AstraZeneca PLC
14 February 2019 07:00 GMT

Full-year and Q4 2018 results

New launches and commercial execution deliver full-year sales growth and a very strong final quarter. 2019 anticipated to be a year of higher year-on-year sales growth combined with operating leverage.

The final quarter of the year saw a very strong performance, including Product Sales growth of 5% (8% at CER[1]) to $5,768m. In the year, Product Sales increased by 4% to $21,049m, reflecting the performance of new medicines[2] (+81%) and the sustained strength of Emerging Markets (+12%, +13% at CER); China sales increased by 28% (25% at CER) in the year. Oncology sales increased by 50% (49% at CER) in FY 2018, with *Tagrisso* and *Lynparza* each doubling in sales, accompanied by a promising performance from *Imfinzi*. *Fasenra* sales reached $297m in its first full year, performing exceptionally well in the countries where it was launched.

In addition, Earnings Per Share (EPS) benefited from a low tax rate. The pipeline produced further positive developments and 2019 is expected to be another busy year for news flow.

	FY 2018			Q4 2018		
	$m	% change		$m	% change	
		Actual	CER		Actual	CER
Product Sales	21,049	4	4	5,768	5	8
Externalisation Revenue	1,041	(55)	(55)	649	n/m	n/m
Total Revenue	22,090	(2)	(2)	6,417	11	14
Reported Operating Profit[3]	3,387	(8)	(7)	1,077	57	54
Core Operating Profit[4]	5,672	(17)	(17)	2,192	23	23
Reported Earnings Per Share (EPS)	$1.70	(28)	(29)	$0.82	(21)	(22)
Core EPS	$3.46	(19)	(19)	$1.58	22	22

Pascal Soriot, Chief Executive Officer, commenting on the results said:
"Closing the year with another strong quarter, our performance confirmed that AstraZeneca has returned to growth. Our new medicines performed particularly well across the therapy areas and the Emerging Markets business went from strength to strength. 2019 will be a year of focus on continued pipeline delivery and flawless commercial execution. The performance of our new medicines demonstrated the ability of our commercial teams to convert the pipeline into successful medicines.

As we recently entered a new phase in our strategic development, we have refined our organisation to position ourselves for the next phase of our journey. The changes are designed to further integrate research and development and accelerate decision-making and the launches of new medicines, consolidating what we believe is already one of the most exciting and productive pipelines in the industry. We are also enhancing our commercial units to increase collaboration with our R&D organisation, enabling greater commitment to our main therapy areas; we want AstraZeneca to be more agile, collaborative and focused as we enter a period of sustained growth.

Our strategy and plans remain unchanged, with sales growth and a focus on cost management anticipated to drive growing operating profit. I'm pleased that we are fully on track to meet these commitments as we build a sustainable level of growth and a pipeline that is benefitting more and more patients around the world."

Financial summary

- Product Sales increased by 4% in the year to $21,049m; new medicines generated incremental sales of $2.8bn at CER. Total Revenue declined by 2% in the year to $22,090m, driven by a 55% decline in Externalisation Revenue to $1,041m, with the year-on-year performance partly reflecting the impact of $997m of Initial Externalisation Revenue recognised in FY 2017 as part of the *Lynparza* collaboration with MSD[5]

- The Reported Gross Margin declined by three percentage points to 77% in the year, partly reflecting restructuring charges associated with biologic-medicine manufacturing facilities, the comparative effect of

manufacturing variances in the first half of 2017 and the impact of the *Lynparza* collaboration with MSD; the Core Gross Margin declined by two percentage points to 80%

