Q1 2018 Financial Results

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

April 26, 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 the 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;
- the potential uncertainty resulting from the announcement by Takeda Pharmaceutical Company Limited that it is considering making a possible offer for Shire; 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		Thomas Dittrich *CFO*
3. Summary		Flemming Ornskov, MD, MPH *CEO*
4. Q & A		

Shire

We continued to deliver against our key priorities

Key Achievements in Q1

Solid commercial execution

- Product **sales growth of +7%**
- Growth driven **by Immunology, recently-launched products, and international** expansion

Continue to advance pipeline

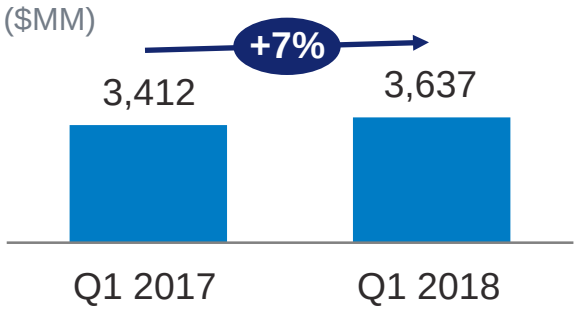
- **Innovative pipeline** with 15 programs in Phase 3 and 7 in registration
- **Lanadelumab filed in US, Europe and Canada**

Progress on portfolio optimization

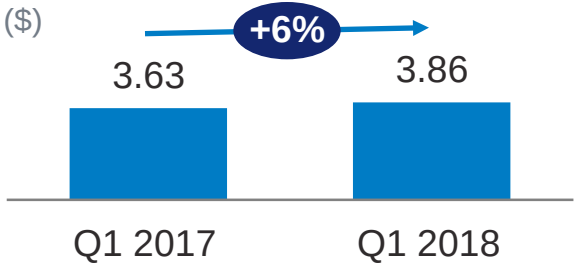
- Sale of Oncology business announced – **Sharpens focus on rare disease leadership and unlocks embedded value**

Solid Q1 commercial and financial performance

Product sales



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



Financial highlights

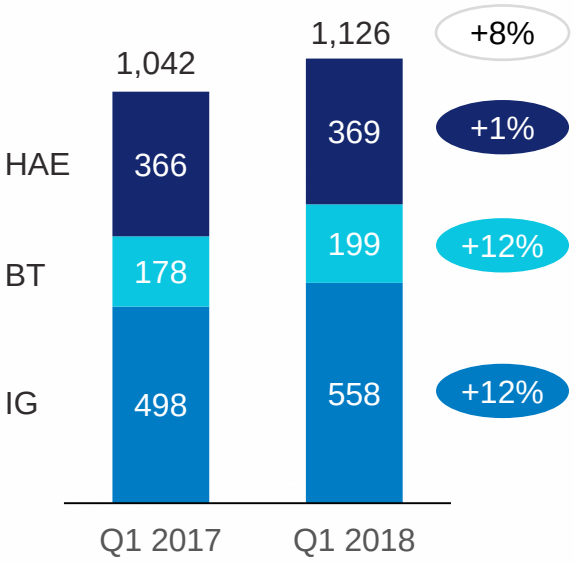
- Product sales of $3.6B and **+7% growth; +3% on a CER basis[2][4]**
- Revenues of $3.8B and +5% growth
- Non GAAP diluted **EPS growth of +6%[1][4]**
- Non GAAP Free Cash Flow[3][4] **grew to $0.9B**

(1) The most directly comparable measure under US GAAP is diluted EPS-ADS (Q1 2018: $1.81, Q1 2017: $1.23).
(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. (Q1 2018: $1.0B).
(4) See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

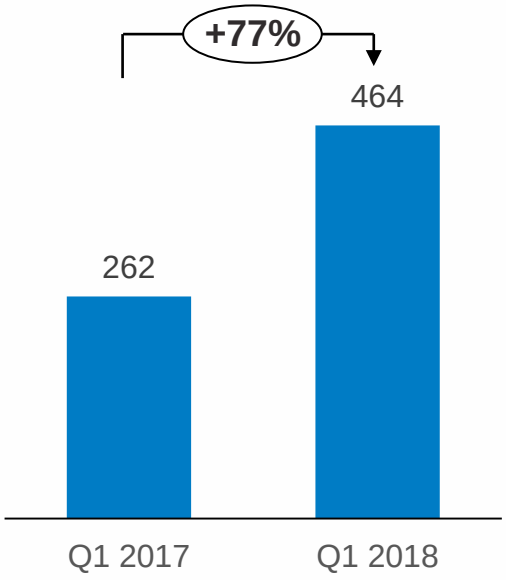
Solid execution across key growth drivers

Product sales, $MM

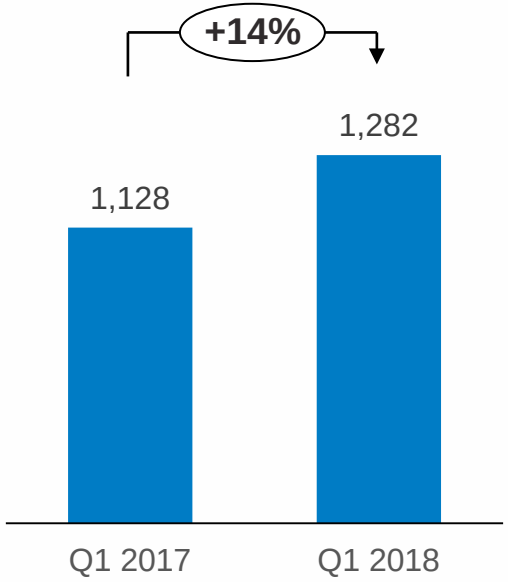
Immunology franchise



Recently launched products(1)



