Press Release

Shire Delivers 7% Product Sales Growth and Robust Pipeline Progress in Q1 2018

Growth driven by Immunology, recently-launched products, and international expansion

Innovative pipeline progresses with 15 programs in Phase 3 and 7 programs in registration including lanadelumab

Delivers Non GAAP diluted earnings per ADS of $3.86, up 6% year-on-year; GAAP diluted earnings per ADS were $1.81, up 47%

$1.0 billion in net operating cash flow enabled continued debt pay down

April 26, 2018 – Shire plc (Shire) (LSE: SHP, NASDAQ: SHPG), the leading global biotech company focused on rare diseases, announces unaudited results for the three months ended March 31, 2018.

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

“Shire is off to a good start in 2018 delivering on our key priorities of commercial execution, pipeline progression, debt pay down, and portfolio optimization. We generated product sales growth of 7% in the first quarter reaching $3.6 billion with important contributions from our Immunology franchise, recently-launched products, and international markets. We delivered $1.0 billion in net operating cash flow allowing us to remain on track towards our debt pay down target.

“We continue to advance our innovative pipeline with seven programs in registration including lanadelumab, the first monoclonal antibody being evaluated to prevent hereditary angioedema attacks, with the potential to change the treatment paradigm for this serious and sometimes life threatening rare disease.

“As part of the ongoing review of our portfolio, we recently announced an agreement for the sale of our Oncology franchise for $2.4 billion allowing us to unlock embedded value and sharpen our focus."

Product and Pipeline Highlights

Regulatory updates

- Advanced lanadelumab with accelerated approval pathways underway in the U.S. (PDUFA date of August 26, 2018), Europe, and Canada.
- Gained FDA acceptance for additional key filings: CINRYZE sBLA for pediatric use, including Priority Review; prucalopride NDA; and Calaspargase Pegol BLA.
- Achieved marketing approval of XIIDRA (lifitegrast ophthalmic solution 5%) in Canada and ADYNOVI in E.U.
- Obtained Breakthrough Therapy Designation for maribavir for cytomegalovirus (CMV) infection in transplant patients from FDA.

Clinical and business development updates

- Agreed to divest Oncology franchise to Servier S.A.S. for $2.4 billion.
- Formed pre-clinical research collaboration to evaluate a potential enzyme replacement therapy using NanoMedSyn’s proprietary synthetic derivatives.

Note: Growth rates are on a reported basis unless mentioned otherwise.

Financial Highlights

	Q1 2018	Reported Growth	Non GAAP CER[1]
Product sales Rare Disease[2]	$2,719 million	+10%	+6%
Product sales Neuroscience[2]	$918 million	-2%	-4%
Total product sales	$3,637 million	+7%	+3%
Total revenues	$3,766 million	+5%	+2%
Rare Disease contribution margin[2]	$1,367 million	+2%	
Neuroscience contribution margin[2]	$770 million	-3%	
Operating income from continuing operations	$694 million	+40%	
Non GAAP operating income[1]	$1,467 million	+1%	-3%
Net income	$551 million	+47%	
Non GAAP net income[1]	$1,173 million	+6%	
Diluted earnings per ADS[3]	$1.81	+47%	
Non GAAP diluted earnings per ADS[1][3]	$3.86	+6%	+2%
Net cash provided by operating activities	$1,010 million	+120%	
Non GAAP free cash flow[1]	$918 million	+272%	
Key ratios			
Rare Disease contribution margin percentage[2][4]	48%	-3ppc	
Neuroscience contribution margin percentage[2][4]	82%	+0ppc	
Net income margin[4][5]	15%	+5ppc	
Non GAAP EBITDA margin[1][4][5]	43%	-1ppc	

[1] The Non GAAP financial measures included within this release are explained on pages 26 – 27, and are reconciled to the most directly comparable financial measures prepared in accordance with U.S. GAAP on pages 20 – 22.
[2] In 2018, Shire created two business segments: a Rare Disease division and a Neuroscience division. As a result, Shire now reports its financial results based on these new segments. Segment contribution margin represents total revenue less cost of sales, direct R&D, and direct selling and marketing expenses. Segment contribution margin percentage represents segment contribution margin as a percentage of segment revenue. For further information, refer to Note 3: Segment reporting on page 19.
[3] Diluted weighted average number of ordinary shares of 912.1 million.
[4] Percentage point change (ppc).
[5] Calculated as a percentage of total revenues.

Product sales growth

- Achieved product sales growth of 10% in our Rare Disease division, with increases across all franchises on a reported basis, driven by Immunology, Hematology, Internal Medicine, and Ophthalmics.
- Delivered growth of recently launched products of 77%, primarily due to ADYNOVATE, CUVITRU, and GATTEX, as well as XIIDRA with script growth of 27% since Q1 2017.
- Experienced decline of 2% in product sales in our Neuroscience division due to the genericization of LIALDA in the second half of 2017. Excluding the impact of LIALDA, Neuroscience grew 12%, primarily driven by VYVANSE.

