.
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September YTD 2016 reported performance metrics

Year on Year Growth:	YTD 2016[1]
Product sales	62%
Non GAAP R&D[2][10]	35%
Non GAAP SG&A[3][10]	54%
Combined Non GAAP R&D and SG&A[4][10]	47%

Ratios: As % of Product Sales	YTD 2016[1]	YTD 2015
Non GAAP gross margin[5][10]	79.3%	85.4%
Non GAAP R&D[6][10]	12%	15%
Non GAAP SG&A[7][10]	27%	28%
Non GAAP EBITDA[8][9][10]	40%	43%

(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 2016: -16%).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (YTD 2016: +49%).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (YTD 2016: +19%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Gross Margin (YTD 2016: 62.0%, YTD 2015: 83.9%). Excluding royalties and other revenues and cost of sales related to contract manufacturing revenue.
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (YTD 2016: 14%, YTD 2015: 27%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (YTD 2016: 28%, YTD 2015: 30%).
(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income Margin (YTD 2016: -2%, YTD 2015: 22%). Excluding royalties and other revenues and cost of sales related to contract manufacturing revenue.
(9) Non GAAP earnings before interest, tax, depreciation and amortization ("EBITDA") as a percentage of product sales, excluding royalties and other revenues and cost of sales related to contract manufacturing revenue.
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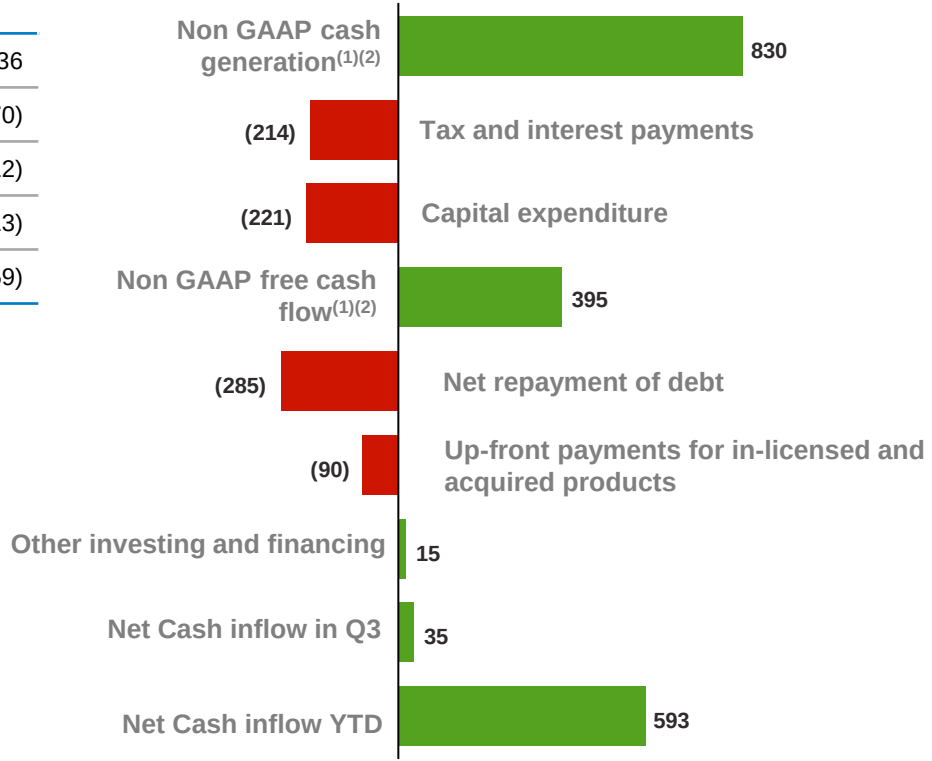
Strong Non GAAP cash generation; deleveraging begins post Baxalta acquisition

$m	September 30, 2016	June 30, 2016	December 31, 2015
Cash and cash equivalents	729	693	136
Long term borrowings	(20,989)	(21,312)	(70)
Short term borrowings	(2,737)	(2,715)	(1,512)
Other debt	(349)	(344)	(13)
Non GAAP net debt[2]	(23,346)	(23,678)	(1,459)



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Reiterating 2016 Non GAAP guidance

