Press Release

Shire reports Q3 2016 results with record revenues and reiterates full year Non GAAP guidance

Very strong U.S. launch for XIIDRA; marks outstanding entry into ophthalmics

Baxalta integration progressing well with synergy initiatives ahead of plan

November 1, 2016 – Shire plc (Shire) (LSE: SHP, NASDAQ: SHPG) announces unaudited results for the three months ended September 30, 2016.

Financial Highlights	**Q3 2016[1]**	**Growth[1]**	**Non GAAP CER[1][2]**
Product sales	$3,315 million	+110%	+111%
Product sales excluding Baxalta products	$1,769 million	+12%	+13%
Total revenues	$3,452 million	+109%	+109%
US GAAP operating loss from continuing operations	($406 million)	(189%)	
Non GAAP operating income[2]	$1,254 million	+73%	+71%
US GAAP net income margin[3][4]	(11%)	(38ppc)	
Non GAAP EBITDA margin[2][4]	38%	(5ppc)	
US GAAP net loss	($387 million)	(185%)	
Non GAAP net income[2]	$962 million	+50%	
US GAAP diluted losses per ADS	($1.29)	(156%)	
Non GAAP diluted earnings per ADS[2]	$3.17	(2%)	(3%)
US GAAP net cash provided by operating activities	$526 million	(6%)	
Non GAAP cash generation[2]	$830 million	+41%	
Non GAAP free cash flow[2]	$395 million	(27%)	

[1] Results include Baxalta Inc. (Baxalta) (acquired on June 3, 2016) and Dyax Corp. (Dyax) (acquired on January 22, 2016), unless otherwise noted. Percentages compare to equivalent 2015 period. [2] The Non GAAP financial measures included within this release are explained on pages 27 – 28, and are reconciled to the most directly comparable financial measures prepared in accordance with US GAAP on pages 21 – 23. [3] US GAAP net income as a percentage of total revenues. [4] Percentage point change (ppc).

Financial highlights

- Very strong launch results for XIIDRA; 64,732 scripts written through October 21, with a market share of 16%.
- Product sales growth of 110% in Q3 2016 to $3.3 billion, driven by record legacy Shire product sales and the inclusion of legacy Baxalta franchises.
- Underlying growth in Q3 2016 hematology and immunology businesses largely in line with overall market trends; pro forma sales growth of legacy Baxalta products impacted by the timing of large orders.
- Q3 2016 year to date growth for legacy Shire product sales was 15% (16% on a Non GAAP CER basis) and legacy Baxalta was 7% on a pro forma basis (8% on a Non GAAP CER pro forma basis), in line with our expectations.

Baxalta integration

- Operating expense synergy initiatives ahead of schedule, including manufacturing footprint optimization review.
- Sharp focus on transitioning legacy Baxalta products onto Shire's commercial platform and operating execution.
- Issued $12.1 billion aggregate principal debt at a weighted average interest rate of 2.6%; net proceeds used to fully repay bridge facility for financing Baxalta transaction.

Pipeline progress

- Pipeline continuing to deliver with U.S. Food and Drug Administration (FDA) approval of CUVITRU, and European Commission (EC) Marketing Authorization for ONIVYDE accompanied by Orphan Drug Designation.
- Fully enrolled Phase 3 study for SHP643 in prophylaxis of hereditary angioedema with results expected in the first half of 2017.
- FDA resubmission of SHP465 for the treatment of ADHD on track to be made in Q4 2016.

Flemming Ornskov, M.D., M.P.H., Shire Chief Executive Officer, commented:

“During the third quarter, we made rapid progress integrating our new company while delivering record quarterly product sales growth and remaining on track to meet our full year Non GAAP guidance. The launch of XIIDRA is off to a very strong start, and we are using this momentum to build a leadership position in pharmaceutical ophthalmics. Commercial execution remains a top priority across the business. Also, our robust pipeline is continuing to advance, and we look forward to highlighting key programs during our upcoming Investor Day. The changes we are applying to the legacy Baxalta business are similar to the One Shire initiative we undertook in 2013-2014, which set off a period of strong growth and profitability. I am highly confident about Shire’s future growth prospects.”

FINANCIAL SUMMARY - THIRD QUARTER 2016

Revenues

- Total product sales increased 110% versus Q3 2015 (up 111% on a Non GAAP CER basis) to $3,315 million (Q3 2015: $1,577 million), primarily due to the inclusion of $1,546 million of legacy Baxalta sales.
- Excluding Baxalta, product sales increased 12% (13% on a Non GAAP CER basis) with all legacy Shire franchises exhibiting growth in Q3 2016, with Neuroscience up 15%, Genetic Diseases up 5% and Internal Medicine up 15% compared with Q3 2015. Following the launch of XIIDRA in August 2016, our Ophthalmology franchise contributed sales of $14 million.
- Royalties and other revenues increased 75% to $137 million, as Q3 2016 benefited from additional revenue acquired with Baxalta, primarily related to contract manufacturing activities.

Operating results

- Research and Development (R&D) expenses increased by 112% compared with Q3 2015, primarily due to the inclusion of Baxalta and Dyax operating costs, and costs related to licensing SHP647. Non GAAP R&D increased by 68% in Q3 2016 primarily due to the inclusion of Baxalta and Dyax operating costs.
- Selling, General and Administrative (SG&A) expenses increased by 98% compared with Q3 2015, primarily due to the inclusion of Baxalta operating costs and XIIDRA launch costs. Non GAAP SG&A increased by 103% in Q3 2016.
- On a US GAAP basis, the operating loss was $406 million in Q3 2016 (Q3 2015: operating income of $456 million). The operating loss in Q3 2016 was primarily due to the impact of acquisition accounting, including higher amortization of inventory fair value step up and amortization of acquired intangible assets, combined with higher integration and acquisition costs. Non GAAP operating income increased 73% to $1,254 million (Q3 2015: $725 million), primarily due to the inclusion of a full quarter of Baxalta operating income and higher revenue from legacy Shire products.
- Non GAAP EBITDA margin (excluding royalties and other revenue, and cost of sales related to contract manufacturing revenues) was 38% (Q3 2015: 43%). The decrease was primarily due to the impact of a full quarter of lower margin product franchises acquired with Baxalta and XIIDRA launch costs.

