

Executing Our Growth Strategy

Q1 2017 Results

May 2, 2017

Flemming Ornskov, MD, MPH – CEO

Jeff Poulton – CFO



“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 may decrease its business flexibility and increase borrowing costs; 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. Business update



Flemming Ornskov, MD, MPH

2. Financial review



Jeff Poulton

3. Summary



Flemming Ornskov, MD, MPH

4. Q & A

Shire continues to make excellent progress towards its near and long-term strategic and financial goals



Strong business performance delivered in Q1

GROWTH



- Achieved quarterly product sales of \$3.4B
 - An increase of 110% from Q1 2016
- Delivered Non GAAP diluted earnings per ADS of \$3.63⁽¹⁾⁽⁴⁾
 - An increase of 14% from Q1 2016
- Q1 pro forma product sales grew 9%⁽²⁾
- Continued advancement of late-stage clinical portfolio

EFFICIENCY



- Baxalta integration continues to track ahead of plan
- Synergy targets ahead of plan and on-track for Year 3 guidance
- Non GAAP EBITDA margin of 44% compared to 40% in Q4 2016⁽³⁾⁽⁴⁾
- Supply network study in process

CAPITAL ALLOCATION



- \$423 million net repayment of debt in Q1
- On track to meet our 2-3x Non GAAP net debt / EBITDA target by end of 2017⁽⁴⁾
- Capital expenditures on track
 - Covington plasma facility on plan for anticipated initial regulatory approval in 2018



(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Diluted EPS-ADS (Q1 2017: \$1.23, Q1 2016: \$2.12).

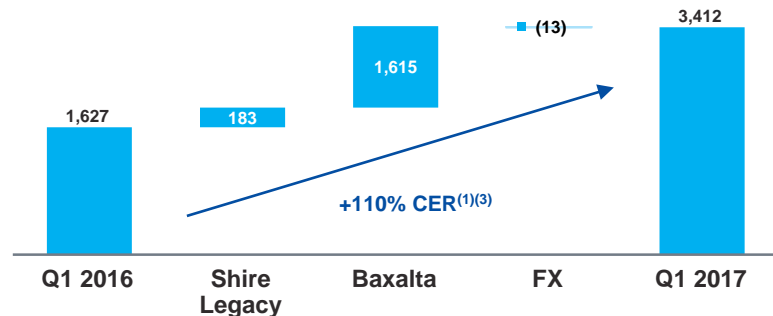
(2) Growth rates represent Q1 2017 reported sales compared to recast 2016 pro forma sales as previously disclosed by Baxalta following the separation from Baxter.

(3) 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 (Q1 2017: 10%, Q4 2016: 12%).

(4) See slide 33 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 29 to 32 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Robust product sales growth and Non GAAP earnings

PRODUCT SALES (\$MM)



NON GAAP DILUTED EARNINGS PER ADS⁽²⁾⁽³⁾



FINANCIAL HIGHLIGHTS

- Addition of Baxalta franchises led to product sales of \$3.4B and 110% growth
- On a pro forma basis, total product sales were 9% higher in Q1 2017 compared to Q1 2016
 - Legacy Shire franchises delivered 11% growth, while legacy Baxalta franchises grew 8% on a pro forma basis
- Non GAAP diluted earnings per ADS growth of 14%⁽²⁾⁽³⁾
- Operating cash flow grew 18% to \$459MM

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Q1 sales growth generated across our diversified portfolio

Hematology
sales \$871MM; +4%⁽¹⁾



- Strong INHIBITOR THERAPIES growth of 12% on a pro forma basis

Genetic Diseases
sales \$696MM; +14%



- CINRYZE sales increased 38% due to an increase in the number of patients on therapy and the impact of stocking following an improvement in supply levels in Q1

Immunology
sales \$676MM; +12%⁽¹⁾



- Strong demand seen for both our immunoglobulin franchise, including newly launched CUVITRU, as well as BIO THERAPEUTICS products, including ALBUMIN

Neuroscience
sales \$653MM; +4%



- VYVANSE continued to perform strongly, with growth driven by increased use in adults in the U.S., pricing improvement, and continued international expansion
- Overall franchise growth was negatively impacted by increased generic competition in the ADDERALL XR market

Internal medicine
sales \$419MM; +9%



- LIALDA sales benefiting from continued market share growth
- Growth from new patient adds on GATTEX and NATPARA

Oncology
sales \$58MM; +13%⁽¹⁾



- ONCASPAR continues to perform well in the U.S.; further growth expected internationally, as commercial launches are initiated across Europe
- Initial launch of ONIVYDE in Europe proceeding well

Ophthalmics
sales \$39MM; N/A



- Positive contribution from XIIDRA with strong early prescription trends and market share gains

Key pipeline progressions in 2017

REGULATORY APPROVALS

- NATPAR (Hypoparathyroidism) received EU conditional marketing authorization
- CINRYZE (HAE) approved in EU for label extension to prevent and treat HAE attacks in pediatric patients
- INTUNIV (ADHD) approved in Japan
- VYVANSE (ADHD) chewable tablets approved in U.S.