Operating performance

- Generated Non GAAP diluted earnings per ADS of $3.86, an increase of 6%, as Q1 2018 benefited from higher product sales and a lower tax rate, which were partially offset by lower gross margins due to Q1 2017 favorability from the timing of changes in the costs to manufacture certain products.
- Reported Non GAAP EBITDA margin of 43%, a slight decline from Q1 2017, with continued benefit from operating efficiencies in SG&A offset by lower gross margins as discussed above.
- Rare Disease reported contribution margin of $1,367 million, or 48%, and Neuroscience reported contribution margin of $770 million, or 82%.

Strong cash flow

- Strong free cash flow enabled an $866 million reduction in Non GAAP net debt during the quarter.

FINANCIAL SUMMARY - FIRST QUARTER 2018 COMPARED TO FIRST QUARTER 2017

Revenues

- Delivered total revenues of $3,766 million representing growth of 5%.
- Rare Disease product sales increased 10% to $2,719 million (Q1 2017: $2,472 million), with growth across all franchises on a reported basis and growth from recently launched products. Rare Disease product sales also benefited from favorable foreign currency exchange in our international markets.
- Neuroscience product sales decreased 2% to $918 million (Q1 2017: $940 million), due to the launch of generic competition for LIALDA in the second half of 2017. Excluding the impact from LIALDA, Neuroscience product sales grew 12%.
- Royalties and other revenues decreased 20% to $129 million (Q1 2017: $160 million), primarily due to the reclassification of ADDERALL XR from royalty revenue to product sales and other accounting changes as required under the new revenue accounting standard as well as lower SENSIPAR royalties.

Operating results

- Rare Disease contribution margin percentage was approximately 48% (Q1 2017: 51%), a slight decline from the prior year due to lower gross margins on sales, partially offset by lower selling and marketing costs.
- Neuroscience contribution margin percentage was flat at 82% (Q1 2017: 82%), as the decline in sales due to LIALDA was offset by lower costs.
- Operating income increased 40% to $694 million (Q1 2017: $497 million), primarily due to lower expense related to the unwind of inventory fair value adjustments, partially offset by higher amortization of acquired intangible assets and integration and acquisition costs.
- Non GAAP operating income increased 1% to $1,467 million (Q1 2017: $1,454 million), with the benefit of our on-going cost reduction initiatives and operating synergies offset by lower gross margins as Q1 2017 reflected favorability from the timing of changes in the costs to manufacture certain products.
- Non GAAP EBITDA margin was slightly down to 43% (Q1 2017: 44%), primarily due to the lower gross margin referred to above offset by ongoing cost reduction initiatives and operating expense synergies.

Earnings per share (EPS)

- Diluted earnings per American Depository Share (ADS) increased 47% to $1.81 (Q1 2017: 1.23). The increase was primarily driven by operating income as noted above, combined with lower expense related to the unwind of inventory fair value adjustments.
- Non GAAP diluted earnings per ADS increased 6% to $3.86 (Q1 2017: 3.63) as Q1 2018 benefited from higher product sales and a lower tax rate partially offset by a lower gross margin.

Cash flows

- Net cash provided by operating activities increased 120% to $1,010 million (Q1 2017: $459 million), driven by improvements in working capital, higher operating profitability, and a favorable comparison period as the Q1 2017 period included a payment of $346 million associated with the settlement of the DERMAGRAFT litigation.
- Non GAAP free cash flow increased 272% to $918 million (Q1 2017: $247 million), primarily due to the growth in net cash provided by operating activities noted above and a decrease in capital expenditures.

Debt

- Non GAAP net debt as of March 31, 2018 decreased $866 million since December 31, 2017, to $18,203 million (December 31, 2017: $19,069 million). A combination of Shire's Non GAAP free cash flow and existing cash balances were utilized to repay debt during the quarter. Non GAAP net debt represents aggregate long and short term borrowings of $18,172 million, and capital leases of $350 million, partially offset by cash and cash equivalents of $318 million.

OUTLOOK

Our 2018 guidance, which continues to include our Oncology franchise, remains unchanged. It will be updated to remove the Oncology franchise upon the close of this pending sale later this year. Similarly, our 2020 guidance remains unchanged and will be updated to remove the Oncology franchise upon the close of this pending sale later this year.

The Non GAAP diluted earnings per ADS forecast assumes a weighted average number of 915 million fully diluted ordinary shares outstanding for 2018.

Our U.S. GAAP diluted earnings per ADS outlook reflects anticipated amortization, integration, and reorganization costs.

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.

Full Year 2018	**U.S. GAAP Outlook**	**Non GAAP Outlook[1]**
Total revenue[2]	$15.4 - $15.9 billion	$15.4 - $15.9 billion
Gross margin as a percentage of total revenue[3]	71.0% - 73.0%	73.5% - 75.5%
Combined R&D and SG&A	$5.2 - $5.4 billion	$4.9 - $5.1 billion
Net interest/other	$450 - $550 million	$450 - $550 million
Effective tax rate	15% - 17%	16% - 18%
Diluted earnings per ADS[4]	$7.30 - $7.90	$14.90 - $15.50

[1] For a list of items excluded from Non GAAP Outlook, refer to pages 26 - 27 of this release.
[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] Gross margin as a percentage of total revenues excludes amortization of acquired intangible assets.
[4] See page 22 for a reconciliation between U.S. GAAP diluted earnings per ADS and Non GAAP diluted earnings per ADS.

