Q3 2018 Financial Results

Flemming Ornskov, MD, MPH – CEO
Thomas Dittrich – CFO

November 1st, 2018

Shire

“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 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 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;
- the potential uncertainty among our employees, customers, suppliers, and other business partners resulting from the announcement by Takeda Pharmaceutical Company Limited on May 8, 2018 of a recommended offer for Shire under the U.K. Takeover Code; 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 “ITEM1A: Risk Factors”, and in Shire’s 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.

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Agenda

1. Business update		Flemming Ornskov, MD, MPH *CEO*
2. Financial review		Thomas Dittrich *CFO*
3. Summary		Flemming Ornskov, MD, MPH *CEO*
4. Q & A		

We continue to deliver against our key priorities

Key Q3 Achievements

Continued commercial execution

- Product sales **grew 6%** driven by Immunology, recently-launched products, and international expansion
- **Product sales growth across all franchises(1)** on a Non GAAP CER basis(2)(3)

Innovative pipeline progress

- **TAKHZYRO approved** in US and Canada and **positive CHMP** opinion received
- **Continued pipeline progression**

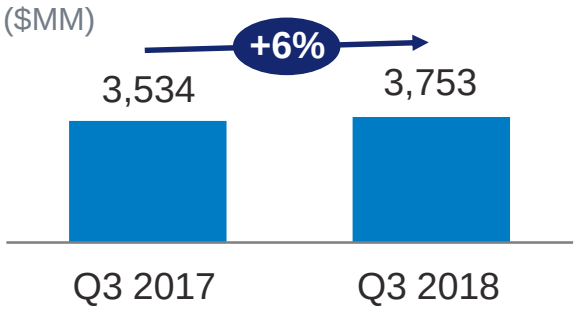
Other key updates

- **Completed sale of Oncology** franchise in Aug 2018 at an attractive multiple
- Completed **$2.3B debt repurchase** with Oncology sale proceeds
- **Takeda integration planning** ongoing; closing expected in H1 2019

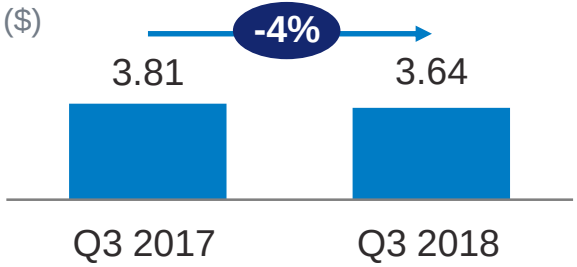
(1) Excluding the Oncology franchise.
(2) Growth rates are at Constant Exchange Rate, a Non GAAP financial measure. CER growth is computed by restating 2018 results using average 2017 foreign exchange rates for the relevant period.
(3) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above.

Solid Q3 commercial and financial performance

Product sales



Non GAAP Diluted Earnings per ADS[1][4]



Financial highlights

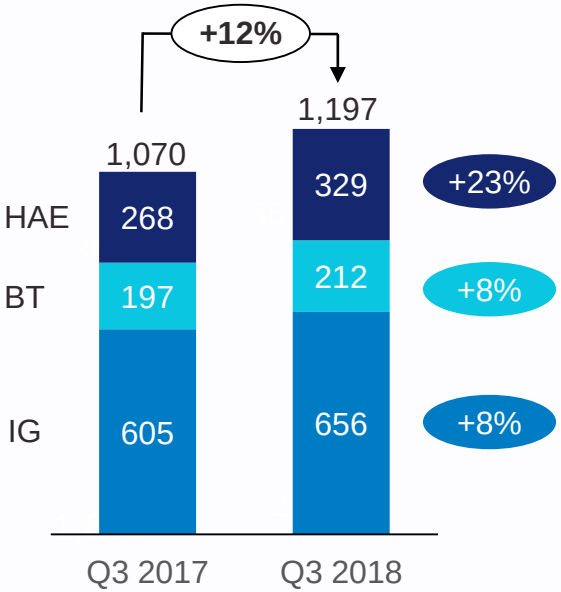
- Product sales of $3.8B and **+6% growth; +7% on a CER basis[2][4]**
- Revenues of $3.9B and +5% growth
- Non GAAP **EBITDA growth of +1%[4]**
- Non GAAP diluted **EPS decline of -4%[1][4]**
- Non GAAP Free Cash Flow[3][4] **of $0.97B, up +8%**
- YTD Non GAAP **net debt[5] pay-down of $3.9B**

(1) The most directly comparable measure under US GAAP is diluted EPS-ADS (Q3 2018: $1.75, Q3 2017: $1.81).
(2) Growth rates are at Constant Exchange Rate, a Non GAAP financial measure. CER growth is computed by restating 2018 results using average 2017 foreign exchange rates for the relevant period.
(3) The most directly comparable measure under US GAAP is net cash provided by operating activities. (Q3 2018: $0.9B).
(4) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 26 to 28 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
(5) Non GAAP net debt represents cash and cash equivalents less short and long term borrowings, capital leases, and other debt.

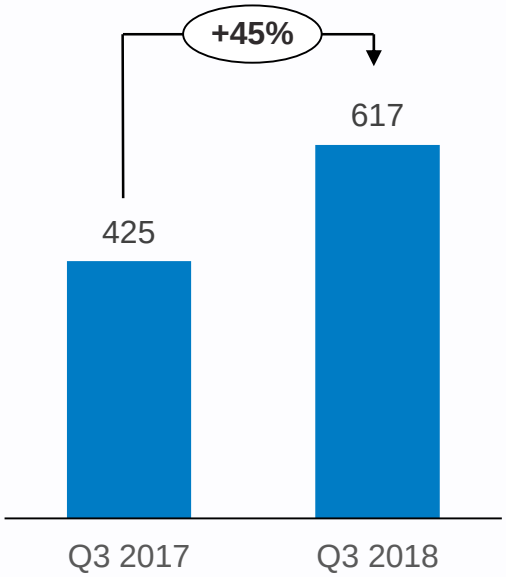
Continued execution across key growth drivers