CLINICAL UPDATES

- Acceptance of FDA filing for SHP465 (ADHD)
 - PDUFA date set for June 2017
- Fast Track FDA Designation
 - SHP655 (cTTP)
- Investigational New Drug (IND) application filed for SHP639 (Glaucoma)
- Initiation of Phase 3 trials
 - SHP640 (Infectious Conjunctivitis)
 - SHP620 (2nd Phase 3 for CMV infection)
- Completed enrollment in SHP643 open-label extension study
- Licensed investigational program from Parion Sciences (Dry Eye Disease)

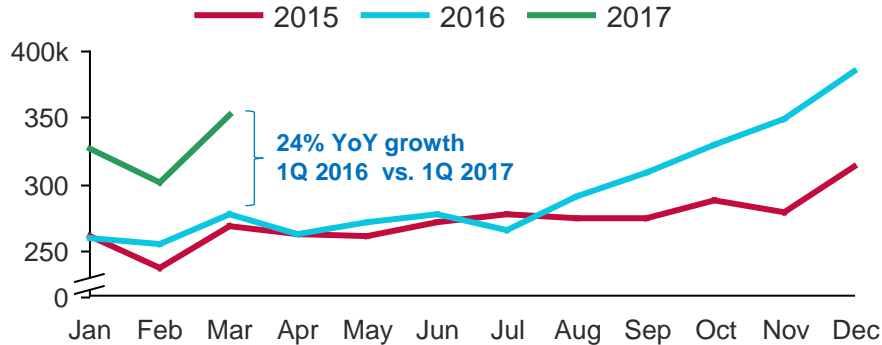
XIIDRA market position continues to grow

XIIDRA RX trends

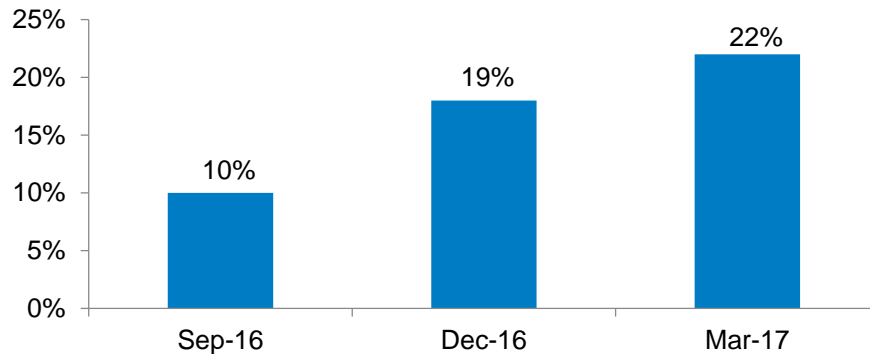
>400K
Total scripts
through
March 2017

~76K
RXs prescribed
in March 2017;
*Best month
since launch*

IMS monthly TRx volume, Total Dry Eye Disease (DED) market



XIIDRA overall market share since launch



ADDITIONAL PROGRESS

- >30K physicians have prescribed XIIDRA to-date
- GTN discounts and patient refills continue to improve quarter over quarter
- Progressing with Medicare Part D coverage; accounts for 40%+ of total market
- EU regulatory filing on track for Q3 2017
- Discussions with PMDA in Japan ongoing



HAE market continues to be core growth driver with SHP643 data expected in Q2

Current Market Dynamics

- Demand for FIRAZYR and CINRYZE continues to grow – combined sales growth of 21% in Q1
- Increasing diagnosis and treatment rates in U.S. and international markets
- International markets remain highly underpenetrated

CINRYZE Supply

- Supply improvements seen with no product stock-outs in Q1
- Progressing plans to provide internal capacity to supply approximately 30% of total demand