Earnings per share (EPS)

- On a US GAAP basis, diluted losses per American Depositary Shares (ADS) were $1.29 (Q3 2015: earnings per ADS of $2.29). The Q3 2016 loss was primarily due to lower US GAAP operating income resulting from the impact of acquisition accounting, including higher amortization of inventory fair value step up and amortization of acquired intangible assets, combined with higher integration and acquisition costs, all primarily related to the Baxalta transaction.
- Non GAAP diluted earnings per ADS decreased 2% to $3.17 (Q3 2015: $3.24), as higher Non GAAP operating income was more than offset by the additional shares issued as consideration for the Baxalta transaction.

Cash flows

- On a US GAAP basis, net cash provided by operating activities decreased 6% to $526 million (Q3 2015: $561 million), primarily due to a payment associated with the termination of a biosimilar collaboration acquired with Baxalta, an increase in costs related to the Baxalta integration and higher tax and interest payments, partially offset by strong cash receipts from higher sales.
- Non GAAP cash generation increased 41% to $830 million (Q3 2015: $588 million), primarily due to strong cash receipts from higher sales, partially offset by a payment associated with the termination of a biosimilar collaboration acquired with Baxalta and an increase in costs related to the Baxalta integration.
- Non GAAP free cash flow decreased 27% to $395 million (Q3 2015: $539 million), primarily due to the decrease in net cash provided by operating activities described above combined with an increase in capital expenditures of $199 million in support of manufacturing operations.

Debt

- Non GAAP net debt at September 30, 2016 was $23,346 million (December 31, 2015: $1,459 million) representing aggregate long and short term borrowings of $23,726 million, primarily used to fund the acquisitions of Baxalta and Dyax and other debt primarily related to capital leases of $349 million, partially offset by cash and cash equivalents of $729 million.

OUTLOOK

After our first full quarter following the acquisition of Baxalta, we are reiterating our non-GAAP guidance from Q2 2016 and updating our US GAAP guidance.

The full year 2016 guidance includes the legacy Baxalta business as of June 3, 2016. The guidance includes expected operating cost synergy savings for 2016 based on our target of at least $700 million in year three post close.

The Non GAAP diluted earnings per ADS forecast assumes a weighted average number of 778 million fully diluted ordinary shares outstanding for 2016 following the equity issuance for the Baxalta transaction.

Our US GAAP diluted earnings per ADS outlook has been updated to reflect an increase in integration costs related to the Baxalta transaction, costs related to licensing SHP647 and reorganization costs associated with the planned closure of a facility in our Los Angeles manufacturing site.

Full Year 2016	**US GAAP Outlook**	**Non GAAP Outlook[1]**
Total product sales	$10.8 - $11 billion	$10.8 - $11 billion
Royalties & other revenues	$490 - $530 million	$490 - $530 million
Gross margin	58% - 60%	77% - 79%
Combined R&D and SG&A	$4.3 - $4.7 billion	$4.1 - $4.4 billion
Net interest/other	$500 - $550 million	$400 - $450 million
Effective tax rate[2]	92% - 136%	16% - 18%
Diluted earnings per ADS[3]	($1.10) - ($0.70)	$12.70 - $13.10

[1] For a list of items excluded from Non GAAP Outlook, refer to pages 27-28 of this release.
[2] For 2016, we expect our effective tax benefit rate on GAAP pre-tax losses from operations to be in the range of 92% - 136%. The GAAP effective tax rate for 2016 is highly sensitive to the relative quantum of profit or loss before tax, leading to the wide range of the expected GAAP effective tax rate.
[3] See page 23 for a reconciliation between US GAAP diluted earnings per ADS and Non GAAP diluted earnings per ADS.

RECENT DEVELOPMENTS

Financing

Senior notes issuance

- On September 23, 2016, Shire issued $12.1 billion aggregate principal amount of senior notes, consisting of four series:
    - $3.3 billion 1.900% Senior Notes due 2019;
    - $3.3 billion 2.400% Senior Notes due 2021;
    - $2.5 billion 2.875% Senior Notes due 2023; and
    - $3.0 billion 3.200% Senior Notes due 2026

- Shire used the net proceeds to fully repay amounts outstanding under its January 2016 bridge facility agreement, which were used to finance its acquisition of Baxalta and for general corporate purposes.

Business Development

Pacritinib for the treatment of myelofibrosis

- On October 21, 2016, Shire and CTI BioPharma Corp. (CTI) entered into an Asset Return and Termination Agreement pursuant to which the license arrangement between the parties was terminated in its entirety and all rights relating to pacritnib were returned to CTI.

Biosimilars (etanercept and adalimumab)

- Shire has terminated its relationship with SFJ Pharmaceuticals, Inc. and its biosimilar collaboration with Coherus BioSciences, Inc. Additionally, Shire has delivered notice of exercise of its right to terminate its biosimilar collaboration with Momenta Pharmaceuticals, Inc. and such termination will be effective upon expiration of the applicable termination notice period. These collaborations were acquired through the Baxalta acquisition.

Products

ONIVYDE for the treatment of pancreatic cancer

- On October 18, 2016, Shire announced that the EC granted Marketing Authorization to ONIVYDE (pegylated liposomal irinotecan hydrochloride trihydrate), for the treatment of metastatic adenocarcinoma of the pancreas, in combination with 5-fluorouracil and leucovorin, in adult patients who have progressed following gemcitabine-based therapy. This approval is accompanied by an Orphan Drug Designation for ONIVYDE.

VYVANSE for the treatment of moderate to severe binge eating disorder (BED)

- On September 30, 2016, Health Canada approved VYVANSE for the treatment of BED in adults. The launch is on track for Q4 2016.

- On October 17, 2016, Shire announced the approval of a supplemental NDA by the FDA. The VYVANSE label will include the new longer-term maintenance of efficacy data in adults with moderate to severe BED.

LIALDA for the treatment of ulcerative colitis

- On September 28, 2016, Mochida Pharmaceutical Co., Ltd announced that the Japanese Ministry of Health, Labour and Welfare approved LIALDA 1200mg for the treatment of adults with ulcerative colitis.