Product sales, $MM

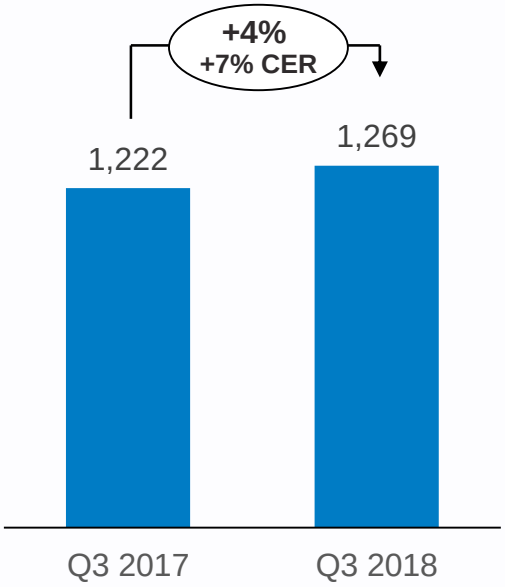
Immunology franchise



Recently launched products[1][2]



International markets[2]

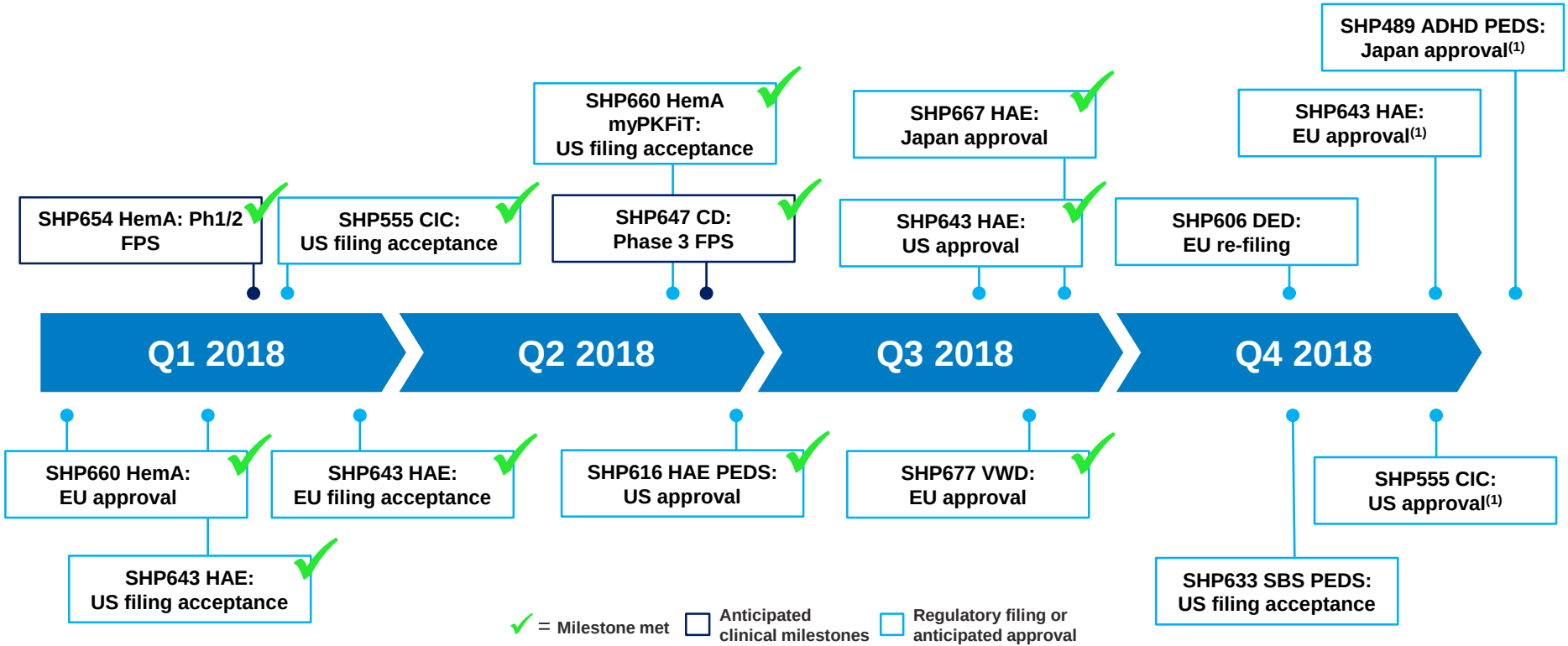


(1) Products launched between 2013 and 2018: HYQVIA, CUVITRU, XIIDRA, MYDAIS, ADYNOVATE, VOVENDI, RIXUBIS, OBIZUR, NATPARA, GATTEX, AND TAKHZYRO.

(2) Recently launched products and international markets exclude Oncology.

Note: HAE: Hereditary Angioedema; BT: Bio Therapeutics; IG: Immunoglobulin.

Good progress advancing the pipeline



(1) Subject to regulatory approval.
All approvals based on standard regulatory review timelines. Programs with Breakthrough Designation reflect accelerated review/approvals.
Note: Timings are approximated to the nearest quarter.
CD: Crohn's Disease; DED: Dry Eye Disease; CIC: Chronic Idiopathic Constipation; HAE: Hereditary Angioedema; VWD: Von Willebrand Disease; ADHD: Attention Deficit Hyperactivity Disorder; FPS: First Patient Screened; HemA: Hemophilia A; PEDS: Pediatric; SBS: Short Bowel Syndrome.