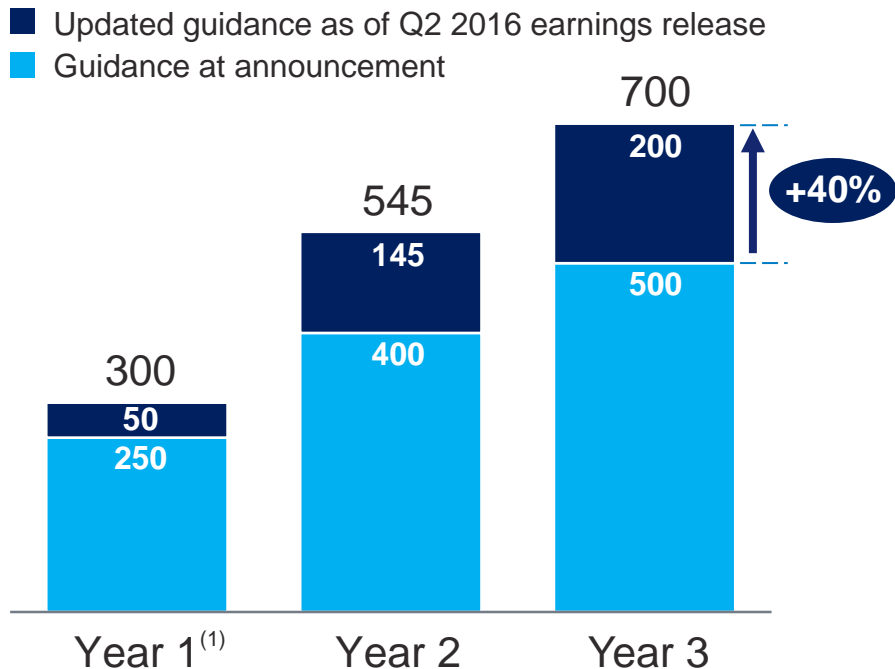
SHP643 Status

- Phase 1b data published in the New England Journal of Medicine
- Phase 3 top-line data expected in Q2 2017
- Open-label extension trial completed enrollment

SHP643 Potential Opportunities

- Potential to improve on the efficacy, safety, and convenience of current treatment options
- Expand utilization of prophylaxis treatment
- Increase penetration rates in international markets
- Secure Shire's long-term leadership position in HAE
- Improve gross margins for Shire's overall business

On target to achieve at least \$700MM in cost synergies



(1) Year 1 denotes the time period beginning June 2016 and ending May 2017.

Q1 PROGRESS

Organizational Design

- Benefiting from simplified structure initiated in 2H 2016
- Streamlined global marketing and R&D project management functions

Consolidation Activities

- Consolidation of U.S. and international sites progressing
- Opened two shared service centers to more efficiently support global operations
- Supply network study ongoing

Systems Integrations

- Completed integration to a single people management platform
- Significant number of business service operations transitioned from Baxter and Baxalta to Shire
- Enterprise resource planning system (ERP) integration progressing and on track

Financial review

Jeff Poulton
Chief Financial Officer



Q1 2017 reported key financials summary

	Q1 2017 \$MM ⁽¹⁾	Q1 2016 \$MM	Reported Growth	CER Growth ⁽²⁾⁽⁸⁾
Product sales	3,412	1,627	+110%	+110%
Royalties and other revenues	160	82	+95%	+96%
Total revenue	3,572	1,709	+109%	+110%
Non GAAP combined R&D and SG&A⁽³⁾⁽⁸⁾	1,221	651	+88%	+89%
Non GAAP EBITDA⁽⁴⁾⁽⁸⁾	1,576	831	+90%	+90%
Non GAAP EBITDA margin⁽⁵⁾⁽⁸⁾	44%	49%	-5 ppc	n/a
Non GAAP effective tax rate⁽⁶⁾⁽⁸⁾	16%	18%	n/a	n/a
Non GAAP diluted EPS – ADS⁽⁷⁾⁽⁸⁾	3.63	3.19	+14%	+14%
Net cash provided by operating activities	459	390	+18%	n/a

(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).

(2) 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.

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q1 2017: \$1,268m, Q1 2016: \$692m).

(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income (Q1 2017: \$375m Q1 2016: \$419m).

(5) 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 (Q1 2017: 10%, Q1 2016: 25%).

(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Effective Tax Rate (Q1 2017: 2%, Q1 2016: 17%).

(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Diluted EPS-ADS (Q1 2017: \$1.23, Q1 2016: \$2.12).

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Q1 product sales performance pro forma⁽¹⁾

<u>\$MM</u>	Q1 2017 Sales			Pro forma growth vs. 2016	
	<u>U.S.</u>	<u>International</u>	<u>Total</u>	<u>Reported</u>	<u>CER⁽²⁾⁽³⁾</u>
Hemophilia	341	309	650	1%	1%
Inhibitor Therapies	71	150	221	12%	14%
Hematology Total	412	459	871	4%	4%
CINRYZE	216	10	226	38%	38%
FIRAZYR	112	17	129	0%	0%
KALBITOR	12	-	12	13%	13%
ELAPRASE	38	102	141	14%	14%
REPLAGAL	-	110	110	6%	8%
VPRIV	36	44	80	-5%	-3%
Genetic Disease Total	413	283	696	14%	14%
VYVANSE	509	55	564	11%	10%
ADDERALL XR	59	6	65	-34%	-35%
Other Neuroscience	2	23	25	12%	15%
Neuroscience Total	569	84	653	4%	4%
Immunoglobulin Therapies	405	93	498	10%	11%
Bio Therapeutics	70	108	178	19%	21%
Immunology Total	475	201	676	12%	13%
LIALDA	153	22	175	4%	4%
PENTASA	69	-	69	8%	8%
GATTEX	57	12	69	33%	34%
NATPARA	30	-	30	90%	90%
Other Internal Medicine	25	51	76	-10%	-9%
Internal Medicine Total	334	85	419	9%	9%
Oncology	42	16	58	13%	13%
Ophthalmology	39	-	39	n/a	n/a
Total Product Sales	2,285	1,128	3,412	9%	10%



- (1) Growth rates represent Q1 2017 reported sales compared to recast 2016 pro forma sales as previously disclosed by Baxalta following the separation from Baxter.
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Q1 2017 reported performance metrics

