Full Year 2017 Financial Results

Flemming Ornskov, MD, MPH – CEO
John Miller – CFO, *ad interim*

February 14, 2018

“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, projected revenues, 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 depends on third parties to supply certain inputs and services critical to its operations including certain inputs, services and ingredients critical to its manufacturing processes. 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;
- the nature of producing plasma-based therapies 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;
- failure to comply with laws and regulations governing the sales and marketing of its products could materially impact Shire’s revenues and profitability;
- Shire’s products and product candidates face substantial competition in the product markets in which it operates, including competition from generics;
- Shire’s patented products are subject to significant 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 Shire’s revenues, financial condition or results of operations;
- Shire may fail to obtain, maintain, enforce or defend the intellectual property rights required to conduct its business;
- Shire faces intense competition for highly qualified personnel from other companies and organizations;
- failure to successfully execute or attain strategic objectives from Shire’s acquisitions and growth strategy 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, could have negative consequences for Shire’s business and increase the risk of non-payment by Shire’s customers;
- changes in foreign currency exchange rates and interest rates could have a material adverse effect on Shire’s operating results and liquidity;
- Shire is subject to evolving and complex tax laws, which may result in additional liabilities that may adversely affect the Shire’s financial condition or results of operations;
- if a marketed product fails to work effectively or causes adverse side effects, this could result in damage to Shire’s reputation, the withdrawal of the product and legal action against Shire;
- 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 faces risks relating to the expected exit of the United Kingdom from the European Union;
- Shire incurred substantial additional indebtedness to finance the Baxalta acquisition, which has increased its borrowing costs and may decrease its business flexibility;
- Shire’s ongoing strategic review of its Neuroscience franchise may distract management and employees and may not lead to improved operating performance or financial results; there can be no guarantee that, once completed, Shire’s strategic review will result in any additional strategic changes beyond those that have already been announced; 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 *CEO*
2. Financial review		John Miller *CFO, Ad Interim*
3. Summary		Flemming Ornskov, MD, MPH *CEO*
4. Q & A		

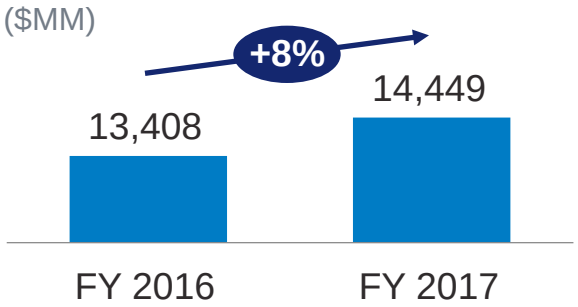
We delivered on the key priorities for 2017

- Commercial execution and new product launches
- Further integration
- Debt pay-down
- Pipeline progression
- Optimize portfolio and strengthen focus

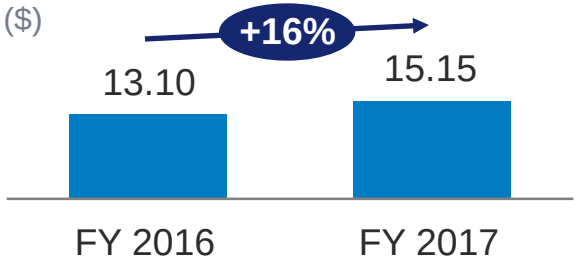
RARE DISEASES LEADER ▸ FUELING GROWTH

Strong commercial and financial performance

Product sales[1]



Non GAAP Diluted Earnings per ADS[2][4]

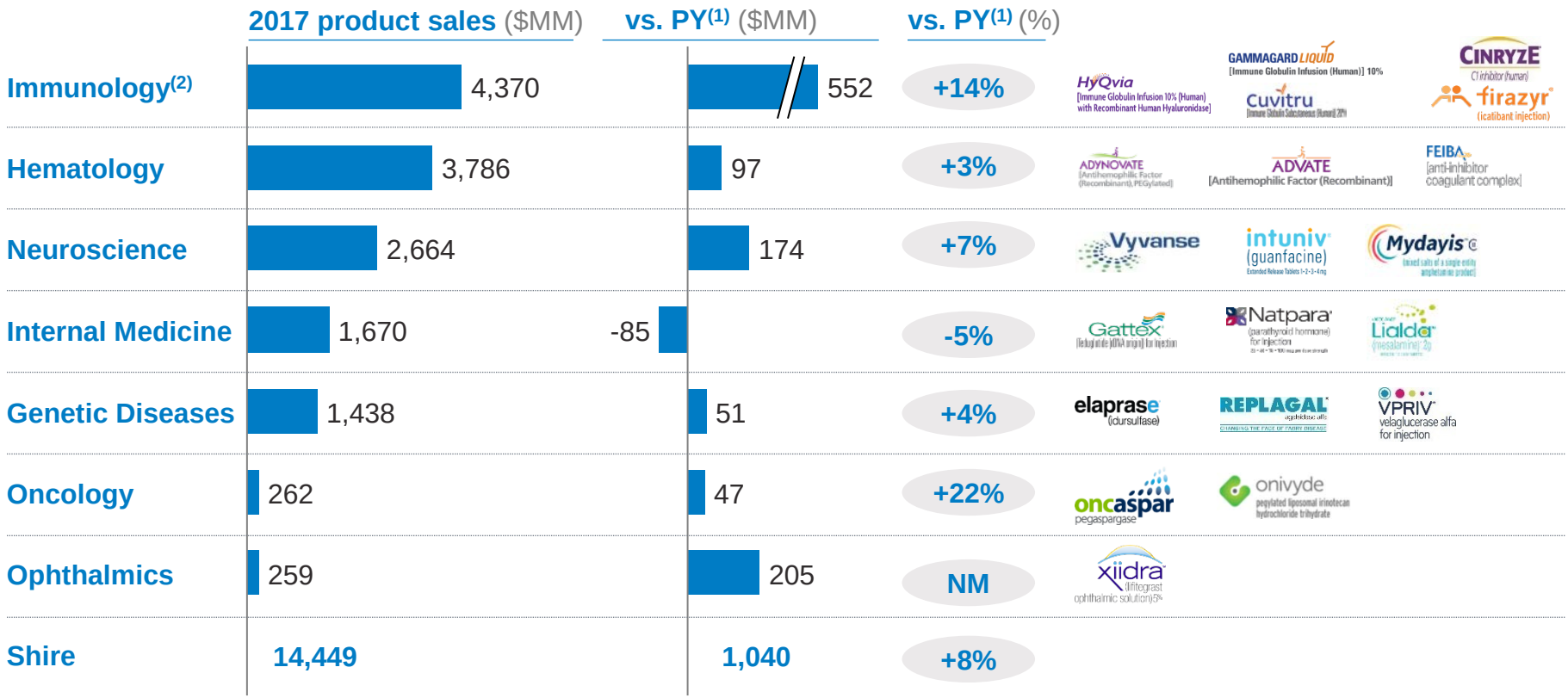


Financial highlights

- Product sales of $14.4B and **+8% pro forma growth** (33% on reported basis)
- Total Non GAAP revenues of $15.1B[3] and 8% growth (32% on reported basis)
- Non GAAP diluted **EPS growth of 16%[2][4]**
- Net cash provided by operating activities grew **+60% to $4.3B**

(1) 2016 product sales are on a pro forma basis, which include results from 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 diluted EPS-ADS (FY 2017: $14.05, FY 2016: $1.27).
(3) Non GAAP total revenues exclude the receipt of an upfront license fee of $75MM. The most directly comparable measure under US GAAP is total revenues (FY 2017: $15.2B).
(4) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

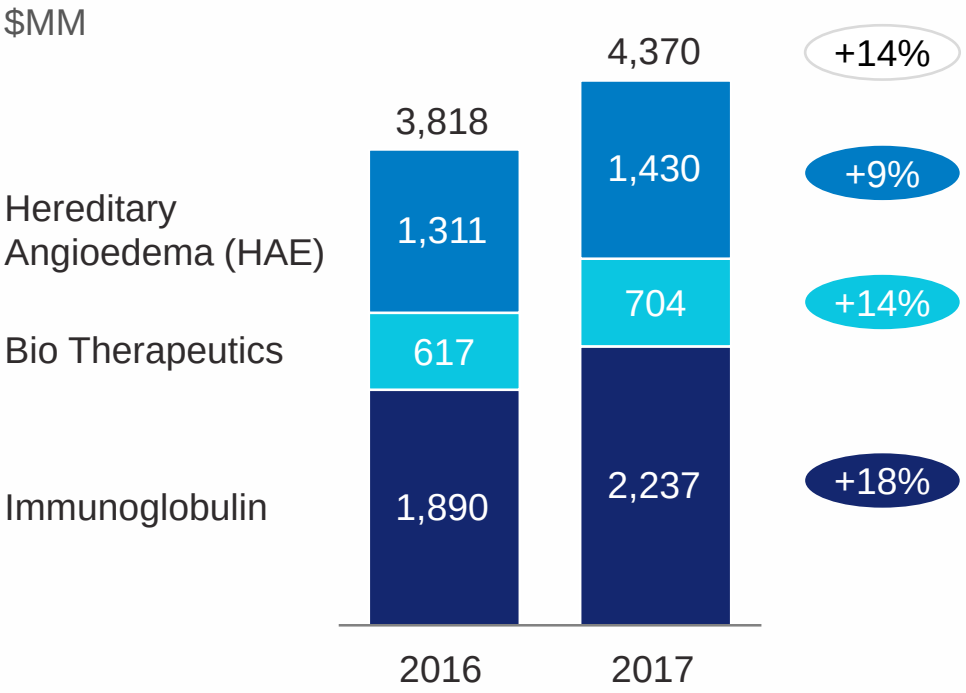
Strong performance across our diversified portfolio, Immunology as largest franchise and core growth engine



(1) Growth rates and product sales represent the full year 2017 results compared to pro forma 2016 results including Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) For 2017 reporting (including comparative information), HAE sales have been reclassified to the Immunology franchise from Genetic Diseases.