TAKHZYRO launched in US and global regulatory progress on track

TAKHZYRO™
(lanadelumab-flyo) injection

- **First monoclonal antibody** to prevent hereditary angioedema attacks
- Potential to **change treatment paradigm** and drive HAE franchise growth in **International markets**
- Subcutaneous **injection in <1 minute for most patients**, with a recommended starting dose of once every 2 weeks
- **Encouraging early launch trajectory** in the US

Regulatory progress

- **US: Approved** after priority review, orphan drug, and breakthrough designations
- **EU: Received CHMP positive opinion,** EC decision on marketing authorization expected December 2018
- **Canada: Approved** after priority review
- **Switzerland: Application validated**, orphan drug designation
- **Australia: Priority review**, orphan drug designation

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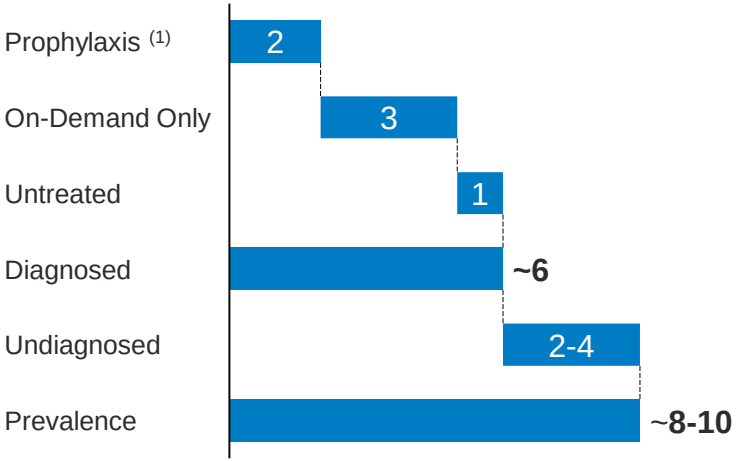
Opportunity to drive HAE preventive therapy both in US and International markets

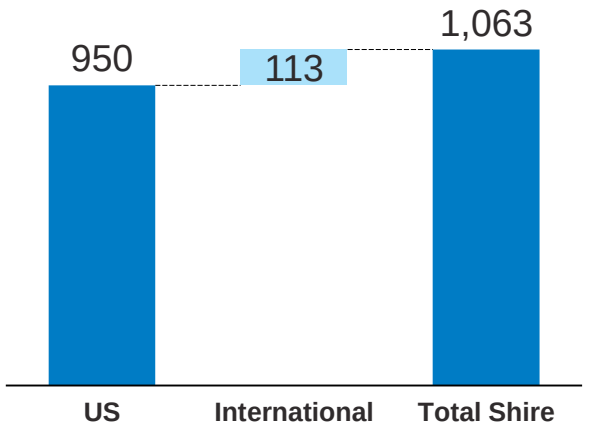
Clear unmet medical need in the US

Estimated US HAE Patients (thousands)



2018 YTD Shire HAE Sales

$MM



(1) Prophylaxis group also includes patients using on-demand treatment in a prophylaxis manner