RECENT DEVELOPMENTS

Corporate

Sale of Oncology franchise

- On April 16, 2018, Shire announced it has entered into a definitive agreement with Servier S.A.S. to sell its Oncology franchise for $2.4 billion.

Formation of Global Commission to End the Diagnostic Odyssey for Children

- On February 20, 2018, Shire, Microsoft, and EURORDIS-Rare Diseases Europe announced a strategic initiative to accelerate time to diagnosis for children with rare diseases.

Business Development

Collaboration with NanoMedSyn

- On March 26, 2018, Shire and NanoMedSyn announced a collaboration to conduct pre-clinical research to evaluate a potential enzyme replacement therapy using NanoMedSyn's proprietary synthetic derivatives named AMFA.

Products

VONVENDI for perioperative management of bleeding in adult patients with von Willebrand disease (VWD)

- On April 17, 2018, Shire announced that the U.S. Food and Drug Administration (FDA) approved VONVENDI, a recombinant von Willebrand factor treatment for perioperative management of bleeding in adults with VWD. This approval builds on the previously approved on-demand treatment and control of bleeding episodes indication.

myPKFiT for ADVATE software

- On March 5, 2018, Shire announced the U.S. availability of myPKFiT for ADVATE, a free web-based software for healthcare professionals that is the first and only pharmacokinetic dosing software cleared by the FDA for use with certain hemophilia A patients treated with ADVATE.

CINRYZE for pediatric hereditary angioedema (HAE)

- On February 15, 2018, Shire announced that the FDA had accepted the CINRYZE (C1 esterase inhibitor [human]) supplemental Biologics License Application to expand the currently approved indication to include children aged 6 years and older with HAE. The filing received priority review designation from the FDA.

Pipeline

Lanadelumab (SHP643) for the treatment of HAE

- On February 23, 2018, Shire announced that the FDA had accepted the Biologics License Application (BLA) and granted priority review for lanadelumab with a PDUFA date of August 26, 2018.
- On February 27, 2018, Shire announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) had granted an accelerated assessment for lanadelumab. On March 29, 2018, Shire announced that the EMA had validated its marketing authorization application (MAA) and also reported that Health Canada had completed screening and accepted the New Drug Submission (NDS) under priority review.
- On April 18, 2018, Shire announced that Swissmedic validated the MAA for lanadelumab.

Prucalopride (SHP555) for the treatment of chronic idiopathic constipation (CIC)

- On March 5, 2018, Shire announced that the FDA had accepted the submission of a New Drug Application (NDA) for prucalopride, which is being evaluated as a potential once-daily treatment option for CIC in adults, with a PDUFA date of December 21, 2018.

Calaspargase Pegol (SHP663) for the treatment of acute lymphoblastic leukemia (ALL)

- On February 28, 2018, Shire announced that the FDA had accepted the BLA for Calaspargase Pegol.

Board Committee Change

On April 25, 2018, Gail Fosler, Non-Executive Director of Shire, was appointed as a member of the Remuneration Committee.

As previously announced, following the conclusion of our Annual General Meeting on April 24, 2018, Anne Minto, Dominic Blakemore, and William Burns have stepped down from the Board of Directors. Following the departure of William Burns from the Board of Directors, Olivier Bohuon has been appointed Senior Independent Director of the Board.

ADDITIONAL INFORMATION

The following additional information is included in this press release:

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Dial in details for the **live conference call** for investors at 14:00 BST / 9:00 EDT on April 26, 2018:

U.K. dial in:	0800 358 9473 or +44 333 300 0804
U.S. dial in:	1 855 857 0686 or 1 631 913 1422
International Access Numbers:	Click here
Password/Conf ID:	83293759#
Live Webcast:	Click here

The quarterly earnings presentation will be available today at 13:00 BST / 8:00 EDT on:

- Shire.com Investors section

- Shire's IR Briefcase in the iTunes Store

OVERVIEW OF FIRST QUARTER 2018 FINANCIAL RESULTS COMPARED TO FIRST QUARTER 2017

In 2018, Shire created two business segments: a Rare Disease division and a Neuroscience division. As a result, Shire now reports its financial performance based on these new segments (including comparative information).

1. Product sales

Total product sales increased 7% to $3,637 million (2017: $3,412 million). Rare Disease product sales growth was 10% with revenue increases across all franchises on a reported basis. Neuroscience product sales declined by 2% due to generic competition for LIALDA, offset by an increase in sales for VYVANSE. Product sales in Q1 2018 also reflect a benefit from favorable foreign currency exchange rates.