Commercial execution in Immunology business with sustainable growth drivers

Immunology product sales(1)



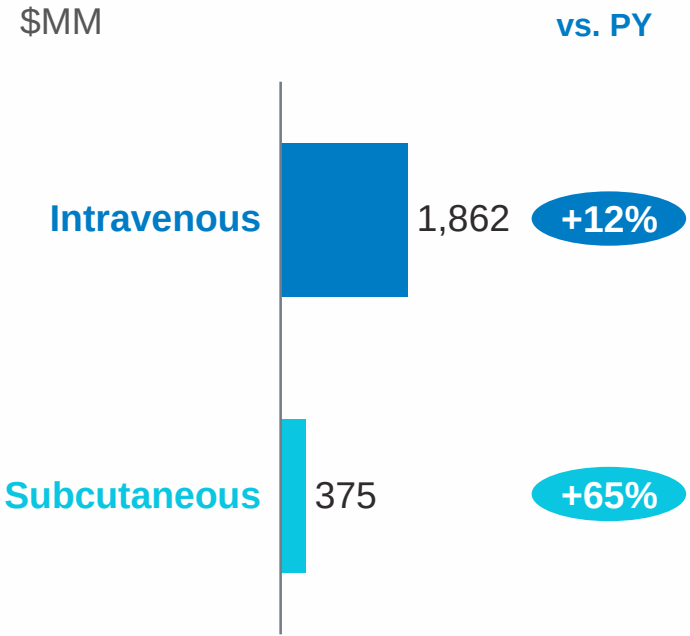
Key growth drivers

- Integration of **HAE and Immunology** commercial teams
- Strong demand for **subcutaneous** portfolio
- Increasing **focus on execution** (e.g., market penetration, geographic expansion)
- Improving **patient experiences** (e.g., patient services, delivery systems)

(1) 2016 product sales are on a pro forma basis, which include results from Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).

Subcutaneous products driving strong growth with product differentiation

2017 Immunoglobulin product sales



Shire Subcutaneous (SC) Portfolio

Cuvitru preferred weekly SC option

HyQvia preferred monthly SC option

Improved outcome	Lower rate of infection or hospitalization due to infection compared to IVIG
Convenience	Easier self-administration[1]

(1) After adequate training.

Recent launches continue on a high growth trajectory

Recently launched products(1)

Immunology
- HyQvia [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]
- Cuvitru [Immune Globulin Subcutaneous (Human)] 20%

Ophthalmics
- xiidra (lifitegrast ophthalmic solution)5%

Neuroscience
- Mydayis

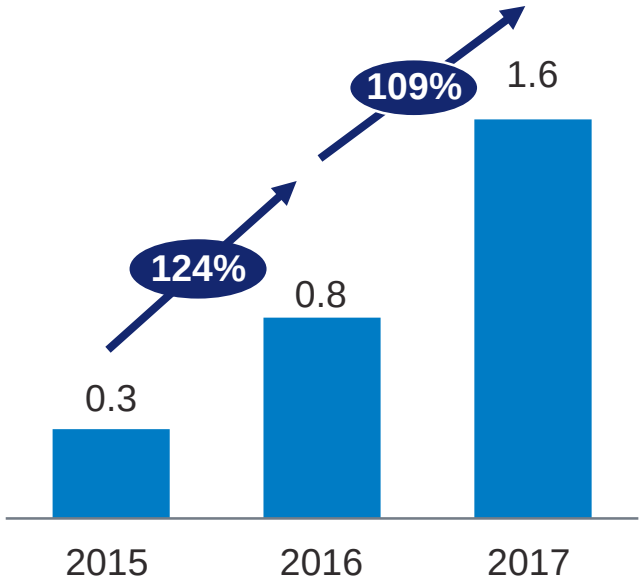
Hematology
- ADYNOVATE [Antihemophilic Factor (Recombinant), PEGylated]
- vonvendi [von Willebrand factor (Recombinant)]
- RIXUBIS [COAGULATION FACTOR IX (RECOMBINANT)]
- Obizur [Antihemophilic Factor (Recombinant), Porcine Sequence]

Internal Medicine
- Natpara (parathyroid hormone) for Injection
- Gattex [Teduglutide [rDNA origin]] for Injection

Oncology
- onivyde (irinotecan liposome injection)

... contribute substantially to current and anticipated future sales(2)

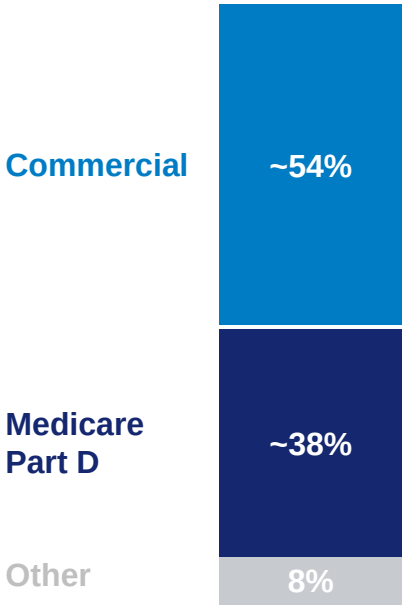
Net product sales, $B



(1) Products launched between 2013 and 2017.
(2) 2016 product sales are on a pro forma basis, which include results from Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).

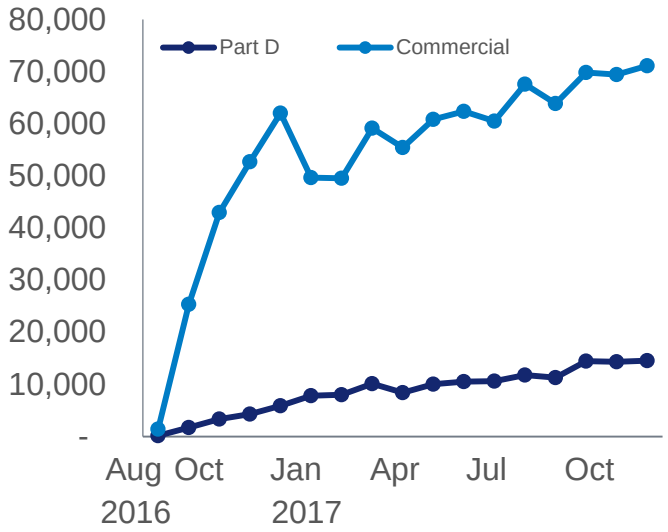
Ophthalmics – XIIDRA with strong performance in the Commercial segment

Dry-eye market by payor coverage



XIIDRA NBRx share(1)

XIIDRA monthly TRx history(2)



- Total dry eye disease **market has grown 23%** in 2017 – flat before XIIDRA launched
- In Commercial segment, **6 out of 10** new patients starting now on XIIDRA
- Key priority to **improve access in Medicare** market in 2018

(1) New-to-Brand script data for November 2017. This excludes conversion within a brand (e.g., Restasis unit-dose to multi-dose).
(2) IMS APLD (Anonymized patient level data) data. IMS data: IMS information is an estimate derived from the use of information under license from the following IMS Health Information service: IMS PlanTrak. IMS expressly reserves all rights including rights of copying, distribution and republication.

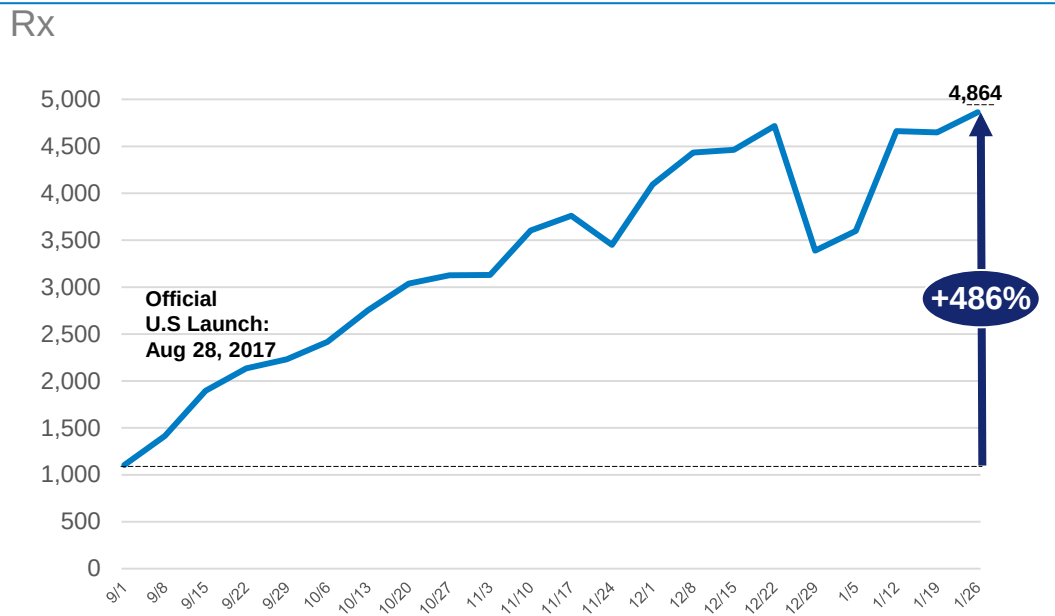
Neuroscience – MYDAYIS as best-in-class launch in ADHD

MYDAYIS launch in US(1) (Total Rx)

~10K
Unique prescribers(1)

~30K
Unique patients(1)

~80K
Total prescriptions(1)



(1) IMS PlanTrak* and Connective Rx redemption data from approval to 1/26/17. IMS data: IMS information is an estimate derived from the use of information under license from the following IMS Health Information service: IMS PlanTrak. IMS expressly reserves all rights including rights of copying, distribution and republication.

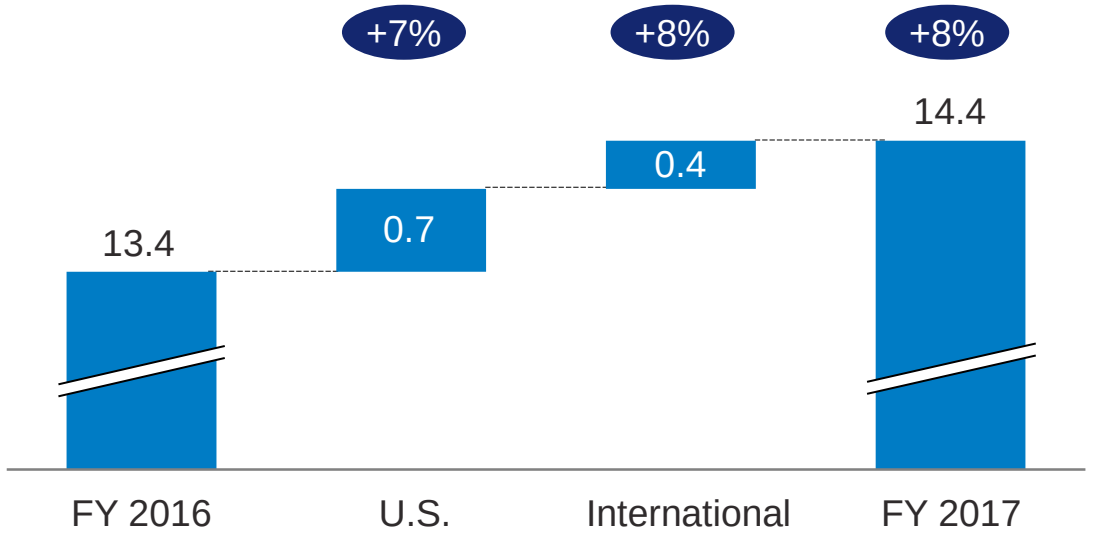
Expanded global footprint contributing significantly to growth

Global expansion accelerated with Baxalta…

2015	2017
Therapies available in 50 countries	Therapies available in >100 countries
Commercial presence in 34 countries	Commercial presence in 70 countries

… leading to meaningful contribution to growth from the International Business

2017 Pro Forma Product Sales Growth(1) ($MM)



(1) 2016 product sales are on a pro forma basis, which include results from Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).