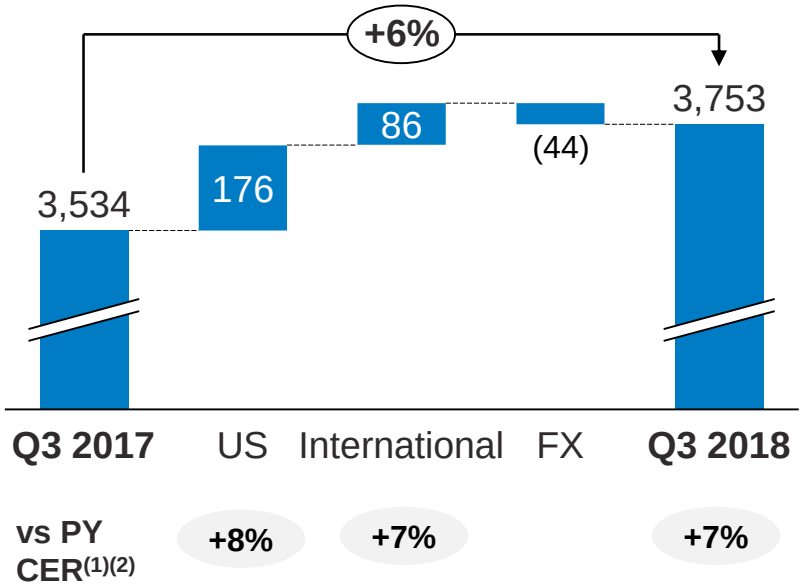
Source: Shire Internal Estimate

Financial Review

Thomas Dittrich
Chief Financial Officer

Product sales growth of +7% at constant exchange rates

Product Sales in $MM

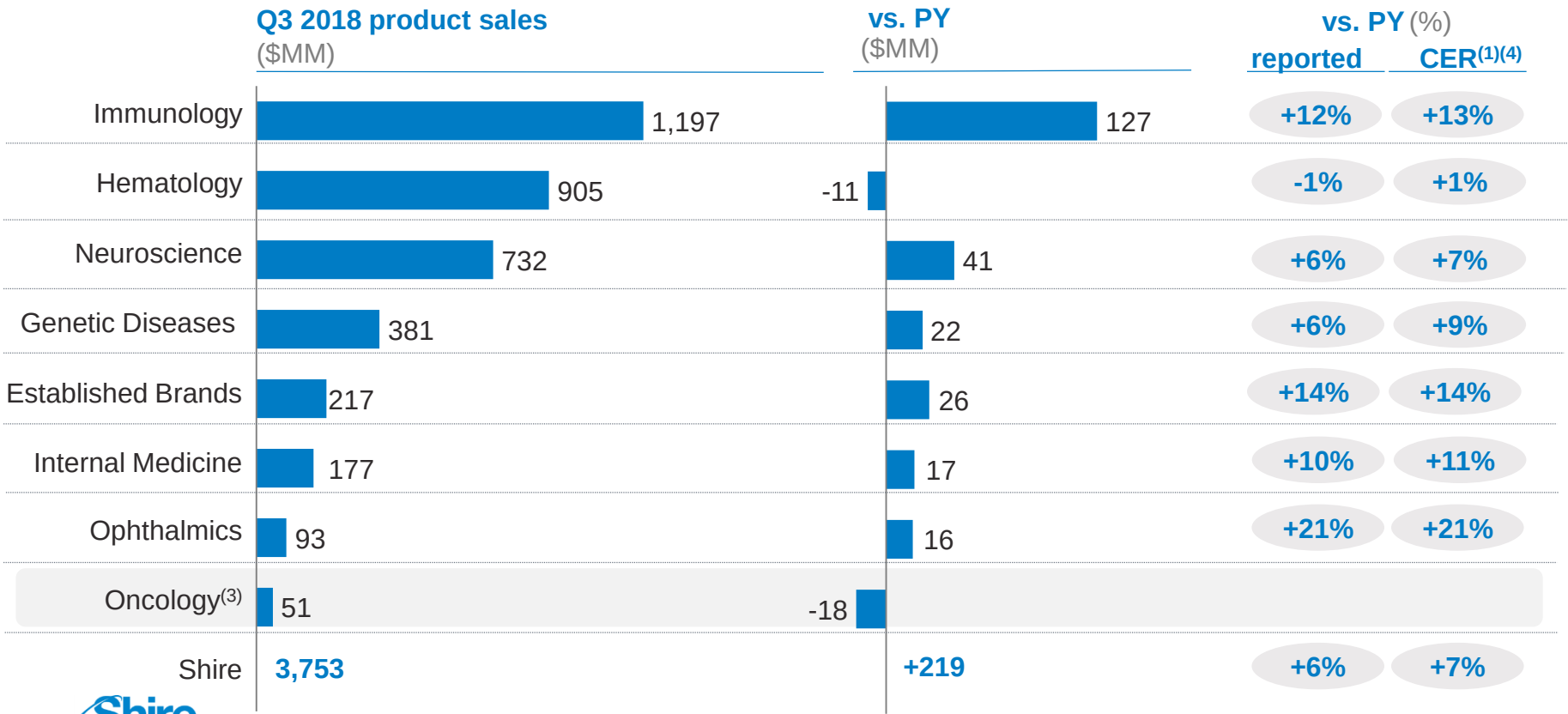


Comments

- Significant growth contribution from **recently-launched products**
- **Unfavorable foreign exchange** rates impacted growth by 1 percentage point
- Oncology sale: Q3 2018 only includes **2 months of Oncology sales**

(1) Growth rates are at Constant Exchange Rate, a Non GAAP financial measure. CER growth is computed by restating 2018 results using average 2017 foreign exchange rates for the relevant period.
(2) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above.

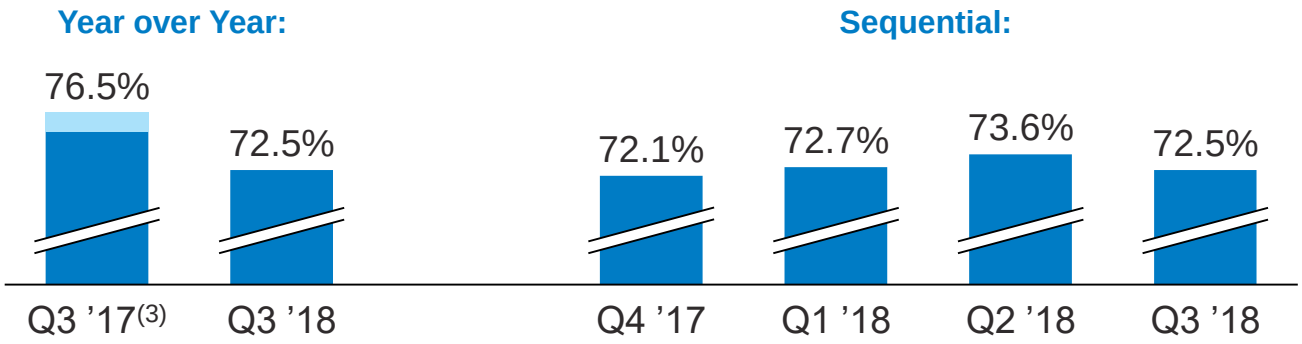
Growth in all franchises on a CER basis(2)



(1) Growth rates are at Constant Exchange Rate, a Non GAAP financial measure. CER growth is computed by restating 2018 results using average 2017 foreign exchange rates for the relevant period.
(2) Excluding the Oncology franchise.
(3) Completed sale of Oncology franchise to Servier on Aug 31st 2018.
(4) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above.

Gross margin overview

Non GAAP gross margin[1][2] % of total revenue



- Q3 2017 benefitted significantly (~250 basis points) from **favorable phasing of Baxalta-related** manufacturing costs
- Q3 2018 year-over-year and sequential comparisons impacted by **headwinds from foreign exchange rates and revenue mix**

(1) The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (Q3 2018: 70.1%, Q2 2018: 71.7%, Q1 2018: 69.9%, Q2 2017: 70.4%, Q4 2017: 69.5%, Q3 2017: 72.9%).
(2) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 26 to 28 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
(3) Blue shading represents ~250 basis point benefit from favorability from the timing of changes in the costs to manufacture certain products.

Q3 P&L reflecting solid commercial execution

$MM	Q3 2018	Q3 2017	YoY Change
Product sales	**3,753**	**3,534**	**+6%**
Royalties and other revenues	119	164	-27%
Total revenues	**3,872**	**3,698**	**+5%**
Non GAAP gross profit	**2,805**	**2,830**	**-1%**
Non GAAP gross margin	*72.5%*	*76.5%*	*-4.0 ppc*
Non GAAP R&D	**393**	**392**	**+0%**
Non GAAP SG&A	**780**	**820**	**-5%**
Non GAAP combined R&D and SG&A	**1,173**	**1,212**	**-3%**
Combined Non GAAP R&D and SG&A %	*30.3%*	*32.8%*	*-2.5 ppc*
Non GAAP EBITDA	**1,633**	**1,618**	**+1%**
Non GAAP EBITDA margin	*42.2%*	*43.8%*	*-1.6 ppc*
Non GAAP depreciation	158	120	+31%
Non GAAP other expense, net	168	134	+25%
Non GAAP effective tax rate	**14.7%**	**14.9%**	*-0.2 ppc*
Non GAAP net income	**1,119**	**1,158**	**-3%**
Non GAAP EPS	**3.64**	**3.81**	**-4%**

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See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 26 to 28 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
Note: YoY=Year over Year.