Rare Disease division

(in millions) **Rare Disease**	U.S. Sales	International Sales	**Total Sales**	Total Sales Year on year growth Reported	 Non GAAP CER
IMMUNOGLOBULIN THERAPIES	$ 421.6	$ 136.3	**$ 557.9**	+12%	+10%
HEREDITARY ANGIOEDEMA	332.4	36.4	**368.8**	+1%	-0%
BIO THERAPEUTICS	82.5	116.7	**199.2**	+12%	+7%
Immunology	**836.5**	**289.4**	**1,125.9**	+8%	+6%
HEMOPHILIA	393.1	349.7	**742.8**	+14%	+10%
INHIBITOR THERAPIES	60.6	149.2	**209.8**	-5%	-10%
Hematology	**453.7**	**498.9**	**952.6**	+9%	+5%
REPLAGAL	—	124.2	**124.2**	+13%	+3%
ELAPRASE	41.0	77.4	**118.4**	-16%	-22%
VPRIV	36.7	53.2	**89.9**	+13%	+7%
Genetic Diseases	**77.7**	**254.8**	**332.5**	+1%	-7%
GATTEX/REVESTIVE	80.3	15.9	**96.2**	+39%	+37%
NATPARA/NATPAR	43.2	1.8	**45.0**	+52%	+51%
Other Internal Medicine[(1)]	0.7	37.0	**37.7**	+13%	+0%
Internal Medicine	**124.2**	**54.7**	**178.9**	+35%	+31%
Oncology	**43.4**	**23.5**	**66.9**	+15%	+10%
Ophthalmics	**61.6**	**0.5**	**62.1**	+61%	+61%
Total Rare Disease product sales	**$ 1,597.1**	**$ 1,121.8**	**$ 2,718.9**	+10%	+6%

[(1)] Other Internal Medicine includes AGRYLIN, PLENADREN, and RESOLOR.

Immunology
Immunology product sales were $1,126 million in Q1 2018. Our immunoglobulin therapies and bio therapeutics each reported growth of 12%. Immunoglobulin therapies growth was primarily driven by continued growth in subcutaneous products, international markets, and increased demand in the U.S., partially offset by U.S. destocking compared to the prior year. HAE product sales were up 1% with FIRAZYR growth offset by a decline in CINRYZE. FIRAZYR results benefited from stocking during the current quarter compared to slight destocking in the prior year. FIRAZYR also benefited from price increases and, to a lesser extent, higher demand. CINRYZE's year-over-year decline resulted from destocking in the quarter as well as an impact on demand from a competitor launch. Bio therapeutics growth was driven by demand and favorable foreign currency exchange.

Hematology
Hematology product sales were $953 million in Q1 2018, with growth in both our U.S. and international markets driven by ADYNOVATE. Our U.S. market growth included an increase in demand as well as stocking. Our international markets growth included the benefits from favorable foreign currency exchange.

Genetic Diseases
Genetic Diseases product sales increased 1% to $333 million, driven by increased sales for REPLAGAL and VPRIV in international markets, partially offset by decreased sales of ELAPRASE that was impacted by timing of large shipments in Q1 2018 compared to Q1 2017.

Internal Medicine
Internal Medicine sales increased 35% to $179 million, driven by strong growth from GATTEX/REVESTIVE and NATPARA/NATPAR of 39% and 52%, respectively, primarily due to an increase in patients on therapy, and to a lesser extent, the benefit of price increases.

Oncology
Oncology product sales increased 15% to $67 million, with growth driven by increased demand in our international markets and the benefit of a price increase.

Ophthalmics
Ophthalmics product sales relate to XIIDRA, which contributed $62 million of product sales with 27% prescription growth compared to Q1 2017.

Neuroscience division

(in millions) **Neuroscience**	U.S. Sales	International Sales	**Total Sales**	Total Sales Year on year growth Reported	 Non GAAP CER
VYVANSE	$ 557.2	$ 71.6	**$ 628.8**	+12%	+11%
ADDERALL XR	72.1	3.9	**76.0**	+17%	+17%
PENTASA	72.4	—	**72.4**	+5%	+5%
LIALDA/MEZAVANT	30.5	31.5	**62.0**	-65%	-66%
MYDAYIS	4.5	—	**4.5**	N/A	N/A
Other Neuroscience[(1)]	21.2	53.3	**74.5**	+11%	+4%
Total Neuroscience product sales	**$ 757.9**	**$ 160.3**	**$ 918.2**	-2%	-4%

[(1)] Other Neuroscience includes FOSRENOL, INTUNIV, EQUASYM, BUCCOLAM, and CARBATROL.

Neuroscience
Neuroscience product sales, which now include PENTASA and LIALDA/MEZAVANT, were $918 million in Q1 2018. VYVANSE product sales increased 12% primarily due to a price increase, stocking, and growth in our international markets. LIALDA/MEZAVANT sales decreased due to generic competition, which began in the second half of 2017.

2. Royalties and other revenues

(in millions)	Revenue	Year on year reported growth
Rare Disease royalties and other revenues	**$ 109.4**	-16%
Neuroscience royalties and other revenues	**19.2**	-34%
Royalties and other revenues	**$ 128.6**	-20%

Royalties and other revenues decreased 20% primarily due to the reclassification of ADDERALL XR from royalty revenue to product sales and other accounting changes as required under the new revenue accounting standard and lower SENSIPAR royalties.

3. Financial details

Cost of sales

(in millions)	Q1 2018	Q1 2017
Cost of sales (U.S. GAAP)	**$ 1,132.4**	$ 1,327.0
Expense related to the unwind of inventory fair value adjustments	**(33.5)**	(480.4)
Depreciation	**(72.7)**	(72.1)
Non GAAP cost of sales	**$ 1,026.2**	$ 774.5
U.S. GAAP cost of sales as a percentage of total revenues	***30%***	*37%*
Non GAAP cost of sales as a percentage of total revenues	***27%***	*22%*

Cost of sales as a percentage of total revenues decreased by 7% to 30% primarily due to lower expense related to the unwind of inventory fair value adjustments.