- Total Reported Operating Expenses of $16,294m were stable in the year (a decline of 1% at CER). Total Core Operating Expenses increased by 5% (4% at CER) to $14,248m:
  - Reported R&D Expenses, which increased by 3% in the year to $5,932m, contained Intangible Asset Impairment charges of $539m (FY 2017: $101m), including a $470m charge in respect of MEDI0680. Core R&D Expenses declined by 3% to $5,266m, driven by efficiency savings and resource optimisation
  - Reported SG&A Expenses declined by 2% in the year (3% at CER) to $10,031m; Core SG&A Expenses increased by 10% (9% at CER) to $8,651m, reflecting support for new medicines and growth in China
- Reported Other Operating Income and Expense increased by 38% to $2,527m, reflecting divestment transactions, while Core Other Operating Income and Expense increased by 10% in the year to $2,147m. The difference between the Reported and Core performances was represented by a legal settlement in the first half of the year
- As indicated, restructuring expenses declined to $697m in the year (FY 2017: $807m). Designed to drive further efficiencies in the operations network, the Company recently decided to close two biologic-medicine manufacturing sites in Colorado, US. Associated with the closures, the Company expects to incur $0.4bn of one-time restructuring charges, the majority of which would be non-cash expenses; $0.3bn of these charges were recognised in FY 2018 as a result of impairments of site-related assets and inventory
- As indicated, capital expenditure declined to $1,043m (FY 2017: $1,326m)
- Reported EPS of $1.70 in the year represented a decline of 28% (29% at CER). Both Reported and Core EPS were impacted primarily by a decline in Externalisation Revenue, as well as the Gross Margin
- Core EPS declined by 19% to $3.46, despite a favourable impact resulting from a lower Core Tax Rate of 11% reflecting a $245m favourable adjustment to deferred taxes arising from recently-announced reduction in Dutch corporate income-tax rate; enacted in December 2018, it equated to $0.19 per share. Milestone revenue of $70m from MSD that related to the rapid regulatory approval in the US of *Lynparza* as a 1st-line maintenance treatment for *BRCA*-mutated (*BRCA*m) advanced ovarian cancer was received earlier than anticipated
- The Board has reaffirmed its commitment to the progressive dividend policy; a second interim dividend of $1.90 per share has been declared post year end, taking the unchanged full-year dividend per share to $2.80

Commercial summary

- Oncology
  Sales growth of 50% in the year (49% at CER) to $6,028m, including:
  - *Tagrisso* sales of $1,860m, representing growth of 95% (93% at CER), with increased use as a 2nd-line treatment for EGFR[6] T790M-mutated[7] NSCLC[8] patients and the 2018 approvals in the 1st-line EGFR-mutated (EGFRm) setting as a new standard of care (SoC). *Tagrisso,* based on the performance in FY 2018, is anticipated to be AstraZeneca's biggest-selling medicine in 2019
  - *Imfinzi* sales of $633m (FY 2017: $19m), reflecting ongoing launches for the treatment of patients with unresectable, Stage III NSCLC. The majority of sales of *Imfinzi* were in the US; the favourable impact of additional potential launches in other markets is yet to come
  - *Lynparza* sales of $647m, representing growth of 118% (116% at CER), driven by expanded use in the treatment of ovarian cancer and the medicine's first approvals for use in the treatment of breast cancer. The recent approval of *Lynparza* as a 1st-line treatment of patients with *BRCA*m ovarian cancer in the US is expected to support further expanded use

- New CVRM[9]
  Sales growth of 12% in the year to $4,004m, including:

  - *Farxiga* sales of $1,391m, with growth of 30% that included a sales increase of 45% in Emerging Markets (52% at CER) to $336m

  - *Bydureon* sales of $584m, an increase of 2% (1% at CER) that was driven by an encouraging *Bydureon BCise* launch in the US. Total Q4 2018 sales declined by 6% (5% at CER) to $138m, reflecting ongoing production constraints

  - *Brilinta* sales of $1,321m, representing growth of 22% (21% at CER), due to continued market penetration in the treatment of acute coronary syndrome and high-risk post-myocardial infarction (HRPMI). Total *Brilinta* sales increased by 26% in Q4 2018 (29% at CER) to $376m

- Respiratory
  Sales growth of 4% in the year (3% at CER) to $4,911m, including:

  - A *Symbicort* sales decline of 9% (10% at CER) to $2,561m, as competitive price pressures in the US continued, despite a market-share increase for the medicine. China sales of *Symbicort* increased by 36% (32% at CER) to $240m

  - *Pulmicort* sales growth of 9% (8% at CER) to $1,286m

  - *Fasenra* sales of $297m (Q4 2018: $125m), consolidating its position in the IL-5 class of severe-asthma medicines, performing exceptionally well in the countries where it was launched

- Emerging Markets
  The Company's largest region by Product Sales, with growth of 12% in the year (13% at CER) to $6,891m, including:

  - A China sales increase of 28% (25% at CER) to $3,795m. Q4 2018 sales in China increased by 17% (22% at CER) to $948m, despite Q4 2017 year-on-year growth of 33% (30% at CER). Oncology sales in China increased by 44% in the year (41% at CER) to $810m, partly underpinned by the launch of *Tagrisso* in China in 2017. *Tagrisso* was recently added to the National Reimbursement Drug List (NRDL) for the treatment of 2nd-line EGFR T790M-mutated NSCLC

  - An ex-China sales decline of 3% (an increase of 1% at CER) to $3,096m, partly impacted by the loss of Product Sales as a result of divestments. The quarter, however, saw a significantly-improved performance as the impact of divestments diminished, with every Emerging Markets sub-region delivering growth at CER and total ex-China Emerging Markets stable sales of $818m (an increase of 10% at CER). Notable performances in the quarter included sales in Brazil (stable, +23% at CER) and (non-China) Asia-Pacific (+10%, +13% at CER)

Organisational changes
As AstraZeneca recently entered a new phase in its strategic development, the Company announced in January 2019 organisational changes to enhance scientific innovation and commercial success.

The new structure simplifies R&D functions from discovery to late-stage development into Oncology and BioPharmaceuticals, or BioPharma. The new Oncology R&D function will be led by a world-renowned expert in the field, José Baselga and the BioPharma R&D function will be led by Mene Pangalos, who was previously responsible for the Company's Innovative Medicines and Early Development Biotech Unit.

The same approach has been applied to the majority of the Company's commercial operations. The commercial unit for Oncology will continue to be led by Dave Fredrickson and the commercial unit for BioPharma will be led by Ruud Dobber, most recently responsible for the Company's commercial operations in North America. The Emerging Markets commercial unit remains under the leadership of Leon Wang.

The goals of the reorganisation are to:

- Further increase focus on the Company's main therapy areas
- Integrate R&D functions for agile decision making and more flexible resource allocation
- Increase collaboration between the R&D and commercial functions

The R&D and commercial functions will each be represented on the Senior Executive Team of AstraZeneca and report to Chief Executive Officer (CEO), Pascal Soriot. The functions will share many common areas including basic biology and science platforms as well as medicine supply, manufacturing and IT infrastructure to improve efficiency. These resources will continue to be allocated on a Company-wide basis, according to the overall therapy-area considerations and strategy.

As AstraZeneca entered a period of sustained growth, the reorganisation was designed to enable the Company to be more agile, collaborative and be very focused on the main therapy areas. Further details of the changes can be found in the Corporate & Business Development section.

Pipeline highlights

The following table highlights significant developments in the late-stage pipeline since the prior results announcement:

Regulatory approvals	- *Lynparza* - ovarian cancer (1st line) (SOLO-1): regulatory approval (US) - roxadustat - anaemia in dialysis patients: regulatory approval (CN) - *Bevespi* - COPD[10]: regulatory approval (EU) - *Linzess* (linaclotide) - inflammatory bowel syndrome w/constipation (IBS-C): regulatory approval (CN)
Regulatory submissions and/or acceptances	- *Imfinzi* - unresectable, Stage III NSCLC: regulatory submission (CN); acceptance (OS[11] data) (US) - *Farxiga* - type-1 diabetes: regulatory submission acceptance (US) - *Fasenra* - severe, eosinophilic asthma; self-administration: submission acceptance (US, EU)
Major Phase III data readouts or other significant developments	- *Tagrisso* - EGFRm NSCLC (1st line): priority review (CN) - *Imfinzi* +/- treme - NSCLC (1st line) (MYSTIC): did not meet OS primary endpoints - *Imfinzi* +/- treme - head & neck cancer (2nd line): did not meet OS primary endpoints - *Lynparza* - ovarian cancer (1st line) (SOLO-1): priority review (CN) - *Lynparza* - ovarian cancer (3rd line+): met response rate primary endpoint - *Forxiga* - type-1 diabetes: CHMP[12] positive opinion (EU) - roxadustat - anaemia of CKD[13]: met primary efficacy endpoints - *Fasenra* - eosinophilic granulomatosis with polyangiitis: Orphan Drug Designation (US) - *Fasenra* - hypereosinophilic syndrome: Orphan Drug Designation (US) - PT010 - COPD: priority review (CN) - MEDI8897- lower respiratory tract infection: Breakthrough Therapy Designation (US), PRIME[14] designation (EU)

FY 2019 guidance
The Company today provides FY 2019 guidance. All measures in this section are at CER. Company guidance is on Product Sales and Core EPS only. All guidance and indications provided assume that the UK's anticipated forthcoming exit from the European Union, even in the event of no deal, proceeds in an orderly manner such that the impact is within the range expected, following the Company's extensive preparations for such eventuality.

Product Sales	A high single-digit percentage increase

In addition to the aforementioned Product Sales growth, the Company anticipates productivity gains and operating leverage in FY 2019. Core Operating Profit is anticipated to grow at a faster rate than Product Sales, despite an expected decline in the sum of Externalisation Revenue and Other Operating Income and Expense vs. the prior year. More details are provided below.

Core EPS	$3.50 to $3.70

Core EPS is anticipated to be impacted by a higher Core Tax Rate in FY 2019, following a low Core Tax Rate in FY 2018. The rate in FY 2019, indicated below, reflects the anticipated geographical mix of profits, as well as the impact of externalisation and divestment transactions anticipated to complete in FY 2019.

Variations in performance between quarters can be expected to continue. The Company is unable to provide guidance and indications on a Reported basis because the Company cannot reliably forecast material elements of the Reported result, including the fair-value adjustments arising on acquisition-related liabilities, intangible-asset impairment charges and legal-settlement provisions. Please refer to the section Cautionary Statements Regarding Forward-Looking Statements at the end of this announcement.

FY 2019 indications
Outside of guidance, the Company provides indications at CER for FY 2019 vs. the prior year:

- As part of its long-term growth strategy, the Company remains committed to focusing on appropriate cash-generating and value-accretive externalisation, collaboration and divestment transactions that reflect the ongoing productivity of the pipeline and the Company's increasing focus on its main therapy areas. The sum of Externalisation Revenue and Core Other Operating Income and Expense, however, is anticipated to decline vs. the prior year

- Core Operating Expenses are expected to increase by a low single-digit percentage. Specific support for medicine launches and China sales delivered compelling results in FY 2018 and elements of that support will continue. The Company will retain flexibility in its investment approach

- Core Operating Profit is anticipated to increase, ahead of Product Sales, by a mid-teens percentage vs. FY 2018.

- Capital expenditure is expected to be broadly stable and restructuring expenses are targeted to reduce vs. the prior year

- A Core Tax Rate of 18-22% (FY 2018: 11%)

Currency impact
The Company's foreign-exchange rate sensitivity analysis is contained within the Operating and Financial Review and, if foreign-exchange rates for February to December 2019 were to remain at the average of rates seen in January 2019, it is anticipated that there would be a low single-digit percentage adverse impact on Product Sales and Core EPS.