Cash Flow & Balance Sheet
On track with our leverage target for 2018

		Q3 '18 $B	Q3 '17 $B	YoY Change	Q2 '18 $B	QoQ Change
Key Cash Flow Items	Capital expenditure	0.2	0.2	0.0	0.2	0.0
	Non GAAP free cash flow[1][2]	1.0	0.9	0.1	0.8	0.2
	Dividends paid	-	-	-	0.28	(0.28)
Key Balance Sheet Items	Cash & cash equivalents	0.2	0.2	(0.0)	0.3	(0.1)
	Debt outstanding	15.3	20.6	(5.2)	17.9	(2.6)
	Non GAAP net debt[2][3]	15.2	20.4	(5.2)	17.7	(2.5)
	Non GAAP net debt[3]/ Non GAAP EBITDA[4] ratio[2]	2.3x	3.2x	-0.9x	2.7x	-0.4x

(1) The most directly comparable measure under US GAAP is Net cash provided by operating activities (Q3 2018 $858m; Q3 2017 $1,055m; Q2 2018 $940m).
(2) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 26 to 28 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
(3) Non GAAP net debt represents cash and cash equivalents less short and long term borrowings, capital leases and other debt.
(4) Non GAAP EBITDA represents 12 months trailing Non GAAP EBITDA.
Note: YoY=Year over Year; QoQ=Quarter over Quarter.

FY guidance adjusted for sale of Oncology only, absorbing significant FX headwinds

	Full Year 2018 Guidance [1]		Oncology impact		Updated guidance, excluding Oncology
Total revenue[1]	$15.4 - $15.9 billion	→	- $0.1 billion	→	$15.3 - $15.8 billion
Non GAAP diluted EPS – ADS	$14.90 - $15.50	→	- $0.13	→	$14.77 - $15.37

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

Summary

Continued focus on execution and innovation in 2018

Operational Focus	▪ Maintaining **strong focus on 2018 performance**, with YTD 6% product sales growth
TAKHZYRO Approval	▪ Now **approved in the US and Canada**, with encouraging early trajectory in the US ▪ Potential for TAKHZYRO to expand the HAE prophylaxis market in the US and globally
Covington Approval	▪ **FDA approval in June 2018** for GAMMAGARD product; Albumin now filed for approval ▪ Expected to add ~**30% capacity** to internal plasma manufacturing network once fully operational
Oncology Divestment	▪ Completed $2.4B **sale of Oncology franchise to Servier** at an attractive multiple ▪ Immediately used proceeds to accelerate debt pay-down
Takeda Acquisition	▪ **Takeda received regulatory clearances** including US, Japan and China ▪ Joint **integration planning** efforts are ongoing
Key Upcoming Milestones	▪ Additional potential **TAKHZYRO** global regulatory approvals (e.g. EU)(1) ▪ **Prucalopride** US PDUFA date December 21, 2018 ▪ **Closing of** acquisition by Takeda **expected in H1 2019 subject to shareholder approval** of both companies and additional regulatory clearances

(1) Subject to regulatory review and approval

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Pipeline overview

RESEARCH AND PRECLINICAL	PHASE 1	PHASE 2		PHASE 3		REGISTRATION	2018 APPROVALS
30+ programs • Internally developed and via partnership • Both rare disease and specialty conditions • Multiple modalities including NCEs, MAbs, proteins, and gene therapy	**SHP611** (MLD)	**SHP607**[1] (Chronic Lung Disease)	**SHP652** (SLE)	**SHP609** (Hunter IT) Ph 2/3	**SHP633** (Pediatric SBS) *LCM for GATTEX*	**SHP489 – Japan** (ADHD) *LCM for VYVANSE*	**SHP660**[3] **– EU** (Hemophilia A) *LCM for ADYNOVATE*
	SHP631 (Hunter CNS)	**SHP615- U.S.** (Seizures) *LCM for BUCCOLAM*	**SHP659** (Dry Eye Disease)	**SHP615 – Japan** (Seizures) *LCM for BUCCOLAM*	**SHP640** (Infectious Conjunctivitis)	**SHP555 – US** (CIC)	**SHP677** (VWD) *LCM for VONVENDI*
	SHP634 – Japan (Hypoparathyroidism) *LCM for NATPARA*	**SHP625**[2] (PFIC)	**SHP625** (ALGS)	**SHP616 – Japan** (HAE Prophylaxis) *LCM for CINRYZE*	**SHP647** (UC)	**SHP606 – EU**[4] (Dry Eye Disease) LCM for XIIDRA	**SHP643**[2] (HAE Prophylaxis) *TAKHZYRO*
	SHP639 (Glaucoma)			**SHP616 SC** (HAE Prophylaxis) *LCM for CINRYZE*	**SHP647** (CD)	**SHP643 EU** (HAE Prophylaxis)	**SHP616 US** (Pediatric HAE) *LCM for CINRYZE*
	SHP654 (Hemophilia A, Gene Therapy)			**SHP616** (AMR) *LCM for CINRYZE*	**SHP655** (cTTP)	**SHP667 - Japan** (HAE) *LCM for FIRAZYR*	
	SHP680 (Neurological Conditions)			**SHP620**[2] (CMV infection in transplant patients)	**SHP671** (CIDP) *LCM for HYQVIA*		
				SHP621[2] (EoE)	**SHP671** (Pediatric PID) *LCM for HYQVIA*		
				SHP633 – Japan (Adult SBS) *LCM for GATTEX*	**SHP672** (CHAWI surgery) *LCM for OBIZUR*		

SOURCE: Pipeline as of Oct 2018.