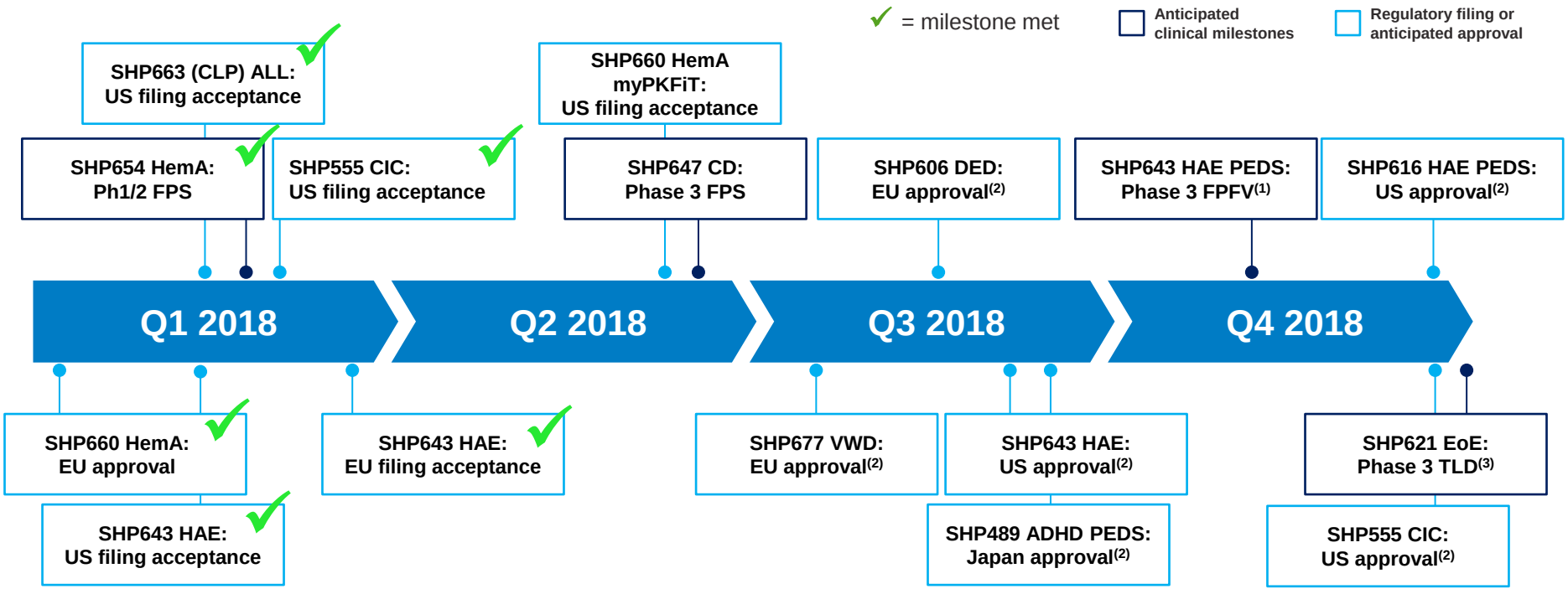
International markets



(1) Products launched between 2013 and 2017: HYQIVA, CUVITRU, XIIDRA, MYDAYIS, ADYNOVATE, VONVENDI, RIXUBIS, OBIZUR, NATPARA, GATTEX, ONIVYDE.

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

2018 Key pipeline events on track



(1) Pending PWR approval by FDA.
(2) Subject to regulatory approval.
(3) Top line data for induction study (301).

All approvals based on standard regulatory review timelines. Programs with Breakthrough Designation reflect accelerated review/approvals.

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; PWD Pediatric Written Request; HemA: Hemophilia A; CLP: Calaspargase Pegol; TLD: Top Line Data; Peds: Pediatric.

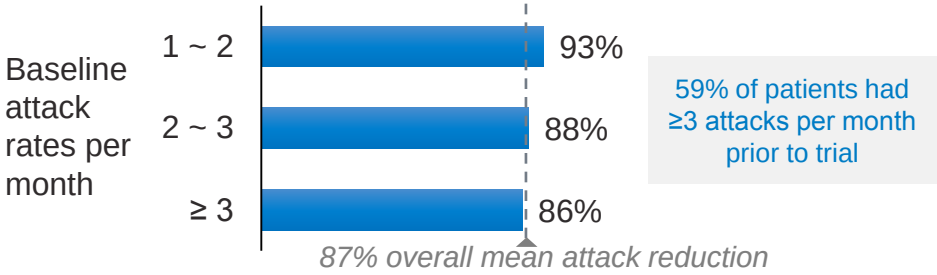
Progress on lanadelumab regulatory status and additional data(1)

Lanadelumab (SHP643) regulatory status

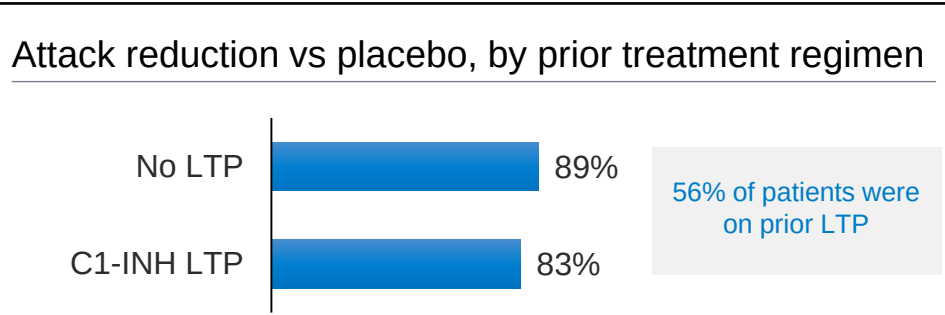
- **US:** Filing accepted, priority review, orphan drug designation
- **EU:** Application validated, accelerated assessment, orphan drug designation
- **Canada:** Filing accepted, priority review
- **Switzerland:** Application validated, orphan drug designation
- **Australia:** Priority review, orphan drug designation

Lanadelumab dosed at 300mg every 2 weeks

Efficacy regardless of baseline attack frequency



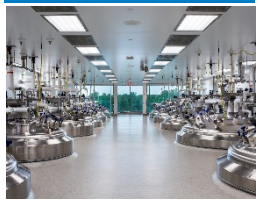
Efficacy in patients on prior LTP with C1-INH



(1) Posters presented at 2018 American Academy of Allergy, Asthma and Immunology / World Allergy Organization Joint Congress, March 2018 (Phase 3 HELP Study).
Note: The HELP Study was a phase 3, randomized, double-blind, parallel-arm, placebo-controlled study. 9 Eligible patients were aged ≥12 years with type I/II HAE and ≥1 attack during a 4-week run-in period. Patients were randomized to receive treatment for 26 weeks (days 0–182; Figure 1). All patients, including those in the placebo arm, had access to on-demand therapy to treat acute attacks during the treatment period. Long-term prophylaxis (LTP). C1 inhibitor (C1-INH).

