Press Release

Shire Delivers Product Sales Growth of 6% and Continues to Execute Against Key Priorities in Q3 2018

Delivered product sales of $3.8 billion; growth driven by Immunology, recently-launched products, and international expansion

Received U.S. Food and Drug Administration and Health Canada approval for TAKHZYRO (lanadelumab-flyo) and launched in the U.S.

Accelerated debt pay-down through proceeds from the $2.4 billion sale of the Oncology franchise and strong net operating cash flow

November 1, 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 September 30, 2018.

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

"We continue to deliver solid growth and pay down our debt while advancing our late-stage pipeline. Our focus on commercial execution led to 6% growth in product sales to $3.8 billion in the third quarter overcoming foreign exchange headwinds. Our growth was once again driven by our Immunology franchise, recently-launched products, and expansion in international markets. Proceeds from the sale of our Oncology franchise coupled with strong free cash flow allowed us to reduce net debt by $3.9 billion year to date.

"We recently launched TAKHZYRO, the first monoclonal antibody to prevent hereditary angioedema (HAE) attacks, in the U.S. We also gained approval for this innovative treatment in Canada and received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) recommending marketing authorization in Europe.

"Takeda's proposed acquisition of Shire remains on track to close in H1 2019, subject to shareholder approval of both companies and additional regulatory approvals. While integration planning is ongoing, our solid performance through the third quarter of 2018 demonstrates our continued focus on delivering for patients and executing against our key priorities."

Financial Highlights

	Q3 2018[1]	Reported Growth[1]	Non GAAP CER[1][2]
Product sales	$3,753 million	+6%	+7%
Total revenues	$3,872 million	+5%	+6%
Operating income from continuing operations	$956 million	+35%	
Non GAAP operating income[2]	$1,475 million	-2%	-1%
Net income margin[3][4]	14%	-1ppc	
Non GAAP EBITDA margin[2][3][4]	42%	-2ppc	
Net income	$537 million	-2%	
Non GAAP net income[2]	$1,119 million	-3%	
Diluted earnings per ADS[5]	$1.75	-3%	
Non GAAP diluted earnings per ADS[2][5]	$3.64	-4%	-4%
Net cash provided by operating activities	$858 million	-19%	
Non GAAP free cash flow[2]	$971 million	+8%	

[1] Results include the Oncology franchise until the date of its sale on August 31, 2018.
[2] The Non GAAP financial measures included within this release are explained on pages 27 – 28, and are reconciled to the most directly comparable financial measures prepared in accordance with U.S. GAAP on pages 19 – 22.
[3] Percentage point change (ppc).
[4] Calculated as a percentage of total revenues.
[5] Diluted weighted average number of ordinary shares of 921.1 million.

Product sales growth

- All franchises demonstrated product sales growth on a Non GAAP constant exchange rate basis, excluding Oncology which was sold during the quarter.
- Encouraging early trajectory of TAKHZYRO since U.S. launch on August 23, 2018 with $51 million in initial launch stocking.
- Growth of recently-launched products of 45%, primarily due to TAKHZYRO, ADYNOVATE, CUVITRU, and XIIDRA.

Operating performance

- Generated Non GAAP diluted earnings per ADS of $3.64, a decrease of 4%, as product sales growth and operating expense discipline were offset by unfavorable foreign exchange, lower gross margins, and unrealized losses on equity investments.
- Reported Non GAAP EBITDA margin of 42%, a slight decline from Q3 2017, primarily due to lower gross margins, as Q3 2017 reflected favorability from the timing of changes in the costs to manufacture certain products, partially offset by ongoing cost discipline and operating expense synergies.

Cash flow

- Proceeds from the sale of our Oncology franchise and strong free cash flow during the year enabled a $3,915 million reduction in Non GAAP net debt since December 31, 2017.

FINANCIAL SUMMARY - THIRD QUARTER 2018 COMPARED TO THIRD QUARTER 2017

Revenues

- Delivered total revenues of $3,872 million representing growth of 5%.
- Product sales increased 6% to $3,753 million (Q3 2017: $3,534 million), driven by Immunology, up 12%, Neuroscience, up 6%, Genetic Diseases, up 6%, Internal Medicine, up 10%, and Ophthalmics, up 21%.
- Royalties and other revenues decreased 27% to $119 million (Q3 2017: $164 million), primarily due to certain royalty expirations, the reclassification of ADDERALL XR from royalty revenue to product sales, and other changes as required under the new revenue accounting standard.

Operating results

- Operating income increased 35% to $956 million (Q3 2017: $709 million), due to the gain on the sale of Shire's Oncology franchise and lower integration and acquisition costs, partially offset by increased reorganization costs.
- Non GAAP operating income decreased 2% to $1,475 million (Q3 2017: $1,498 million), primarily due to lower gross margins as Q3 2017 reflected favorability from the timing of changes in the costs to manufacture certain products.
- Non GAAP EBITDA margin was slightly down to 42% (Q3 2017: 44%), primarily due to lower gross margins partially offset by ongoing cost discipline and operating expense synergies.

Earnings per share (EPS)

- Diluted earnings per American Depository Share (ADS) decreased 3% to $1.75 (Q3 2017: $1.81), primarily due to increased reorganization costs and income taxes, offset by the gain on the sale of Shire's Oncology franchise.
- Non GAAP diluted earnings per ADS decreased 4% to $3.64 (Q3 2017: $3.81) as product sales growth and operating expense discipline were offset by unfavorable foreign exchange, lower gross margins, and unrealized losses on equity investments.

Cash flows

- Net cash provided by operating activities decreased 19% to $858 million (Q3 2017: $1,055 million), driven by a $251 million contingent consideration payment to former shareholders of Dyax Corp. due to the approval of TAKHZYRO.
- Non GAAP free cash flow increased 8% to $971 million (Q3 2017: $901 million). Non GAAP free cash flow includes capital expenditures of $203 million (Q3 2017: $174 million) and excludes payments relating to milestone and license arrangements of $316 million (Q3 2017: $20 million).