(1) SHP607 originally developed for ROP - Retinopathy of Prematurity; (2) Granted breakthrough designation by FDA; (3) Aproved in U.S. for on-demand, prophylaxis in adults and children and in perioperative management. (4) SHP606 EU Filing Strategy changed to Centralized Procedure.
Note: Phase 2/3 programs shown as Phase 3; LCM: Life cycle management – while these products are approved for certain indications, they are under investigation for other indications and subject to regulatory approval. Oncology assets removed due to divesture to Servier
MLD- Metachromatic Leukodystrophy; CNS- Central Nervous System; PFIC- Progressive Familial Intrahepatic cholestasis; ALGS- Alagille Syndrome; SLE- Systemic Lupus Erythematosus; CMV- Cytomegalovirus; EoE- Eosinophilic Esophagitis; UC- Ulcerative Colitis; CD- Crohn's Disease; cTTP- Congenital Thrombotic Thrombocytopenic Purpura; CIDP- Chronic Inflammatory Demyelinating Polyradiculoneuropathy; PID- Primary Immunodeficiency Diseases; CHAWI- Congenital Hemophilia A with Inhibitors; CIC- Chronic Idiopathic Constipation; ADHD- Attention Deficit Hyperactivity Disorder; HAE- Hereditary Angioedema; VWD- Von Willebrand Disease; SBS: Short Bowel Syndrome

Rare indication

Non-rare indication

Q3 product sales performance

$MM	Q3 2018 Sales U.S.	Q3 2018 Sales International	Q3 2018 Sales Total	YoY Growth Reported	YoY Growth CER[1][6]
Immunoglobulin Therapies	531	125	656	+8%	+10%
Hereditary Angioedema[2]	291	38	329	+23%	+23%
Bio Therapeutics	92	120	212	+8%	+9%
Immunology Total	**914**	**283**	**1,197**	**+12%**	**+13%**
Hemophilia	387	349	736	+1%	+3%
Inhibitor Therapies	45	124	169	-11%	-8%
Hematology Total	**431**	**474**	**905**	**-1%**	**+1%**
VYVANSE	529	67	595	+11%	+11%
ADDERALL XR	72	5	76	-28%	-28%
MYDAYIS	19	-	19	+89%	+89%
Other Neuroscience[3]	1	40	41	+13%	+15%
Neuroscience Total	**620**	**112**	**732**	**+6%**	**+7%**
ELAPRASE	42	129	171	+12%	+15%
REPLAGAL	-	123	123	+5%	+8%
VPRIV	39	49	88	-2%	-2%
Genetic Diseases Total	**81**	**301**	**381**	**+6%**	**+9%**
LIALDA/MEZAVANT	89	30	119	+37%	+38%
PENTASA	66	-	66	-9%	-9%
Other Established Brands[4]	11	21	32	+0%	+1%
Established Brands Total	**165**	**51**	**217**	**+14%**	**+14%**
GATTEX/REVESTIVE	82	15	97	+14%	+15%
NATPARA/NATPAR	48	3	51	+30%	+30%
Other Internal Medicine[5]	0	29	29	-21%	-19%
Internal Medicine Total	**130**	**47**	**177**	**+10%**	**+11%**
Ophthalmics	92	1	93	+21%	+21%
Oncology	33	17	51	N/M	N/M
Total Product Sales	**2,467**	**1,286**	**3,753**	**+6%**	**+7%**

(1) Growth rates are at Constant Exchange Rate, a Non GAAP financial measure. CER growth is computed by restating 2018 results using average 2017 foreign exchange rates for the relevant period.
(2) For 2018 reporting (including comparative information), HAE sales have been reclassified to Immunology from Genetic Diseases.
(3) Other Neuroscience includes INTUNIV, EQUASYM, and BUCCOLAM.
(4) Other Established Brands includes FOSRENOL and CARBATROL.
(5) Other Internal Medicine includes AGRYLIN, PLENADREN, and RESOLOR.
(6) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 26 to 28 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

HAE franchise details

Product Sales

	2016					2017					2018		
$MM	**Q1**	**Q2**	**Q3**	**Q4**	**FY**	**Q1**	**Q2**	**Q3**	**Q4**	**FY**	**Q1**	**Q2**	**Q3**
CINRYZE	**164**	**173**	**165**	**178**	**680**	**226**	**176**	**57**	**241**	**699**	**147**	**136**	**117**
US	156	164	152	168	639	216	165	46	229	657	135	124	105
International	8	10	14	10	42	10	11	11	11	43	12	12	12
FIRAZYR	**128**	**137**	**146**	**167**	**579**	**129**	**137**	**196**	**202**	**663**	**206**	**211**	**140**
US	113	120	129	149	511	112	118	174	178	581	182	185	114
International	15	17	17	18	68	17	19	22	24	82	24	27	26
KALBITOR	**10**	**18**	**11**	**13**	**52**	**12**	**21**	**16**	**19**	**67**	**15**	**17**	**20**
US	10	18	11	13	52	12	21	16	19	67	15	17	20
International	-	-	-	-	-	-	-	-	-	-	-	-	-
TAKHZYRO	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**51**
US	-	-	-	-	-	-	-	-	-	-	-	-	51
International	-	-	-	-	-	-	-	-	-	-	-	-	-
Total HAE	**303**	**327**	**323**	**358**	**1,311**	**366**	**334**	**268**	**461**	**1,430**	**369**	**365**	**329**
Growth	*+26%*	*+35%*	*+4%*	*+33%*	*+23%*	*+21%*	*+2%*	*-17%*	*+29%*	*+9%*	*+1%*	*+9%*	*+23%*

Reported regional product sales and growth analysis

Q3 2018	US	EU	LATAM	APAC[(1)]	Other	Total
Product Sales $MM	2,467	594	184	234	274	3,753
% of Product Sales	66%	16%	5%	6%	7%	
YoY Growth	**+8%**	**-11%**	**+32%**	**+4%**	**+27%**	**+6%**

(1) APAC region includes Japan.

Income statement growth analysis

$MM	2017 Q1	2017 Q2	2017 Q3	2017 Q4	2017 FY	2018 Q1	2018 Q2	2018 Q3
Total product sales	$3,412	$3,592	$3,534	$3,911	$14,449	$3,637	$3,809	$3,753
versus prior year	*+110%*	*+55%*	*+7%*	*+8%*	*+33%*	*+7%*	*+6%*	*+6%*
Non GAAP royalties & other revenues[(1)(8)]	$160	$154	$164	$159	$637	$129	$111	$119
versus prior year	*+95%*	*+44%*	*+20%*	*-14%*	*+25%*	*-20%*	*-28%*	*-27%*
Non GAAP revenues[(2)(8)]	$3,572	$3,746	$3,698	$4,070	$15,086	$3,766	$3,920	$3,872
versus prior year	*+109%*	*+54%*	*+7%*	*+7%*	*+32%*	*+5%*	*+5%*	*+5%*
Non GAAP gross margin[(3)(8)]	78.3%	76.1%	76.5%	72.1%	75.6%	72.7%	73.6%	72.5%
Combined Non GAAP R&D and SG&A[(4)(8)]	$1,221	$1,237	$1,212	$1,247	$4,917	$1,133	$1,256	$1,173
versus prior year	+88%	+32%	-2%	-8%	+18%	-7%	*+2%*	*-3%*
Non GAAP EBITDA Margin[(5)(8)]	44%	43%	44%	41%	43%	43%	42%	42%
Non GAAP tax rate[(6)(8)]	16%	16%	15%	14%	15%	14%	16%	15%
Non GAAP diluted Earnings per ADS[(7)(8)]	$3.63	$3.73	$3.81	$3.98	$15.15	$3.86	$3.88	$3.64
versus prior year	*+14%*	*+10%*	*+20%*	*+18%*	*+16%*	*+6%*	*+4%*	*-4%*