CUVITRU for the treatment of primary immunodeficiency disorders

- On September 14, 2016, Shire announced that the FDA granted approval for CUVITRU [Immune Globulin Subcutaneous (Human), 20% Solution] in adult and pediatric patients two years of age and older.

XIIDRA for the treatment of dry eye disease

- On August 29, 2016, Shire announced that XIIDRA (lifitegrast ophthalmic solution) 5%, a twice-daily prescription eye drop indicated for the treatment of both the signs and symptoms of dry eye disease, became available by prescription in the U.S. The FDA approved XIIDRA on July 11, 2016.

- On October 28, 2016, a New Drug Submission (NDS) was filed with Health Canada for lifitegrast ophthalmic solution 5%. This submission marks the first step towards Shire's international expansion activities for lifitegrast.

VONVENDI for the treatment of adults affected by von Willebrand disease (VWD)

- On August 9, 2016, Shire announced the U.S. launch of VONVENDI [von Willebrand factor (Recombinant)], the only recombinant treatment for adults living with VWD.

Pipeline

SHP610 for the treatment of Sanfilippo Syndrome type A (MPS-IIIA) (Sanfilippo A)

- The Phase 2b study of SHP610 in pediatric patients with early stage Sanfilippo A did not meet its primary endpoint of slowing the cognitive decline in patients. Shire intends to terminate all clinical trials of SHP610 and plans to publish the results of the SHP610 program for the benefit of the Sanfilippo community.

SHP643 for the treatment of Hereditary Angioedema

- The pivotal Phase 3 study completed enrollment in September 2016 with 125 patients enrolled. The topline data readout is expected in Q2 2017.

SHP609 for the treatment of Hunter Syndrome

- The pivotal Phase 3 study completed enrollment in September 2016 with 49 patients enrolled. The topline data readout is expected in Q4 2017.

Legal Proceedings

Patent Trial and Appeal Board issues decision regarding GATTEX patent

- On October 21, 2016, the U.S. Patent & Trademark Office's Patent Trial and Appeal Board (PATB) issued a decision holding certain claims of U.S. Patent 7,056,886 (the '886 patent) invalid, following an inter partes review (IPR) challenge by the Coalition for Affordable Drugs II L.L.C. (CFAD). Shire is currently reviewing the decision and will decide whether to appeal. The PTAB had earlier declined to review certain claims of the '886 patent that had been challenged by CFAD. Claims of the FDA Orange Book-listed '886 patent that were not reviewed in the IPR proceedings remain in force. In addition, GATTEX has orphan drug exclusivity until December 2019, and is also protected by Orange Book-listed patents expiring in 2020 and 2025.

Patent Trial and Appeal Board upholds the validity of LIALDA patent

- On October 5, 2016, Shire announced that the PTAB issued a decision upholding the validity of U.S. Patent No. 6,773,720, related to LIALDA.

District Court issues ruling in Hatch Waxman Case regarding LIALDA

- On September 16, 2016, the U.S. District Court for the District of Delaware ruled that Cadilla Healthcare Ltd./ Zydus Pharmaceuticals (USA) Inc.'s (Zydus) proposed generic version of LIALDA does not infringe U.S Patent No. 6,773,720 (the '720 patent). Shire has appealed this ruling to the Court of Appeals of the Federal Circuit. Shire believes that the proposed Zydus product infringes the '720 patent and will continue to vigorously defend its intellectual property rights.

ADDITIONAL INFORMATION

The following additional information is included in this press release:

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Dial in details for the **live conference call** for investors at 14:00 GMT / 10:00 EDT on November 1, 2016:

UK dial in:	0808 237 0030 or 020 3139 4830
US dial in:	1 866 928 7517 or 1 718 873 9077
International Access Numbers:	Click here
Password/Conf ID:	42020034#
Live Webcast:	Click here

The quarterly earnings presentation will be available today at 13:00 GMT / 09:00 EDT on:

- Shire.com Investors section

- Shire's IR Briefcase in the iTunes Store

OVERVIEW OF THIRD QUARTER 2016 FINANCIAL RESULTS

1. Product Sales

For the three months ended Q3 2016, product sales increased 110% to $3,315 million (Q3 2015: $1,577 million), primarily due to the Baxalta transaction. Excluding legacy Baxalta, product sales increased 12% (up 13% on a Non GAAP CER basis).

(in millions) **Product sales**	U.S. Sales	International Sales	**Total Sales**	Total Sales Year on year growth Reported	 Non GAAP CER
HEMOPHILIA	$ 354.8	$ 347.6	**$ 702.4**	N/A	N/A
INHIBITOR THERAPIES	73.3	108.4	**181.7**	N/A	N/A
Hematology total	**428.1**	**456.0**	**884.1**	N/A	N/A
CINRYZE	151.6	13.8	**165.4**	-12%	-12%
ELAPRASE	38.0	108.7	**146.7**	+9%	+11%
FIRAZYR	129.1	17.2	**146.3**	+19%	+19%
REPLAGAL	—	118.9	**118.9**	+7%	+7%
VPRIV	39.8	47.9	**87.7**	+3%	+4%
KALBITOR	11.1	—	**11.1**	N/A	N/A
Genetic Diseases total	**369.6**	**306.5**	**676.1**	+5%	+6%
VYVANSE	467.7	44.9	**512.6**	+20%	+20%
ADDERALL XR	75.3	5.2	**80.5**	+3%	+3%
Other Neuroscience	3.4	20.0	**23.4**	-21%	-18%
Neuroscience total	**546.4**	**70.1**	**616.5**	+15%	+16%
IMMUNOGLOBULIN THERAPIES	381.2	91.3	**472.5**	N/A	N/A
BIO THERAPEUTICS	71.6	62.4	**134.0**	N/A	N/A
Immunology total	**452.8**	**153.7**	**606.5**	N/A	N/A
LIALDA/MEZAVANT	188.4	20.2	**208.6**	+18%	+18%
PENTASA	85.4	—	**85.4**	-3%	-3%
GATTEX/REVESTIVE	49.5	8.6	**58.1**	+35%	+36%
NATPARA	23.3	—	**23.3**	+238%	+238%
Other Internal Medicine	35.0	52.3	**87.3**	+0%	+1%
Internal Medicine total	**381.6**	**81.1**	**462.7**	+15%	+16%
Oncology total	**44.9**	**10.5**	**55.4**	N/A	N/A
Ophthalmology total	**14.1**	**—**	**14.1**	N/A	N/A
Total product sales	**$ 2,237.5**	**$ 1,077.9**	**$ 3,315.4**	+110%	+111%

Hematology
The Hematology franchise was acquired with Baxalta in June 2016 and includes sales of recombinant and plasma-derived hemophilia products (primarily factor VIII and factor IX) and inhibitor therapies. Reported product sales in Q3 2016 were $884 million and represent 56 percentage points of Shire's reported product sales growth. Underlying pro forma Q3 2016 growth in Hematology was largely in line with market trends, but was impacted by the timing or large orders.