Full Year 2016 Dynamics

	Impact of FX Rates on Guidance	Guidance
Total product sales	-2% to -3%	$10.8 - $11 billion
Royalties & other revenues		$490 - $530 million
Non GAAP gross margin[3]		77% - 79%
Non GAAP combined R&D and SG&A[3]		$4.1 - $4.4 billion
Non GAAP net interest/other[3]		$400 - $450 million
Non GAAP effective tax rate[3]		16% - 18%
Non GAAP diluted earnings per ADS[1][2]	-1% to 1%	$12.70 - $13.10
2016 fully diluted weighted average shares[2]		778 million
Capital Expenditure		~$800 million

Our 2016 Outlook is based on YTD 2016 actual exchange rates and the July 12, 2016 exchange rates holding for Q4 2016 (€:$1.11, £:$1.32, CHF:$1.01, CAD:$0.77, ¥:$0.0096). The estimated impact of a 10% appreciation in the US Dollar against the respective currency, over the last three months of the year, on our 2016 Guidance is as follows:

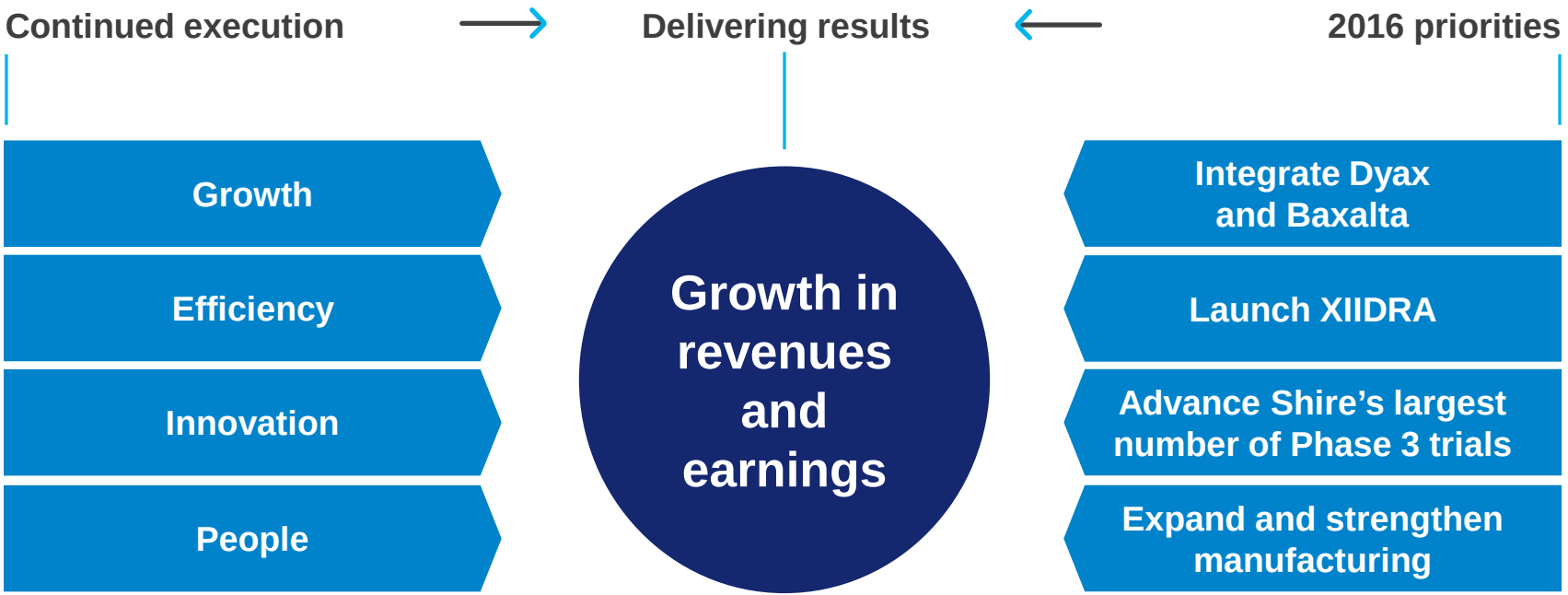
	Revenue	Earnings
EUR	(1.6%)	(2.3%)
GBP	(0.2%)	(0.3%)
CHF	(0.1%)	0.1%
CAD	(0.1%)	(0.3%)
JPY	(0.3%)	(0.6%)
Other	(0.5%)	(0.7%)

(1) This is a Non GAAP financial measure. The diluted earnings per ADS forecast assumes a weighted average number of fully diluted ordinary shares outstanding of 778 million for 2016 following the equity issuance for the Baxalta transaction.
(2) 2016 fully diluted weighted average shares based on YTD actual weighted average shares of 731 million.
(3) This is a Non GAAP financial measure. See slide 36 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Summary

Flemming Ornskov, MD, MPH

We remain focused on delivering growth in revenues and earnings through continued execution of our strategy



The global leader in Rare Diseases and highly specialized conditions.