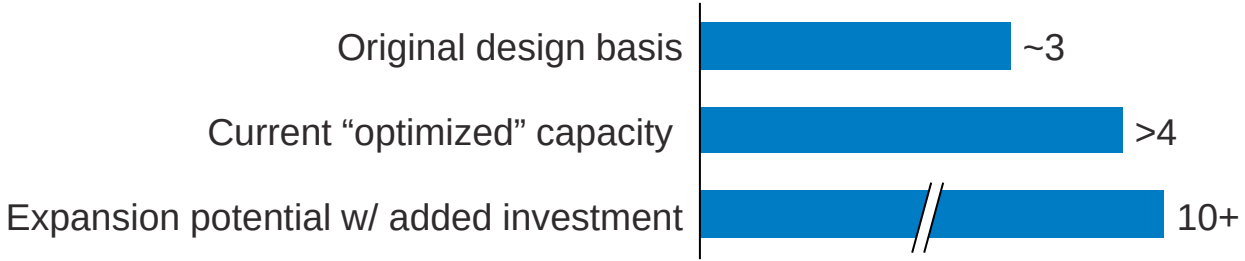
Covington site supporting continued growth of Immunology franchise

Fully integrated end-to-end production site

Plasma testing	Fractionation	Purification	Filling	Packaging
BioLife PLASMA SERVICES				

Flexible design for future expansion

Fractionation capacity, million liters



- 900 associates already engaged in production
- Site includes already approved BioLife testing and storage facility
- FDA approval expected this year(1)

Shire

(1) Subject to regulatory approval.

Announced sale of Oncology business will unlock embedded value

Portfolio optimization

Continuing to evaluate our portfolio for opportunities to **unlock further value** and **sharpen our focus** on rare disease leadership with **selective disposals of non-strategic assets**

Sale of Oncology

- Oncology business not core to Shire's **longer-term strategy**
- Selling price of $2.4B with **attractive multiple** of 9.2 times 2017 revenues
- Sharpens focus on our **leadership in rare diseases**

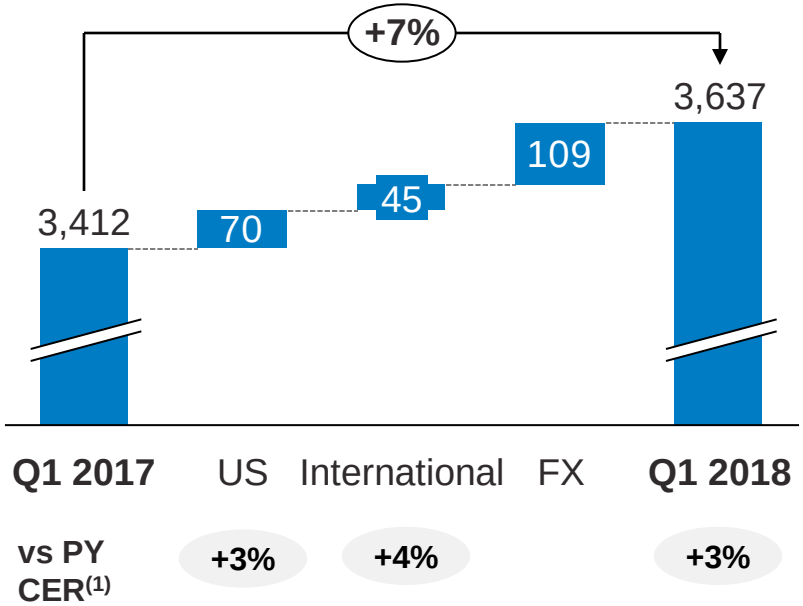
Note: Anticipated closing in Q2 or Q3 2018.

Financial Review

Thomas Dittrich
Chief Financial Officer

+7% product sales growth while absorbing ~$110M impact from LIALDA generic competition

Product Sales in $MM

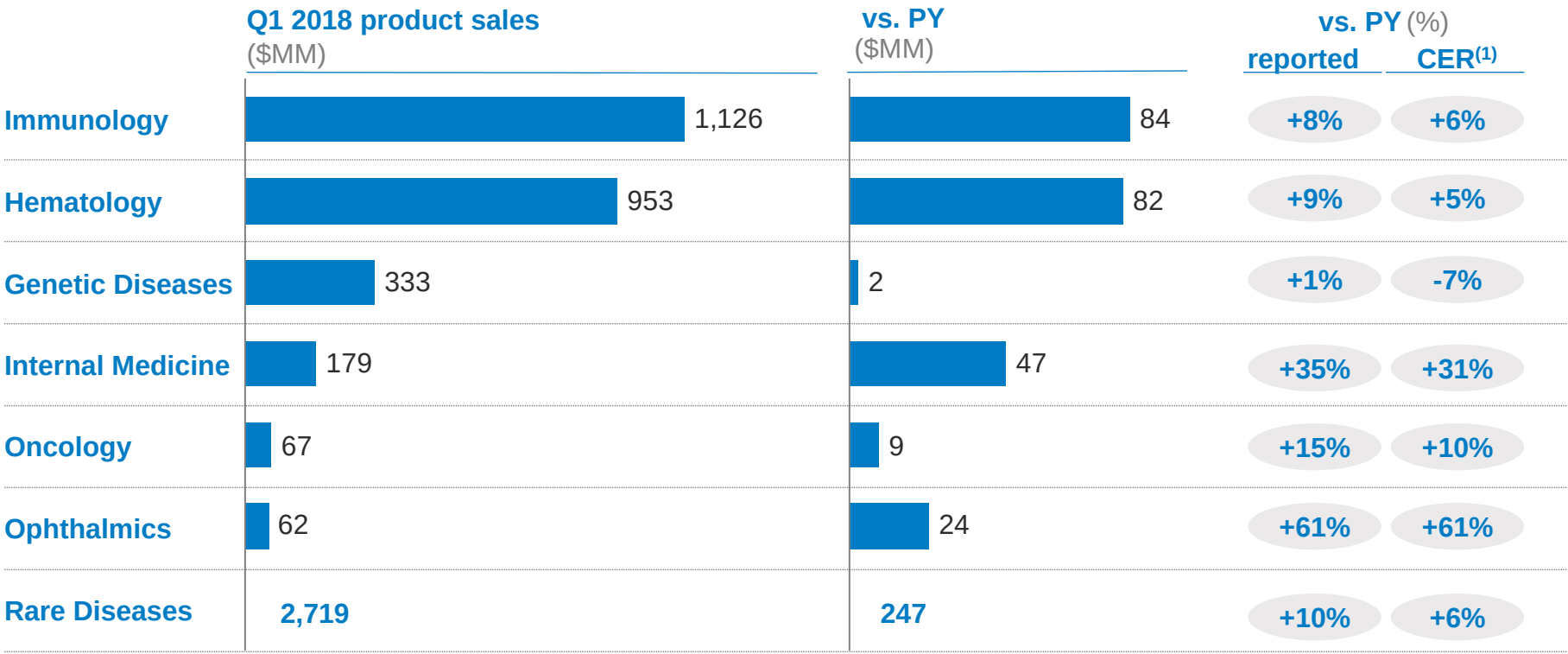


Comments

- **Solid demand growth** overall, excluding the impact of LIALDA generic competition
- **Significant growth contribution from recently launched products**, including CUVITRU, HYQVIA, ADYNOVATE, GATTEX, NATPARA, and XIIDRA
- **Favorable foreign exchange rates added 3 points** of growth overall, **offsetting the impact** from LIALDA generic competition