Non GAAP cost of sales as a percentage of total revenues increased by 5% to 27% primarily due to lower gross margins as Q1 2017 reflected favorability from the timing of changes in the costs to manufacture certain products.

R&D

(in millions)	Q1 2018	Q1 2017
R&D (U.S. GAAP)	**$ 405.2**	$ 379.3
Costs relating to license arrangements	**(10.0)**	—
Depreciation	**(10.7)**	(13.4)
Non GAAP R&D	**$ 384.5**	$ 365.9
U.S. GAAP R&D as a percentage of total revenues	***11%***	*11%*
Non GAAP R&D as a percentage of total revenues	***10%***	*10%*

R&D increased by $26 million, or 7%, primarily due to continued investment in late stage programs and upfront payments associated with license arrangements. R&D as a percentage of total revenues remained consistent with Q1 2017.

Non GAAP R&D increased by $19 million, or 5%, primarily due to continued investment in late stage programs. Non GAAP R&D as a percentage of total revenues remained consistent with Q1 2017.

SG&A

(in millions)	Q1 2018	Q1 2017
SG&A (U.S. GAAP)	**$ 804.8**	$ 888.9
One-time employee related costs	**—**	4.0
Depreciation	**(56.8)**	(37.4)
Non GAAP SG&A	**$ 748.0**	$ 855.5
U.S. GAAP SG&A as a percentage of total revenues	***21%***	*25%*
Non GAAP SG&A as a percentage of total revenues	***20%***	*24%*

SG&A decreased by $84 million, or 9%, primarily due to on-going cost reduction initiatives and operating synergies, as well as a reduction in marketing costs.

Non GAAP SG&A decreased by $108 million, or 13%. Non GAAP SG&A as a percentage of total revenues decreased 4 percentage points, for the reasons described above.

Amortization of acquired intangible assets

In Q1 2018, Shire recorded amortization of acquired intangible assets of $484 million (Q1 2017: $364 million), primarily related to the acceleration of CINRYZE amortization with the expected launch of SHP643, subject to regulatory approval.

Integration and acquisition costs

In Q1 2018, Shire recorded integration and acquisition costs of $240 million, including an impairment of a manufacturing facility, as well as third party professional fees and other expenses primarily related to the integration of Baxalta. In Q1 2017, Shire recorded integration and acquisition costs of $116 million, primarily related to the integration of Baxalta. These costs included stock compensation, third-party professional fees, and expenses associated with facility consolidations.

Other expense, net

(in millions)	**Q1 2018**	Q1 2017
Other expense, net (U.S. GAAP)	**$ (101.2)**	$ (134.7)
Amortization of one-time upfront borrowing costs for Baxalta and Dyax	**1.7**	1.8
Fair value adjustment for joint venture net written option	**(8.0)**	—
Non GAAP other expense, net	**$ (107.5)**	$ (132.9)

Other expense, net decreased by $34 million, primarily due to an unrealized gain in publicly traded equity securities and lower interest expense resulting from debt paydown, inclusive of a fair value adjustment for a joint venture net written option.

Non GAAP other expense, net decreased by $25 million, primarily due to an unrealized gain in publicly traded equity securities and lower interest expense.

Taxation

(in millions)	**Q1 2018**	Q1 2017
Income tax expense (U.S. GAAP)	**$ (43.3)**	$ (6.8)
U.S. tax reform Non GAAP tax adjustment	**(21.3)**	—
Other Non GAAP tax adjustments	**(122.2)**	(210.9)
Non GAAP Income tax expense	**$ (186.8)**	$ (217.7)
U.S. GAAP effective tax rate	***7%***	*2%*
Non GAAP effective tax rate	***14%***	*16%*

The effective tax rate on U.S. GAAP income in Q1 2018 was 7% (Q1 2017: 2%) and on a Non GAAP basis was 14% (Q1 2017: 16%).

The effective rate in Q1 2018 on U.S. GAAP income from continuing operations has been affected by certain provisions of the U.S. Tax Cuts and Jobs Act (Tax Act) passed in December 2017, which enacts a U.S. federal tax rate of 21% along with anti-deferral provisions and new limitations on certain deductions required under the Tax Act. Additionally, certain discrete events occurred during Q1 2018, including the recording of a net tax benefit for income tax reserves, which impacted the rate favorably for the quarter.

Discontinued operations

There was no gain or loss from discontinued operations in Q1 2018. The gain in Q1 2017 was $20 million, net of tax benefit of $12 million, primarily due to the return of funds previously held in escrow related to the acquisition of the DERMAGRAFT business.