Solidifying our leadership in rare and highly specialized diseases

Delivering

- Record product sales performance
- Strong growth from legacy Shire products, including XIIDRA launch
- Remain on target and on track to deliver our non GAAP full year 2016 guidance

Integrating

- Integration proceeding ahead of relevant benchmarks
- Ahead of synergy target YTD, and on-track for Year 3 guidance
- Manufacturing network optimization underway

Upgrading

- Integrating legacy Baxalta franchises into Shire's commercial model
- Combined approach for commercial ops, market access, patient services
- Expanding geographic reach of our product portfolio and services

Innovating

- New product approvals (CUVITRU & ONIVYDE) and key product launches (XIIDRA & VONVENDI) since Q2 results
- Driving late stage, global assets SHP643 (HAE) and SHP647 (IBD)
- Innovative clinical pipeline with promising late-stage programs

Questions and Answers

APPENDIX

Reported Regional Product Sales and Pro-forma Growth Analysis

Q3 2016	US	EU	LATAM	APAC[3]	Other	Total
Product Sales $m[1]	2,238	611	133	164	170	3,315
% of Product Sales	67%	18%	4%	5%	5%	
Pro Forma YoY Growth[2]	11%	5%	-24%	1%	-16%	6%

YTD 2016	US	EU	LATAM	APAC[3]	Other	Total
Product Sales $m[1]	5,059	1,277	262	276	391	7,265
% of Product Sales	70%	18%	4%	4%	5%	
Pro Forma YoY Growth[2]	15%	6%	1%	12%	-4%	11%

(1) Results from continuing operations including Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) Growth rates represent the Q3/YTD pro-forma sales compared to recast Q3/YTD 2015 pro-forma sales as previously disclosed by Baxalta following its separation from Baxter.
(3) APAC region includes Japan.

Royalties and Other Revenues

	Q3 2016 $m[1]	Q3 2015 $m	Reported Growth	CER Growth[3][4]
SENSIPAR	39	35	+11%	+11%
3TC and ZEFFIX	16	12	+36%	+36%
FOSRENOL	14	13	+4%	-12%
ADDERALL XR	5	7	-34%	-33%
Other Royalties	19	9	+97%	+96%
Royalties	**92**	**76**	**+20%**	**+18%**
Other Revenues	6	2	n/m	n/m
Contract Manufacturing Revenue[2]	39	-	n/a	n/a
Total Royalties & Other Revenues	**137**	**78**	**+75%**	**+72%**

(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) Prior to acquisition, Baxalta reported contract manufacturing revenue within Bio Therapeutics.
(3) Growth rates are at constant exchange rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2016 performance (restated using 2015 exchange rates for the relevant period) to actual 2015 reported performance.
(4) See slide 36 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Income statement growth analysis

	2015 Q1	2015 Q2	2015 Q3	2015 Q4	2015 FY	2016 Q1(1)	2016 Q2(1)	2016 Q3(1)
Total Product Sales	$1,423m	$1,476m	$1,577m	$1,624m	$6,100m	$1,627m	$2,322m	$3,315m
versus prior year	+9%	+0%	+2%	+8%	+5%	+14%	+57%	+110%
Royalties & Other Revenues	$65m	$82m	$78m	$92m	$317m	$82m	$107m	$137m
versus prior year	+68%	+150%	+73%	+22%	+65%	+26%	+31%	+75%
Total Revenue	$1,488m	$1,558m	$1,655m	$1,716m	$6,417m	$1,709m	$2,429m	$3,452m
versus prior year	+11%	+4%	+4%	+9%	+7%	+15%	+57%	+109%
Non GAAP Gross Margin (2)(7)	86%	86%	84%	86%	86%	86%	80%	75%
Combined Non GAAP R&D and SG&A(3)(7)	$571m	$697m	$652m	$688m	$2,608m	$651m	$934m	$1,239m
versus prior year	+6%	+16%	+5%	+2%	+7%	+14%	+34%	+90%
Non GAAP EBITDA Margin(4)(7)	46%	39%	43%	43%	43%	46%	40%	38%
Non GAAP Tax Rate(5)(7)	17%	13%	10%	21%	16%	18%	16%	13%
Non GAAP diluted Earnings per ADS(6)(7)	$2.84	$2.63	$3.24	$2.97	$11.68	$3.19	$3.38	$3.17
versus prior year	+20%	-2%	+11%	+13%	+10%	+12%	+29%	-2%