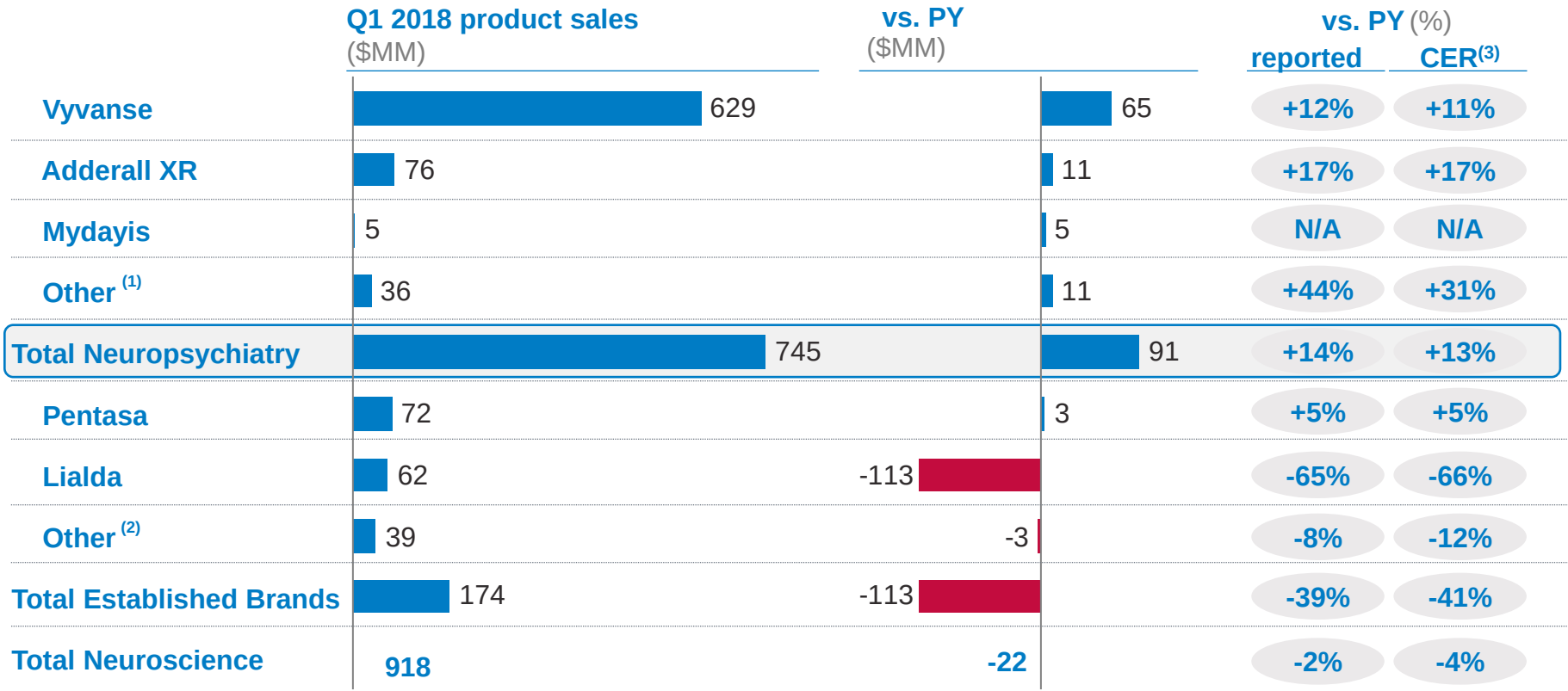
(1) Growth rates are at Constant Exchange Rate, a Non GAAP financial measure. CER growth is computed by restating 2018 results using average 2017 foreign exchange rates for the relevant period.

Rare Disease division product sales grew +10% vs prior year



(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.

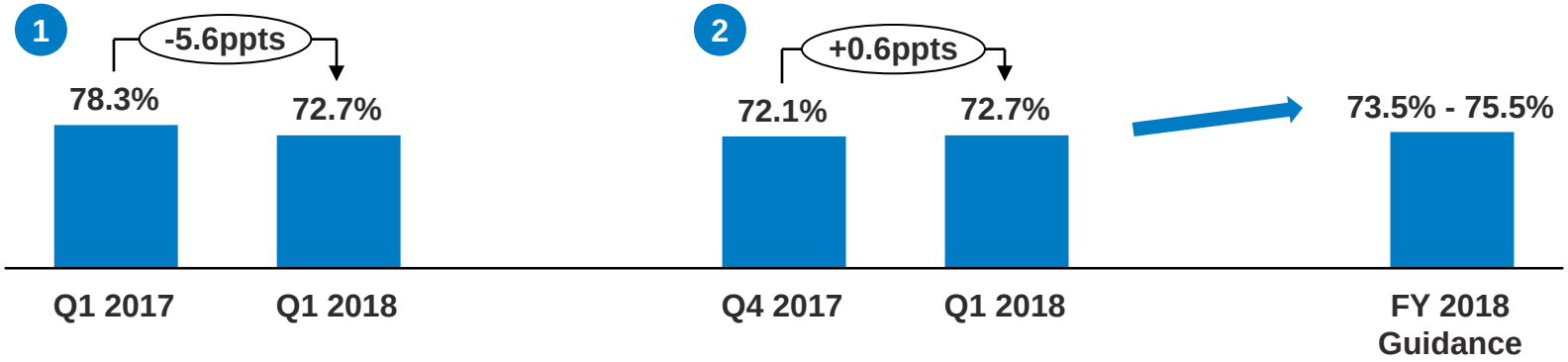
Neuroscience division with +14% sales growth excluding Established Brands



(1) Includes Intuniv, Equasym and Buccolam.
(2) Includes Fosrenol, Carbatrol, Equetro and Reminyl.
(3) 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.