FINANCIAL INFORMATION

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Unaudited U.S. GAAP Consolidated Balance Sheets

(in millions, except par value of shares)

	March 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	**$ 317.7**	$ 472.4
Restricted cash	**35.5**	39.4
Accounts receivable, net	**3,140.5**	3,009.8
Inventories	**3,340.8**	3,291.5
Prepaid expenses and other current assets	**1,080.5**	795.3
Total current assets	**7,915.0**	7,608.4
Non-current assets:		
Investments	**271.8**	241.1
Property, plant and equipment (PP&E), net	**6,460.1**	6,635.4
Goodwill	**19,988.6**	19,831.7
Intangible assets, net	**32,864.3**	33,046.1
Deferred tax asset	**189.2**	188.8
Other non-current assets	**179.8**	205.4
Total assets	**$ 67,868.8**	$ 67,756.9
LIABILITIES AND EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	**$ 3,939.0**	$ 4,184.5
Short term borrowings and capital leases	**1,787.2**	2,788.7
Other current liabilities	**1,218.4**	908.8
Total current liabilities	**6,944.6**	7,882.0
Non-current liabilities:		
Long term borrowings and capital leases	**16,733.7**	16,752.4
Deferred tax liability	**4,716.4**	4,748.2
Other non-current liabilities	**2,074.1**	2,197.9
Total liabilities	**30,468.8**	31,580.5
Equity:		
Common stock of 5p par value; 1,500 shares authorized; and 918.9 shares issued and outstanding (2017: 1,500 shares authorized; and 917.1 shares issued and outstanding)	**81.7**	81.6
Additional paid-in capital	**25,156.6**	25,082.2
Treasury stock: 8.2 shares (2017: 8.4 shares)	**(279.1)**	(283.0)
Accumulated other comprehensive income	**1,846.1**	1,375.0
Retained earnings	**10,594.7**	9,920.6
Total equity	**37,400.0**	36,176.4
Total liabilities and equity	**$ 67,868.8**	$ 67,756.9

Unaudited U.S. GAAP Consolidated Statements of Operations
(in millions)

	3 months ended March 31,	
	2018	2017
Revenues:		
Product sales	**$ 3,637.1**	$ 3,412.3
Royalties & other revenues	**128.6**	160.0
Total revenues	**3,765.7**	3,572.3
Costs and expenses:		
Cost of sales	**1,132.4**	1,327.0
Research and development	**405.2**	379.3
Selling, general and administrative	**804.8**	888.9
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)
Total operating expenses	**3,071.4**	3,075.2
Operating income from continuing operations	**694.3**	497.1
Interest income	**2.6**	3.1
Interest expense	**(127.0)**	(142.3)
Other income, net	**23.2**	4.5
Total other expense, net	**(101.2)**	(134.7)
Income from continuing operations before income taxes and equity in earnings/ (losses) of equity method investees	**593.1**	362.4
Income taxes	**(43.3)**	(6.8)
Equity in earnings/(losses) of equity method investees, net of taxes	**0.8**	(0.8)
Income from continuing operations, net of taxes	**550.6**	354.8
Gain from discontinued operations, net of taxes	**—**	20.2
Net income	**$ 550.6**	$ 375.0

Unaudited U.S. GAAP Consolidated Statements of Operations (continued)

(in millions, except per share amounts)

	3 months ended March 31,	
	2018	2017
Earnings per Ordinary Share – basic		
Earnings from continuing operations	**$ 0.61**	$ 0.39
Earnings from discontinued operations	**—**	0.02
Earnings per Ordinary Share – basic	**$ 0.61**	$ 0.41
Earnings per ADS – basic	**$ 1.82**	$ 1.24
Earnings per Ordinary Share – diluted		
Earnings from continuing operations	**$ 0.60**	$ 0.39
Earnings from discontinued operations	**—**	0.02
Earnings per Ordinary Share – diluted	**$ 0.60**	$ 0.41
Earnings per ADS – diluted	**$ 1.81**	$ 1.23
Weighted average number of shares:		
Basic	**909.5**	904.1
Diluted	**912.1**	911.8

Unaudited U.S. GAAP Consolidated Statements of Cash Flows
(in millions)

	3 months ended March 31,	
	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income	**$ 550.6**	$ 375.0
Adjustments to reconcile net income to net cash provided by operating activities:		
Depreciation and amortization	**624.2**	486.9
Share-based compensation	**41.0**	52.7
Expense related to the unwind of inventory fair value adjustments	**33.5**	480.4
Change in deferred taxes	**(50.4)**	(135.5)
Change in fair value of contingent consideration	**18.9**	(3.5)
Impairment of PP&E and other	**137.5**	—
Other, net	**13.6**	30.0
Changes in operating assets and liabilities:		
Increase in accounts receivable	**(291.7)**	(35.3)
Increase in sales deduction accrual	**282.6**	17.5
Increase in inventory	**(40.2)**	(151.8)
(Increase)/decrease in prepayments and other assets	**(136.7)**	14.2
Decrease in accounts payable and other liabilities	**(172.6)**	(671.5)
Net cash provided by operating activities	**1,010.3**	459.1
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of PP&E	**(177.8)**	(212.5)
Other, net	**(11.1)**	1.2
Net cash used in investing activities	**(188.9)**	(211.3)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from revolving line of credit, long term and short term borrowings	**423.3**	1,401.9
Repayment of revolving line of credit, long term and short term borrowings	**(1,439.4)**	(1,825.7)
Proceeds from issuance of stock for share-based compensation arrangements	**40.5**	42.1
Other, net	**(6.5)**	(20.1)
Net cash used in financing activities	**(982.1)**	(401.8)
Effect of foreign exchange rate changes on cash and cash equivalents and restricted cash	**2.1**	2.7
Net decrease in cash and cash equivalents and restricted cash	**(158.6)**	(151.3)
Cash and cash equivalents and restricted cash at beginning of period	**511.8**	554.4
Cash and cash equivalents and restricted cash at end of period	**$ 353.2**	$ 403.1