Genetic Diseases
Genetic Diseases product sales in Q3 2016 increased 5% (up 6% on a Non GAAP CER basis) compared with Q3 2015, led by strong patient growth in FIRAZYR and across our LSD portfolio.

FIRAZYR sales increased 19% in Q3 2016 compared with Q3 2015 due to an increase in the number of patients on therapy in both U.S. and international markets. The growth was held back by lower utilization per patient. CINRYZE sales decreased by 12% in Q3 2016 compared with Q3 2015, as an increase in the number of patients on therapy was more than offset by destocking and reduced utilization as a result of a U.S. supply constraint. Shire has taken steps to increase CINRYZE production and expects to return to normalized supply by early 2017.

Neuroscience
Neuroscience product sales increased 15% (up 16% on a Non GAAP CER basis) in Q3 2016 compared with Q3 2015 with growth primarily driven by VYVANSE.

VYVANSE sales increased 20% due to year-over-year prescription growth in the U.S., the benefit of a price increase taken since Q3 2015 and, to a lesser extent, increased stocking in Q3 2016 and growth in our international markets.

Immunology
The Immunology franchise was acquired with Baxalta in June 2016 and includes sales of antibody-replacement immunoglobulin and bio therapeutics therapies. Reported product sales in Q3 2016 were $607 million and represent 38 percentage points of Shire's reported product sales growth. Underlying pro forma Q3 2016 growth in Immunology was largely in line with market trends, but was impacted by the timing or large orders, particularly our Bio Therapeutics portfolio.

Internal Medicine
Internal Medicine product sales increased 15% (up 16% on a Non GAAP CER basis) in Q3 2016, with strong growth from LIALDA/MEZAVANT, GATTEX/REVESTIVE and NATPARA.

LIALDA/MEZAVANT sales increased 18% due to an increase in prescription demand, resulting in a market share of 40% at the end of Q3 2016 and the impact of a price increase taken since Q3 2015.

GATTEX/REVESTIVE and NATPARA continued to perform well with sales increasing 35% and 238%, respectively, primarily due to an increase in the numbers of patients on therapy.

Oncology
The Oncology franchise was acquired with Baxalta in June 2016 and includes sales of ONCASPAR. Reported sales in Q3 2016 were $55 million and represent 4 percentage points of Shire's reported product sales growth.

Ophthalmology
Product sales relate to XIIDRA, which was made available to patients on August 29, 2016. XIIDRA contributed $14 million of product sales in Q3 2016, primarily due to initial launch stocking.

Baxalta pro forma product sales growth
The following table presents Q3 2016 reported legacy Baxalta product sales compared with recast Q3 2015 pro forma sales as previously reported by Baxalta following the separation from Baxter.

(in millions)				Pro forma Year on year growth	
Reported product sales	U.S. Sales	International Sales	**Total Sales**	Reported	Non GAAP CER
HEMOPHILIA	$ 354.8	$ 347.6	**$ 702.4**	-5%	-5%
INHIBITOR THERAPIES	73.3	108.4	**181.7**	-13%	-13%
Hematology total	**428.1**	**456.0**	**884.1**	-6%	-6%
IMMUNOGLOBULIN THERAPIES	381.2	91.3	**472.5**	+8%	+9%
BIO THERAPEUTICS	71.6	62.4	**134.0**	-6%	-5%
Immunology total	**452.8**	**153.7**	**606.5**	+5%	+5%
Oncology total	**44.9**	**10.5**	**55.4**	+64%	+64%
Total	**$ 925.8**	**$ 620.2**	**$ 1,546.0**	-1%	-1%

2. Royalties and other revenues

(in millions)	Revenue	Year on year growth Reported	Year on year growth Non GAAP CER
SENSIPAR Royalties	**$ 38.7**	+11%	+11%
3TC and ZEFFIX Royalties	**16.2**	+36%	+36%
FOSRENOL Royalties	**13.7**	+4%	-12%
ADDERALL XR Royalties	**4.7**	-34%	-33%
Other Royalties and Revenues	**63.4**	+466%	+462%
Total Royalties and Other Revenues	**$ 136.7**	+75%	+72%

Royalties and Other Revenues increased 75% in Q3 2016 compared with Q3 2015, primarily due to $39 million of contract manufacturing revenue acquired with Baxalta.

3. Financial Details

Cost of sales

(in millions)	Q3 2016	% of product sales	Q3 2015	% of product sales
Cost of sales (US GAAP)	**$ 1,736.2**		$ 262.7	
Cost of contract manufacturing revenue	**(44.2)**		**—**	
Cost of product sales	**1,692.0**	**51%**	262.7	17%
Amortization of inventory fair value step-up	**(803.8)**		(6.7)	
Inventory write-down relating to the planned closure of a facility at the Los Angeles manufacturing site	**(11.6)**		—	
Costs of employee retention awards following AbbVie Inc.'s (AbbVie) terminated offer	**—**		(1.0)	
Depreciation	**(54.5)**		(9.6)	
Non GAAP cost of product sales	**$ 822.1**	**25%**	$ 245.4	16%

US GAAP cost of product sales as a percentage of product sales increased in Q3 2016, primarily due to the impact of higher amortization of inventory fair value step-ups in 2016 following the acquisitions of Baxalta and Dyax and, to a lesser extent, the impact of lower margin product franchises acquired with Baxalta.

Non GAAP cost of product sales as a percentage of product sales increased to 25% in Q3 2016, primarily due to the impact of lower margin product franchises acquired with Baxalta.