Debt

- Non GAAP net debt as of September 30, 2018 decreased $3,915 million since December 31, 2017, to $15,154 million (December 31, 2017: $19,069 million). A combination of proceeds from the sale of Shire's Oncology franchise, Non GAAP free cash flow, and existing cash balances were utilized to repay debt during the year. Non GAAP net debt represents aggregate long and short term borrowings of $14,980 million, and capital leases of $367 million, partially offset by cash and cash equivalents of $193 million.

OUTLOOK

Our 2018 guidance, presented in the table below, has been updated to adjust for the sale of our Oncology franchise, which closed on August 31, 2018. Similarly, our projected 2020 revenue target has been updated to $16.5 - $17.5 billion, reflecting the removal of $0.5 billion of Oncology sales in our original projection. We continue to expect to achieve mid-forties Non GAAP EBITDA margin by 2020, which remains unchanged after considering the impact of the sale of our Oncology franchise.

Our Non GAAP diluted earnings per ADS outlook assumes a weighted average number of 917 million fully diluted ordinary shares outstanding for 2018.

Our U.S. GAAP diluted earnings per ADS outlook reflects anticipated amortization, integration, acquisition, and reorganization costs, as well as the gain on sale of our Oncology franchise and the impact from debt repurchase.

Risks associated with this outlook include the potential uncertainty resulting from the announcement by Takeda Pharmaceutical Company Limited (Takeda) on May 8, 2018 of a recommended offer for Shire under the U.K. Takeover Code.

Full Year 2018	**U.S. GAAP Outlook**	**Non GAAP Outlook[1]**
Total revenue[2]	$15.3 - $15.8 billion	$15.3 - $15.8 billion
Diluted earnings per ADS[3]	$7.17 - $7.77	$14.77 - $15.37

[1] For a list of items excluded from Non GAAP Outlook, refer to pages 27 - 28 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] See page 22 for a reconciliation between U.S. GAAP diluted earnings per ADS and Non GAAP diluted earnings per ADS.

RECENT DEVELOPMENTS

Corporate

- The acquisition of Shire by Takeda is expected to close in H1 2019, subject to receipt of additional regulatory clearances and approval by the shareholders of both companies. Takeda has already received clearances from regulatory agencies in the U.S., Japan, China, and other countries and is in discussions with the European Commission as part of its Phase 1 review of the proposed acquisition.

Business Development

Sale of Oncology franchise

- On August 31, 2018, Shire announced it had completed the sale of its Oncology franchise to Servier S.A.S. (Servier) for $2.4 billion. The franchise included the global rights to ONCASPAR and ex-U.S. and ex-Taiwan rights to ONIVYDE, as well as Oncology pipeline assets.

Acquisition of sanaplasma AG

- On September 6, 2018, Shire announced the acquisition of sanaplasma AG, a source plasma collection company headquartered in Switzerland. Sanaplasma AG adds 14 new centers in the Czech Republic and Hungary to Shire's European-based plasma collection network.

Financing

- On September 11, 2018, Shire completed a $2.3 billion cash tender offer to repurchase certain of its outstanding senior notes. The tender offer was funded from the proceeds of the sale of its Oncology franchise.

Products

TAKHZYRO, a first-of-its-kind monoclonal antibody (mAb) preventive treatment for HAE

- On August 23, 2018, Shire announced that the U.S. Food and Drug Administration (FDA) had approved TAKHZYRO injection, for prophylaxis to prevent attacks of HAE in patients 12 years of age and older.
- On September 20, 2018, Shire announced that Health Canada had authorized TAKHZYRO for routine prevention of attacks of HAE in patients 12 years of age and older.
- On October 19, 2018, Shire announced that the CHMP of the European Medicines Agency (EMA) had issued a positive opinion recommending the granting of marketing authorization in the European Union (EU) for lanadelumab for the prevention of HAE attacks.

FIRAZYR for the treatment of HAE attacks in Japan

- On September 21, 2018, Shire announced that the Ministry of Health, Labour and Welfare in Japan had granted manufacturing and marketing authorization for FIRAZYR, for the acute treatment of HAE attacks in adult patients with HAE.

VEYVONDI, for adults with von Willebrand disease (VWD)

- On September 12, 2018, Shire announced that the European Commission had granted Marketing Authorization for VEYVONDI, for the treatment of bleeding events and treatment/prevention of surgical bleeding in adults (age 18 and older) with VWD when desmopressin treatment alone is ineffective or not indicated.

INTUNIV, for the treatment of attention deficit hyperactivity disorder (ADHD) in adults

- On August 13, 2018, Shire announced that its partner in Japan, Shionogi & Co., Ltd had submitted a New Drug Application (NDA) for the manufacture and marketing in Japan of INTUNIV.

Pipeline

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

- On October 18, 2018, Shire announced that the FDA Gastrointestinal Drugs Advisory Committee voted unanimously that the risk-benefit profile of prucalopride supports the approval of this NDA, which has a Prescription Drug User Fee Act (PDUFA) date of December 21, 2018.

Facilities

- On October 25, 2018, Shire announced it had filed a second submission to the FDA for approval to manufacture albumin therapy at its new plasma manufacturing facility near Covington, Georgia.