Excellent pipeline progression in 2017

54 MAJOR MARKET FILINGS

126 PRODUCT APPROVALS GLOBALLY

9 PHASE 3 STUDIES COMPLETED

Major Approvals & Launches

- **Approval and Launch of MYDAYIS** for ADHD in adults and adolescents in the US
- **Approval and Launch of NATPAR** for hypoparathyroidism in EU
- **Approval for lyophilized ONCASPAR** for ALL in EU
- **Approval and Launch of INTUNIV** for ADHD in Japan
- **Approval for FIRAZYR** for acute HAE attacks in pediatric patients in EU
- **CHMP Positive Opinion for ADYNOVI** for adults and adolescents with Hemophilia A

Development Progress

- **10 Dossiers submitted**
- **2 FDA Fast Track Designations, 2 Orphan Drug Designations, 1 Breakthrough Therapy Designation**
- **3 INDs submitted**
- **Initiated 6 Phase 3 Global Programs (and two Phase 3 studies in Japan)**
- **Licensing SHP659 for DED**
- **Licensing agreement with Novimmune S.A. and Rani Therapeutics**

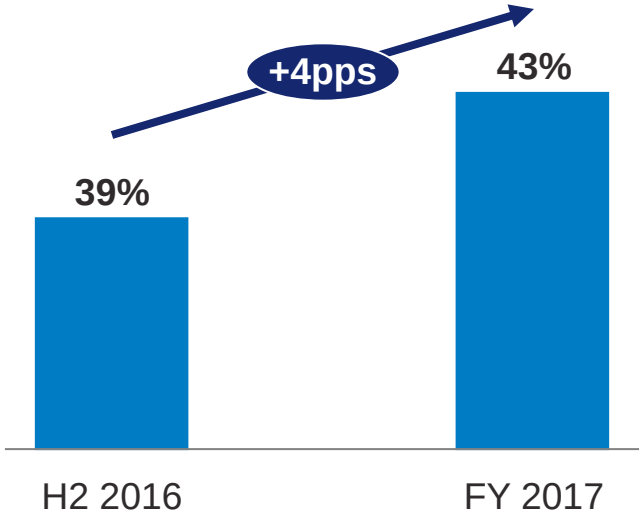
Building innovation hub in Cambridge

- **New state-of-the-art research lab facility in Kendall Square – occupancy in H1 2018**

Note: DED: dry eye disease; HAE: hereditary angioedema; ALL: acute lymphoblastic leukemia; ADHD: attention deficit hyperactivity disorder.

Significant improvement of operating margins

Non GAAP EBITDA margin[1][2]



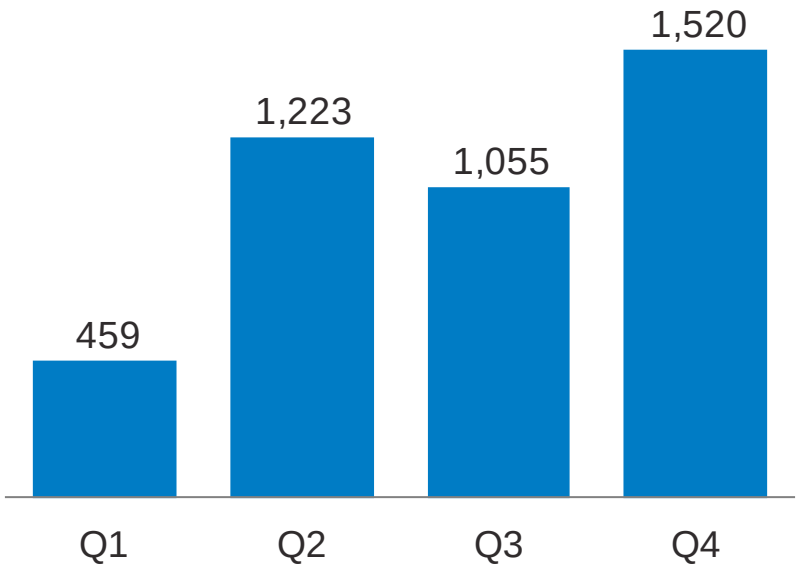
- **Commercial Integration** completed quickly, all major site moves done
- **Synergy realization** ahead of plan
- On track to achieve **~$700M in synergies** by year 3

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income margin (FY 2017: 28%, H2 2016: 1%).
(2) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Strong cash flow generation enabled rapid debt pay down

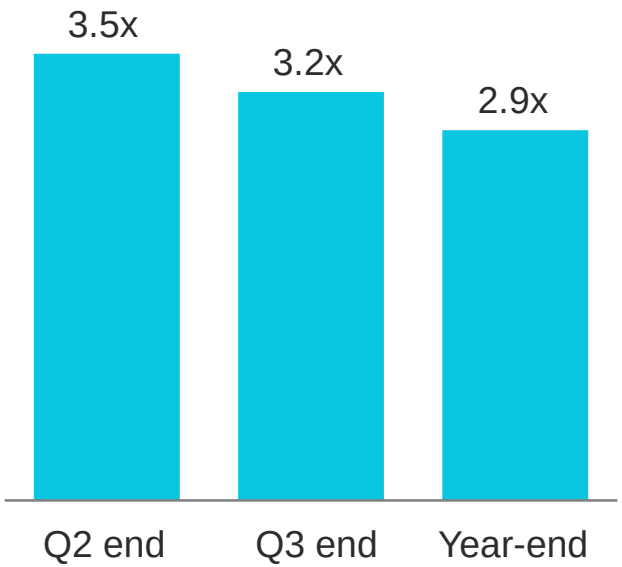
Net cash provided by operating activities

2017, $MM



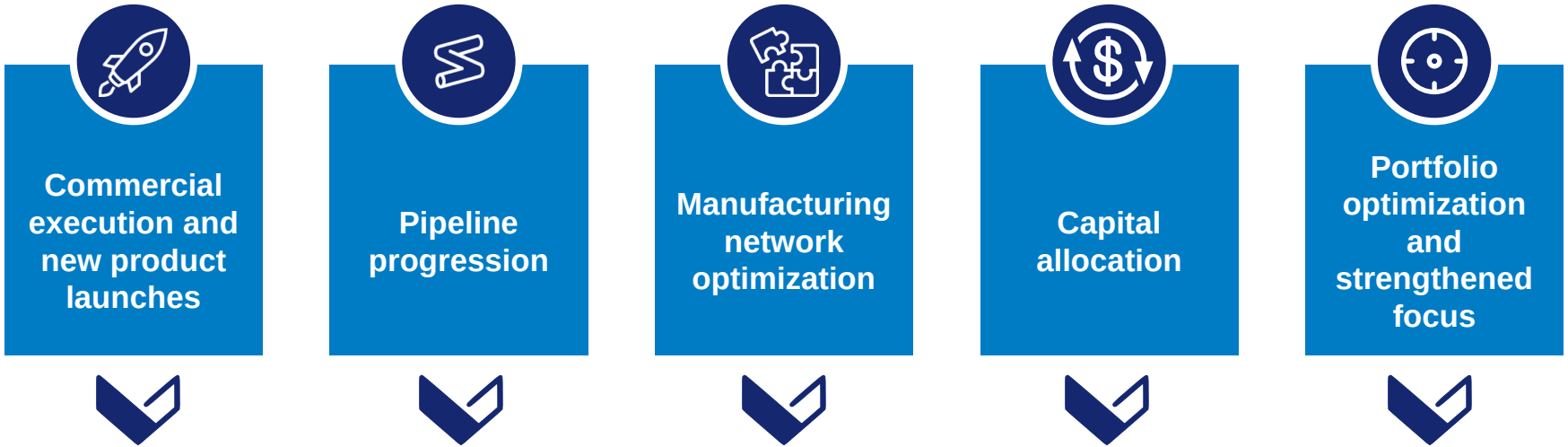
Leverage ratio

2017, Non GAAP net debt / EBITDA(1)



(1) Non GAAP net debt / EBITDA is a Non GAAP financial measure. Non GAAP net debt represents cash and cash equivalents less short and long term borrowings, capital leases and other debt. EBITDA represents 12 months trailing Non GAAP EBITDA. The most directly comparable measure for EBITDA under US GAAP is net income. See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Key priorities for 2018 – continue to execute and innovate



- Strengthen Rare Disease leadership with Immunology and innovation
- Invest in Neuroscience to expand beyond ADHD and enhance optionality

Lanadelumab – key pillar for market leadership in HAE(1)

"Achieved attack-free results for the majority of HAE patients, in the Phase III trial taking Lanadelumab every two weeks, once steady state is achieved(2)"

Efficacy approaching attack free

- Overall **87% attack reduction** over 26 weeks(2)
- **During steady state** stage of trial (day 70-182)(2)
  - **91% attack reduction**
  - **8 out of 10 patients attack free**

Enhancing patients' treatment experience

- Simple and convenient subcutaneous injection that **takes <1 minute to self-administer, every 2 weeks**
- **75% reduction in number of injections** vs traditional preventive therapies
- Based on an Angioedema Quality of Life (QoL) Questionnaire, subjects reported **improved health-related QoL** compared to placebo(3)

(1) Subject to regulatory approval.
(2) Study DX-2930-03 with lanadelumab 300 mg q2wks vs placebo for the duration of the 6-month study (P<0.001). Primary efficacy endpoint LS mean monthly attack rate, Day 0 to 182; secondary endpoints - reduction of HAE attacks that required acute treatment, were moderate or severe, or started after day 14 (Poisson regression model); estimated steady state period (day 70-182); 77% of patients attack free (day 70-182).
(3) Change in AE-QoL total and domain scores and minimal clinically important difference from day 0 to 182 (Weller et al, 2016).