R&D

(in millions)	Q3 2016	% of product sales	Q3 2015	% of product sales
R&D (US GAAP)	**$ 511.1**	**15%**	$ 241.2	15%
Costs relating to license arrangements	**(110.0)**		—	
Costs of employee retention awards following AbbVie's terminated offer	**—**		(2.0)	
Depreciation	**(9.0)**		(5.5)	
Non GAAP R&D	**$ 392.1**	**12%**	$ 233.7	15%

US GAAP R&D increased by $270 million, or 112%, primarily due to the inclusion of Baxalta and Dyax costs, and costs related to licensing SHP647.

Non GAAP R&D increased by $158 million, or 68%, in Q3 2016 primarily due to the inclusion of Baxalta and Dyax costs. Non GAAP R&D expense as a percentage of product sales decreased 3 percentage points.

SG&A

(in millions)	Q3 2016	% of product sales	Q3 2015	% of product sales
SG&A (US GAAP)[1]	**$ 875.6**	**26%**	$ 442.3	28%
Legal and litigation costs	**0.5**		(1.7)	
Costs incurred in connection with AbbVie's terminated offer	**—**		(5.0)	
Depreciation	**(29.6)**		(17.8)	
Non GAAP SG&A	**$ 846.5**	**26%**	$ 417.8	26%

US GAAP SG&A increased by $433 million, or 98%, primarily due to the inclusion of Baxalta related costs and XIIDRA launch costs.

Non GAAP SG&A increased by $429 million, or 103%, compared with Q3 2015. Q3 2016 Non GAAP SG&A as a percentage of product sales remained consistent with Q3 2015 at 26%.

[1] Reported SG&A for periods prior to Q3 2016 have been recast to exclude amortization of acquired intangible assets, which is now presented as a separate line item in the Unaudited Consolidated Statements of Operations.

Integration and acquisition costs

In Q3 2016, Shire recorded integration and acquisition costs of $285 million, primarily related to the Baxalta and Dyax transactions.

In Q3 2015, Shire recorded integration and acquisition costs of $90 million, which included costs related to the integration of NPS and the proposed combination with Baxalta of $31 million. Additionally there was a net charge of $59 million for the change in fair value of contingent consideration liabilities, primarily related to SHP625 (acquired with Lumena).

Amortization of acquired intangible assets

In Q3 2016, Shire recorded amortization of acquired intangible assets of $355 million (Q3 2015: $133 million). The increase primarily related to amortization on the intangible assets acquired with the Baxalta and Dyax transactions.

Reorganization costs

In Q3 2016, Shire recorded reorganization costs of $101 million, primarily related to the planned closure of a facility at the Los Angeles manufacturing site.

In Q3 2015, Shire recorded reorganization costs of $31 million, primarily related to the relocation of roles from Pennsylvania to Massachusetts.

Other expense, net

(in millions)	Q3 2016	Q3 2015
Other expense, net (US GAAP)	**$ (191.3)**	$ (0.3)
Amortization of one-time upfront borrowing costs for Baxalta and Dyax	**47.4**	—
Gain on sale of long term investments	**—**	(10.4)
Non GAAP Other expense, net	**$ (143.9)**	$ (10.7)

US GAAP Other expense, net increased $191 million, primarily due to higher interest expense and amortization of one-time borrowing costs incurred on borrowings, including the write off of certain financing costs related to the bridge facility for the Baxalta transaction. During Q3 2016, the bridge facility was fully repaid with the proceeds from the $12.1 billion public debt offering.

Non GAAP Other expense, net increased $133 million, primarily due to higher interest expense as noted above.

Taxation

(in millions)	Q3 2016	Effective tax rate	Q3 2015	Effective tax rate
Income tax benefit (US GAAP)	**$ 229.6**	**38%**	$ 22.3	(5%)
Tax effect of adjustments	**(377.3)**		(94.4)	
Non GAAP Income tax charge	**$ (147.7)**	**13%**	$ (72.1)	10%

The effective tax rate on US GAAP income in Q3 2016 was 38% (Q3 2015: -5%) and on a Non GAAP basis was 13% (Q3 2015: 10%).

The effective tax rate in Q3 2016 on US GAAP income from continuing operations is higher primarily due to the combined impact of the relative quantum of the profit before tax for the period by jurisdiction and the reversal of deferred tax liabilities from the Baxalta acquisition (including in higher tax territories), inventory and intangible asset amortization, as well as acquisition and integration costs.

The Q3 2015 GAAP tax rate was negative primarily due to the release of certain valuation allowances and the effect of the finalization of various tax returns during the period.

The Q3 2016 Non GAAP tax rate is higher than the same period in 2015, primarily due to relatively higher discrete benefits in Q3 2015 compared with Q3 2016 in relation to the release of certain valuation allowances and the effect of the finalization of various tax returns.

Discontinued operations

The loss from discontinued operations in Q3 2016 was $18 million, net of tax, primarily due to legal contingencies related to the divested DERMAGRAFT business. The loss in Q3 2015 was $24 million, net of tax, primarily related to a change in estimate for onerous lease provisions.

FINANCIAL INFORMATION

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Unaudited US GAAP Consolidated Balance Sheets
(in millions, except par value of shares)

	September 30, 2016	December 31, 2015
ASSETS		
Current assets:		
Cash and cash equivalents	**$ 728.6**	$ 135.5
Restricted cash	**20.1**	86.0
Accounts receivable, net	**2,633.4**	1,201.2
Inventories	**4,857.1**	635.4
Prepaid expenses and other current assets	**665.3**	197.4
Total current assets	**8,904.5**	2,255.5
Non-current assets:		
Investments	**191.8**	50.8
Property, plant and equipment (PP&E), net	**6,527.7**	828.1
Goodwill	**14,850.6**	4,147.8
Other intangible assets, net	**38,871.5**	9,173.3
Deferred tax asset	**109.0**	121.0
Other non-current assets	**296.2**	33.3
Total assets	**$ 69,751.3**	$ 16,609.8
LIABILITIES AND EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	**$ 4,021.7**	$ 2,050.6
Short term borrowings	**2,737.1**	1,511.5
Other current liabilities	**352.1**	144.0
Total current liabilities	**7,110.9**	3,706.1
Non-current liabilities:		
Long term borrowings	**20,988.9**	69.9
Deferred tax liability	**9,326.5**	2,205.9
Other non-current liabilities	**2,539.3**	798.8
Total liabilities	**39,965.6**	6,780.7
Equity:		
Common stock of 5p par value; 1,000 shares authorized; and 910.9 shares issued and outstanding (2015: 1,000 shares authorized; and 601.1 shares issued and outstanding)	**81.3**	58.9
Additional paid-in capital	**24,631.3**	4,486.3
Treasury stock: 9.1 shares (2015: 9.7 shares)	**(302.2)**	(320.6)
Accumulated other comprehensive loss	**(134.2)**	(183.8)
Retained earnings	**5,509.5**	5,788.3
Total equity	**29,785.7**	9,829.1
Total liabilities and equity	**$ 69,751.3**	$ 16,609.8