ADDITIONAL INFORMATION

The following additional information is included in this press release:

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Dial in details for the **live conference call** for investors at 14:00 GMT / 10:00 EDT on November 1, 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:	28705371 #
Live Webcast:	Click here

The quarterly earnings presentation will be available today at 13:00 GMT / 9:00 EDT on:

- Shire.com Investors section

- Shire's IR Briefcase in the iTunes Store

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

1. Product sales

Product sales increased 6% to $3,753 million (Q3 2017: $3,534 million), driven by Immunology, up 12%, Neuroscience, up 6%, Genetic Diseases, up 6%, Internal Medicine, up 10%, and Ophthalmics, up 21%. Product sales include TAKHZYRO, which was launched on August 23, 2018, and results for Oncology through August 31, 2018, the date the sale of the franchise was completed.

(in millions) **Product sales by franchise**	U.S. Sales	International Sales	**Total Sales**	Total Sales Year on year growth Reported	 Non GAAP CER
IMMUNOGLOBULIN THERAPIES	$ 530.7	$ 125.2	**$ 655.9**	+8%	+10%
HEREDITARY ANGIOEDEMA	291.3	37.7	**329.0**	+23%	+23%
BIO THERAPEUTICS	91.9	120.4	**212.3**	+8%	+9%
Immunology	**913.9**	**283.3**	**1,197.2**	+12%	+13%
HEMOPHILIA	386.6	349.3	**735.9**	+1%	+3%
INHIBITOR THERAPIES	44.7	124.4	**169.1**	-11%	-8%
Hematology	**431.3**	**473.7**	**905.0**	-1%	+1%
VYVANSE	528.5	66.5	**595.0**	+11%	+11%
ADDERALL XR	71.5	4.8	**76.3**	-28%	-28%
MYDAYIS	19.3	—	**19.3**	+89%	+89%
Other Neuroscience[(1)]	0.9	40.2	**41.1**	+13%	+15%
Neuroscience	**620.2**	**111.5**	**731.7**	+6%	+7%
ELAPRASE	41.7	128.9	**170.6**	+12%	+15%
REPLAGAL	—	123.0	**123.0**	+5%	+8%
VPRIV	39.0	48.8	**87.8**	-2%	-2%
Genetic Diseases	**80.7**	**300.7**	**381.4**	+6%	+9%
LIALDA/MEZAVANT	88.9	30.2	**119.1**	+37%	+38%
PENTASA	65.7	—	**65.7**	-9%	-9%
Other Established Brands[(2)]	10.7	21.0	**31.7**	+0%	+1%
Established Brands	**165.3**	**51.2**	**216.5**	+14%	+14%
GATTEX/REVESTIVE	82.2	14.9	**97.1**	+14%	+15%
NATPARA/NATPAR	47.8	3.2	**51.0**	+30%	+30%
Other Internal Medicine[(3)]	0.1	28.9	**29.0**	-21%	-19%
Internal Medicine	**130.1**	**47.0**	**177.1**	+10%	+11%
Ophthalmics	**92.1**	**1.3**	**93.4**	+21%	+21%
Oncology[(4)]	**33.4**	**17.1**	**50.5**	N/M	N/M
Total product sales	**$ 2,467.0**	**$ 1,285.8**	**$ 3,752.8**	+6%	+7%

[(1)] Other Neuroscience includes INTUNIV, EQUASYM, and BUCCOLAM.
[(2)] Other Established Brands includes FOSRENOL and CARBATROL.
[(3)] Other Internal Medicine includes AGRYLIN, PLENADREN, and RESOLOR.
[(4)] Results include the Oncology franchise until the date of its sale on August 31, 2018.

Immunology
Immunology product sales were $1,197 million in Q3 2018. Immunoglobulin therapies and bio therapeutics were each up 8% mainly due to increased demand. HAE product sales were up 23%, which included $51 million of TAKHZYRO product sales for initial launch stocking. HAE product sales also reflected higher CINRYZE product sales as Q3 2017 included the impact of supply constraints, offset by destocking of FIRAZYR.

Hematology
Hematology product sales were $905 million in Q3 2018. Sales of inhibitor therapies declined 11% due to new competition, while sales of hemophilia therapies increased by 1% with continued growth of our extended half-life product, ADYNOVATE.

Neuroscience
Neuroscience product sales were $732 million in Q3 2018. VYVANSE product sales increased 11% due to a U.S. price increase and continued growth in our international markets.

Genetic Diseases
Genetic Diseases product sales increased 6% to $381 million, driven by increased sales for ELAPRASE and REPLAGAL primarily in our international markets.

Established Brands
Established Brands products sales increased 14% to $217 million, with the impact of generic competition offset by favorable sales deductions and some stocking for LIALDA in Q3 2018 compared to Q3 2017.

Internal Medicine
Internal Medicine product sales increased 10% to $177 million, driven by demand growth for GATTEX/REVESTIVE and NATPARA/NATPAR.

Ophthalmics
Ophthalmics product sales increased 21% to $93 million due to XIIDRA demand growth.

Oncology
As a result of the sale of Shire's Oncology franchise, completed on August 31, 2018, Oncology product sales decreased to $51 million from $69 million in Q3 2017.

2. Royalties and other revenues

(in millions)	Revenue	Year on year reported growth
Royalties	**$ 45.1**	-60%
Other revenues	**73.8**	+41%
Royalties and other revenues	**$ 118.9**	-27%

Royalties and other revenues decreased 27%, primarily due to certain royalty expirations, the reclassification of ADDERALL XR from royalty revenue to product sales, and other changes as required under the new revenue accounting standard.

3. Financial details

Cost of sales

(in millions)	Q3 2018	Q3 2017
Cost of sales (U.S. GAAP)	**$ 1,157.6**	$ 1,001.4
Expense related to the unwind of inventory fair value adjustments	**(1.6)**	(63.3)
Depreciation	**(89.4)**	(70.1)
Non GAAP cost of sales	**$ 1,066.6**	$ 868.0
U.S. GAAP cost of sales as a percentage of total revenues	***30%***	*27%*
Non GAAP cost of sales as a percentage of total revenues	***28%***	*23%*

Cost of sales as a percentage of total revenues increased by 3 percentage points to 30%, primarily due to lower gross margins as Q3 2017 reflected favorability from the timing of changes in the costs to manufacture certain products.