(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. The most directly comparable measure under US GAAP is Gross Margin (Q3 2016: 47.6%, Q3 2015: 83.3%). Excluding royalties and other revenues and cost of sales related to contract manufacturing revenue.
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q3 2016: +103%, Q3 2015: -1%).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income Margin (Q3 2016: -11%, Q3 2015: 27%). Excluding royalties and other revenues and cost of sales related to contract manufacturing revenue.
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Tax rate (Q3 2016: 38%, Q3 2015: -5%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q3 2016: -$1.29, Q3 2015: $2.29).
(7) See slide 36 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Non GAAP cash flow measures

Non GAAP cash generation[1][2] and Non GAAP free cash flow[1][2] reconciliation	Q3 2016 $m	Q3 2015 $m	Reported Growth
Non GAAP cash generation[1][2]	**830**	**588**	**+41%**
Tax and interest payments, net	(214)	(26)	
Up-front payments for in-licensed and acquired products	(90)	-	
US GAAP Net cash provided by operating activities	**526**	**561**	**-6%**
Capital expenditures	(221)	(22)	
Up-front payments for in-licensed and acquired products	90	-	
Non GAAP free cash flow[1][2]	**395**	**539**	**-27%**

(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 36 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Non GAAP net debt

$m	September 30, 2016	June 30, 2016	December 31, 2015
Cash and cash equivalents	729	693	136
Long term borrowings	(20,989)	(21,312)	(70)
Short term borrowings	(2,737)	(2,715)	(1,512)
Other debt	(349)	(344)	(13)
Non GAAP net debt	(23,346)	(23,678)	(1,459)

At September 30, 2016 Shire had issued $12.1bn of Senior Notes (with maturity dates of 3 years and beyond) to refinance the bridge loan that was utilized to finance the Baxalta acquisition. The company had assumed $5bn of Baxalta Senior Notes (with maturity dates of 2018 and beyond) upon the acquisition. In addition, it had a $5.6bn term loan that was fully utilized to finance the Dyax acquisition and amortizes until its final maturity in 2018. Its $2.1bn revolving credit facility matures in 2020.

Q3 2016 – Operating Income US GAAP and Non GAAP

	Q3 2016 $m[1]	Q3 2015 $m	Reported Growth
Non GAAP Operating Income [2][3] from continuing operations	**1,254**	**725**	**+73%**
Integration and acquisition activities	(1,198)	(97)	
Intangible asset amortization	(355)	(133)	
Reorganization costs	(107)	(31)	
Legal and litigation costs	1	(2)	
Other	-	(8)	
US GAAP Operating (loss)/Income from continuing operations	**(406)**	**456**	**-189%**

(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 US GAAP Operating Income from continuing operations (see details above).
(3) See slide 36 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

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

($M)	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	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 (loss)/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 (loss)/earnings per ADS	**($1.29)**	**$0.88**	**$3.32**	**$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: Amortization of inventory fair value adjustments primarily associated with Baxalta and Dyax ($803.8 million), acquisition and integration costs primarily associated with Dyax and Baxalta ($274.3 million), SHP647 (Pfizer) upfront & milestone payment ($110.0 million), charges 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 ($11.6 million) relating to the planned closure of a facility at the Los Angeles manufacturing site, and exit and severance costs ($86.2 million), costs relating to termination of the Krems, Austria building project ($10.0 million), costs relating to the relocation of staff from Chesterbrook to Lexington and closure of the Basingstoke office ($5.2 million), net gain on re-measurement of DAYTRANA contingent consideration to fair value ($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; and

(e) 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.