Year on Year Growth:	Q1 2017⁽¹⁾
Product sales	110%
Non GAAP R&D⁽²⁾⁽⁹⁾	73%
Non GAAP SG&A⁽³⁾⁽⁹⁾	95%
Combined Non GAAP R&D and SG&A⁽⁴⁾⁽⁹⁾	88%

Ratios: As % of Total Revenue	Q1 2017⁽¹⁾	Q1 2016
Non GAAP gross margin⁽⁵⁾⁽⁹⁾	78.3%	86.7%
Non GAAP R&D⁽⁶⁾⁽⁹⁾	10%	12%
Non GAAP SG&A⁽⁷⁾⁽⁹⁾	24%	26%
Non GAAP EBITDA⁽⁸⁾⁽⁹⁾	44%	49%

(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 (Q1 2017: +75%).

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (Q1 2017: +87%).

(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q1 2017: +83%).

(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Gross Margin (Q1 2017: 62.9%, Q1 2016: 85.5%).

(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (Q1 2017: 11%, Q1 2016: 13%).

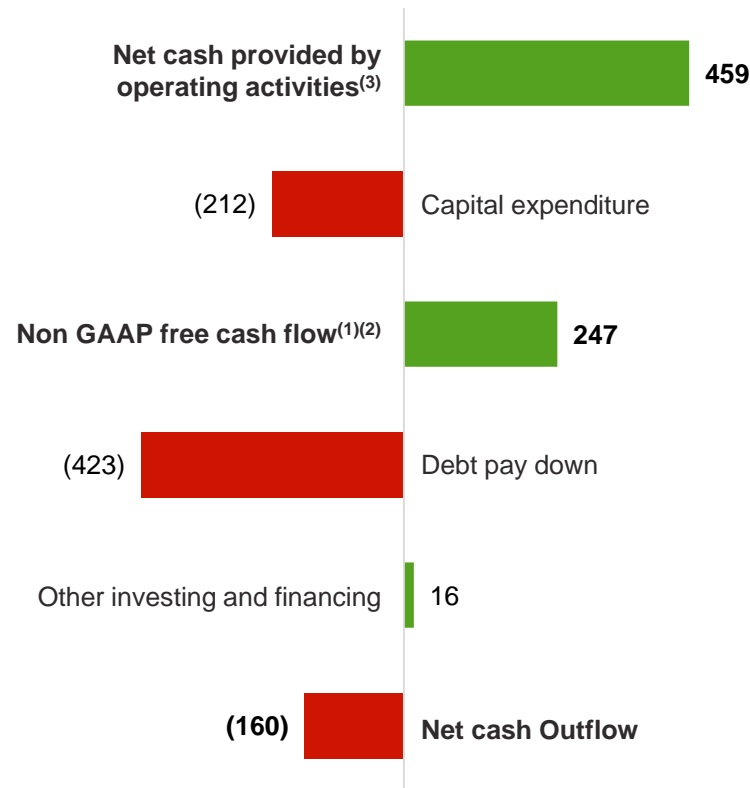
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (Q1 2017: 25%, Q1 2016: 28%).

(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income Margin (Q1 2017: 10%, Q1 2016: 25%).

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Operating cash flow continues to drive debt reduction

\$ MM	March 31, 2017	December 31, 2016	Increase/ (Decrease)
Cash and cash equivalents	369	529	(160)
Long term borrowings	19,151	19,553	
Short term borrowings	3,043	3,062	
Capital leases and other debt	352	354	
Total borrowings, capital leases, and other debt	22,546	22,969	(423)
Non GAAP net debt⁽²⁾	22,176	22,439	(263)



(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net cash provided by operating activities (Q1 2017: \$459m, Q1 2016: \$390m).
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(3) Net cash provided by operating activities was held back by payment of \$346m associated with the settlement of the Dermagraft litigation.

2017 Guidance reiterated

	Full year 2017 Dynamics	
	Guidance	Impact of FX Rates on Guidance
Product Sales	\$14.5 - \$14.8 billion	-1% to -2%
Royalties & other revenues	\$600 - \$700 million	
Non GAAP gross margin ⁽¹⁾ (as % of total revenue)	74.5% - 76.5%	
Non GAAP combined R&D and SG&A ⁽¹⁾	\$5.0 - \$5.3 billion	
Non GAAP depreciation ⁽¹⁾	\$400 - \$450 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⁾	\$14.60 - \$15.20	-1% to -2%
2017 fully diluted weighted average shares	914 million	
Capital Expenditure	~\$1 billion	



Expected Phasing of Product Sales

- Current pro forma product sales guidance implies ~9% growth vs. 2016
- As previously communicated, 1H 2017 product sales growth is expected to be lower than our FY annual growth rate guidance due to strong 1H 2016 pro-forma comparables
- Historic pro forma product sales from 2016:
 - Q1 2016: \$3.12B
 - Q2 2016: \$3.35B
 - Q3 2016: \$3.32B
 - Q4 2016: \$3.62B