Non GAAP cost of sales as a percentage of total revenues increased by 5 percentage points to 28%, as noted above.

R&D

(in millions)	**Q3 2018**	Q3 2017
R&D (U.S. GAAP)	**$ 407.2**	$ 402.8
Program wind-down costs	**(3.3)**	—
Depreciation	**(10.9)**	(10.8)
Non GAAP R&D	**$ 393.0**	$ 392.0
U.S. GAAP R&D as a percentage of total revenues	***11%***	*11%*
Non GAAP R&D as a percentage of total revenues	***10%***	*11%*

R&D increased $4 million, or 1%, primarily due to continued investment in late stage and launch programs offset by savings on discontinued programs. R&D as a percentage of total revenues remained consistent with Q3 2017.

Non GAAP R&D was flat. Non GAAP R&D as a percentage of total revenues decreased 1 percentage point.

SG&A

(in millions)	**Q3 2018**	Q3 2017
SG&A (U.S. GAAP)	**$ 836.8**	$ 859.7
Legal and litigation costs	**—**	(1.0)
Depreciation	**(57.3)**	(39.0)
Non GAAP SG&A	**$ 779.5**	$ 819.7
U.S. GAAP SG&A as a percentage of total revenues	***22%***	*23%*
Non GAAP SG&A as a percentage of total revenues	***20%***	*22%*

SG&A decreased $23 million, or 3%, primarily due to the benefits of on-going cost discipline and operating synergies partially offset by increased depreciation.

Non GAAP SG&A decreased by $40 million, or 5%, due to the benefits of on-going cost discipline and operating synergies.

Amortization of acquired intangible assets

In Q3 2018, Shire recorded amortization of acquired intangible assets of $434 million (Q3 2017: $482 million). The decrease was primarily related to amortization for CINRYZE and the sale of Oncology assets, including ONCASPAR and ONIVYDE, partially offset by amortization for TAKHZYRO, which was approved in Q3 2018.

Integration and acquisition costs

In Q3 2018, Shire recorded integration and acquisition costs of $93 million, primarily related to changes in fair value of contingent consideration and costs related to the proposed Takeda transaction.

In Q3 2017, Shire recorded integration and acquisition costs of $237 million, primarily related to the Baxalta transaction. Costs included asset impairment charges, employee severance, the acceleration of stock compensation, third-party professional fees, and expenses associated with facility consolidations.

Reorganization costs

In Q3 2018, Shire recorded reorganization costs of $255 million, primarily related to expenses associated with office facility closures. In Q3 2017, Shire recorded reorganization costs of $5 million.

Gain/loss on sale of Oncology and product rights

In Q3 2018, Shire recorded a gain from the sale of its Oncology franchise of $267 million. In Q3 2017, Shire recorded a loss on sale of product rights of less than $1 million.

Other expense, net

(in millions)	**Q3 2018**	Q3 2017
Other expense, net (U.S. GAAP)	**$ (220.0)**	$ (140.5)
Amortization of one-time upfront borrowing costs for Baxalta and Dyax	**—**	1.9
Gain on sale of non-core investments	**—**	4.3
Costs related to bond tender offer	**40.6**	—
Fair value adjustment for joint venture net written option	**11.0**	—
Non GAAP other expense, net	**$ (168.4)**	$ (134.3)

Other expense, net increased by $80 million, primarily due to costs related to the cash tender offer for the repurchase of $2.3 billion of Shire's outstanding senior notes.

Non GAAP other expense, net increased by $34 million, primarily due to unrealized losses in equity investments and net losses on foreign exchange revaluations.

Taxation

(in millions)	**Q3 2018**	Q3 2017
Income tax expense (U.S. GAAP)	**$ (203.3)**	$ (13.5)
Other Non GAAP tax adjustments	**10.7**	(189.0)
Non GAAP income tax expense	**$ (192.6)**	$ (202.5)
U.S. GAAP effective tax rate	***28%***	*2%*
Non GAAP effective tax rate	***15%***	*15%*

The effective tax rate on U.S. GAAP income in Q3 2018 was 28% (Q3 2017: 2%) and on a Non GAAP basis was 15% (Q3 2017: 15%).

The effective rate in Q3 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.

Income tax expense was increased by $60 million during the three months ended September 30, 2018 due to continued refinement of Shire's provisional computations under the Tax Act. The increase in the tax expense recorded during the three months ended September 30, 2018 was due to 1) an adjustment to U.S. deferred tax balances recorded as of December 31, 2017 related to the corporate income tax rate reduction of $15 million; and 2) an increase of $45 million related to the repatriation toll charge. The change in the toll charge was partially driven by an adjustment of $31 million related to the tax rates applied to certain drivers of the provisional repatriation toll charge in 2017, as well as the finalization of inputs to the calculation of the repatriation toll charge and the refinement of Shire's computation for the various guidance and regulations issued during 2018.

Shire will continue to assess the financial statement impact of the applicable provisions of the Tax Act upon enactment. It is expected that additional interpretive guidance will be issued during the measurement period that may change how Shire has computed the provisional amounts for the year ended December 31, 2017. Consequently, Shire continues to assert that all amounts recorded and disclosed to date remain provisional.