(1) The most directly comparable measure under US GAAP is royalties and other revenues (Q3 2018: $119m; Q3 2017: $164m).
(2) The most directly comparable measure under US GAAP is total revenues (Q3 2018: $3,872m; Q3 2017: $3,698m).
(3) The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (Q3 2018: 30%, Q3 2017: 27%).
(4) The most directly comparable measure under US GAAP is combined R&D and SG&A (Q3 2018: $1,244m, Q3 2017: $1,263m).
(5) The most directly comparable measure under US GAAP is net income margin as a percentage of total revenues (Q3 2018: 14%, Q3 2017: 15%).
(6) The most directly comparable measure under US GAAP is tax rate (Q3 2018: 28%, Q3 2017: 2%).
(7) The most directly comparable measure under US GAAP is EPS-ADS (Q3 2018: $1.75, Q3 2017: $1.81).
(8) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 26 to 28 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	Q3 2018 $MM	Q3 2017 $MM	Reported Growth
Net cash provided by operating activities	**858**	**1,055**	**-19%**
Capital expenditure	(203)	(174)	
Payments relating to milestone and license arrangements	316	20	
Non GAAP free cash flow[(1)(2)]	**971**	**901**	**+8%**

(1) The most directly comparable measure under US GAAP is Net cash provided by operating activities (see details above).
(2) See slide 29 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 26 to 28 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

GAAP to Non GAAP reconciliation
For the three months ended September 30, 2018

$MM	GAAP	Adjustments					Non GAAP
		(a)	(b)	(c)	(d)	(e)	
Total Revenues	**3,871.7**	**-**	**-**	**-**	**-**	**-**	**3,871.7**
Costs and expenses:							
Cost of sales	1,157.6	-	(1.6)	-	-	(89.4)	1,066.6
R&D	407.2	-	-	-	(3.3)	(10.9)	393.0
SG&A	836.8	-	-	-	-	(57.3)	779.5
Amortization of acquired intangible assets	433.7	(433.7)	-	-	-	-	-
Integration and acquisition costs	93.0	-	(93.0)	-	-	-	-
Reorganization costs	254.8	-	-	(254.8)	-	-	-
Gain on sale of Oncology and product rights	(267.2)	-	-	267.2	-	-	-
Depreciation	-	-	-	-	-	157.6	157.6
Total operating expenses	2,915.9	(433.7)	(94.6)	12.4	(3.3)	-	2,396.7
Operating Income	**955.8**	**433.7**	**94.6**	**(12.4)**	**3.3**	**-**	**1,475.0**
Total other expense, net	(220.0)	-	-	-	51.6	-	(168.4)
Income from continuing operations before income taxes and equity earnings of equity method investees	735.8	433.7	94.6	(12.4)	54.9	-	1,306.6
Income taxes	(203.3)	(28.9)	(19.7)	4.3	55.0	-	(192.6)
Equity in earnings of equity method investees, net of taxes	4.7	-	-	-	-	-	4.7
Income from continuing operations	**537.2**	**404.8**	**74.9**	**(8.1)**	**109.9**	**-**	**1,118.7**
Net income	**537.2**	**404.8**	**74.9**	**(8.1)**	**109.9**	**-**	**1,118.7**
No. of Shares	921.1						921.1
Diluted earnings per ADS	**$1.75**	**$1.32**	**$0.24**	**($0.03)**	**$0.36**	**-**	**$3.64**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired ($433.7 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 ($1.6 million), acquisition and integration costs associated with Baxalta ($29.9 million), primarily for facility consolidations, Takeda ($46.6 million), reclass of costs to gain on sale of Oncology upon closing in Q3 2018 ($37.9 million credit), net charge related to the change in the fair value of contingent consideration liabilities ($54.5 million), and tax effect of adjustments;

(c) Divestments, reorganizations and discontinued operations: Reorganization costs primarily relating to facility consolidations ($254.8 million) and gain on sale of Oncology franchise ($267.2 million), and tax effect of adjustments;

(d) Other: Program wind-down costs ($3.3 million), loss on fair value adjustment for joint venture net written option ($11.0 million), charges related to cash tender offer ($40.6 million), income tax due to U.S. tax reform ($59.9 million), and tax effect of other adjustments; and

(e) Depreciation reclassification: Depreciation of $157.6 million included in cost of product sales, R&D, and SG&A for US GAAP separately disclosed for the presentation of Non GAAP earnings.

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

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

The following items are included in Adjustments:

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

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

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

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

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

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

Shire

GAAP net income to Non GAAP EBITDA reconciliation
For the three months ended September 30, 2018 and 2017

	3 months ended September 30,	
	2018	2017
U.S. GAAP net income	**$ 537.2**	$ 550.8
Add back/(deduct):		
Loss/(gain) from discontinued operations, net of taxes	**—**	0.4
Equity in (losses)/earnings of equity method investees, net of taxes	**(4.7)**	3.4
Income taxes	**203.3**	13.5
Other expense, net	**220.0**	140.5
U.S. GAAP operating income from continuing operations	**955.8**	708.6
Add back/(deduct) Non GAAP adjustments:		
Expense related to the unwind of inventory fair value adjustments	**1.6**	63.3
Program wind-down and one-time employee related costs	**3.3**	—
Legal and litigation costs	**—**	1.0
Amortization of acquired intangible assets	**433.7**	482.4
Integration and acquisition costs	**93.0**	237.0
Reorganization costs	**254.8**	5.4
(Gain)/loss on sale of Oncology and product rights	**(267.2)**	0.3
Depreciation	**157.6**	119.9
Non GAAP EBITDA	**1,632.6**	1,617.9
Depreciation	**(157.6)**	(119.9)
Non GAAP operating income	**$ 1,475.0**	$ 1,498.0
Net income margin[(1)]	**14%**	15 %
Non GAAP EBITDA margin[(2)]	**42%**	44 %

(1) Net income as a percentage of total revenues.
(2) Non GAAP EBITDA as a percentage of total revenues.