Our 2017 Outlook is based on January 13, 2017 actual exchange rates (€:\$1.06, £:\$1.22, CHF:\$0.99, CAD:\$0.76, ¥:\$0.0087). 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	(1.3%)	(0.8%)
GBP	(0.2%)	(0.3%)
CHF	(0.1%)	0.1%
CAD	(0.2%)	(0.4%)
JPY	(0.2%)	(0.5%)
Other	(0.3%)	(0.2%)

Summary

Flemming Ornskov, MD, MPH



Key priorities for 2017



Commercial execution and new product launches



Further integration



Pipeline progression



Optimize portfolio and strengthen focus



Debt pay-down



RARE DISEASES LEADER ► FUELING GROWTH

Thank you... Questions and Answers



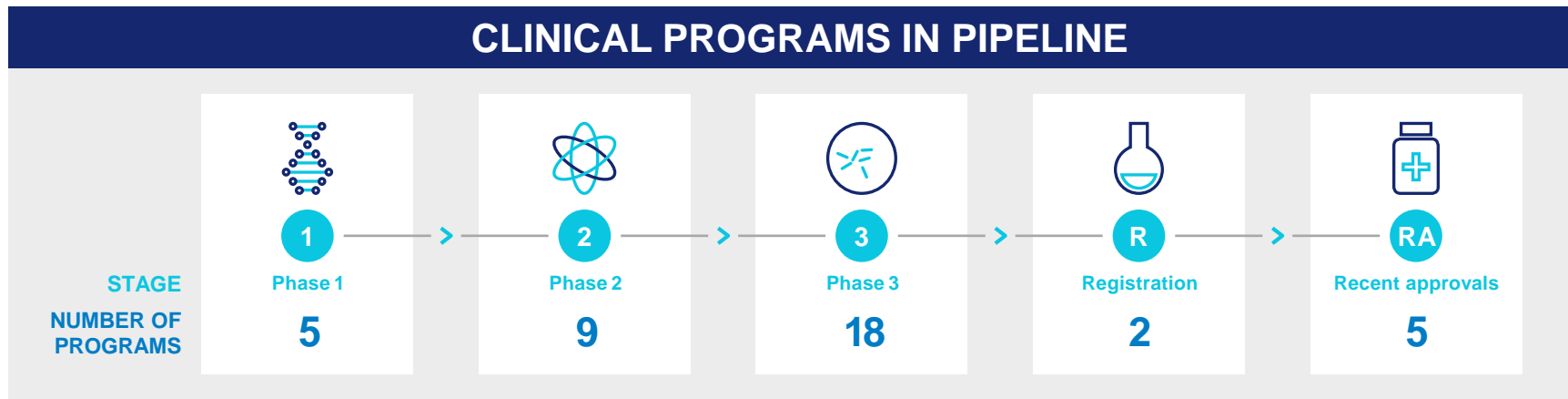
APPENDIX

Innovation is the lifeblood of our current and future success

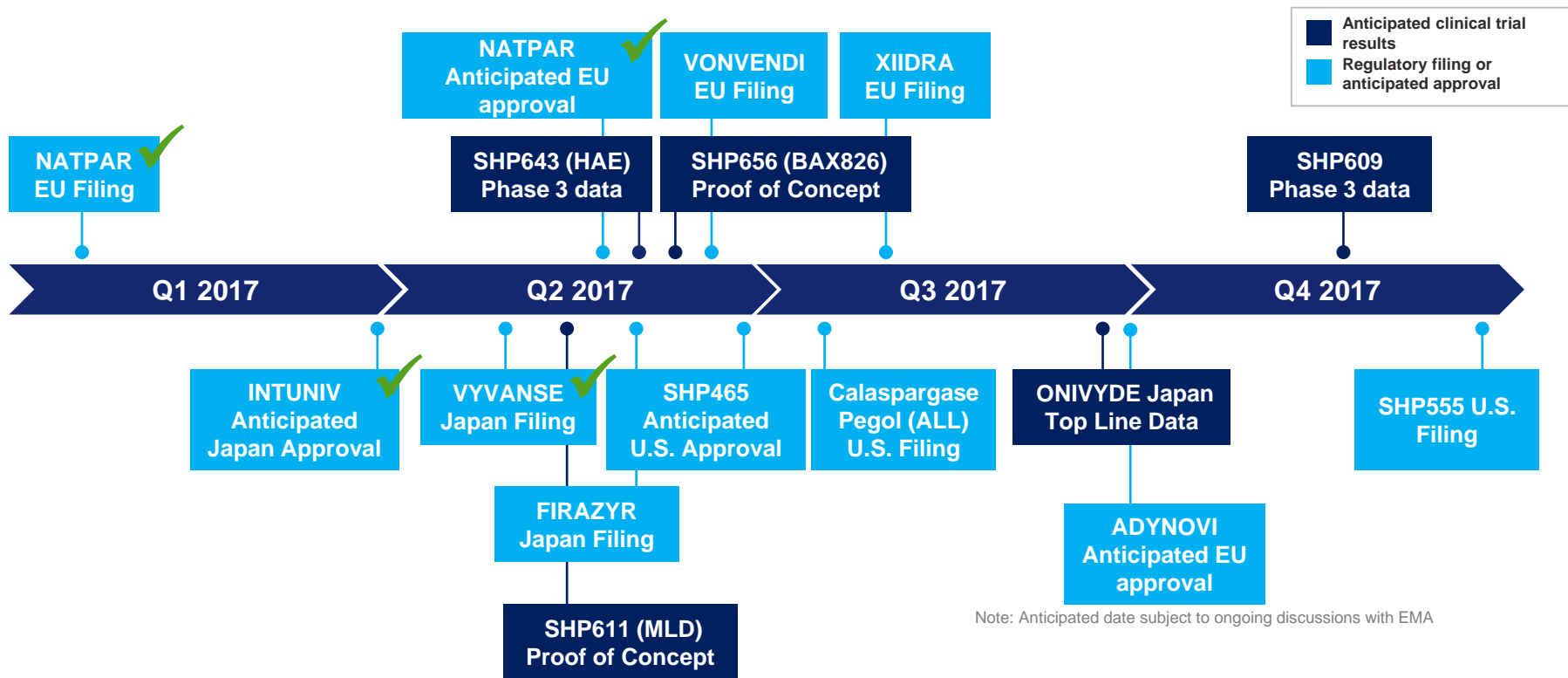
We focus our innovation across areas with **high unmet medical need**