Innovative R&D pipeline with several near-term catalysts

Clinical Programs in Pipeline

STAGE	Phase 1	Phase 2	Phase 3	Registration	Recent approvals
NUMBER OF PROGRAMS	7	10	15	8	7

Key Program Highlights[1] for 2018

- ADYNOVI (Hem A) – EU approval in January
- SHP643 (HAE) – US approval expected H2
- XIIDRA (DED) – EU approval expected H2
- VYVANSE (ADHD) – Japan approval expected mid-year
- SHP643 (HAE) – Pediatric Phase 3 start expected Q4[2]
- SHP647 (CD) – Phase 3 start expected H1
  (UC indication started Q4 2017)
- SHP621 (EoE) – Topline data expected Q4 2018 / Q1 2019
- SHP654 (GT Hem A) – First patient screened Q1

SOURCE: Pipeline as of January 2018.
NOTES: UC: ulcerative colitis; DED: dry eye disease; CIC: chronic idiopathic constipation; HAE: hereditary angioedema; CD: Crohn's disease; EoE: eosinophilic esophagitis; GT: genetic therapy.
(1) All programs subject to regulatory approval.
(2) Subject to FDA PWR approval.

State-of-the-art plasma fractionation site expected to start operation in H1 2018(1)

Covington, GA

Key facts

GAMMAGARD LIQUID Flexbumin

- One of the **largest greenfield** site projects in the US
- CAPEX investment **>$1B**
- Manufacturing campus **>1M square feet**
- Potential to employ **~1,500 people** at full ramp up
- Expected to receive FDA license and **start production in H1 2018(1)**

Fueling growth for our Immunoglobulin/Bio therapeutics businesses

Expected to increases Shire's fractionation capacity by 30%

Shire

(1) Subject to regulatory approval.

Financial Review

John Miller
Chief Financial Officer, *Ad Interim*

FY 2017 reported key financials summary

	FY 2017 $MM[(1)]	FY 2016 $MM[(1)]	Reported Growth	CER Growth[(2)(10)]	FY Guidance as updated at Q2'17	Actual vs. Guidance
Product sales	14,449	10,886	+33%	+33%	$14.3 - $14.6 billion	✓
Non GAAP royalties and other revenues[(3)(10)]	637	511	+25%	+25%	$600 - $700 million	✓
Non GAAP total revenues[(4)(10)]	15,086	11,397	+32%	+32%		
Non GAAP combined R&D and SG&A[(5)(10)]	4,917	4,178	+18%	+17%	$4.9 - $5.1 billion	✓
Non GAAP EBITDA[(6)(10)]	6,492	4,710	+38%	+38%		
Non GAAP EBITDA margin[(7)(10)]	43%	41%	2 ppc	n/a		
Non GAAP effective tax rate[(8)(10)]	15%	16%	n/a	n/a	16% - 17%	✓
Non GAAP diluted EPS – ADS[(9)(10)]	15.15	13.10	+16%	+16%	$14.80 - $15.20	✓
Net cash provided by operating activities	4,257	2,659	+60%	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 royalties and other revenues (FY 2017: $712m; FY 2016: $511m).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is total revenues (FY 2017: $15,161m; FY 2016: $11,397m).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is combined R&D and SG&A (FY 2017: $5,294m, FY 2016: $4,455m).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income (FY 2017: $4,272m, FY 2016: $327m).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income margin as a percentage of total revenues (FY 2017: 28%, FY 2016: 3%).
(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is effective tax rate (FY 2017: benefit of 125%, FY 2016: benefit of 26%).
(9) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is diluted EPS-ADS (FY 2017: $14.05, FY 2016: $1.27).
(10) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

FY product sales performance pro forma[1]

$MM	FY 2017 Sales U.S.	FY 2017 Sales International	FY 2017 Sales Total	Pro forma growth vs. 2016 Reported	Pro forma growth vs. 2016 CER[2][4]
Immunoglobulin Therapies	1,789	448	2,237	+18%	+19%
Hereditary Angioedema[3]	1,305	124	1,430	+9%	+9%
Bio Therapeutics	316	388	704	+14%	+14%
Immunology Total	**3,410**	**960**	**4,370**	**+14%**	**+15%**
Hemophilia	1,478	1,479	2,957	+3%	+3%
Inhibitor Therapies	279	549	828	+2%	+2%
Hematology Total	**1,757**	**2,028**	**3,786**	**+3%**	**+3%**
VYVANSE	1,917	244	2,161	+7%	+7%
ADDERALL XR	328	20	348	-4%	-4%
MYDAYIS	22	-	22	N/A	N/A
Other Neuroscience	17	116	133	+18%	+19%
Neuroscience Total	**2,284**	**380**	**2,664**	**+7%**	**+7%**
LIALDA/MEZAVANT	473	96	569	-28%	-28%
GATTEX/REVESTIVE	288	48	336	+53%	+53%
PENTASA	313	-	313	+1%	+1%
NATPARA/NATPAR	146	1	147	+73%	+73%
Other Internal Medicine	82	222	305	-13%	-13%
Internal Medicine Total	**1,302**	**368**	**1,670**	**-5%**	**-5%**
ELAPRASE	163	453	616	+5%	+3%
REPLAGAL	-	472	472	+4%	+4%
VPRIV	150	200	350	+1%	+1%
Genetic Diseases Total	**313**	**1,125**	**1,438**	**+4%**	**+3%**
Oncology	185	77	262	+22%	+21%
Ophthalmics	259	-	259	N/M	N/M
Total Product Sales	**9,511**	**4,938**	**14,449**	**+8%**	**+8%**

(1) Growth rates represent the FY 2017 reported sales compared to 2016 pro forma sales including 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.
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FY 2017 reported performance metrics

Year on Year Growth:	FY 2017[1]
Product sales	33%
Non GAAP R&D[2][9]	22%
Non GAAP SG&A[3][9]	16%
Combined Non GAAP R&D and SG&A[4][9]	18%

Ratios: As % of Non GAAP total revenues	FY 2017[1]	FY 2016[1]
Non GAAP gross margin[5][9]	76%	78%
Non GAAP R&D[6][9]	10%	11%
Non GAAP SG&A[7][9]	22%	25%
Non GAAP EBITDA[8][9]	43%	41%

(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 (FY 2017: +22%).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (FY 2017: +17%).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is combined R&D and SG&A (FY 2017: +19%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (FY 2017: 69%, FY 2016: 67%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D as a percentage of total revenues (FY 2017: 12%, FY 2016: 13%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A as a percentage of total revenues (FY 2017: 23%, FY 2016: 26%).
(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income margin as a percentage of total revenues (FY 2017: 28%, FY 2016: 3%).
(9) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

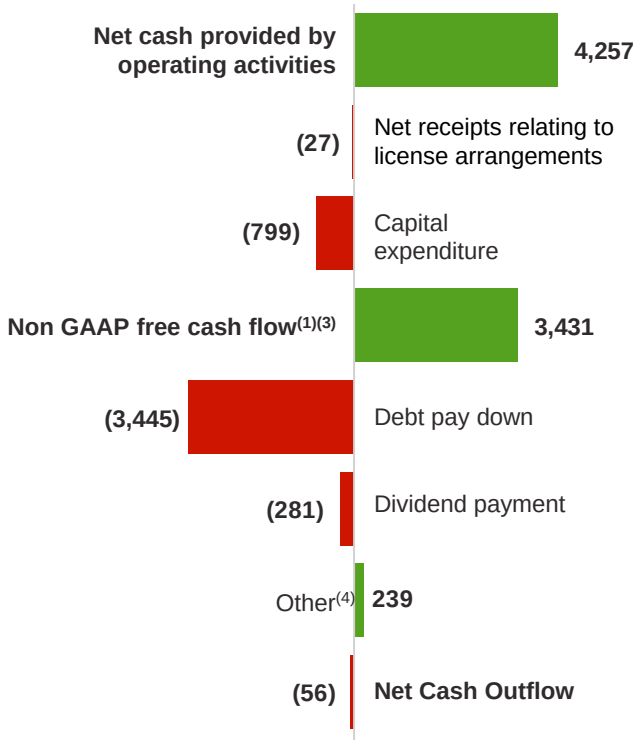
Strong 2017 operating cash flow drives $3.4B reduction in Non GAAP net debt

2017 Non GAAP Net Debt Progression

$MM	September 30, 2017	December 31, 2017	Q4 Change	December 31, 2016	FY Change
Cash and cash equivalents	**209**	**472**	**263**	**529**	**(56)**
Long term borrowings	17,614	16,411		19,553	
Short term borrowings	2,622	2,781		3,062	
Capital leases	349	349		354	
Total borrowings, capital leases, and other debt	**20,585**	**19,541**	**(1,044)**	**22,969**	**(3,427)**
Non GAAP net debt[3]	**20,376**	**19,069**	**(1,307)**	**22,439**	**(3,370)**

Leverage at December 31, 2017
Non GAAP net debt / EBITDA ratio[2][3] 2.9x

FY 2017 Cash Flow $MM



(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net cash provided by operating activities (FY 2017: $4,257m).
(2) Non GAAP net debt / EBITDA is a Non GAAP financial measure. Non GAAP net debt represents cash and cash equivalents less short and long term borrowings, capital leases and other debt. EBITDA represents 12 months trailing Non GAAP EBITDA. The most directly comparable measure for EBITDA under US GAAP is net income.
(3) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
(4) Includes $134M related to proceeds from issuance of stock for share-base compensation arrangements and $89M related to proceeds from sale of investments.