Selected Notes to the Unaudited U.S. GAAP Financial Statements

(1) Earnings Per Share (EPS)

(in millions)

	3 months ended March 31,	
	2018	2017
Income from continuing operations	**$ 550.6**	$ 354.8
Gain from discontinued operations	**—**	20.2
Numerator for EPS	**$ 550.6**	$ 375.0
Weighted average number of shares:		
Basic	**909.5**	904.1
Effect of dilutive shares:		
Share based awards to employees	**2.6**	7.7
Diluted	**912.1**	911.8

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

Share based awards to employees	**15.9**	7.3

Selected Notes to the Unaudited U.S. GAAP Financial Statements

(2) Analysis of revenues
(in millions)

	3 months ended March 31,	
	2018	2017
Product sales by segment		
IMMUNOGLOBULIN THERAPIES	**$ 557.9**	$ 498.3
HEREDITARY ANGIOEDEMA	**368.8**	366.1
BIO THERAPEUTICS	**199.2**	177.9
Immunology	**1,125.9**	1,042.3
HEMOPHILIA	**742.8**	650.4
INHIBITOR THERAPIES	**209.8**	220.5
Hematology	**952.6**	870.9
REPLAGAL	**124.2**	109.7
ELAPRASE	**118.4**	140.6
VPRIV	**89.9**	79.8
Genetic Diseases	**332.5**	330.1
GATTEX/REVESTIVE	**96.2**	69.0
NATPARA/NATPAR	**45.0**	29.7
Other Internal Medicine	**37.7**	33.4
Internal Medicine	**178.9**	132.1
Oncology	**66.9**	58.3
Ophthalmics	**62.1**	38.6
Total Rare Disease product sales	**2,718.9**	2,472.3
VYVANSE	**628.8**	563.7
ADDERALL XR	**76.0**	64.9
PENTASA	**72.4**	69.1
LIALDA/MEZAVANT	**62.0**	175.1
MYDAYIS	**4.5**	—
Other Neuroscience	**74.5**	67.2
Total Neuroscience product sales	**918.2**	940.0
Total product sales	**3,637.1**	3,412.3
Royalties and other revenues		
Royalties	**70.6**	105.1
Other revenues	**58.0**	54.9
Total royalties and other revenues	**128.6**	160.0
Total revenues	**$ 3,765.7**	$ 3,572.3

Selected Notes to the Unaudited U.S. GAAP Financial Statements

(3) Segment reporting
(in millions)

Segment contribution for each segment represents total revenues, less cost of sales, direct selling and marketing expenses, and direct R&D expenses. Comparative financial information for 2017 was restated. There are no intersegment sales or intersegment allocations of expenses.

The following items are excluded from segment contribution:
- certain unallocated shared functional costs;
- amortization and depreciation expense;
- general and administrative expenses; and
- other items such as asset impairment charges, acquisition and integration costs, restructuring charges, costs related to licensing arrangement, and non-recurring or unusual charges.

	3 months ended March 31,	
	2018	2017
Revenues:		
Rare Disease	**$ 2,828.3**	$ 2,603.3
Neuroscience	**937.4**	969.0
Total revenues	**3,765.7**	3,572.3
Segment contribution:		
Rare Disease	**1,366.6**	1,339.7
Neuroscience	**769.9**	792.6
Total segment contribution	**2,136.5**	2,132.3
Less: reconciling items to operating income from continuing operations		
Unallocated corporate and shared functional costs, including G&A expenses	**529.5**	555.9
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	**10.0**	—
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
Operating income from continuing operations	**694.3**	497.1
Operating margin %	**18%**	14%
Other expense, net	**(101.2)**	(134.7)
Income from continuing operations before taxes and equity in earnings/(losses) of equity method investees	**$ 593.1**	$ 362.4

Non GAAP reconciliations

(in millions)

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

	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	**10.0**	—
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.

Reconciliation of revenues to Non GAAP Gross Margin:

	3 months ended March 31,	
	2018	2017
Revenues	**$ 3,765.7**	$ 3,572.3
Cost of sales (U.S. GAAP)	**(1,132.4)**	(1,327.0)
U.S. GAAP gross margin	**2,633.3**	2,245.3
Add back Non GAAP adjustments:		
Expense related to the unwind of inventory fair value adjustments	**33.5**	480.4
Depreciation	**72.7**	72.1
Non GAAP gross margin	**$ 2,739.5**	$ 2,797.8
U.S. GAAP gross margin[(1)(2)]	**69.9%**	62.9%
Non GAAP gross margin[(2)]	**72.7%**	78.3%

[(1)] U.S. GAAP gross margin excluded amortization of acquired intangible assets.

[(2)] U.S. GAAP gross margin as a percentage of total revenues. Non GAAP gross margin as a percentage of total revenues.