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



Key anticipated events in next 12 months



Pipeline is robust at all stages of development

RESEARCH AND PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGISTRATION	RECENT APPROVALS		
<p>35+ programs</p> <ul style="list-style-type: none"> Internally developed and via partnership Both rare disease and specialty conditions Multiple modalities including NCEs, MABs, proteins, and gene therapy 	SHP611 (MLD)	ONIVYDE (Pancreatic Cancer, 1 st line)	SHP625 ⁽⁴⁾ (PFIC)	SHP609 (Hunter IT) Ph 2/3	OBIZUR (CHAWI surgery)	ADYNOVATE ⁽⁵⁾ – EU (Hemophilia A)	CUVITRU – U.S. and EU (PID)
	SHP623 ⁽¹⁾ (rC1-INH) (NMO)	ONIVYDE - Japan ⁽²⁾ (Pancreatic Cancer, post gemcitabine)	SHP625 (ALGS)	SHP621 ⁽⁴⁾ (EoE)	OBIZUR (CHAWI on demand)	SHP465 – U.S. (ADHD)	ONIVYDE – EU (Pancreatic Cancer, Line 2)
	SHP631 (Hunter CNS)	SHP607 ⁽³⁾ (Complications of Prematurity)	SHP626 (NASH)	SHP643 ⁽⁴⁾ (HAE Prophylaxis)	CALASPARGASE PEGOL (ALL)		NATPAR – EU (Hypoparathyroidism)
	SHP655 (BAX930) (cTTP)	SHP647 (UC)	SHP647 (CD)	FIRAZYR – Japan (Acute HAE) Ph 2/3	10% HYQVIA+KIOVIG (CIDP)		INTUNIV – Japan (ADHD)
	SHP656 (BAX826) (Hemophilia A)		SHP652 (SM101) (SLE)	CINRYZE – Japan (HAE Prophylaxis)	Alpha-1 ANTITRYPSIN (Acute GvHD)		XIIDRA – U.S. (Dry eye)
			CINRYZE SC (HAE Prophylaxis)	SHP555 – US (Chronic Constipation)			
			GATTEX – Japan (Adult SBS)	VYVANSE – Japan (ADHD) Ph2/3			
			VONVENDI (VWD)	SHP620 (CMV infection in transplant patients)			
			SHP616 AMR	SHP640 (Infectious Conjunctivitis)			

Rare indication
 Non-rare indication



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

(1) rC1-INH previously being developed as SHP623 for HAE prophylaxis; After Ph1 completion will be developed for NMO; (2) Registrational study;

(3) SHP607 originally developed for ROP; (4) Granted breakthrough designation by FDA; (5) Approved in U.S. for on-demand, prophylaxis in adults and children and in perioperative management. EU in registration for treatment and prophylaxis of bleeding in patients with haemophilia A.

Note: Phase 2/3 programs shown as Phase 3.

Reported regional product sales and pro forma growth analysis

Q1 2017	US	EU	LATAM	APAC ⁽³⁾	Other	Total
Product Sales \$MM ⁽¹⁾	2,285	584	174	195	175	3,412
% of Product Sales	67%	17%	5%	6%	5%	
Pro forma YoY Growth ⁽²⁾	8%	1%	89%	13%	7%	9%



(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).

(2) Growth rates represent Q1 2017 reported sales compared to recast 2016 pro forma sales as previously disclosed by Baxalta following the separation from Baxter.

(3) APAC region includes Japan.