FINANCIAL INFORMATION

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Unaudited U.S. GAAP Consolidated Balance Sheets
(in millions, except par value of shares)

	September 30, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	**$ 193.2**	$ 472.4
Restricted cash	**39.9**	39.4
Accounts receivable, net	**3,207.4**	3,009.8
Inventories	**3,458.7**	3,291.5
Other current assets	**900.1**	795.3
Total current assets	**7,799.3**	7,608.4
Non-current assets:		
Investments	**470.7**	241.1
Property, plant and equipment (PP&E), net	**6,453.0**	6,635.4
Goodwill	**19,095.0**	19,831.7
Intangible assets, net	**29,625.4**	33,046.1
Deferred tax asset	**151.2**	188.8
Other non-current assets	**171.3**	205.4
Total assets	**$ 63,765.9**	$ 67,756.9
LIABILITIES AND EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	**$ 4,025.1**	$ 4,184.5
Short term borrowings and capital leases	**4,248.7**	2,788.7
Other current liabilities	**237.8**	908.8
Total current liabilities	**8,511.6**	7,882.0
Non-current liabilities:		
Long term borrowings and capital leases	**11,098.0**	16,752.4
Deferred tax liability	**4,571.2**	4,748.2
Other non-current liabilities	**2,294.9**	2,197.9
Total liabilities	**26,475.7**	31,580.5
Equity:		
Common stock of 5p par value; 1,500 shares authorized; and 922.1 shares issued and outstanding (2017: 1,500 shares authorized; and 917.1 shares issued and outstanding)	**81.9**	81.6
Additional paid-in capital	**25,390.2**	25,082.2
Treasury stock: 7.5 shares (2017: 8.4 shares)	**(260.7)**	(283.0)
Accumulated other comprehensive income	**626.4**	1,375.0
Retained earnings	**11,452.4**	9,920.6
Total equity	**37,290.2**	36,176.4
Total liabilities and equity	**$ 63,765.9**	$ 67,756.9

Unaudited U.S. GAAP Consolidated Statements of Operations

(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
Revenues:				
Product sales	**$ 3,752.8**	$ 3,533.8	**$ 11,198.5**	$ 10,537.9
Royalties and other revenues	**118.9**	163.8	**358.4**	477.8
Total revenues	**3,871.7**	3,697.6	**11,556.9**	11,015.7
Costs and expenses:				
Cost of sales	**1,157.6**	1,001.4	**3,398.3**	3,437.3
Research and development	**407.2**	402.8	**1,240.0**	1,324.5
Selling, general and administrative	**836.8**	859.7	**2,549.3**	2,647.7
Amortization of acquired intangible assets	**433.7**	482.4	**1,375.3**	1,280.5
Integration and acquisition costs	**93.0**	237.0	**512.0**	696.7
Reorganization costs	**254.8**	5.4	**268.9**	24.5
(Gain)/loss on sale of Oncology and product rights	**(267.2)**	0.3	**(267.2)**	(0.4)
Total operating expenses	**2,915.9**	2,989.0	**9,076.6**	9,410.8
Operating income from continuing operations	**955.8**	708.6	**2,480.3**	1,604.9
Interest income	**1.3**	1.5	**4.8**	5.7
Interest expense	**(125.2)**	(141.8)	**(378.1)**	(425.4)
Other (expense)/income, net	**(96.1)**	(0.2)	**(43.9)**	6.8
Total other expense, net	**(220.0)**	(140.5)	**(417.2)**	(412.9)
Income from continuing operations before income taxes and equity in earnings of equity method investees	**735.8**	568.1	**2,063.1**	1,192.0
Income taxes	**(203.3)**	(13.5)	**(371.0)**	(44.6)
Equity in earnings/(losses) of equity method investees, net of taxes	**4.7**	(3.4)	**11.2**	0.1
Income from continuing operations, net of taxes	**537.2**	551.2	**1,703.3**	1,147.5
(Loss)/gain from discontinued operations, net of taxes	**—**	(0.4)	**—**	18.6
Net income	**$ 537.2**	$ 550.8	**$ 1,703.3**	$ 1,166.1

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

(in millions, except per share amounts)

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
Earnings per Ordinary Share – basic				
Earnings from continuing operations	**$ 0.59**	$ 0.61	**$ 1.87**	$ 1.27
Earnings from discontinued operations	**—**	—	**—**	0.02
Earnings per Ordinary Share – basic	**$ 0.59**	$ 0.61	**$ 1.87**	$ 1.29
Earnings per ADS – basic	**$ 1.76**	$ 1.82	**$ 5.60**	$ 3.86
Earnings per Ordinary Share – diluted				
Earnings from continuing operations	**$ 0.58**	$ 0.60	**$ 1.86**	$ 1.26
Earnings from discontinued operations	**—**	—	**—**	0.02
Earnings per Ordinary Share – diluted	**$ 0.58**	$ 0.60	**$ 1.86**	$ 1.28
Earnings per ADS – diluted	**$ 1.75**	$ 1.81	**$ 5.57**	$ 3.84
Weighted average number of shares:				
Basic	**914.0**	907.2	**912.0**	905.9
Diluted	**921.1**	911.6	**916.9**	912.1