Non GAAP gross margin[(1)(2)] is on track for FY guidance range

Non GAAP gross margin[(1)(2)] % of revenue



- **Q1 2017 benefitted** from favorable phasing of Baxalta-related manufacturing costs
- Q1 2018 includes **incremental Covington** expenses and headwinds from mix

- **QoQ gross margin improvement** driven by **productivity gains**

- **On track for FY gross margin** guidance driven by sales mix (growth of recently launched products)

(1) The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (Q1 2018: 69.9%, Q1 2017: 62.9%, Q4 2017: 69.5%).
(2) See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

+6% Non GAAP EPS growth driven by sales performance, increased productivity and tax benefits, partially offset by lower gross margin

$MM	Q1 2018	Q1 2017	YoY Change
Product sales	**3,637**	**3,412**	**+7%**
Royalties and other revenues	129	160	-20%
Total Revenue	**3,766**	**3,572**	**+5%**
Non GAAP gross profit	**2,740**	**2,798**	**-2%**
Non GAAP gross margin	*72.7%*	*78.3%*	*-5.6 ppc*
Non GAAP R&D	**385**	**366**	**+5%**
Non GAAP SG&A	**748**	**856**	**-13%**
Non GAAP combined R&D and SG&A	**1,133**	**1,221**	**-7%**
Combined Non GAAP R&D and SG&A %	*30.1%*	*34.2%*	*-4.1 ppc*
Non GAAP EBITDA	**1,607**	**1,576**	**+2%**
Non GAAP EBITDA Margin	*42.7%*	*44.1%*	*-1.5 ppc*
Non GAAP effective tax rate	**13.7%**	**16.5%**	*-2.7 ppc*
Non GAAP Net Income	**1,173**	**1,102**	**+6%**
Non GAAP EPS	**3.86**	**3.63**	**+6%**

See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 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 to meet our leverage target for 2018

		Q1 ’18 $B	Q1 ’17 $B	YoY Change	Q4 ’17 $B	QoQ Change
Key Cash Flow Items	Capital expenditure	0.2	0.2	(0.0)	0.2	(0.1)
	Non GAAP free cash flow[(1)(4)]	0.9	0.2	0.7	1.2	(0.3)
	Dividends paid	-	-	N/A	0.0	N/A
Key Balance Sheet Items	Cash & equivalents	0.3	0.4	(0.1)	0.5	(0.2)
	Debt outstanding	18.5	22.5	(4.0)	19.5	(1.0)
	Non GAAP net debt[(2)(4)]	18.2	22.2	(4.0)	19.1	(0.9)
	Non GAAP net debt[(2)] / Non GAAP EBITDA[(3)] ratio[(4)]	2.8x	4.1x	-1.3x	2.9x	-0.1x

(1) The most directly comparable measure under US GAAP is Net cash provided by operating activities (Q1 2018 $1,010m; Q1 2017 $459m; Q4 2017 $1,520m).
(2) Non GAAP net debt represents cash and cash equivalents less short and long term borrowings, capital leases and other debt.
(3) Non GAAP EBITDA represents 12 months trailing Non GAAP EBITDA.
(4) See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.
Note: YoY=Year over Year; QoQ=Quarter over Quarter.

2018 guidance unchanged

	Full Year 2018 Guidance[1]
Total Revenue[2]	$15.4 - $15.9 billion
Non GAAP gross margin[3] (as % of total revenue)	73.5% - 75.5%
Non GAAP combined R&D and SG&A[3]	$4.9 - $5.1 billion
Non GAAP Depreciation[3]	$575 - $625 million
Non GAAP Net Interest[3]	$450 - $550 million
Non GAAP effective tax rate[3]	16% - 18%
Non GAAP diluted EPS – ADS[3]	$14.90 - $15.50
Capital Expenditure	$800 - $900 million

	Revenue	Earnings
EUR	-1.5%	-1.0%
GBP	-0.2%	-0.3%
CHF	-0.1%	0.1%
CAD	-0.2%	-0.1%
JPY	-0.2%	-0.4%
Other	-0.5%	-0.5%

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:

Note: Risks associated with this outlook include the potential uncertainty resulting from the announcement by Takeda Pharmaceutical Company Limited that it is considering making a possible offer for Shire.

(1) Full year 2018 guidance will be updated to remove the Oncology franchise upon the close of this pending sale later this year.
(2) Management is providing guidance for total revenue. Total revenue is comprised of total product sales and royalties & other revenues. Pursuant to a change in U.S. GAAP related to accounting for revenue, certain revenue formerly classified as royalties are now recorded as product sales.
(3) See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Financial summary – Performance on track