Non GAAP measures

This press release 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, net; Non GAAP tax adjustments; 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.

Out-license, divestments, reorganizations, and discontinued operations:
- Revenue from up-front and milestone receipts from out-license arrangements;
- Gains and losses on the sale of non-core assets;
- Costs associated with restructuring and reorganization activities;
- Termination costs; and
- Gains/(losses) from divestitures and 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 26 to 28 of this presentation.

Non GAAP CER growth is computed by restating 2018 results using average 2017 foreign exchange rates for the relevant period.

Average exchange rates used by Shire for the three months ended September 30, 2018 were $1.31:£1.00 and $1.17:€1.00 (2017: $1.31:£1.00 and $1.17:€1.00).

A reconciliation of 2020 Non GAAP EBITDA margin to U.S. GAAP net income margin 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.

Profit forecasts

On February 14, 2018, Shire published its full year 2018 outlook for total revenue of $15.4 – $15.9 billion, GAAP diluted EPS of $7.30 – $7.90, and non-GAAP diluted EPS of $14.90-$15.50 (the "Full Year 2018 Outlook"). Shire also announced "We are committed to achieving our projected revenue target of $17-$18 billion in 2020" and "With the already disclosed manufacturing and SG&A cost reduction initiatives, we are on track to achieve mid-forties Non-GAAP EBITDA margin by 2020" (the "Mid-Term Outlook").

Both the Full Year 2018 Outlook and the Mid-Term Outlook comprised all Shire franchises, including Oncology. Earlier in the year, Shire announced that it had entered into an agreement with Servier for the sale of its Oncology franchise for $2.4 billion as part of its strategy to unlock value and sharpen its focus on rare disease leadership. The transaction closed on August 31, 2018. The U.S. GAAP Full Year 2018 Outlook has also been updated for the gain from the sale of the Oncology franchise, bond retirement with the proceeds of the sale and resulting interest reduction, and reorganization costs. Accordingly, the Full Year 2018 Outlook and the Mid-Term Outlook are no longer valid and Shire has updated the Full Year 2018 Outlook and the Mid-Term Outlook to adjust for the sale of the Oncology franchise as follows:

Full Year 2018 Outlook

Full year 2018 U.S. GAAP outlook for total revenue is expected to be $15.3 – $15.8 billion and diluted earnings per ADS is expected to be $7.17 – $7.77.

Full year 2018 Non GAAP outlook for total revenue is expected to be $15.3 – $15.8 billion and diluted earnings per ADS is expected to be $14.77 – $15.37.

Mid-Term Outlook

"Our projected 2020 revenue target has been updated to $16.5 – $17.5 billion."

"We continue to expect to achieve mid-forties Non GAAP EBITDA margin by 2020."

Assumptions and basis of preparation

The Full Year 2018 Outlook and the Mid-Term Outlook (as updated) (the "Profit Forecasts") include "profit forecasts" for the purposes of Rule 28 of the City Code on Takeovers and Mergers (the "Code").

In accordance with Rule 28.1(c) of the Code, the directors of Shire confirm that: (i) the basis of accounting used to prepare the Profit Forecasts is consistent with the accounting policies of Shire (or in the case of the Non GAAP Profit Forecasts, or in the case of the Non GAAP guidance, as adjusted in accordance with Shire's established Non GAAP policy, which excludes the items set out on page 29 in the section "Non GAAP measures", including their tax effect); and (ii) each of the Profit Forecasts has been properly compiled on the basis of the following assumptions:

Assumptions outside the Directors' control

- the Profit Forecasts exclude any future effect resulting from the announcement by Takeda on May 8, 2018 of a recommended offer for Shire under the Code;
- there will be no material change to existing global macroeconomic and political conditions during the year ending December 31, 2018;
- there will be no material changes in market conditions within the pharmaceutical industry over the forecast period to December 31, 2018, in relation to either customer demand or the competitive environment which could impact Shire's products;
- there will be no product shortages caused by unanticipated production issues, such as contamination, which could result in prolonged supply shortages;
- there will be no material changes to Shire's obligations to customers or governments, its ability to negotiate new business, resolve contract disputes, or the retention of key management;
- the Euro, British Pound, and Swiss Franc and other exchange rates against the U.S. dollar, together with inflation, tax, and interest rates in Shire's principal markets, will remain relatively unchanged from the rates underpinning the Profit Forecasts;
- there will be no material adverse events that will have a significant impact on Shire's financial position or performance;
- there will be no material change in legislation, regulatory requirements, or the position of any regulatory bodies impacting Shire's operations or its accounting and tax conclusions, policies, and procedures;
- there will be no significant increases or decreases in the value of publicly-held investments resulting in recognition of material gains or losses; and
- there will be no material change in tax law and practice, including interpretive guidance issued by the IRS with respect to U.S. tax reform, impacting Shire's operations and the jurisdictions in which it earns significant amounts of income, whether earned from third parties or from intercompany transactions.

Assumptions within the Directors' control

- there will be no material change in the present management of Shire or its existing operational strategy prior to the closing of the recommended offer by Takeda announced on May 8, 2018;
- there will be no material future acquisitions, disposals, or licensing arrangements;
- there will be no material change in the debt structure of the Shire Group, other than planned repayments of existing borrowings;
- there will be no material change to the number of diluted shares in issue; and
- Shire's accounting and tax policies, including those related to determining Shire's effective tax rate, will be consistently applied in the financial year to December 31, 2018.