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

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
CASH FLOWS FROM OPERATING ACTIVITIES:				
Net income	**$ 537.2**	$ 550.8	**$ 1,703.3**	$ 1,166.1
Adjustments to reconcile net income to net cash provided by operating activities:				
Depreciation and amortization	**591.3**	602.3	**1,808.1**	1,644.0
Share based compensation	**48.8**	53.3	**135.7**	159.7
Expense related to the unwind of inventory fair value adjustments	**1.6**	63.3	**40.9**	688.7
Change in deferred taxes	**219.1**	(99.1)	**14.2**	(392.4)
Change in fair value of contingent consideration	**54.5**	(3.4)	**100.4**	144.3
Impairment of PP&E and intangible assets	**16.2**	114.0	**169.5**	167.6
Gain on sale of Oncology franchise	**(267.2)**	—	**(267.2)**	—
Other, net	**39.9**	77.6	**(7.2)**	99.2
Changes in operating assets and liabilities:				
Increase in accounts receivable	**(235.7)**	(120.0)	**(362.0)**	(301.5)
(Decrease)/increase in sales deduction accrual	**(60.1)**	36.9	**(22.6)**	94.0
Increase in inventory	**(135.6)**	(73.6)	**(305.4)**	(245.2)
Decrease/(increase) in prepayments and other assets	**106.1**	(34.2)	**44.6**	70.4
Decrease in accounts payable and other liabilities	**(58.5)**	(112.7)	**(244.8)**	(557.8)
Net cash provided by operating activities	**857.6**	1,055.2	**2,807.5**	2,737.1
CASH FLOWS FROM INVESTING ACTIVITIES:				
Proceeds from sale of Oncology franchise	**2,412.2**	—	**2,412.2**	—
Purchases of PP&E	**(203.3)**	(174.4)	**(564.6)**	(565.5)
Acquisition of business, net of cash acquired	**(104.7)**	—	**(104.7)**	—
Proceeds from sale of investments	**31.8**	7.5	**31.8**	48.1
Other, net	**(62.3)**	31.6	**(97.9)**	34.8
Net cash provided by/(used in) investing activities	**2,073.7**	(135.3)	**1,676.8**	(482.6)

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

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
CASH FLOWS FROM FINANCING ACTIVITIES:				
Proceeds from revolving line of credit, long term and short term borrowings	**1,085.0**	1,149.7	**3,735.3**	3,261.6
Repayment of revolving line of credit, long term and short term borrowings	**(3,706.7)**	(2,136.6)	**(7,969.0)**	(5,664.5)
Payment of contingent consideration	**(396.0)**	—	**(396.0)**	—
Payment of dividend	**—**	—	**(276.6)**	(234.7)
Proceeds from issuance of stock for share-based compensation arrangements	**47.1**	12.7	**180.8**	92.2
Other, net	**(18.7)**	(2.2)	**(25.6)**	(26.2)
Net cash used in financing activities	**(2,989.3)**	(976.4)	**(4,751.1)**	(2,571.6)
Effect of foreign exchange rate changes on cash and cash equivalents	**(3.6)**	2.1	**(11.9)**	6.2
Net decrease in cash, cash equivalents, and restricted cash	**(61.6)**	(54.4)	**(278.7)**	(310.9)
Cash, cash equivalents, and restricted cash at beginning of period	**294.7**	298.0	**511.8**	554.5
Cash, cash equivalents, and restricted cash at end of period	**$ 233.1**	$ 243.6	**$ 233.1**	$ 243.6

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

(1) Earnings Per Share (EPS)

(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
Income from continuing operations	**$ 537.2**	$ 551.2	**$ 1,703.3**	$ 1,147.5
(Loss)/gain from discontinued operations	**—**	(0.4)	**—**	18.6
Numerator for EPS	**$ 537.2**	$ 550.8	**$ 1,703.3**	$ 1,166.1
Weighted average number of shares:				
Basic	**914.0**	907.2	**912.0**	905.9
Effect of dilutive shares:				
Share based awards to employees	**7.1**	4.4	**4.9**	6.2
Diluted	**921.1**	911.6	**916.9**	912.1

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

Share based awards to employees	**10.0**	16.2	**13.4**	14.8

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

(2) Analysis of revenues
(in millions)

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
Product sales by franchise				
IMMUNOGLOBULIN THERAPIES	**$ 655.9**	$ 605.1	**$ 1,825.9**	$ 1,613.9
HEREDITARY ANGIOEDEMA	**329.0**	268.4	**1,063.0**	968.4
BIO THERAPEUTICS	**212.3**	196.6	**583.7**	546.7
Immunology	**1,197.2**	1,070.1	**3,472.6**	3,129.0
HEMOPHILIA	**735.9**	725.3	**2,225.4**	2,119.6
INHIBITOR THERAPIES	**169.1**	190.7	**583.2**	631.9
Hematology	**905.0**	916.0	**2,808.6**	2,751.5
VYVANSE	**595.0**	538.4	**1,779.8**	1,620.3
ADDERALL XR	**76.3**	106.0	**232.1**	242.3
MYDAYIS	**19.3**	10.2	**40.4**	25.9
Other Neuroscience	**41.1**	36.5	**117.8**	91.3
Neuroscience	**731.7**	691.1	**2,170.1**	1,979.8
ELAPRASE	**170.6**	152.9	**465.5**	454.5
REPLAGAL	**123.0**	117.2	**372.8**	349.0
VPRIV	**87.8**	89.6	**267.3**	257.3
Genetic Diseases	**381.4**	359.7	**1,105.6**	1,060.8
LIALDA/MEZAVANT	**119.1**	86.7	**287.0**	469.6
PENTASA	**65.7**	72.1	**215.6**	224.5
Other Established Brands	**31.7**	31.7	**105.9**	122.3
Established Brands	**216.5**	190.5	**608.5**	816.4
GATTEX/REVESTIVE	**97.1**	84.9	**326.8**	229.2
NATPARA/NATPAR	**51.0**	39.1	**160.8**	103.3
Other Internal Medicine	**29.0**	36.5	**101.3**	105.2
Internal Medicine	**177.1**	160.5	**588.9**	437.7
Ophthalmics	**93.4**	77.4	**255.8**	173.4
Oncology	**50.5**	68.5	**188.4**	189.3
Total product sales	**3,752.8**	3,533.8	**11,198.5**	10,537.9
Royalties and other revenues				
Royalties	**45.1**	111.4	**175.4**	329.7
Other revenues	**73.8**	52.4	**183.0**	148.1
Total royalties and other revenues	**118.9**	163.8	**358.4**	477.8
Total revenues	**$ 3,871.7**	$ 3,697.6	**$ 11,556.9**	$ 11,015.7

Non GAAP reconciliations

(in millions)