2018

- **Solid execution in Q1 - on track to deliver 2018 guidance(1)**

Longer Term Outlook

- **No change to 2020 guidance(1)**

Capital Allocation

- **Working on disciplined and balanced capital allocation program**

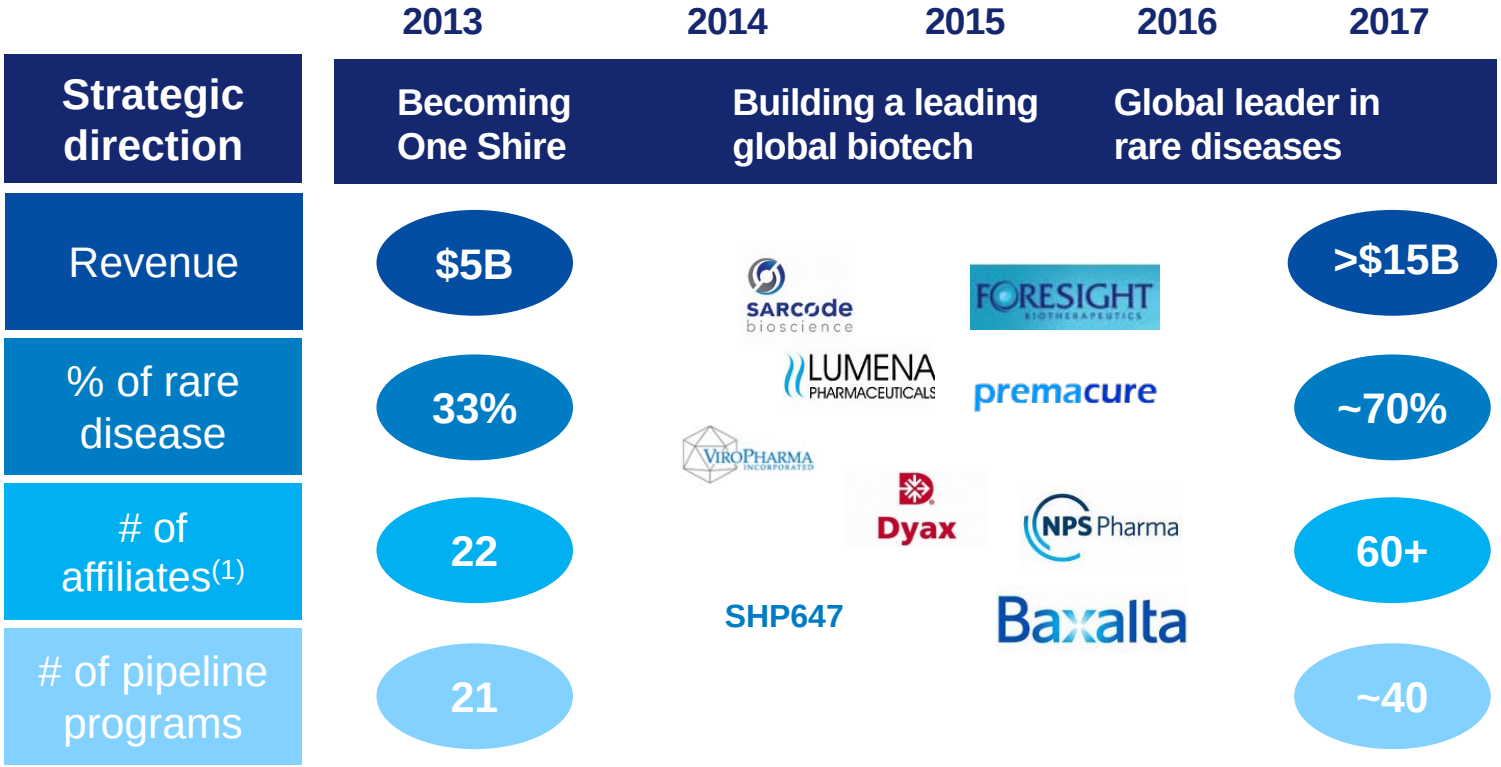
Note: Risks associated with this outlook include the potential uncertainty resulting from the announcement by Takeda Pharmaceutical Company Limited that it is considering making a possible offer for Shire.

(1) To be adjusted for the sale of the Oncology business after closing of the transaction.

Summary

Flemming Ornskov, MD, MPH
Chief Executive Officer

Putting Q1 2018 performance in perspective



(1) Number of countries with commercial operations.

Key milestones for the remainder of 2018

- **Covington** site(1) approval
- **Lanadelumab** approval in US(1) and potential approvals in Europe & Canada(1)
- **VYVANSE** approval in Japan(1)
- **XIIDRA** approval in EU(1)
- **Prucalopride** approval in US(1)

(1) 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

Pipeline overview

RESEARCH AND PRECLINICAL

35+ programs

- Internally developed and via partnership
- Both rare disease and specialty conditions
- Multiple modalities including NCEs, MAbs, proteins, and gene therapy

PHASE 1

- **SHP611** (MLD)
- **SHP631** (Hunter CNS)
- **SHP634 – Japan** (Hypoparathyroidism) *LCM for NATPARA*
- **SHP639** (Glaucoma)
- **SHP654** (Hemophilia A, Gene Therapy)
- **SHP673** (Small Cell Lung Cancer, 2nd Line) *LCM for ONIVYDE*
- **SHP680** (Neurological Conditions)

PHASE 2

- **SHP607**(1) (Chronic Lung Disease)
- **SHP615- U.S.** (Seizures) *LCM for BUCCOLAM*
- **SHP625**(2) (PFIC)
- **SHP625** (ALGS)
- **SHP626** (NASH)
- **SHP647** (CD)
- **SHP652**(4) (SLE)
- **SHP659** (Dry Eye Disease)
- **SHP673 – Japan** (Pancreatic Cancer, Post Gemcitabine) *LCM for ONIVYDE*
- **SHP673** (Pancreatic Cancer, 1st line) *LCM for ONIVYDE*

PHASE 3

- **SHP609** (Hunter IT) Ph 2/3
- **SHP615 – Japan** (Seizures) *LCM for BUCCOLAM*
- **SHP616 – Japan** (HAE Prophylaxis) *LCM for CINRYZE*
- **SHP616 SC** (HAE Prophylaxis) *LCM for CINRYZE*
- **SHP616** (AMR) *LCM for CINRYZE*
- **SHP620**(2) (CMV infection in transplant patients)
- **SHP621**(2) (EoE)
- **SHP633 – Japan** (Adult SBS) *LCM for GATTEX*
- **SHP633** (Pediatric SBS) *LCM for GATTEX*
- **SHP640** (Infectious Conjunctivitis)
- **SHP647** (UC)
- **SHP655** (cTTP)
- **SHP671** (CIDP) *LCM for HYQVIA*
- **SHP671** (Pediatric PID) *LCM for HYQVIA*
- **SHP672** (CHAWI surgery) *LCM for OBIZUR*

REGISTRATION

- **SHP489 – Japan** (ADHD) *LCM for VYVANSE*
- **SHP555 – US** (CIC)
- **SHP606 – EU** (Dry Eye Disease) LCM for XIIDRA
- **SHP643**(2) (HAE Prophylaxis)
- **SHP663** (ALL) *LCM for ONCASPAR*
- **SHP667 - Japan** (HAE) *LCM for FIRAZYR*
- **SHP677** (VWD) *LCM for VONVENDI*

2018 APPROVALS

- **SHP660**(3) **– EU** (Hemophilia A) *LCM for ADYNOVATE*

SOURCE: Pipeline as of April 2018.

(1) SHP607 originally developed for ROP; (2) Granted breakthrough designation by FDA; (3) Aproved in U.S. for on-demand, prophylaxis in adults and children and in perioperative management. (4) Working closely with the FDA to resolve their questions.

Note: Phase 2/3 programs shown as Phase 3; LCM: Life cycle management – while this product is approved for certain indications, it is under investigation for other indications and subject to regulatory approval.