2018 guidance

Full Year 2018 Dynamics

	Guidance
Product sales	$14.9 - $15.3 billion
Royalties & other revenues	$500 - $600 million
Non GAAP gross margin(1)	73.5% - 75.5%
Non GAAP combined R&D and SG&A(1)	$4.9 - $5.1 billion
Non GAAP depreciation(1)	$575 - $625 million
Non GAAP net interest/other(1)	$450 - $550 million
Non GAAP effective tax rate(1)	16% - 18%
Non GAAP diluted earnings per ADS(1)	$14.90 - $15.50
Capital Expenditure	$800 - $900 million

Our 2018 outlook is based on January 30th, 2018 actual exchange rates (€:$1.242422, £:$1.417678, CHF:$1.071076, CAD:$0.811779, ¥:$0.009184). The estimated impact of a 10% appreciation in the US Dollar against the respective currency, over the remainder of the year, on our 2018 Guidance is as follows:

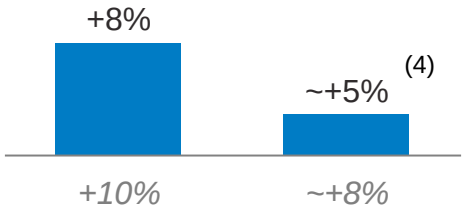
	Revenues	Earnings
EUR	-1.4%	-0.5%
GBP	-0.2%	-0.3%
CHF	-0.1%	0.0%
CAD	-0.2%	-0.3%
JPY	-0.2%	-0.4%
Other	-0.5%	-0.5%

(1) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Anticipated 2018 dynamics – accelerated generic competition and Covington investment provide headwind to sales and profit growth

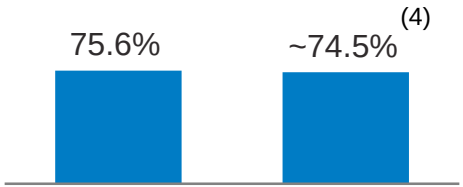
Sales Growth (pro forma)

Before Gx impact



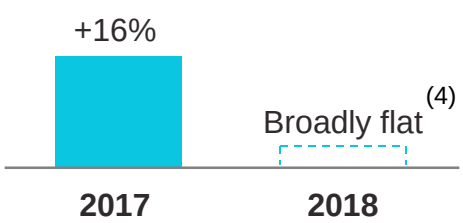
- Potential **Gx impact up to ~3-4% of sales**
- **Healthy underlying growth** from rare disease as well as Neuroscience business

Non GAAP Gross Margin(1)(3), % of Revenue



- Negative Impact on margin as we **start up Covington**
- Unfavorable impact due to **sales mix** (genericization of high margin small molecule products)
- Expected **reduction in royalties** in 2018

Non GAAP EPS Growth(2)(3)



- **Increased depreciation of ~ $100m** mainly due to Covington investment and other manufacturing and integration related projects
- **2018 tax rate:** 16-18%

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (FY 2017: 69.0%).
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is diluted EPS-ADS (FY 2017: $14.05, FY 2016: $1.27).
(3) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
(4) Commentary based on mid-range of 2018 Guidance.

Dynamics beyond 2018 – continued growth to 2020 revenue and Non GAAP EBITDA margin targets

Anticipated dynamics

- Continued strong growth in **Immunology business**
- Continued growth of **recently launched products**
- Sales uptake following potential launch of **SHP643**(1)
- Portfolio expansion in **large international markets** (Japan and China)
- Strong focus on **manufacturing network optimization** fueling growth and margins
- **Competitive entry** in hemophilia
- Continued **generic competition** and **industry pricing pressure**

Expectations by 2020

- Revenue of $17-18B
- Non GAAP EBITDA margin(2) of mid 40's (% of revenues)
- Non GAAP tax rate(2): 16-18%

(1) Subject to regulatory approval.
(2) A reconciliation of 2020 Non GAAP measure to the US GAAP equivalent cannot be provided because we are unable to forecast with reasonable certainty many of the items necessary to calculate such comparable GAAP measures. See slide 43 for additional information.

Note: Our 2020 outlook is based on January 30th, 2018 actual exchange rates (€:$1.242422, £:$1.417678, CHF:$1.071076, CAD:$0.811779, ¥:$0.009184).

Outlook for Hematology Franchise

2017 hematology product sales, $B

Inhibitor Sales (FEIBA)

- Greater level of **unmet need**
- **Bypassing agent still needed** – 37% of emicizumab patients still experience bleeds
- Historically ~40% of patients require both FEIBA and NOVOSEVEN, or do not respond to one

Could face ~50% FEIBA erosion by 2022

Non-Inhibitor Sales (ADVATE / ADYNOVATE)(1)

- **Factor VIII standard of care** with decades of efficacy and safety data
- **Growing market with continued innovations** in Factor VIII treatment with extended half life and personalized prophylaxis
- Emicizumab full **clinical data not yet public**

Cautiously assume erosion of up to 30% by 2022

Long-term efficacy & safety data, and real-world physician & patient experience will determine outcome

(1) Sales only shown for ADVATE and ADYNOVATE; excluding plasma derived and first generation products to treat Hemophilia A, treatments for other Hemophilia conditions such as Hemophilia B and Von Willebrand Disease.

Summary

Flemming Ornskov, MD, MPH
Chief Executive Officer

Shire

Shire has transformed into the leading global biotech focused on rare diseases while delivering strong financial performance

1 Rare disease leader

- **Innovative, rare disease-focused biotech** committed to differentiated and high patient-impact medicines
- **Global footprint**: ~23K employees in 70 countries

2 Strong portfolio

- Seven franchises, five with **over $1B in annual revenue** with multiple leading brands

3 Clear biotech profile

- **~65% of 2017 sales** from biologics

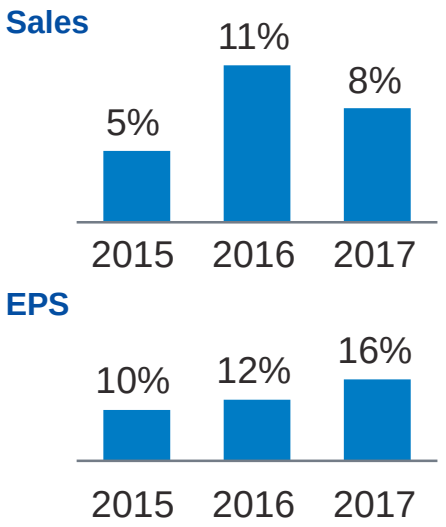
4 Robust R&D pipeline

- **40 programs** in clinical development, 15 in Phase 3
- 2 FDA **Fast Track** Designations, 2 **Orphan Drug** Designations, 1 **Breakthrough Therapy** Designation in 2017

5 Patient focus

- **Advancing diagnostics** (diagnostic toolkits, biomarkers in genetic diseases)
- **Precision medicine** (e.g., ADVATE+myPKFiT)

Product sales (pro forma)(1) and Non GAAP EPS growth(2)(3)



(1) 2016 product sales are on a pro forma basis, which include results from 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 diluted EPS-ADS (FY 2017: $14.05, FY 2016: $1.27, FY 2015: $6.59).
(3) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

In 2017 – delivering strong performance
In 2018 – investing for future growth and value creation

Strong 2017

- **Strong performance, delivering on all key priorities**
  - 8% product sales growth[1]; 16% Non GAAP EPS growth[2][4]
  - 4 pps Non GAAP EBITDA margin[3][4] improvement (vs. H2 2016); debt pay-down
  - Robust pipeline progression

Challenges in 2018

- **Potential for accelerated genericization** impacting top & bottom line
- **Covington investment site start-up** negatively impacting margins in the short term
- Increased competition in Hematology and HAE

Opportunities in 2018

- **Topline growth driven by healthy and sustainable business drivers**
  - Immunology
  - Launch of new products, especially potential launch of SHP643[5]
  - International markets

Projections for 2019 and beyond

- **Continued growth** for sales and EPS projected to meet our 2020 goal
  - **Revenues $17-18B**
  - **Mid 40's** Non GAAP EBITDA margin

(1) 2016 product sales are on a pro forma basis, which include results from 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 diluted EPS-ADS (FY 2017: $14.05, FY 2016: $1.27).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income margin (FY 2017: 28%, H2 2016: 1%).
(4) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
(5) Subject to regulatory approval.

Shire

In the fight against rare disease, where there's a will, there's always a way.

Champion the fight against rare disease with us at shire.com

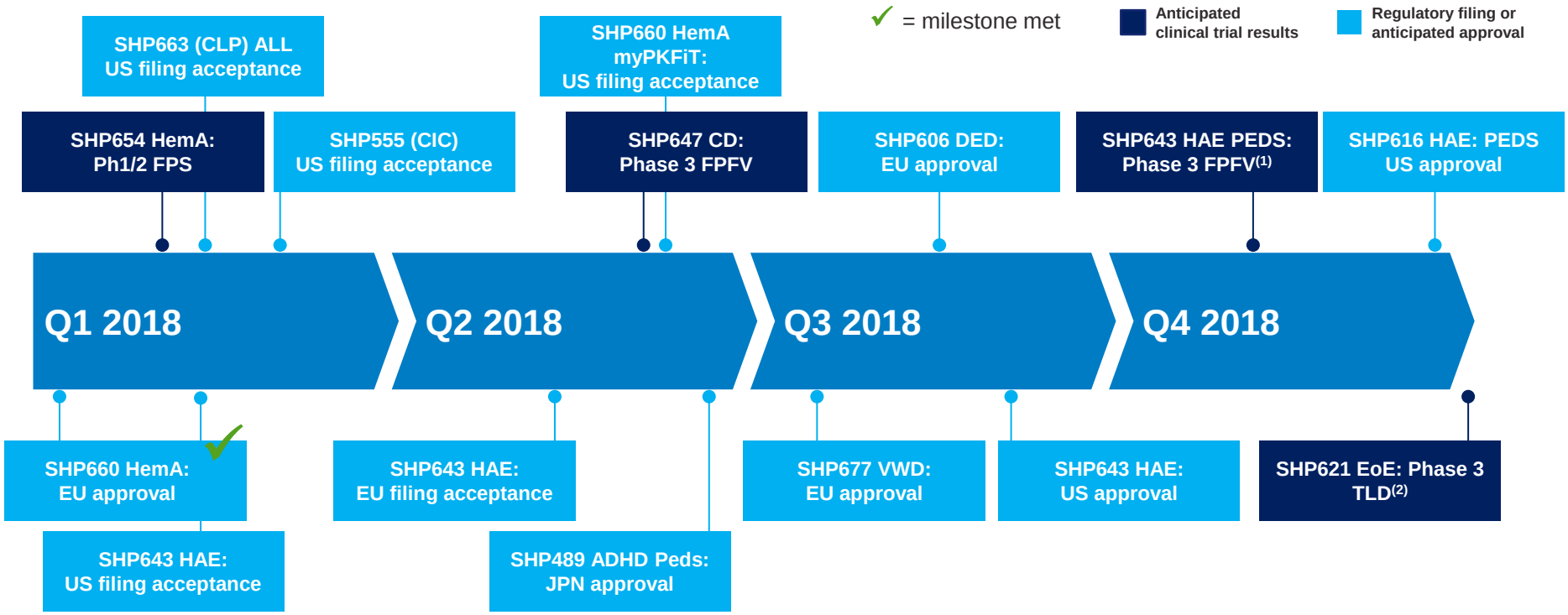
Significant progress expected for our late stage pipeline in 2018

Therapeutic area	Phase 3 starts	Regulatory filings and approvals[1] ✓ = milestone met
Hematology		• SHP661 (ADYNOVI) Hemophilia approval – EU ✓ • SHP667 (VWD) approval – EU • ADYNOVATE+myPKFiT – US filing acceptance
Immunology including HAE	• SHP643 (Peds)[2]	• SHP643 (HAE) filing acceptance – US, EU • SHP643 (HAE) approval – US • SHP616 (CINRYZE) Peds approval – US
Neuroscience	• SHP615 (Seizures) US[3]	• SHP489 (VYVANSE) Peds approval – JPN
Internal medicine	• SHP633 SBS (bridging) JPN • SHP647 CD • SHP647 UC (Maintenance)	• SHP555 (CIC) filing acceptance – US
Ophthalmics		• SHP606 (XIIDRA) DED approval – EU
Oncology		• SHP663 (CLP) ALL filing acceptance – US • SHP663 (CLP) ALL approval – US

(1) Subject to regulatory approval.
(2) Subject to FDA PWR approval.
(3) Q4 2018 / Q1 2019.