Unaudited US GAAP Consolidated Statements of Operations
(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
Revenues:				
Product sales	**$ 3,315.4**	$ 1,576.8	**$ 7,264.8**	$ 4,476.2
Royalties & other revenues	**136.7**	78.2	**325.7**	224.8
Total revenues	**3,452.1**	1,655.0	**7,590.5**	4,701.0
Costs and expenses:				
Cost of sales	**1,736.2**	262.7	**2,762.9**	718.5
Research and development	**511.1**	241.2	**1,023.0**	1,210.8
Selling, general and administrative[(1)]	**875.6**	442.3	**2,025.8**	1,356.6
Amortization of acquired intangible assets	**354.9**	132.7	**702.5**	352.3
Integration and acquisition costs	**284.5**	89.9	**738.6**	(46.8)
Reorganization costs	**101.4**	31.1	**115.7**	59.6
Gain on sale of product rights	**(5.7)**	(0.7)	**(12.2)**	(13.0)
Total operating expenses	**3,858.0**	1,199.2	**7,356.3**	3,638.0
Operating (loss)/income from continuing operations	**(405.9)**	455.8	**234.2**	1,063.0
Interest income	**9.3**	0.8	**11.9**	3.4
Interest expense	**(186.9)**	(10.7)	**(318.8)**	(31.6)
Other (expense)/income, net	**(13.7)**	9.6	**(16.2)**	11.9
Total other expense, net	**(191.3)**	(0.3)	**(323.1)**	(16.3)
(Loss)/income from continuing operations before income taxes and equity in losses of equity method investees	**(597.2)**	455.5	**(88.9)**	1,046.7
Income taxes	**229.6**	22.3	**218.4**	9.0
Equity in losses of equity method investees, net of taxes	**(0.9)**	(0.7)	**(1.9)**	(1.6)
(Loss)/income from continuing operations, net of taxes	**(368.5)**	477.1	**127.6**	1,054.1
Loss from discontinued operations, net of taxes	**(18.3)**	(24.3)	**(257.5)**	(31.3)
Net (loss)/income	**$ (386.8)**	$ 452.8	**$ (129.9)**	$ 1,022.8

[(1)] Reported SG&A for periods prior to September 30, 2016 have been recast to exclude amortization of acquired intangible assets, which is now presented as a separate line item.

Unaudited US GAAP Consolidated Statements of Operations (continued)
(in millions, except per share amounts)

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
(Loss)/earnings per Ordinary Share – basic				
(Loss)/earnings from continuing operations	**$ (0.41)**	$ 0.81	**$ 0.18**	$ 1.79
Loss from discontinued operations	**(0.02)**	(0.04)	**(0.36)**	(0.06)
(Loss)/earnings per Ordinary Share – basic	**$ (0.43)**	$ 0.77	**$ (0.18)**	$ 1.73
(Loss)/earnings per ADS – basic	**$ (1.29)**	$ 2.30	**$ (0.54)**	$ 5.20
(Loss)/earnings per Ordinary Share – diluted				
(Loss)/earnings from continuing operations	**$ (0.41)**	$ 0.80	**$ 0.18**	$ 1.78
Loss from discontinued operations	**(0.02)**	(0.04)	**(0.36)**	(0.06)
(Loss)/earnings per Ordinary Share – diluted	**$ (0.43)**	$ 0.76	**$ (0.18)**	$ 1.72
(Loss)/earnings per ADS – diluted	**$ (1.29)**	$ 2.29	**$ (0.54)**	$ 5.17
Weighted average number of shares:				
Basic	**900.2**	590.9	**725.5**	590.2
Diluted	**900.2**	593.4	**725.5**	593.2

Unaudited US GAAP Consolidated Statements of Cash Flows
(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
CASH FLOWS FROM OPERATING ACTIVITIES:				
Net (loss)/income	**$ (386.8)**	$ 452.8	**$ (129.9)**	$ 1,022.8
Adjustments to reconcile net (loss)/income to net cash provided by operating activities:				
Depreciation and amortization	**448.0**	165.6	**877.8**	457.4
Share based compensation	**74.8**	26.5	**269.6**	70.8
Amortization of deferred financing fees	**71.6**	3.6	**121.7**	8.0
Amortization of inventory fair value step-up	**803.8**	6.7	**1,097.3**	23.0
Change in deferred taxes	**(217.7)**	(98.9)	**(546.9)**	(178.3)
Change in fair value of contingent consideration	**10.2**	59.2	**(34.8)**	(196.5)
Impairment of intangible assets	**—**	—	**8.9**	523.3
Impairment of PP&E	**86.5**	—	**89.2**	—
Other, net	**55.6**	(18.5)	**35.3**	(23.2)
Changes in operating assets and liabilities:				
Increase in accounts receivable	**(230.2)**	(203.2)	**(411.2)**	(288.1)
Increase in sales deduction accrual	**41.8**	62.7	**108.2**	100.0
(Increase)/decrease in inventory	**(111.6)**	15.7	**(228.0)**	(21.7)
(Increase)/decrease in prepayments and other assets	**(92.9)**	(7.2)	**(66.4)**	21.2
(Decrease)/increase in accounts payable and other liabilities	**(27.5)**	96.3	**315.2**	56.5
Net cash provided by operating activities	**525.6**	561.3	**1,506.0**	1,575.2
CASH FLOWS FROM INVESTING ACTIVITIES:				
Purchases of PP&E and non-current investments	**(223.4)**	(22.6)	**(402.5)**	(67.3)
Purchases of businesses, net of cash acquired	**—**	(304.2)	**(17,476.2)**	(5,553.4)
Proceeds from short-term investments	**—**	—	**—**	67.0
Proceeds from disposal of non-current investments	**0.6**	14.1	**0.6**	18.5
Movements in restricted cash	**1.1**	(28.5)	**68.3**	(48.0)
Proceeds received on sale of product rights	**2.2**	5.7	**7.8**	14.5
Other, net	**(7.0)**	3.6	**(9.3)**	2.7
Net cash used in investing activities	**(226.5)**	(331.9)	**(17,811.3)**	(5,566.0)