Sustainability
AstraZeneca's sustainability ambition is founded on making science accessible and operating in a way that recognises the interconnection between business growth, the needs of society and the limitations of the planet. The Company's sustainability ambition is reinforced by its purpose and values, which are intrinsic to its business model and ensures that the delivery of its strategy broadens access to medicines, minimises the environmental footprint of medicines and processes and ensures that all business activities are underpinned by the highest levels of ethics and transparency. A full update on the Company's sustainability progress is shown in the Sustainability section of this announcement.

Notes
The following notes refer to pages 1-5:

1. Constant exchange rates. These are financial measures that are not accounted for according to generally-accepted accounting principles (GAAP) because they remove the effects of currency movements from Reported results.

2. *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Lumoxiti*, *Farxiga*, *Brilinta*, *Lokelma*, *Fasenra* and *Bevespi*. These new medicines are pillars in the main therapy areas and are important platforms for future growth.

3. Reported financial measures are the financial results presented in accordance with International Financial Reporting Standards, as reported by the European Union and as issued by the International Accounting Standards Board.

4. Core financial measures. These are non-GAAP financial measures because, unlike Reported performance, they cannot be derived directly from the information in the Group Financial Statements. See the Operating and Financial Review for a definition of Core financial measures and a reconciliation of Core to Reported financial measures.

5. Merck & Co., Inc., Kenilworth, NJ, US, known as MSD outside the US and Canada.

6. Epidermal growth factor receptor.

7. Substitution of threonine (T) with methionine (M) at position 790 of exon 20 mutation.

8. Non-small cell lung cancer.

9. New Cardiovascular, Renal and Metabolism, incorporating Diabetes medicines, *Brilinta* and *Lokelma*.

10. Chronic obstructive pulmonary disease.

11. Overall survival.

12. Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA).

13. Chronic kidney disease.

14. PRIority MEdicines.

Pipeline: forthcoming major news flow
Innovation is critical to addressing unmet patient needs and is at the heart of the Company's growth strategy. The focus on research and development is designed to yield strong results from the pipeline.

H1 2019	- *Tagrisso* - EGFRm NSCLC (1st line): regulatory decision (CN) - *Imfinzi* +/- treme - head & neck cancer (1st line): data readout, regulatory submission - *Lynparza* - breast cancer: regulatory decision (EU) - *Lynparza* - pancreatic cancer: data readout - *Brilinta* - CAD[15] / type-2 diabetes CVOT[16]: data readout - *Forxiga* - type-1 diabetes: regulatory decision (EU, JP) - *Farxiga* - type-2 diabetes CVOT: regulatory submission - roxadustat - anaemia: data readout (pooled safety), regulatory submission (US) - *Duaklir* - COPD: regulatory decision (US)
H2 2019	- *Tagrisso* - EGFRm NSCLC (1st line): data readout (final OS) - *Imfinzi* - unresectable, Stage III NSCLC: regulatory decision (CN) - *Imfinzi* + treme - NSCLC (1st line) (NEPTUNE): data readout, regulatory submission - *Imfinzi* +/- treme - NSCLC (1st line) (POSEIDON): data readout, regulatory submission - *Imfinzi* +/- treme - small-cell lung cancer: data readout, regulatory submission - *Imfinzi* +/- treme - bladder cancer (1st line): data readout, regulatory submission - *Lynparza* - ovarian cancer (1st line) (SOLO-1): regulatory decision (EU, JP, CN) - *Lynparza* - pancreatic cancer: regulatory submission - *Lynparza* - ovarian cancer (1st line) (PAOLA-1): data readout - *Lynparza* - prostate cancer (2nd line, castration-resistant): data readout - *Calquence* - CLL[17]: data readout, regulatory submission - selumetinib - NF1: regulatory submission - *Brilinta* - CAD / type-2 diabetes CVOT: regulatory submission - *Farxiga* - type-1 diabetes: regulatory decision (US) - *Lokelma* - hyperkalaemia: regulatory submission (JP) - *Symbicort* - mild asthma: regulatory decision (EU), regulatory submission (CN) - *Bevespi* - COPD: regulatory decision (JP, CN) - *Fasenra* - self administration: regulatory decision (US, EU) - PT010 - COPD: regulatory decision (JP, CN), regulatory submission (US, EU) - PT010 - COPD: data readout (ETHOS)

[15] Coronary artery disease.
[16] Cardiovascular outcomes trial.
[17] Chronic lymphocytic leukaemia.