(f) Impact of dilutive shares

Shire

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

($M)	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	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 (loss)/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)
(Loss)/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 (loss)/earnings per ADS	**($0.54)**	**$2.16**	**$6.69**	**$1.35**	**$0.04**	**-**		**$9.71**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Impairment of SHP627 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: Amortization of inventory fair value adjustments primarily associated with NPS, Dyax and Baxalta ($1,097.3 million), acquisition and integration costs primarily associated with NPS, Dyax and Baxalta ($703.7 million), SHP647 (Pfizer) upfront & milestone payment ($110.0 million), charges related to the change in the fair value of contingent consideration liabilities ($34.9 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 ($11.6 million) relating to the planned closure of a facility at the Los Angeles manufacturing site, and exit and severance costs ($86.2 million), costs relating to termination of the Krems, Austria building project ($10.0 million), costs relating to the relocation of staff from Chesterbrook to Lexington and closure of the Basingstoke office ($19.5 million), net gain on re-measurement of DAYTRANA contingent consideration to fair value ($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; and

(e) 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.

(f) Impact of dilutive shares

Shire

GAAP to Non GAAP Reconciliation
For the three months ended September 30, 2015

($M)	GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**1,655.0**	**-**	**-**	**-**	**-**	**-**	**-**	**1,655.0**
Costs and expenses:								
Cost of product sales	262.7	-	(6.7)	-	-	(1.0)	(9.6)	245.4
R&D	241.2	-	-	-	-	(2.0)	(5.5)	233.7
SG&A	442.3	-	-	-	(1.7)	(5.0)	(17.8)	417.8
Amortization	132.7	(132.7)	-	-	-	-	-	-
Integration and acquisition costs	89.9	-	(89.9)	-	-	-	-	-
Reorganization costs	31.1	-	-	(31.1)	-	-	-	-
Gain on sale of product rights	(0.7)	-	-	0.7	-	-	-	-
Depreciation	-	-	-	-	-	-	32.9	32.9
Total operating expenses	1,199.2	(132.7)	(96.6)	(30.4)	(1.7)	(8.0)	-	929.8
Operating Income	**455.8**	**132.7**	**96.6**	**30.4**	**1.7**	**8.0**	**-**	**725.2**
Total other expense, net	(0.3)	-	-	(10.4)	-	-	-	(10.7)
(Loss)/income from continuing operations before income taxes and equity losses of equity method investees	455.5	132.7	96.6	20.0	1.7	8.0	-	714.5
Income taxes	22.3	(52.3)	(33.0)	(6.2)	(0.6)	(2.3)	-	(72.1)
Equity in losses of equity method investees, net of ta	(0.7)	-	-	-	-	-	-	(0.7)
Income from continuing operations	**477.1**	**80.4**	**63.6**	**13.8**	**1.1**	**5.7**	**-**	**641.7**
Loss from discontinued operations, net of tax	(24.3)	-	-	24.3	-	-	-	-
Net income	**452.8**	**80.4**	**63.6**	**38.1**	**1.1**	**5.7**	**-**	**641.7**
No. of Shares	593.4	-	-	-	-	-	-	593.4
Diluted earnings per ADS	**$2.29**	**$0.40**	**$0.32**	**$0.19**	**$0.01**	**$0.03**	**-**	**$3.24**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired ($132.7 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Unwind of NPS inventory fair value adjustments ($6.7 million), acquisition and integration costs associated with NPS, ViroPharma and the proposed combination with Baxalta ($30.7 million), charges related to the change in fair value of contingent consideration liabilities ($59.2 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Gain on re-measurement of DAYTRANA contingent consideration to fair value ($0.7 million), costs relating to the One Shire reorganization, including costs relating to the relocation of staff from Chesterbrook to Lexington ($31.1 million), gain on sale of long-term investment ($10.4 million), tax effect of adjustments, and loss from discontinued operations, net of tax ($24.3 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($1.7 million), and tax effect of adjustments;

(e) Other: Costs associated with AbbVie's terminated offer for Shire ($8.0 million), and tax effect of adjustments; and

(f) Depreciation reclassification: Depreciation of $32.9 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