Unaudited US GAAP Consolidated Statements of Cash Flows (continued)
(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
CASH FLOWS FROM FINANCING ACTIVITIES:				
Proceeds from revolving line of credit, long term and short term borrowings	**12,847.3**	725.2	**31,742.3**	3,650.8
Repayment of revolving line of credit, long term and short term borrowings	**(13,132.6)**	(955.2)	**(14,632.9)**	(2,486.1)
Payment of dividend	**—**	—	**(130.2)**	(110.2)
Debt issuance costs	**(58.7)**	0.4	**(171.0)**	(3.3)
Proceeds from exercise of options	**98.7**	—	**98.9**	—
Other, net	**(18.3)**	(18.0)	**(6.5)**	3.7
Net cash (used in)/provided by financing activities	**(263.6)**	(247.6)	**16,900.6**	1,054.9
Effect of foreign exchange rate changes on cash and cash equivalents	**(0.3)**	(0.9)	**(2.2)**	(1.6)
Net increase/(decrease) in cash and cash equivalents	**35.2**	(19.1)	**593.1**	(2,937.5)
Cash and cash equivalents at beginning of period	**693.4**	64.0	**135.5**	2,982.4
Cash and cash equivalents at end of period	**$ 728.6**	$ 44.9	**$ 728.6**	$ 44.9

Selected Notes to the Unaudited US GAAP Financial Statements

(1) Earnings Per Share (EPS)

(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
(Loss)/income from continuing operations	**$ (368.5)**	$ 477.1	**$ 127.6**	$ 1,054.1
Loss from discontinued operations	**(18.3)**	(24.3)	**(257.5)**	(31.3)
Numerator for EPS	**$ (386.8)**	$ 452.8	**$ (129.9)**	$ 1,022.8
Weighted average number of shares:				
Basic	**900.2**	590.9	**725.5**	590.2
Effect of dilutive shares:				
Share based awards to employees	**—**	2.5	**—**	3.0
Diluted	**900.2**	593.4	**725.5**	593.2

The share equivalents not included in the calculation of the diluted weighted average number of shares are shown below:

Share based awards to employees	**14.6**	3.9	**9.7**	3.3

Selected Notes to the Unaudited US GAAP Financial Statements

(2) Analysis of revenues
(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
Product sales:				
HEMOPHILIA	**$ 702.4**	$ —	**$ 978.0**	$ —
INHIBITOR THERAPIES	**181.7**	—	**255.7**	—
Hematology total	**884.1**	—	**1,233.7**	—
CINRYZE	**165.4**	187.5	**502.6**	474.4
ELAPRASE	**146.7**	134.0	**424.3**	405.5
FIRAZYR	**146.3**	123.2	**411.3**	319.8
REPLAGAL	**118.9**	111.1	**340.5**	325.5
VPRIV	**87.7**	85.1	**259.3**	256.2
KALBITOR	**11.1**	—	**39.2**	—
Genetic Diseases total	**676.1**	640.9	**1,977.2**	1,781.4
VYVANSE	**512.6**	427.3	**1,539.5**	1,268.9
ADDERALL XR	**80.5**	78.0	**281.1**	259.7
Other Neuroscience	**23.4**	29.5	**81.2**	81.9
Neuroscience total	**616.5**	534.8	**1,901.8**	1,610.5
IMMUNOGLOBULIN THERAPIES	**472.5**	—	**610.7**	—
BIO THERAPEUTICS	**134.0**	—	**185.3**	—
Immunology total	**606.5**	—	**796.0**	—
LIALDA/MEZAVANT	**208.6**	176.6	**570.3**	483.0
PENTASA	**85.4**	87.7	**222.3**	232.7
GATTEX/REVESTIVE	**58.1**	43.0	**154.3**	95.2
NATPARA	**23.3**	6.9	**58.8**	12.8
Other Internal Medicine	**87.3**	86.9	**260.6**	260.6
Internal Medicine total	**462.7**	401.1	**1,266.3**	1,084.3
Oncology total	**55.4**	—	**75.7**	—
Ophthalmology total	**14.1**	—	**14.1**	—
Total product sales	**3,315.4**	1,576.8	**7,264.8**	4,476.2
Royalties and Other Revenues:				
SENSIPAR Royalties	**38.7**	34.8	**112.2**	80.0
3TC and ZEFFIX Royalties	**16.2**	11.9	**43.3**	29.9
FOSRENOL Royalties	**13.7**	13.2	**34.3**	32.4
ADDERALL XR Royalties	**4.7**	7.1	**15.7**	22.2
Other Royalties and Revenues	**63.4**	11.2	**120.2**	60.3
Total Royalties and Other Revenues	**136.7**	78.2	**325.7**	224.8
Total Revenues	**$ 3,452.1**	$ 1,655.0	**$ 7,590.5**	$ 4,701.0

Non GAAP reconciliations

(in millions)

Reconciliation of US GAAP net (loss)/income to Non GAAP EBITDA:

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
US GAAP Net (loss)/income	**$ (386.8)**	$ 452.8	**$ (129.9)**	$ 1,022.8
Add back/(deduct):				
Loss from discontinued operations, net of tax	**18.3**	24.3	**257.5**	31.3
Equity in losses of equity method investees, net of taxes	**0.9**	0.7	**1.9**	1.6
Income taxes	**(229.6)**	(22.3)	**(218.4)**	(9.0)
Other expense, net	**191.3**	0.3	**323.1**	16.3
US GAAP Operating (loss)/income from continuing operations	**(405.9)**	455.8	**234.2**	1,063.0
Add back/(deduct) Non GAAP adjustments:				
Acquisition and integration activities	**1,198.3**	96.6	**1,945.9**	(23.8)
Amortization of acquired intangible assets	**354.9**	132.7	**702.5**	352.3
Divestments and reorganizations	**107.3**	30.4	**115.1**	46.6
Depreciation	**93.1**	32.9	**175.3**	105.1
Legal and litigation costs	**(0.5)**	1.7	**16.1**	4.4
Impairment of intangible assets	**—**	—	**8.9**	523.3
Other	**—**	8.0	**—**	56.0
Non GAAP EBITDA	**1,347.2**	758.1	**3,198.0**	2,126.9
Depreciation	(93.1)	(32.9)	(175.3)	(105.1)
Non GAAP Operating income	**$1,254.1**	$ 725.2	**$3,022.7**	$ 2,021.8
Net (loss)/income margin[(1)]	**(11%)**	27%	**(2%)**	22%
Non GAAP EBITDA margin[(2)]	**38%**	43%	**40%**	43%

[(1)] Net income as a percentage of total revenues.

[(2)] Non GAAP EBITDA as a percentage of product sales, excluding royalties and other revenues, and cost of contract manufacturing revenues.

Reconciliation of US GAAP product sales to Non GAAP Gross Margin:

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
US GAAP Product Sales	**$ 3,315.4**	$ 1,576.8	**$ 7,264.8**	$ 4,476.2
(Deduct)/add back:				
Cost of sales (US GAAP)	**(1,736.2)**	(262.7)	**(2,762.9)**	(718.5)
Cost of contract manufacturing revenue	**44.2**	—	**61.4**	—
Amortization of inventory fair value step-up	**803.8**	6.7	**1,097.3**	23.0
Inventory write-down relating to the planned closure of a facility at the Los Angeles manufacturing site	**11.6**	—	**11.6**	—
Costs of employee retention awards following AbbVie's terminated offer	**—**	1.0	**—**	6.5
Depreciation	**54.5**	9.6	**85.2**	34.4
Non GAAP Gross Margin	**$ 2,493.3**	$ 1,331.4	**$ 5,757.4**	$ 3,821.6
Non GAAP Gross Margin % [(1)]	**75.2%**	84.4%	**79.3%**	85.4%

[(1)] Non GAAP Gross Margin as a percentage of product sales.

Non GAAP reconciliations

(in millions, except per ADS amounts)

Reconciliation of US GAAP diluted earnings per ADS to Non GAAP diluted earnings per ADS:

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
US GAAP diluted (loss)/earnings per ADS	**$ (1.29)**	$ 2.29	**$ (0.54)**	$ 5.17
Amortization and asset impairments	**1.17**	0.67	**2.92**	4.43
Acquisition and integration costs	**4.11**	0.49	**8.36**	(0.12)
Divestments, reorganizations and discontinued operations	**0.43**	0.30	**1.97**	0.41
Legal and litigation costs	**—**	0.01	**0.07**	0.02
Other Non GAAP adjustments	**—**	0.04	**—**	0.28
Tax effect of adjustments above	**(1.25)**	(0.56)	**(3.07)**	(1.48)
Non GAAP diluted earnings per ADS	**$ 3.17**	$ 3.24	**$ 9.71**	$ 8.71

Reconciliation of US GAAP net cash provided by operating activities to Non GAAP cash generation:

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
Net cash provided by operating activities	**$ 525.6**	$ 561.3	**$ 1,506.0**	$ 1,575.2
Tax and interest payments, net	**214.1**	26.4	**579.2**	33.6
Up-front payments for in-licensed and acquired products	**90.0**	—	**90.0**	—
Non GAAP cash generation	**$ 829.7**	$ 587.7	**$ 2,175.2**	$ 1,608.8

Reconciliation of US GAAP net cash provided by operating activities to Non GAAP free cash flow:

	3 months ended September 30,		9 months ended September 30,	
	2016	2015	**2016**	2015
Net cash provided by operating activities	**$ 525.6**	$ 561.3	**$ 1,506.0**	$ 1,575.2
Capital expenditure	**(220.8)**	(22.3)	**(399.6)**	(62.1)
Up-front payments for in-licensed and acquired products	**90.0**	—	**90.0**	—
Non GAAP free cash flow	**$ 394.8**	$ 539.0	**$ 1,196.4**	$ 1,513.1

Non GAAP net debt comprises:

	September 30, 2016	December 31, 2015
Cash and cash equivalents	**$ 728.6**	$ 135.5
Long term borrowings	**(20,988.9)**	(69.9)
Short term borrowings	**(2,737.1)**	(1,511.5)
Other debt	**(348.6)**	(13.4)
Non GAAP net debt	**$ (23,346.0)**	$ (1,459.3)

Non GAAP reconciliations

(in millions, except per ADS amounts)

Reconciliation of full year 2016 US GAAP diluted earnings per ADS Outlook to Non GAAP diluted earnings per ADS Outlook:

	Full Year 2016 Outlook		
	Min		Max
US GAAP diluted earnings per ADS	**$ (1.10)**	**—**	**$ (0.70)**
Amortization and asset impairments		4.13	
Acquisition and integration costs		11.74	
Divestments, reorganizations and discontinued operations		1.96	
Legal and litigation costs		0.06	
Tax effect of adjustments above		(4.09)	
Non GAAP diluted earnings per ADS	**$ 12.70**	**—**	**$ 13.10**

NOTES TO EDITORS

Stephen Williams, Deputy Company Secretary (responsible for arranging the release of this announcement).

Inside Information

This announcement contains inside information.

About Shire

Shire is the leading global biotechnology company focused on serving people with rare diseases and other highly specialized conditions. We strive to develop best-in-class products, many of which are available in more than 100 countries, across core therapeutic areas including Hematology, Immunology, Neuroscience, Ophthalmics, Lysosomal Storage Disorders, Gastrointestinal / Internal Medicine / Endocrine and Hereditary Angioedema; and a growing franchise in Oncology.

Our employees come to work every day with a shared mission: to develop and deliver breakthrough therapies for the hundreds of millions of people in the world affected by rare diseases and other high-need conditions, and who lack effective therapies to live their lives to the fullest.

www.shire.com

THE "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 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, Dyax or 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 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.

NON GAAP MEASURES

This press release 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 presentational 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 23.

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).

TRADEMARKS

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