Royalties and other revenues

	Q1 2017 \$MM ⁽¹⁾	Q1 2016 \$MM	Reported Growth
SENSIPAR	39	38	+3%
3TC and ZEFFIX	15	15	-3%
ADDERALL XR	13	6	+116%
FOSRENOL	9	9	-7%
Other Royalties	31	11	+171%
Royalties	105	79	+33%
Other Revenues	8	3	n/m
Contract Manufacturing Revenue⁽²⁾	46	-	n/a
Total Royalties & Other Revenues	160	82	+95%



(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).

(2) Prior to acquisition, Baxalta reported in Bio Therapeutics business unit as net product sales.

Income statement growth analysis

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

(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 (Q1 2017: 62.9%, Q1 2016: 85.5%).

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q1 2017: +83%, Q1 2016: +13%).

(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 (Q1 2017: 10%, Q1 2016: 25%).

(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Effective Tax rate (Q1 2017: 2%, Q1 2016: 17%).

(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Diluted EPS-ADS (Q1 2017: \$1.23, Q1 2016: \$2.12).

(7) See slide 33 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 29 to 32 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Q1 2017 – Reported performance metrics comparison

Ratios: As % of Total Revenue	Q1 2017⁽¹⁾	Q1 2016
Non GAAP gross margin⁽²⁾⁽¹⁰⁾	78.3%	86.7%
Non GAAP R&D⁽³⁾⁽¹⁰⁾	10%	12%
Non GAAP SG&A⁽⁴⁾⁽¹⁰⁾	24%	26%
Non GAAP EBITDA⁽⁵⁾⁽¹⁰⁾	44%	49%

Ratios: As % of Net Product Sales	Q1 2017⁽¹⁾	Q1 2016
Non GAAP gross margin⁽⁶⁾⁽¹⁰⁾	78.7%	86.0%
Non GAAP R&D⁽⁷⁾⁽¹⁰⁾	11%	13%
Non GAAP SG&A⁽⁸⁾⁽¹⁰⁾	25%	27%
Non GAAP EBITDA⁽⁵⁾⁽⁹⁾⁽¹⁰⁾	43%	46%

(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 Gross Margin (Q1 2017: 62.9%, Q1 2016: 85.5%).

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (Q1 2017: 11%, Q1 2016: 13%).

(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (Q1 2017: 25%, Q1 2016: 28%).

(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income Margin (Q1 2017: 10%, Q1 2016: 25%).

(6) Non GAAP Gross Margin as a percentage of product sales, excludes royalties and other revenues and cost of sales related to contract manufacturing revenue. The most directly comparable measure under US GAAP is Gross Margin (Q1 2017: 62.5%, Q1 2016: 84.7%).

(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (Q1 2017: 11%, Q1 2016: 13%).

(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (Q1 2017: 26%, Q1 2016: 29%).

(9) Non GAAP EBITDA as a percentage of product sales, excludes royalties and other revenues and cost of sales related to contract manufacturing revenue.

(10) See slide 33 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 29 to 32 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Q1 2017 – Operating income US GAAP and Non GAAP

	Q1 2017 \$MM ⁽¹⁾	Q1 2016 \$MM	Reported Growth
Non GAAP Operating Income⁽²⁾⁽³⁾ from continuing operations	1,454	797	+82%
Unwind of inventory fair value adjustments	(480)	(13)	
Integration and acquisition costs	(116)	(91)	
Amortization of acquired intangible assets	(364)	(135)	
Gain on sale of product rights	5	4	
Divestments and reorganization costs	(5)	(3)	
Legal and litigation costs	-	(15)	
Other Non GAAP adjustments	4	-	
US GAAP Operating Income from continuing operations	497	544	-9%



(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 (see details above).

(3) See slide 33 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 29 to 32 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	Q1 2017 \$MM ⁽¹⁾	Q1 2016 \$MM	Reported Growth
Net cash provided by operating activities	459	390	+18%
Capital expenditure	(212)	(52)	
Non GAAP free cash flow⁽¹⁾⁽²⁾	247	338	-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 33 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 29 to 32 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 March 31, 2017

(\$MM)	GAAP	Adjustments					Non GAAP
		(a)	(b)	(c)	(d)	(e)	
Total Revenues	3,572.3	-	-	-	-	-	3,572.3
Costs and expenses:							
Cost of product sales	1,327.0	-	(480.4)	-	-	(72.1)	774.5
R&D	379.3	-	-	-	-	(13.4)	365.9
SG&A	888.9	-	-	-	4.0	(37.4)	855.5
Amortization	364.0	(364.0)	-	-	-	-	-
Integration and acquisition costs	116.0	-	(116.0)	-	-	-	-
Reorganization costs	5.5	-	-	(5.5)	-	-	-
Gain on sale of product rights	(5.5)	-	-	5.5	-	-	-
Depreciation	-	-	-	-	-	122.9	122.9
Total operating expenses	3,075.2	(364.0)	(596.4)	-	4.0	-	2,118.8
Operating income	497.1	364.0	596.4	-	(4.0)	-	1,453.5
Total other expense, net	(134.7)	-	1.8	-	-	-	(132.9)
Income from continuing operations before income taxes and equity losses of equity method investees	362.4	364.0	598.2	-	(4.0)	-	1,320.6
Income taxes	(6.8)	(85.3)	(123.9)	(1.8)	0.1	-	(217.7)
Equity in losses of equity method investees, net of taxes	(0.8)	-	-	-	-	-	(0.8)
Income from continuing operations	354.8	278.7	474.3	(1.8)	(3.9)	-	1,102.1
Gain from discontinued operations, net of tax	20.2	-	-	(20.2)	-	-	-
Net income	375.0	278.7	474.3	(22.0)	(3.9)	-	1,102.1
No. of Shares	911.9						911.9
Diluted earnings per ADS	\$1.23	\$0.92	\$1.56	(\$0.07)	(\$0.01)	-	\$3.63