Note: This list is not exhaustive of all pipeline progress expected in 2018. CD: Crohn's disease; UC: ulcerative colitis; VWD: Von Willebrand disease; DED: dry eye disease; CIC: chronic idiopathic constipation; HAE: hereditary angioedema; L2PaCa: 2nd line pancreatic cancer; CLP: Calaspargase Pegol: ALL: acute lymphoblastic leukemia.

2018 Key Events



Note: Timings are approximated to the nearest quarter and where appropriate subject to regulatory approval.
CD: Crohn's disease; DED: dry eye disease; CIC: chronic idiopathic constipation; HAE: hereditary angioedema; VWD: Von Willebrand disease; ADHD: attention deficit hyperactivity disorder; EoE: eosinophilic esophagitis; FPS: first patient screened; FPFV: first patient first visit; TLD: top-line data.

(1) Subject to FDA PWR approval.
(2) Q4 2018 / Q1 2019.

Key phase 3 pipeline assets expected to deliver future growth

Asset	Potential Indication	Commercial Opportunity and Unmet Need	Expected Phase 3 Data	Potential Initial Launch Year[1]
SHP643 Lanadelumab (Breakthrough, Fast Track and Orphan Drug Designation)[2]	**Hereditary Angioedema (Prophylaxis)**	• Affects ~42,000 people globally[3]; ~60% of global HAE patients undiagnosed; ~30-40% of patients in U.S./EU • Potential to change the treatment paradigm and less frequent administration has the potential to significantly reduce the current prophylaxis treatment burden	**Q2 2017**	**2018**
SHP555 Prucalopride	**Chronic Idiopathic Constipation (CIC)**	• 39M patients in the U.S. with CIC • Unique MOA that helps to stimulate colonic motility	**Q3 2017**	**2019**
SHP620 Maribavir (Orphan Drug Designation)[2]	**Cytomegalo-virus (CMV) infection during transplant**	• There are >100,000 solid organ transplants and >50,000 hematopoietic stem cell transplants performed per year worldwide[4][5] • Current available anti-CMV drugs have limitations in terms of efficacy and safety	**Q2 2019**	**2020**
SHP621 Budesonide (Breakthrough and Orphan Drug Designation)[2]	**Eosinophilic Esophagitis**	• Estimated 200,000+ cases in U.S. (2016), expected to increase due to greater diagnosis, incidence rates and potential treatment options[6] • Potential to be the 1st and only approved agent to treat EoE, for both induction and maintenance	**Q4 2018 / Q1 2019**	**2020**
SHP607 Mecasermin (Fast Track designation)[2]	**Chronic Lung Disease, Broncho-pulmonary Dysplasia (BPD) and Intra-ventricular Hemorrhage (IVH)**	• ~120K pre-term infants born annually before 28 weeks gestational age in U.S./EU/JP/ROW markets with NICU infrastructure[7] • Currently no treatments available / approved to prevent certain severe neonatal complications in pre-term infants	**TBD[9]**	**TBD[9]**
SHP647 IgG2 mAB targeting MAdCAM-1 (Orphan Drug Designation UC & CD pediatric only)[2]	**Inflammatory Bowel Disease - Crohn's Disease (CD) and Ulcerative Colitis (UC)**	• 1.3M CD and 1.8M UC patients with moderate to severe diagnosis across G7 countries[8] • Only anti-integrin directly targeting MAdCAM-1; gut-specific activity, with a potentially differentiated profile	**UC Q3 2020** **CD Q4 2022**	**2022 / 2024**

(1) Initial Launch Years defined as 1st launch in major country.
(2) Designations granted by FDA in the US.
(3) Zuraw BL. Clinical practice. Hereditary Angioedema.N Engl J Med. 2008;359(10):1027-1036.
(4) http://www.who.int/transplantation/gkt/statistics/en/
(5) http://www.who.int/transplantation/hsctx/en/
(6) Dellon E. Gastroenterol Clin North Am. 2014 June; 43(2): 201-218; 2 Kotton CN. Am J Transplant 2013.
(7) Lancet 2012; 379: 2162–72.
(8) Decision Resources Group 2017.
(9) Timelines TBD – ongoing discussions with regulatory authorities.

Note: All assets subject to positive results and regulatory approval.

Q4 2017 reported key financials summary

Top line growth and spend efficiencies supporting double-digit EPS growth

	Q4 2017 $MM	Q4 2016 $MM	Reported Growth	CER Growth[1][9]
Product sales	3,911	3,621	+8%	+7%
Non GAAP royalties and other revenues[2][9]	159	185	-14%	-14%
Non GAAP total revenues[3][9]	4,070	3,806	+7%	+6%
Non GAAP combined R&D and SG&A[4][9]	1,247	1,354	-8%	-9%
Non GAAP EBITDA[5][9]	1,686	1,512	+11%	+10%
Non GAAP EBITDA margin[6][9]	41%	40%	1 ppc	n/a
Non GAAP effective tax rate[7][9]	14%	17%	n/a	n/a
Non GAAP diluted EPS – ADS[8][9]	3.98	3.37	+18%	+17%
Net cash provided by operating activities	1,520	1,153	+32%	n/a

(1) Growth rates are at Constant Exchange Rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2017 performance (restated using 2016 exchange rates for the relevant period) to actual 2016 reported performance.
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is royalties and other revenues (Q4 2017: $234m; Q4 2016: $185m).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is total revenues (Q4 2017: $4,145m; Q4 2016: $3,806m).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is combined R&D and SG&A (Q4 2017: $1,322m, Q4 2016: $1,406m).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income (Q4 2017: $3,105m, Q4 2016: $457m).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income margin as a percentage of total revenues (Q4 2017: 75%, Q4 2016: 12%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is effective tax rate (Q4 2017: benefit of 342%, Q4 2016: charge of 16%).
(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is diluted EPS-ADS (Q4 2017: $10.22, Q4 2016: $1.51).
(9) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Q4 product sales performance

$MM	Q4 2017 Sales U.S.	International	Total	Growth vs. Q4 2016 Reported	CER[1][3]
Immunoglobulin Therapies	489	134	623	+17%	+16%
Hereditary Angioedema[2]	426	35	461	+29%	+28%
Bio Therapeutics	84	73	157	-16%	-17%
Immunology Total	**999**	**242**	**1,241**	**+15%**	**+14%**
Hemophilia	396	441	838	+3%	+2%
Inhibitor Therapies	62	134	196	+0%	-2%
Hematology Total	**458**	**576**	**1,034**	**+3%**	**+1%**
VYVANSE	472	69	541	+14%	+13%
ADDERALL XR	102	4	106	+28%	+28%
MYDAYIS	-4	-	-4	N/A	N/A
Other Neuroscience	4	38	42	+33%	+32%
Neuroscience Total	**573**	**111**	**684**	**+16%**	**+16%**
LIALDA/MEZAVANT	71	29	100	-55%	-56%
GATTEX/REVESTIVE	94	12	106	+63%	+62%
PENTASA	89	-	89	+2%	+2%
NATPARA/NATPAR	43	1	44	+66%	+66%
Other Internal Medicine	14	63	77	-13%	-15%
Internal Medicine Total	**311**	**105**	**416**	**-15%**	**-16%**
ELAPRASE	43	118	161	-2%	-6%
REPLAGAL	-	123	123	+10%	+6%
VPRIV	40	53	93	+7%	+4%
Genetic Diseases Total	**83**	**294**	**377**	**+4%**	**+0%**
Oncology	50	23	72	+32%	+30%
Ophthalmics	86	-	86	N/M	N/M
Total Product Sales	**2,561**	**1,350**	**3,911**	**+8%**	**+7%**

(1) Growth rates are at Constant exchange rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2017 performance (restated using 2016 exchange rates for the relevant period) to actual 2016 reported performance.
(2) For 2017 reporting (including comparative information), HAE sales have been reclassified to the Immunology franchise from Genetic Diseases.
(3) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Q4 2017 reported performance metrics

Year on Year Growth:	Q4 2017
Product sales	8%
Non GAAP R&D[1][8]	4%
Non GAAP SG&A[2][8]	-13%
Combined Non GAAP R&D and SG&A[3][8]	-8%

Ratios: As % of Non GAAP Total Revenue	Q4 2017	Q4 2016
Non GAAP gross margin[4][8]	72%	75%
Non GAAP R&D[5][8]	10%	11%
Non GAAP SG&A[6][8]	20%	25%
Non GAAP EBITDA[7][8]	41%	40%

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (Q4 2017: +5%).
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (Q4 2017: -11%).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is combined R&D and SG&A (Q4 2017: -6%).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (Q4 2017: 70%, Q4 2016: 72%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D as a percentage of total revenues (Q4 2017: 11%, Q4 2016: 11%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A as a percentage of total revenues (Q4 2017: 21%, Q4 2016: 26%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income margin as a percentage of total revenues (Q4 2017: 75%, Q4 2016: 12%).
(8) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Reported regional product sales and pro forma growth analysis

Q4 2017	US	EU	LATAM	APAC[3]	Other	Total
Product Sales $MM	2,561	659	172	219	299	3,911
% of Product Sales	65%	17%	4%	6%	8%	
YoY Growth	**9%**	**11%**	**5%**	**-12%**	**15%**	**8%**

FY 2017	US	EU	LATAM	APAC[3]	Other	Total
Product Sales $MM[1]	9,511	2,533	654	843	908	14,449
% of Product Sales	66%	18%	5%	6%	6%	
Pro Forma YoY Growth[2]	**7%**	**5%**	**13%**	**11%**	**13%**	**8%**

(1) Results include Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) Growth rates represent FY 2017 reported sales compared to recast FY 2016 pro forma sales as previously disclosed by Baxalta following the separation from Baxter.
(3) APAC region includes Japan.