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

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
U.S. GAAP net income	**$ 537.2**	$ 550.8	**$ 1,703.3**	$ 1,166.1
Add back/(deduct):				
Loss/(gain) from discontinued operations, net of taxes	**—**	0.4	**—**	(18.6)
Equity in (earnings)/losses of equity method investees, net of taxes	**(4.7)**	3.4	**(11.2)**	(0.1)
Income taxes	**203.3**	13.5	**371.0**	44.6
Other expense, net	**220.0**	140.5	**417.2**	412.9
U.S. GAAP operating income from continuing operations	**955.8**	708.6	**2,480.3**	1,604.9
Add back/(deduct) Non GAAP adjustments:				
Expense related to the unwind of inventory fair value adjustments	**1.6**	63.3	**40.9**	688.7
Program wind-down and one-time employee related costs	**3.3**	—	**3.3**	(4.0)
Impairment of acquired intangible assets	**—**	—	**10.0**	20.0
Costs relating to license arrangements	**—**	—	**10.0**	123.7
Legal and litigation costs	**—**	1.0	**—**	8.6
Amortization of acquired intangible assets	**433.7**	482.4	**1,375.3**	1,280.5
Integration and acquisition costs	**93.0**	237.0	**512.0**	696.7
Reorganization costs	**254.8**	5.4	**268.9**	24.5
(Gain)/loss on sale of Oncology and product rights	**(267.2)**	0.3	**(267.2)**	(0.4)
Depreciation	**157.6**	119.9	**432.8**	363.5
Non GAAP EBITDA	**1,632.6**	1,617.9	**4,866.3**	4,806.7
Depreciation	**(157.6)**	(119.9)	**(432.8)**	(363.5)
Non GAAP operating income	**$ 1,475.0**	$ 1,498.0	**$ 4,433.5**	$ 4,443.2
Net income margin[(1)]	**14%**	15%	**15%**	11%
Non GAAP EBITDA margin[(2)]	**42%**	44%	**42%**	44%

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

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

Reconciliation of U.S. GAAP gross margin to Non GAAP gross margin:

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
U.S. GAAP total revenues	**$ 3,871.7**	$ 3,697.6	**$ 11,556.9**	$ 11,015.7
Cost of sales (U.S. GAAP)	**(1,157.6)**	(1,001.4)	**(3,398.3)**	(3,437.3)
U.S. GAAP gross margin[1]	**2,714.1**	2,696.2	**8,158.6**	7,578.4
Add back Non GAAP adjustments:				
Expense related to the unwind of inventory fair value adjustments	**1.6**	63.3	**40.9**	688.7
Depreciation	**89.4**	70.1	**228.2**	209.2
Non GAAP gross margin	**$ 2,805.1**	$ 2,829.6	**$ 8,427.7**	$ 8,476.3
U.S. GAAP gross margin [1][2]	***70.1%***	*72.9%*	***70.6%***	*68.8%*
Non GAAP gross margin [2]	***72.5%***	*76.5%*	***72.9%***	*76.9%*

[1] U.S. GAAP gross margin excludes 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.

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

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
U.S. GAAP net income	**$ 537.2**	$ 550.8	**$ 1,703.3**	$ 1,166.1
Expense related to the unwind of inventory fair value adjustments	**1.6**	63.3	**40.9**	688.7
Program wind-down and one-time employee related costs	**3.3**	—	**3.3**	(4.0)
Impairment of acquired intangible assets	**—**	—	**10.0**	20.0
Costs relating to license arrangements	**—**	—	**10.0**	123.7
Legal and litigation costs	**—**	1.0	**—**	8.6
Amortization of acquired intangible assets	**433.7**	482.4	**1,375.3**	1,280.5
Integration and acquisition costs	**93.0**	237.0	**512.0**	696.7
Reorganization costs	**254.8**	5.4	**268.9**	24.5
(Gain)/loss on sale of Oncology and product rights	**(267.2)**	0.3	**(267.2)**	(0.4)
Amortization of one-time upfront borrowing costs for Baxalta and Dyax	**—**	1.9	**2.3**	5.4
Loss/(gain) on sale of non-core investments	**—**	4.3	**—**	(8.9)
Loss/(gain) from discontinued operations	**—**	0.4	**—**	(29.6)
Costs related to bond tender offer	**40.6**	—	**40.6**	—
Fair value adjustment for joint venture net written option	**11.0**	—	**8.0**	—
Non GAAP tax adjustments	**10.7**	(189.0)	**(229.7)**	(576.5)
Non GAAP net income	**$ 1,118.7**	$ 1,157.8	**$ 3,477.7**	$ 3,394.8

Non GAAP reconciliations

(in millions, except per ADS amounts)

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

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
U.S. GAAP diluted earnings per ADS	**$ 1.75**	$ 1.81	**$ 5.57**	$ 3.84
Expense related to the unwind of inventory fair value adjustments	**0.01**	0.21	**0.13**	2.26
Program wind-down and one-time employee related costs	**0.01**	—	**0.01**	(0.01)
Impairment of acquired intangible assets	**—**	—	**0.03**	0.07
Costs relating to license arrangements	**—**	—	**0.03**	0.41
Legal and litigation costs	**—**	0.00	**—**	0.03
Amortization of acquired intangible assets	**1.41**	1.59	**4.50**	4.21
Integration and acquisition costs	**0.30**	0.78	**1.68**	2.29
Reorganization costs	**0.83**	0.02	**0.88**	0.08
(Gain)/loss on sale of Oncology and product rights	**(0.87)**	0.00	**(0.87)**	0.00
Amortization of one-time upfront borrowing costs for Baxalta and Dyax	**—**	0.01	**0.01**	0.02
Loss/(gain) on sale of non-core investments	**—**	0.01	**—**	(0.03)
Loss/(gain) from discontinued operations	**—**	0.00	**—**	(0.10)
Costs related to bond tender offer	**0.13**	—	**0.13**	—
Fair value adjustment for joint venture net written option	**0.04**	—	**0.03**	—
Non GAAP tax adjustments	**0.03**	(0.62)	**(0.75)**	(1.90)
Non GAAP diluted earnings per ADS	**$ 3.64**	$ 3.81	**$ 11.38**	$ 11.17