Rare indication

Non-rare indication

Q1 Rare Disease product sales performance

Product Sales

$MM	Q1 2018 Sales U.S.	Q1 2018 Sales International	Q1 2018 Sales Total	YoY Growth Reported	YoY Growth CER[1][3]
Immunoglobulin Therapies	422	136	558	+12%	+10%
Hereditary Angioedema[2]	332	36	369	+1%	-0%
Bio Therapeutics	83	117	199	+12%	+7%
Immunology Total	**837**	**289**	**1,126**	**+8%**	**+6%**
Hemophilia	393	350	743	+14%	+10%
Inhibitor Therapies	61	149	210	-5%	-10%
Hematology Total	**454**	**499**	**953**	**+9%**	**+5%**
REPLAGAL	-	124	124	+13%	+3%
ELAPRASE	41	77	118	-16%	-22%
VPRIV	37	53	90	+13%	+7%
Genetic Diseases Total	**78**	**255**	**333**	**+1%**	**-7%**
GATTEX/REVESTIVE	80	16	96	+39%	+37%
NATPARA/NATPAR	43	2	45	+52%	+51%
Other Internal Medicine	1	37	38	+13%	+0%
Internal Medicine Total	**124**	**55**	**179**	**+35%**	**+31%**
Oncology Total	43	24	67	+15%	+10%
Ophthalmics Total	62	1	62	+61%	+61%
Total Rare Disease Product Sales	**1,597**	**1,122**	**2,719**	**+10%**	**+6%**

(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 the Immunology franchise from Genetic Diseases.
(3) See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

HAE Franchise Details

Product Sales in $ MM

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

Q1 Neuroscience product sales performance

Product Sales

$MM	Q1 2018 Sales U.S.	Q1 2018 Sales International	Q1 2018 Sales Total	YoY Growth Reported	YoY Growth CER[1][2]
VYVANSE	557	72	629	+12%	+11%
ADDERALL XR	72	4	76	+17%	+17%
PENTASA	72	-	72	+5%	+5%
LIALDA/MEZAVANT	31	32	62	-65%	-66%
MYDAYIS	5	-	5	N/A	N/A
Other Neuroscience	21	53	75	+11%	+4%
Total Neuroscience Product Sales	**758**	**160**	**918**	**-2%**	**-4%**

(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 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

Reported regional product sales and growth analysis

Q1 2018	US	EU	LATAM	APAC[(1)]	Other	Total
Product Sales $MM	2,355	664	154	219	245	3,637
% of Product Sales	65%	18%	4%	6%	7%	
YoY Growth	**+3%**	**+14%**	**-11%**	**+12%**	**+40%**	**+7%**

(1) APAC region includes Japan.

Income statement growth analysis

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

(1) The most directly comparable measure under US GAAP is royalties and other revenues (Q1 2018: $129m; Q1 2017: $160m).
(2) The most directly comparable measure under US GAAP is total revenues (Q1 2018: $3,766m; Q1 2017: $3,572m).
(3) The most directly comparable measure under US GAAP is gross margin as a percentage of total revenues (Q1 2018: 69.9%, Q1 2017: 62.9%).
(4) The most directly comparable measure under US GAAP is combined R&D and SG&A (Q1 2018: $1,210m, Q1 2017: $1,268m).
(5) The most directly comparable measure under US GAAP is net income margin as a percentage of total revenues (Q1 2018: 15%, Q1 2017: 10%).
(6) The most directly comparable measure under US GAAP is tax rate (Q1 2018: 7%, Q1 2017: charge of 2%).
(7) The most directly comparable measure under US GAAP is EPS-ADS (Q1 2018: $1.81, Q1 2017: $1.23).
(8) See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 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	Q1 2018 $MM	Q1 2017 $MM	Reported Growth
Net cash provided by operating activities	**1,010**	**459**	**+120%**
Capital expenditure	(178)	(213)	
Payments relating to license arrangements	85	-	
Non GAAP free cash flow[(1)(2)]	**918**	**247**	**+272%**

(1) The most directly comparable measure under US GAAP is Net cash provided by operating activities (see details above).
(2) See slide 34 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. See slides 30 to 33 for a reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP.

GAAP to Non GAAP reconciliation
For the three months ended March 31, 2018

$MM	GAAP	Adjustments					Non GAAP
		(a)	(b)	(c)	(d)	(e)	
Total Revenues	**3,765.7**	**-**	**-**	**-**	**-**	**-**	**3,765.7**
Costs and expenses:							
Cost of product sales	1,132.4	-	(33.5)	-	-	(72.7)	1,026.2
R&D	405.2	-	(10.0)	-	-	(10.7)	384.5
SG&A	804.8	-	-	-	-	(56.8)	748.0
Amortization of acquired intangible assets	484.0	(484.0)	-	-	-	-	-
Integration and acquisition costs	239.7	-	(239.7)	-	-	-	-
Reorganization costs	5.3	-	-	(5.3)	-	-	-
Depreciation	-	-	-	-	-	140.2	140.2
Total operating expenses	3,071.4	(484.0)	(283.2)	(5.3)	-	-	2,298.9
Operating Income	**694.3**	**484.0**	**283.2**	**5.3**	**-**	**-**	**1,466.8**
Total other expense, net	(101.2)	-	1.7	-	(8.0)	-	(107.5)
Income from continuing operations before income taxes and equity earnings of equity method investees	593.1	484.0	284.9	5.3	(8.0)	-	1,359.3
Income taxes	(43.3)	(70.3)	(50.7)	(1.2)	(21.3)	-	(186.8)
Equity in earnings of equity method investees, net of taxes	0.8	-	-	-	-	-	0.8
Income from continuing operations	**550.6**	**413.7**	**234.2**	**4.1**	**(29.3)**	**-**	**1,173.3**
Net income	**550.6**	**413.7**	**234.2**	**4.1**	**(29.3)**	**-**	**1,173.3**
No. of Shares	912.1						912.1
Diluted earnings per ADS	**$1.81**	**$1.36**	**$0.77**	**$0.01**	**($0.09)**	**-**	**$3.86**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Amortization of intangible assets relating to intellectual property rights acquired ($484.0 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 ($33.5 million), costs relating to license arrangements ($10.0 million), acquisition and integration costs primarily associated with Baxalta ($220.8 million), net charge related to the change in the fair value of contingent consideration liabilities ($18.9 million), amortization of one-time upfront borrowing costs for Dyax ($1.7 million) and tax effect of adjustments;

(c) Out-license, divestments, reorganizations and discontinued operations: Reorganization costs primarily related to facility consolidations ($5.3 million), and tax effect of adjustments;

(d) Other: Gain on fair value adjustment for joint venture net written option ($8.0 million), credit to income taxes due to U.S. tax reform ($21.3 million), and tax effect of other adjustments; and

(e) Depreciation reclassification: Depreciation of $140.2 million included in Cost of product sales, R&D and SG&A for U.S. GAAP separately disclosed for the presentation of Non GAAP earnings.