Income statement growth analysis

$MM	2016 Q1[1]	2016 Q2[1]	2016 Q3[1]	2016 Q4[1]	2016 FY[1]	2017 Q1[1]	2017 Q2[1]	2017 Q3[1]	2017 Q4[1]	2017 FY[1]
Total product sales	$1,627	$2,322	$3,315	$3,621	$10,886	$3,412	$3,592	$3,534	$3,911	$14,449
versus prior year	*+14%*	*+57%*	*+110%*	*+123%*	*+78%*	*+110%*	*+55%*	*+7%*	*+8%*	*+33%*
Non GAAP royalties & other revenues[2][9]	$82	$107	$137	$185	$511	$160	$154	$164	$159	$637
versus prior year	*+26%*	*+31%*	*+75%*	*+101%*	*+61%*	*+95%*	*+44%*	*+20%*	*-14%*	*+25%*
Non GAAP revenues[3][9]	$1,709	$2,429	$3,452	$3,806	$11,397	$3,572	$3,746	$3,698	$4,070	$15,086
versus prior year	*+15%*	*+57%*	*+109%*	*+122%*	*+78%*	*+109%*	*+54%*	*+7%*	*+7%*	*+32%*
Non GAAP gross margin [4][9]	86.7%	80.4%	74.9%	75.3%	78.0%	78.3%	76.1%	76.5%	72.1%	75.6%
Combined Non GAAP R&D and SG&A[5][9]	$651	$934	$1,239	$1,354	$4,178	$1,221	$1,237	$1,212	$1,247	$4,917
versus prior year	+14%	+34%	+90%	+97%	+60%	+88%	+32%	-2%	-8%	+18%
Non GAAP EBITDA Margin[6][9]	49%	42%	39%	40%	41%	44%	43%	44%	41%	43%
Non GAAP tax rate[7][9]	18%	16%	13%	17%	16%	16%	16%	15%	14%	15%
Non GAAP diluted Earnings per ADS[8][9]	$3.19	$3.38	$3.17	$3.37	$13.10	$3.63	$3.73	$3.81	$3.98	$15.15
versus prior year	*+12%*	*+29%*	*-2%*	*+13%*	*+12%*	*+14%*	*+10%*	*+20%*	*+18%*	*+16%*

(1) Results from continuing operations including Baxalta (acquired on June 3, 2016) and Dyax (acquired on January 22, 2016).
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is royalties and other revenues (Q4 2017: $234m; Q4 2016: $185m; FY 2017: $712m; FY 2016: $511m).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is total revenues (Q4 2017: $4,145m; Q4 2016: $3,806m; FY 2017: $15,161m; FY 2016: $11,397m).
(4) This is a Non GAAP financial measure as a percentage of total revenues. The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (Q4 2017: 69.5%, Q4 2016: 72.3%, FY 2017: 69.0%, FY 2016: 66.5%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is combined R&D and SG&A (Q4 2017: -6%, Q4 2016: +68%, FY 2017: +19%, FY 2016: +31%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is net income margin as a percentage of total revenues (Q4 2017: 75%, Q4 2016: 12%, FY 2017: 28%, FY 2016: 3%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is tax rate (Q4 2017: benefit of 342%, Q4 2016: charge of 16%, FY 2017: benefit of 125%, FY 2016: benefit of 26%).
(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q4 2017: $10.22, Q4 2016: $1.51, FY 2017: $14.05, FY 2016: $1.27).
(9) See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 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 to Non GAAP free cash flow reconciliation	FY 2017 $MM	FY 2016 $MM	Reported Growth	Q4 2017 $MM	Q4 2016 $MM	Reported Growth
Net cash provided by operating activities	**4,257**	**2,659**	**+60%**	**1,520**	**1,153**	**+32%**
Receipts relating to license arrangements	(75)	-		(75)	-	
Capital expenditure	(799)	(646)		(233)	(247)	
Payments relating to license arrangements	48	90		8	-	
Non GAAP free cash flow[(1)(2)]	**3,431**	**2,103**	**+63%**	**1,219**	**906**	**+35%**

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is US GAAP Operating Income (see details above).
(2) See See slide 43 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 44 to 47 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

HAE franchise details

Net Product Sales in $ MM

	2016					2017				
	Q1	Q2	Q3	Q4	FY	Q1	Q2	Q3	Q4	FY
CINRYZE	**164.2**	**173.0**	**165.4**	**177.6**	**680.2**	**225.9**	**175.9**	**56.9**	**240.6**	**699.3**
US	155.9	163.5	151.6	167.6	638.6	216.4	164.7	46.2	229.4	656.7
International	8.3	9.5	13.8	10.0	41.6	9.5	11.2	10.7	11.2	42.6
FIRAZYR	**128.3**	**136.7**	**146.3**	**167.2**	**578.5**	**128.5**	**137.4**	**195.5**	**201.6**	**663.0**
US	113.4	119.5	129.1	148.9	510.9	111.6	118.1	173.6	177.9	581.2
International	14.9	17.2	17.2	18.3	67.6	16.9	19.3	21.9	23.7	81.8
KALBITOR	**10.4**	**17.7**	**11.1**	**13.0**	**52.2**	**11.7**	**20.6**	**16.0**	**19.0**	**67.3**
US	10.4	17.7	11.1	13.0	52.2	11.7	20.6	16.0	19.0	67.3
International	-	-	-	-	-	-	-	-	-	-
Total HAE	**302.9**	**327.4**	**322.8**	**357.8**	**1,310.9**	**366.1**	**333.9**	**268.4**	**461.2**	**1,429.6**
Growth	*26%*	*35%*	*4%*	*33%*	*23%*	*21%*	*2%*	*-17%*	*29%*	*9%*

Non GAAP measures

This presentation contains financial measures not prepared in accordance with U.S. GAAP. These measures are referred to as "Non GAAP" measures and include: Non GAAP total revenues; Non GAAP operating income; Non GAAP income tax expense; Non GAAP net income; Non GAAP diluted earnings per ADS; Non GAAP effective tax rate; Non GAAP CER; Non GAAP cost of sales; Non GAAP gross margin; Non GAAP R&D; Non GAAP SG&A; Non GAAP other expense; Non GAAP free cash flow, Non GAAP net debt, Non GAAP EBITDA and Non GAAP EBITDA margin.

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

Shire's management uses Non GAAP financial measures to make operating decisions as they facilitate additional internal comparisons of Shire's performance to historical results and to competitors' 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 differently 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 U.S. GAAP, and Shire's financial results calculated in accordance with U.S. GAAP and reconciliations to those financial statements should be carefully evaluated.

Non GAAP Financial Measure Descriptions

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

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

Acquisitions and integration activities:
- Up-front payments and milestones in respect of in-licensed and acquired products;
- Costs associated with acquisitions, including transaction costs, fair value adjustments on contingent consideration and acquired inventory;
- Costs associated with the integration of companies; and
- 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 U.S. GAAP to Non GAAP measures.

Depreciation, which is included in Cost of sales, R&D and SG&A costs in our U.S. 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, or receipts, for in-licensed and acquired products, but including capital expenditure in the ordinary course of business.

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

A reconciliation of Non GAAP financial measures to the most directly comparable measure under U.S. GAAP is presented on pages 44 to 47.

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 December 31, 2017 were $1.34:£1.00 and $1.18:€1.00 (2016: $1.26:£1.00 and $1.09:€1.00). Average exchange rates used by Shire for the twelve months ended December 31, 2017 were $1.29:£1.00 and $1.13:€1.00 (2016: $1.36:£1.00 and $1.11:€1.00).

2020 Financial Targets

A reconciliation of 2020 Non GAAP EBITDA to US GAAP net income and Non GAAP tax rates to the US GAAP tax rates cannot be provided because we are unable to forecast with reasonable certainty many of the items necessary to calculate such comparable GAAP measures, including asset impairments, acquisitions and integration related expenses, divestments, reorganizations and discontinued operations related expenses, legal settlement costs, as well as other unusual or non-recurring gains or losses . These items are uncertain, depend on various factors, and could be material to our results computed in accordance with GAAP. We believe the inherent uncertainties in reconciling Non GAAP measures for periods after 2018 to the most comparable GAAP measures would make the forecasted comparable GAAP measures nearly impossible to predict with reasonable certainty and therefore inherently unreliable.

GAAP to Non GAAP reconciliation
For the twelve months ended December 31, 2017

$MM	GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**15,160.6**	**-**	**-**	**-**	**-**	**(74.6)**	**-**	**15,086.0**
Costs and expenses:								
Cost of product sales	4,700.8	-	(747.8)	-	-	-	(276.1)	3,676.9
R&D	1,763.3	(20.0)	(131.2)	-	-	-	(47.2)	1,564.9
SG&A	3,530.9	-	-	-	(10.6)	4.0	(172.5)	3,351.8
Amortization of acquired intangible assets	1,768.4	(1,768.4)	-	-	-	-	-	-
Integration and acquisition costs	894.5	-	(894.5)	-	-	-	-	-
Reorganization costs	47.9	-	-	(47.9)	-	-	-	-
Gain on sale of product rights	(0.4)	-	-	0.4	-	-	-	-
Depreciation	-	-	-	-	-	-	495.8	495.8
Total operating expenses	12,705.4	(1,788.4)	(1,773.5)	(47.5)	(10.6)	4.0	-	9,089.4
Operating Income	**2,455.2**	**1,788.4**	**1,773.5**	**47.5**	**10.6**	**(78.6)**	**-**	**5,996.6**
Total other expense, net	(561.8)	-	6.1	(28.7)	-	15.0	-	(569.4)
Income from continuing operations before income taxes and equity earnings of equity method investees	1,893.4	1,788.4	1,779.6	18.8	10.6	(63.6)	-	5,427.2
Income taxes	2,357.6	(419.7)	(389.9)	(10.8)	(3.8)	(2,359.0)	-	(825.6)
Equity in earnings of equity method investees, net of taxes	2.5	-	-	-	-	-	-	2.5
Income from continuing operations	**4,253.5**	**1,368.7**	**1,389.7**	**8.0**	**6.8**	**(2,422.6)**	**-**	**4,604.1**
Gain from discontinued operations, net of tax	18.0	-	-	(18.0)	-	-	-	-
Net income	**4,271.5**	**1,368.7**	**1,389.7**	**(10.0)**	**6.8**	**(2,422.6)**	**-**	**4,604.1**
No. of Shares	912.0							912.0
Diluted earnings per ADS	**$14.05**	**$4.50**	**$4.57**	**($0.03)**	**$0.02**	**($7.96)**	**-**	**$15.15**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Impairment of IPR&D intangible asset ($20.0 million), amortization of intangible assets relating to intellectual property rights acquired ($1,768.4 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Baxalta ($747.8 million), costs relating to license arrangements ($131.2 million), acquisition and integration costs primarily associated with Baxalta ($773.8 million), net charge related to the change in the fair value of contingent consideration liabilities primarily related to SHP643 ($120.7 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($6.1 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Reorganization costs primarily relating to facility consolidations ($47.9 million), net gain on sale of product rights ($0.4 million), gains on sale of long-term investments ($28.7 million), tax effect of adjustments and gain from discontinued operations, net of tax ($18.0 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($10.6 million), and tax effect of adjustments;