The following items are included in Adjustments:

- (a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired (\$364.0 million), and tax effect of adjustments;
- (b) Acquisition and integration activities: Unwind of inventory fair value adjustments primarily associated with Baxalta (\$480.4 million), integration costs primarily associated with Baxalta (\$119.5 million), net credit related to the change in the fair value of contingent consideration liabilities (\$3.5 million), amortization of one-time upfront borrowing costs for Dyax (\$1.8 million), and tax effect of adjustments;
- (c) Divestments, reorganizations and discontinued operations: Gain on re-measurement of DAYTRANA contingent consideration to fair value (\$5.5 million), reorganization costs primarily relating to the closure of the Basingstoke office (\$5.5 million), tax effect of adjustments and gain from discontinued operations, net of tax (\$20.2 million);
- (d) Other: One-time net credit to pension expense (\$4.0 million), and tax effect of adjustments; and
- (e) Depreciation reclassification: Depreciation of \$122.9 million included in Cost of sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

GAAP to Non GAAP reconciliation

For the three months ended March 31, 2016

(\$MM)	GAAP	Adjustments					Non GAAP
		(a)	(b)	(c)	(d)	(e)	
Total Revenues	1,709.3	-	-	-	-	-	1,709.3
Costs and expenses:							
Cost of product sales	248.6	-	(12.8)	-	-	(8.3)	227.5
R&D	217.1	-	-	-	-	(5.9)	211.2
SG&A	474.9	-	-	-	(15.0)	(20.1)	439.8
Amortization	134.6	(134.6)	-	-	-	-	-
Integration and acquisition costs	91.1	-	(91.1)	-	-	-	-
Reorganization costs	3.3	-	-	(3.3)	-	-	-
Gain on sale of product rights	(4.2)	-	-	4.2	-	-	-
Depreciation	-	-	-	-	-	34.3	34.3
Total operating expenses	1,165.4	(134.6)	(103.9)	0.9	(15.0)	-	912.8
Operating income	543.9	134.6	103.9	(0.9)	15.0	-	796.5
Total other expense, net	(52.2)	-	18.2	6.0	-	-	(28.0)
Income from continuing operations before income taxes and equity losses of equity method investees	491.7	134.6	122.1	5.1	15.0	-	768.5
Income taxes	(82.1)	(39.6)	(8.4)	(1.0)	(5.5)	-	(136.6)
Equity in losses of equity method investees, net of taxes	(0.1)	-	-	-	-	-	(0.1)
Income from continuing operations	409.5	95.0	113.7	4.1	9.5	-	631.8
Gain from discontinued operations, net of tax	9.5	-	-	(9.5)	-	-	-
Net income	419.0	95.0	113.7	(5.4)	9.5	-	631.8
No. of Shares	593.3	-	-	-	-	-	593.3
Diluted earnings per ADS	\$2.12	\$0.48	\$0.57	(\$0.03)	\$0.05	-	\$3.19

The following items are included in Adjustments:

- (a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired (\$134.6 million), and tax effect of adjustments;
- (b) Acquisition and integration activities: Unwind of inventory fair value adjustments primarily related to NPS and Dyax (\$12.8 million), acquisition and integration costs primarily associated with NPS, Dyax and Baxalta (\$79.7 million), charges related to the change in fair value of contingent consideration liabilities (\$11.4 million), amortization of one-time borrowing costs for Baxalta and Dyax (\$18.2 million), and tax effect of adjustments;
- (c) Divestments, reorganizations and discontinued operations: Gain on re-measurement of DAYTRANA contingent consideration to fair value (\$4.2 million), costs relating to the One Shire reorganization, primarily costs relating to the relocation of staff from Chesterbrook to Lexington (\$3.3 million), loss on divestment of non-core subsidiary (\$6.0 million), tax effect of adjustments, and gain from discontinued operations, net of tax (\$9.5 million);
- (d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs (\$15.0 million), and tax effect of adjustments; and
- (e) Depreciation reclassification: Depreciation of \$34.3 million included in Cost of 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; Combined Non GAAP R&D and 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 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
- Non-controlling 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.

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 March 31, 2017 were \$1.24:£1.00 and \$1.06:€1.00 (2016: \$1.43:£1.00 and \$1.09:€1.00).

See slides 29 to 32 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.