Non GAAP reconciliations

(in millions, except per ADS amounts)

Reconciliation of U.S. GAAP net income to Non GAAP net income:

	3 months ended March 31,	
	2018	2017
U.S. GAAP net income	**$ 550.6**	$ 375.0
Expense related to the unwind of inventory fair value adjustments	**33.5**	480.4
One-time employee related costs	**—**	(4.0)
Costs related to license arrangements	**10.0**	—
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)
Amortization of one-time upfront borrowing costs for Baxalta and Dyax	**1.7**	1.8
Gain from discontinued operations	**—**	(31.8)
Fair value adjustment for joint venture net written option	**(8.0)**	—
Tax effect of adjustments	**(143.5)**	(199.3)
Non GAAP net income	**$ 1,173.3**	$ 1,102.1

Reconciliation of U.S. GAAP diluted earnings per ADS to Non GAAP diluted earnings per ADS:

	3 months ended March 31,	
	2018	2017
U.S. GAAP diluted earnings per ADS	**$ 1.81**	$ 1.23
Expense related to the unwind of inventory fair value adjustments	**0.11**	1.58
One-time employee related costs	**—**	(0.01)
Costs related to license arrangements	**0.03**	—
Amortization of acquired intangible assets	**1.60**	1.20
Integration and acquisition costs	**0.79**	0.38
Reorganization costs	**0.02**	0.02
Gain on sale of product rights	**—**	(0.02)
Amortization of one-time upfront borrowing costs for Baxalta and Dyax	**0.01**	0.01
Gain from discontinued operations	**—**	(0.10)
Fair value adjustment for joint venture net written option	**(0.03)**	—
Non GAAP tax adjustments	**(0.47)**	(0.66)
Non GAAP diluted earnings per ADS	**$ 3.86**	$ 3.63

Reconciliation of U.S. GAAP net cash provided by operating activities to Non GAAP free cash flow:

	3 months ended March 31,	
	2018	2017
Net cash provided by operating activities	**$ 1,010.3**	$ 459.1
Capital expenditures	**(177.8)**	(212.5)
Payments related to license arrangements	**85.0**	—
Non GAAP free cash flow	**$ 917.5**	$ 246.6

Non GAAP reconciliations

(in millions, except per ADS amounts)

Non GAAP net debt comprises:

	March 31, 2018	December 31, 2017
Cash and cash equivalents	**$ 317.7**	$ 472.4
Long term borrowings (excluding capital leases)	**(16,391.8)**	(16,410.7)
Short term borrowings (excluding capital leases)	**(1,779.6)**	(2,781.2)
Capital leases	**(349.5)**	(349.2)
Non GAAP net debt	**$ (18,203.2)**	$ (19,068.7)

Reconciliation of full year 2018 U.S. GAAP diluted earnings per ADS Outlook to Non GAAP diluted earnings per ADS Outlook[(1)]:

	Full Year 2018 Outlook		
	Min		**Max**
U.S. GAAP diluted earnings per ADS	**$ 7.30**		**$ 7.90**
Expense related to the unwind of inventory fair value adjustments		0.12	
Legal and litigation costs		0.05	
Amortization of acquired intangible assets		6.60	
Integration and acquisition costs		2.30	
Reorganization costs		0.03	
Costs relating to license arrangements		0.10	
Non GAAP tax adjustments		(1.60)	
Non GAAP diluted earnings per ADS	**$ 14.90**		**$ 15.50**

(1) Does not take into account the sale of the Oncology franchise.

NOTES TO EDITORS

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

Inside Information

This announcement contains inside information.

About Shire

Shire is the global biotechnology leader serving patients with rare diseases and specialized conditions. We seek to push boundaries through discovering and delivering new possibilities for patient communities who often have few or no other champions. Relentlessly on the edge of what's next, we are serial innovators with a diverse pipeline offering fresh thinking and new hope. Serving patients and partnering with healthcare communities in over 100 countries, we strive to be part of the entire patient journey to enable earlier diagnosis, raise standards of care, accelerate access to treatment, and support patients. Our Rare Disease and Neuroscience divisions support our diverse portfolio of therapeutic areas, including Immunology, Hematology, Genetic Diseases, Internal Medicine, Ophthalmics, Oncology, and neuropsychiatry disorders.

Championing patients is our call to action - it brings the opportunity - and responsibility - to change people's lives.

www.shire.com

THE "SAFE HARBOR" STATEMENT UNDER THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995

Statements included herein that are not historical facts, including without limitation statements concerning future strategy, plans, objectives, expectations and intentions, 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;

- 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.

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 4 and 22 of this announcement 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 franchise 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.

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
- 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 20 to 22.

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.

TRADEMARKS

We own or have rights to trademarks, service marks, or trade names that we use in connection with the operation of our business. In addition, our names, logos, and website names and addresses are owned by us or licensed by us. We also own or have the rights to copyrights that protect the content of our solutions. Solely for convenience, the trademarks, service marks, trade names, and copyrights referred to in this press release are listed without the ©, ®, and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks, trade names, and copyrights. In addition, this press release may include trademarks, service marks, or trade names of other companies. Our use or display of other parties' trademarks, service marks, trade names, or products is not intended to, and does not imply a relationship with, or endorsement or sponsorship of us by, the trademark, service mark, or trade name.