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

	3 months ended September 30,		9 months ended September 30,	
	2018	2017	**2018**	2017
Net cash provided by operating activities	**$ 857.6**	$ 1,055.2	**$ 2,807.5**	$ 2,737.1
Capital expenditures	**(203.3)**	(174.4)	**(564.6)**	(565.5)
Payments relating to milestone and license arrangements	**316.2**	20.0	**401.2**	40.0
Non GAAP free cash flow	**$ 970.5**	$ 900.8	**$ 2,644.1**	$ 2,211.6

Non GAAP net debt comprises:

	September 30, 2018	December 31, 2017
Cash and cash equivalents	**$ 193.2**	$ 472.4
Long term borrowings (excluding capital leases)	**(10,740.7)**	(16,410.7)
Short term borrowings (excluding capital leases)	**(4,239.2)**	(2,781.2)
Capital leases	**(366.8)**	(349.2)
Non GAAP net debt	**$ (15,153.5)**	$ (19,068.7)

Non GAAP reconciliations

(in millions, except per ADS amounts)

Reconciliation of full year 2018 U.S. GAAP diluted earnings per ADS Outlook to Non GAAP diluted earnings per ADS Outlook:

	Full Year 2018 Outlook		
	Min		Max
U.S. GAAP diluted earnings per ADS	**$ 7.17**		**$ 7.77**
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		2.20	
Reorganization costs		0.89	
Costs relating to license arrangements		0.10	
Costs related to bond tender offer		0.13	
Gain from the sale of the Oncology franchise		(0.87)	
Non GAAP tax adjustments		(1.62)	
Non GAAP diluted earnings per ADS	**$ 14.77**		**$ 15.37**

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 diverse portfolio of therapeutic areas includes Immunology, Hematology, Genetic Diseases, Neuroscience, Internal Medicine, and Ophthalmics.

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;

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

a further list and description of risks, uncertainties and other matters can be found in Shire's most recent Annual Report on Form 10-K and in Shire's subsequent Quarterly Reports on Form 10-Q, in each case including those risks outlined in "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

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

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

Full Year 2018 Outlook

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

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

Mid-Term Outlook

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

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

Assumptions and basis of preparation

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

In accordance with Rule 28.1(c) of the Code, the directors of Shire confirm that: (i) the basis of accounting used to prepare the Profit Forecasts is consistent with the accounting policies of Shire (or in the case of the Non GAAP Profit Forecasts, or in the case of the Non GAAP guidance, as adjusted in accordance with Shire's established Non GAAP policy, which excludes the items set out on pages 27 – 28 in the section "Non GAAP measures", including their tax effect); and (ii) each of the Profit Forecasts has been properly compiled on the basis of the following assumptions:

Assumptions outside the Directors' control

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

Assumptions within the Directors' control

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

NON GAAP MEASURES

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

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

Shire's management uses Non GAAP financial measures to make operating decisions as they facilitate additional internal comparisons of Shire's performance to historical results and to competitors' results, and provides them to investors as a supplement to Shire's reported results to provide additional insight into Shire's operating performance. Shire's Remuneration Committee uses certain key Non GAAP measures when assessing the performance and compensation of employees, including Shire's executive directors.

The Non GAAP financial measures used by Shire may be calculated differently from, and therefore may not be comparable to, similarly titled measures used by other companies - refer to the section "Non GAAP Financial Measure Descriptions" below for additional information. In addition, these Non GAAP financial measures should not be considered in isolation as a substitute for, or as superior to, financial measures calculated in accordance with U.S. GAAP, and Shire's financial results calculated in accordance with U.S. GAAP and reconciliations to those financial statements should be carefully evaluated.

Non GAAP Financial Measure Descriptions

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

Amortization and asset impairments:

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

Acquisitions and integration activities:

- Up-front payments and milestones in respect of in-licensed and acquired products;
- Costs associated with acquisitions, including transaction costs, fair value adjustments on contingent consideration and acquired inventory;
- Costs associated with the integration of companies; and
- Non-controlling interests in consolidated variable interest entities.

Out-license, divestments, reorganizations, and discontinued operations:

- Revenue from up-front and milestone receipts from out-license arrangements;
- Gains and losses on the sale of non-core assets;
- Costs associated with restructuring and reorganization activities;
- Termination costs; and
- Gains and losses from divestitures and discontinued operations.

Legal and litigation costs:

- Net legal costs related to the settlement of litigation, government investigations, and other disputes (excluding internal legal team costs).

Additionally, in any given period Shire may have significant, unusual, or non-recurring gains or losses, which it may exclude from its Non GAAP earnings for that period. When applicable, these items would be fully disclosed and incorporated into the required reconciliations from U.S. GAAP to Non GAAP measures.

Depreciation, which is included in Cost of sales, R&D, and SG&A costs in our U.S. GAAP results, has been separately disclosed for presentational purposes.

Free cash flow represents net cash provided by operating activities, excluding up-front and milestone payments, or receipts, for in-licensed and acquired products, but including capital expenditure in the ordinary course of business.

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

A reconciliation of Non GAAP financial measures to the most directly comparable measure under U.S. GAAP is presented on pages 19 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 September 30, 2018 were $1.31:£1.00 and $1.17:€1.00 (2017: $1.31:£1.00 and $1.17:€1.00).

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

TRADEMARKS

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