Shire

GAAP to Non GAAP Reconciliation
For the nine months ended September 30, 2015

($M)	GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**4,701.0**	**-**	**-**	**-**	**-**	**-**	**-**	**4,701.0**
Costs and expenses:								
Cost of product sales	718.5	-	(23.0)	-	-	(6.5)	(34.4)	654.6
R&D	1,210.8	(523.3)	-	-	-	(13.5)	(17.2)	656.8
SG&A	1,356.6	-	-	-	(4.4)	(36.0)	(53.5)	1,262.7
Amortization	352.3	(352.3)	-	-	-	-	-	-
Integration and acquisition costs	(46.8)	-	46.8	-	-	-	-	-
Reorganization costs	59.6	-	-	(59.6)	-	-	-	-
Gain on sale of product rights	(13.0)	-	-	13.0	-	-	-	-
Depreciation	-	-	-	-	-	-	105.1	105.1
Total operating expenses	3,638.0	(875.6)	23.8	(46.6)	(4.4)	(56.0)	-	2,679.2
Operating Income	**1,063.0**	**875.6**	**(23.8)**	**46.6**	**4.4**	**56.0**	-	**2,021.8**
Total other expense, net	(16.3)	-	-	(14.1)	-	(1.1)	-	(31.5)
(Loss)/income from continuing operations before income taxes and equity losses of equity method investees	1,046.7	875.6	(23.8)	32.5	4.4	54.9	-	1,990.3
Income taxes	9.0	(187.9)	(53.1)	(13.3)	(1.6)	(19.3)	-	(266.2)
Equity in losses of equity method investees, net of ta	(1.6)	-	-	-	-	-	-	(1.6)
Income from continuing operations	**1,054.1**	**687.7**	**(76.9)**	**19.2**	**2.8**	**35.6**	**-**	**1,722.5**
Loss from discontinued operations, net of tax	(31.3)	-	-	31.3	-	-	-	-
Net income	**1,022.8**	**687.7**	**(76.9)**	**50.5**	**2.8**	**35.6**	**-**	**1,722.5**
No. of Shares	593.2	**-**	**-**	**-**	**-**	**-**	-	593.2
Diluted earnings per ADS	**$5.17**	**$3.48**	**($0.39)**	**$0.26**	**$0.01**	**$0.18**	**-**	**$8.71**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Impairment of SHP625 IPR&D intangible asset ($346.6 million), impairment of SHP608 IPR&D intangible asset ($176.7 million), amortization of intangible assets relating to intellectual property rights acquired ($352.3 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Unwind of NPS inventory fair value adjustments ($21.7 million), unwind of ViroPharma inventory fair value adjustments ($1.3 million), acquisition and integration costs associated with NPS, ViroPharma and the proposed combination with Baxalta ($149.7 million), net credit related to the change in fair values of contingent consideration liabilities primarily relating to SHP625 and SHP608 ($196.5 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Net gain on divestment of non-core product rights and on re-measurement of DAYTRANA contingent consideration to fair value ($11.9 million), gain on disposal of non-core product rights ($1.1 million), costs relating to the One Shire reorganization, including costs relating to the relocation of staff from Chesterbrook to Lexington ($59.6 million), gain on sale of long term investments ($14.1 million), tax effect of adjustments and loss from discontinued operations, net of tax ($31.3 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($4.4 million), and tax effect of adjustments;

(e) Other: Costs associated with AbbVie's terminated offer for Shire ($56.0 million), interest income received in respect of cash deposited with the Canadian revenue authorities ($1.1 million), and tax effect of adjustments; and

(f) Depreciation reclassification: Depreciation of $105.1 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

Shire

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 product sales; Non GAAP gross margin; Non GAAP R&D; Non GAAP SG&A; Non GAAP other expense; Non GAAP cash generation; Non GAAP free cash flow, Non GAAP net debt, Non GAAP EBITDA and Non GAAP EBITDA margin* (excluding royalties and other revenues and cost of sales related to contract manufacturing revenues).

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 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 product sales, R&D and SG&A costs in our US GAAP results, has been separately disclosed for presentation purposes.

Cash generation represents net cash provided by operating activities, excluding up-front and milestone payments for in-licensed and acquired products, tax and interest payments.

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 and other debt.

A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented on pages 21 to 22.

Non GAAP CER growth is computed by restating 2016 results using average 2015 foreign exchange rates for the relevant period.

Average exchange rates used by Shire for Q3 2016 were $1.32:£1.00 and $1.11:€1.00 (2015: $1.56:£1.00 and $1.11:€1.00). Average exchange rates used by Shire for the nine months to September 30, 2016 were $1.40:£1.00 and $1.11:€1.00 (2015: $1.54:£1.00 and $1.12:€1.00).

See slides 32 to 35 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.