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

$MM	GAAP	Adjustments					Non GAAP
		(a)	(b)	(c)	(d)	(e)	
Total Revenues	**3,572.3**	**-**	**-**	**-**	**-**	**-**	**3,572.3**
Costs and expenses:							
Cost of product sales	1,327.0	-	(480.4)	-	-	(72.1)	774.5
R&D	379.3	-	-	-	-	(13.4)	365.9
SG&A	888.9	-	-	-	4.0	(37.4)	855.5
Amortization of acquired intangible assets	364.0	(364.0)	-	-	-	-	-
Integration and acquisition costs	116.0	-	(116.0)	-	-	-	-
Reorganization costs	5.5	-	-	(5.5)	-	-	-
Gain on sale of product rights	(5.5)	-	-	5.5	-	-	-
Depreciation	-	-	-	-	-	122.9	122.9
Total operating expenses	3,075.2	(364.0)	(596.4)	-	4.0	-	2,118.8
Operating Income	**497.1**	**364.0**	**596.4**	**-**	**(4.0)**	**-**	**1,453.5**
Total other expense, net	(134.7)	-	1.8	-	-	-	(132.9)
Income from continuing operations before income taxes and equity losses of equity method investees	362.4	364.0	598.2	-	(4.0)	-	1,320.6
Income taxes	(6.8)	(85.3)	(123.9)	(1.8)	0.1	-	(217.7)
Equity in losses of equity method investees, net of taxes	(0.8)	-	-	-	-	-	(0.8)
Income from continuing operations	**354.8**	**278.7**	**474.3**	**(1.8)**	**(3.9)**	**-**	**1,102.1**
Loss from discontinued operations, net of tax	20.2	-	-	(20.2)	-	-	-
Net income	**375.0**	**278.7**	**474.3**	**(22.0)**	**(3.9)**	**-**	**1,102.1**
No. of Shares	911.8						911.8
Diluted earnings per ADS	**$1.23**	**$0.92**	**$1.56**	**($0.07)**	**($0.01)**	**-**	**$3.63**

The following items are included in Adjustments:

(a) Amortization and asset impairments: Impairment of intangible assets relating to intellectual property right acquired ($364.0 million), and tax effect of adjustments;

(b) Acquisition and integration activities: Unwind of inventory fair value adjustments primarily associated with Baxalta ($480.4 million), integration costs primarily associated with Baxalta ($119.5 million), net credit related to the change in the fair value of contingent consideration liabilities ($3.5 million), amortization of one-time upfront borrowings costs for Dyax ($1.8 million), and tax effect of adjustments;

(c) Out-license, divestments, reorganizations and discontinued operations: Gain on re-measurement of DAYTRANA contingent consideration to fair value ($5.5 million), reorganization costs primarily related to the closure of the Basingstoke office ($5.5 million), tax effect of adjustments and gain from discontinued operations, net of tax ($20.2 million);

(d) Other: One-time adjustment to pension expense ($4.0 million), and tax effect of adjustments; and

(e) Depreciation reclassification: Depreciation of $122.9 million included in Cost of sales, R&D and SG&A for U.S. GAAP separately disclosed for the presentation of Non GAAP earnings.

GAAP to Non GAAP reconciliation
For the three months ended March 31, 2018 and 2017

Reconciliation of U.S. GAAP net income to
Non GAAP EBITDA and Non GAAP Operating income:

(in millions)	3 months ended March 31,	
	2018	2017
U.S. GAAP Net income	**$ 550.6**	$ 375.0
Add back/(deduct):		
Gain from discontinued operations, net of taxes	**—**	(20.2)
Equity in (earnings)/losses of equity method investees, net of taxes	**(0.8)**	0.8
Income taxes	**43.3**	6.8
Other expense, net	**101.2**	134.7
U.S. GAAP Operating income from continuing operations	**694.3**	497.1
Add back/(deduct) Non GAAP adjustments:		
Expense related to the unwind of inventory fair value adjustments	**33.5**	480.4
One-time employee related costs	**—**	(4.0)
Costs relating to license arrangements	**10**	—
Amortization of acquired intangible assets	**484.0**	364.0
Integration and acquisition costs	**239.7**	116.0
Reorganization costs	**5.3**	5.5
Gain on sale of product rights	**—**	(5.5)
Depreciation	**140.2**	122.9
Non GAAP EBITDA	**1,607.0**	1,576.4
Depreciation	**(140.2)**	(122.9)
Non GAAP Operating income	**$ 1,466.8**	$ 1,453.5
Net income margin[1]	**15 %**	10 %
Non GAAP EBITDA margin[2]	**43 %**	44 %

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

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, 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
- 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 30 to 33.

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 March 31, 2018 were $1.38:£1.00 and $1.22:€1.00 (2017: $1.24:£1.00 and $1.06:€1.00).

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

In its FY 2017 results announcement on February 14, 2018 (FY 2017 Announcement), Shire published its full year 2018 outlook for total revenue[1] of $15.4-$15.9 billion, GAAP diluted EPS of $7.30-$7.90, and non-GAAP diluted EPS of $14.90-$15.50 (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" (Mid-Term Outlook).

Certain of the statements on pages 15, 18 and 19 of this presentation include a "profit forecast" for the purposes of Rule 28 of the City Code on Takeovers and Mergers (the "Code") which was first contained in the FY 2017 Announcement.

In accordance with Rule 28.1(c) of the Code, the directors of Shire confirm that: (i) each of the Full Year 2018 Outlook and the Mid-Term Outlook remains valid and has been properly compiled on the basis of the assumptions stated in the FY 2017 Announcement; and (ii) the basis of accounting used for each of the Full Year 2018 Outlook and the Mid-Term Outlook is consistent with Shire's accounting policies.

The Full Year 2018 Outlook and the Mid-Term Outlook do not take into account, and exclude the impact of, the completion of the sale of the Oncology business to Servier S.A.S. (as announced by Shire on April 16, 2018).

[1] Management is providing guidance for total revenue. Total revenue is comprised of total product sales and royalties & other revenues. Pursuant to a change in U.S. GAAP related to accounting for revenue, certain revenue formerly classified as royalties are now recorded as product sales.