(e) Other: Receipt of upfront license fee ($74.6 million), one-time adjustment to pension expense ($4.0 million), loss on fair value adjustment for joint venture net written option ($15.0 million), income tax adjustment on subsidiary move from Zurich to Zug ($11.1 million), credit to income taxes due to U.S. tax reform ($2,378.3 million), and tax effect of other adjustments; and

(f) Depreciation reclassification: Depreciation of $495.8 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

Shire

GAAP to Non GAAP reconciliation
For the twelve months ended December 31, 2016

$MM	GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**11,396.6**	**-**	**-**	**-**	**-**	**-**	**-**	**11,396.6**
Costs and expenses:								
Cost of product sales	3,816.5	-	(1,118.0)	(18.9)	-	(10.0)	(160.8)	2,508.8
R&D	1,439.8	(8.9)	(110.0)	-	-	-	(34.1)	1,286.8
SG&A	3,015.2	-	-	-	(16.3)	(10.0)	(98.0)	2,890.9
Amortization of acquired intangible assets	1,173.4	(1,173.4)	-	-	-	-	-	-
Integration and acquisition costs	883.9	-	(883.9)	-	-	-	-	-
Reorganization costs	121.4	-	-	(121.4)	-	-	-	-
Gain on sale of product rights	(16.5)	-	-	16.5	-	-	-	-
Depreciation	-	-	-	-	-	-	292.9	292.9
Total operating expenses	10,433.7	(1,182.3)	(2,111.9)	(123.8)	(16.3)	(20.0)	-	6,979.4
Operating Income	**962.9**	**1,182.3**	**2,111.9**	**123.8**	**16.3**	**20.0**	**-**	**4,417.2**
Total other expense, net	(476.8)	-	93.6	6.0	-	-	-	(377.2)
Income from continuing operations before income taxes and equity losses of equity method investees	486.1	1,182.3	2,205.5	129.8	16.3	20.0	-	4,040.0
Income taxes	126.1	(295.4)	(422.7)	(41.8)	(5.9)	(1.1)	-	(640.8)
Equity in losses of equity method investees, net of taxes	(8.7)	-	-	-	-	-	-	(8.7)
Income from continuing operations	**603.5**	**886.9**	**1,782.8**	**88.0**	**10.4**	**18.9**	**-**	**3,390.5**
Loss from discontinued operations, net of tax	(276.1)	-	-	276.1	-	-	-	-
Net income	**327.4**	**886.9**	**1,782.8**	**364.1**	**10.4**	**18.9**	**-**	**3,390.5**
No. of Shares	776.2							776.2
Diluted earnings per ADS	**$1.27**	**$3.43**	**$6.88**	**$1.41**	**$0.04**	**$0.07**	**-**	**$13.10**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Impairment of SHP627 IPR&D intangible asset ($8.9 million), amortization of intangible assets relating to intellectual property rights acquired ($1,173.4 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Dyax and Baxalta ($1,118.0 million), SHP647 (Pfizer) upfront and milestone payments ($110.0 million), acquisition and integration costs primarily associated with NPS, Dyax and Baxalta ($873.0 million), net charge related to the change in the fair value of contingent consideration liabilities ($10.9 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($93.6 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Inventory write-off ($18.9 million) relating to the planned closure of a facility at the Los Angeles manufacturing site, and exit and severance costs ($85.3 million), costs relating to facility consolidations ($36.1 million), net gain on sale of product rights ($11.0 million), net gain on sale of assets ($5.5 million), loss on divestment of non-core subsidiary ($6.0 million), tax effect of adjustments and loss from discontinued operations, net of tax ($276.1 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($16.3 million), and tax effect of adjustments;

(e) Other: One-time adjustment to pension expense ($20.0 million), and tax effect of adjustments; and

(f) Depreciation reclassification: Depreciation of $292.9 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

Shire

GAAP to Non GAAP reconciliation
For the three months ended December 31, 2017

$MM	GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**4,144.9**	**-**	**-**	**-**	**-**	**(74.6)**	**-**	**4,070.3**
Costs and expenses:								
Cost of product sales	1,263.5	-	(59.1)	-	-	-	(66.9)	1,137.5
R&D	438.8	-	(7.5)	-	-	-	(10.2)	421.1
SG&A	883.2	-	-	-	(2.0)	-	(55.2)	826.0
Amortization of acquired intangible assets	487.9	(487.9)	-	-	-	-	-	-
Integration and acquisition costs	197.8	-	(197.8)	-	-	-	-	-
Reorganization costs	23.4	-	-	(23.4)	-	-	-	-
Gain on sale of product rights	-	-	-	-	-	-	-	-
Depreciation	-	-	-	-	-	-	132.3	132.3
Total operating expenses	3,294.6	(487.9)	(264.4)	(23.4)	(2.0)	-	-	2,516.9
Operating Income	**850.3**	**487.9**	**264.4**	**23.4**	**2.0**	**(74.6)**	**-**	**1,553.4**
Total other expense, net	(148.9)	-	0.7	(19.8)	-	15.0	-	(153.0)
Income from continuing operations before income taxes and equity earnings of equity method investees	701.4	487.9	265.1	3.6	2.0	(59.6)	-	1,400.4
Income taxes	2,402.2	(114.5)	(129.3)	(3.2)	(0.7)	(2,348.0)	-	(193.5)
Equity in earnings of equity method investees, net of taxes	2.4	-	-	-	-	-	-	2.4
Income from continuing operations	**3,106.0**	**373.4**	**135.8**	**0.4**	**1.3**	**(2,407.6)**	**-**	**1,209.3**
Loss from discontinued operations, net of tax	(0.6)	-	-	0.6	-	-	-	-
Net income	**3,105.4**	**373.4**	**135.8**	**1.0**	**1.3**	**(2,407.6)**	**-**	**1,209.3**
No. of Shares	911.9	-	-	-	-	-	-	911.9
Diluted earnings per ADS	**$10.22**	**$1.23**	**$0.45**	**-**	**-**	**($7.92)**	**-**	**$3.98**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired ($487.9 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Baxalta ($59.1 million), costs relating to license arrangements ($7.5 million), acquisition and integration costs primarily associated with Baxalta ($221.4 million), net credit related to the change in the fair value of contingent consideration liabilities ($23.6 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($0.7 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Reorganization costs primarily relating to facility consolidations ($23.4 million), gains on sale of long-term investments ($19.8 million), tax effect of adjustments and loss from discontinued operations, net of tax ($0.6 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($2.0 million), and tax effect of adjustments;

(e) Other: Receipt of upfront license fee ($74.6 million), loss on fair value adjustment for joint venture net written option ($15.0 million), credit to income taxes due to U.S. tax reform ($2,378.3 million), and tax effect of other adjustments; and

(f) Depreciation reclassification: Depreciation of $132.3 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

GAAP to Non GAAP reconciliation
For the three months ended December 31, 2016

$MM	GAAP	Adjustments						Non GAAP
		(a)	(b)	(c)	(d)	(e)	(f)	
Total Revenues	**3,806.1**	**-**	**-**	**-**	**-**	**-**	**-**	**3,806.1**
Costs and expenses:								
Cost of product sales	1,053.6	-	(20.7)	(7.3)	-	(10.0)	(75.6)	940.0
R&D	416.8	-	-	-	-	-	(13.4)	403.4
SG&A	989.4	-	-	-	(0.2)	(10.0)	(28.6)	950.6
Amortization of acquired intangible assets	470.9	(470.9)	-	-	-	-	-	-
Integration and acquisition costs	145.3	-	(145.3)	-	-	-	-	-
Reorganization costs	5.7	-	-	(5.7)	-	-	-	-
Gain on sale of product rights	(4.3)	-	-	4.3	-	-	-	-
Depreciation	-	-	-	-	-	-	117.6	117.6
Total operating expenses	3,077.4	(470.9)	(166.0)	(8.7)	(0.2)	(20.0)	-	2,411.6
Operating Income	**728.7**	**470.9**	**166.0**	**8.7**	**0.2**	**20.0**	**-**	**1,394.5**
Total other expense, net	(153.7)	-	2.1	-	-	-	-	(151.6)
Income from continuing operations before income taxes and equity losses of equity method investees	575.0	470.9	168.1	8.7	0.2	20.0	-	1,242.9
Income taxes	(92.3)	(110.5)	(14.5)	6.9	(0.1)	(1.1)	-	(211.6)
Equity in losses of equity method investees, net of taxes	(6.8)	-	-	-	-	-	-	(6.8)
Income from continuing operations	**475.9**	**360.4**	**153.6**	**15.6**	**0.1**	**18.9**	**-**	**1,024.5**
Loss from discontinued operations, net of tax	(18.6)	-	-	18.6	-	-	-	-
Net income	**457.3**	**360.4**	**153.6**	**34.2**	**0.1**	**18.9**	**-**	**1,024.5**
No. of Shares	911.1							911.1
Diluted earnings per ADS	**$1.51**	**$1.19**	**$0.51**	**$0.11**	**-**	**$0.06**	**-**	**$3.37**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired ($470.9 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Expense related to the unwind of inventory fair value adjustments primarily associated with Dyax and Baxalta ($20.7 million), acquisition and integration costs primarily associated with NPS, Dyax and Baxalta ($99.5 million), net charge related to the change in the fair value of contingent consideration liabilities ($45.8 million), amortization of one-time upfront borrowing costs for Baxalta and Dyax ($2.1 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Inventory write-off ($7.3 million) relating to the planned closure of a facility at the Los Angeles manufacturing site, and exit and severance net credit ($0.9 million), costs relating to facility consolidations ($6.6 million), net loss on sale of product rights ($1.2 million), net gain on sale of assets ($5.5 million), tax effect of adjustments and loss from discontinued operations, net of tax ($18.6 million);

(d) Legal and litigation costs: Costs related to litigation, government investigations, other disputes and external legal costs ($0.2 million), and tax effect of adjustments;

(e) Other: One-time adjustment to pension expense ($20.0 million), and tax effect of adjustments; and

(f) Depreciation reclassification: Depreciation of $117.6 million included in Cost of product sales, R&D and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.