2020	- *Imfinzi* - neo-adjuvant NSCLC: data readout - *Lynparza* - ovarian cancer (1st line) (PAOLA-1): regulatory submission - *Lynparza* - prostate cancer (2nd line, castration-resistant): regulatory submission - *Brilinta* - stroke: data readout, regulatory submission - *Farxiga* - heart failure CVOT: data readout, regulatory submission - *Farxiga* - CKD: data readout - *Epanova* - hypertriglyceridaemia CVOT: data readout - *Lokelma* - hyperkalaemia: regulatory submission (CN) - roxadustat - anaemia of myelodysplastic syndrome: data readout - *Fasenra* - nasal polyps: data readout, regulatory submission - tezepelumab - severe asthma: data readout

Conference call
A conference call and webcast for investors and analysts will begin at 12pm UK time today. Details can be accessed via astrazeneca.com.

Reporting calendar
The Company intends to publish its first-quarter financial results on 26 April 2019.

About AstraZeneca
AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in its main therapy areas - Oncology, CVRM and Respiratory. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit astrazeneca.com and follow us on Twitter @AstraZeneca.

Investor Relations

Thomas Kudsk Larsen		+44 203 749 5712
Henry Wheeler	Oncology	+44 203 749 5797
Christer Gruvris	BioPharma - Cardiovascular; Metabolism	+44 203 749 5711
Nick Stone	BioPharma - Respiratory; Renal	+44 203 749 5716
Josie Afolabi	Other	+44 203 749 5631
Craig Marks	Finance; Fixed Income	+44 7881 615 764
Jennifer Kretzmann	Retail Investors; Corporate Access	+44 203 749 5824
US toll-free		+1 866 381 7277

Media Relations

Gonzalo Viña	UK/Global	+44 203 749 5916
Rob Skelding	UK/Global	+44 203 749 5821
Matt Kent	UK/Global	+44 203 749 5906
Jennifer Hursit	UK/Global	+44 7384 799 726
Christina Malmberg Hägerstrand	Sweden	+46 8 552 53 106
Michele Meixell	US	+1 302 885 2677

Table of contents and list of tables

Operating and financial review

All narrative on growth and results in this section is based on actual exchange rates, unless stated otherwise. Financial figures are in US$ millions ($m). The performance shown in this announcement covers the twelve-month period to 31 December 2018 (the year or FY 2018) and the three-month period to 31 December 2018 (the quarter, the fourth quarter or Q4 2018) compared to the twelve-month period to 31 December 2017 (FY 2017) and the three-month period to 31 December 2017 (Q4 2017) respectively, unless stated otherwise. All commentary in the Operating and Financial Review relates to the year, unless stated otherwise.

Core financial measures, EBITDA, Net Debt, Initial Externalisation Revenue and Ongoing Externalisation Revenue are non-GAAP financial measures because they cannot be derived directly from the Group Condensed Consolidated Financial Statements. Management believes that these non-GAAP financial measures, when provided in combination with Reported results, will provide investors and analysts with helpful supplementary information to understand better the financial performance and position of the Company on a comparable basis from period to period. These non-GAAP financial measures are not a substitute for, or superior to, financial measures prepared in accordance with GAAP. Core financial measures are adjusted to exclude certain significant items, such as:

- Amortisation and impairment of intangible assets, including impairment reversals but excluding any charges relating to IT assets

- Charges and provisions related to global restructuring programmes, which includes charges that relate to the impact of global restructuring programmes on capitalised IT assets

- Other specified items, principally comprising acquisition-related costs, which include fair-value adjustments and the imputed finance charge relating to contingent consideration on business combinations, legal settlements and foreign-exchange gains and losses on certain non-structural intra-group loans

Details on the nature of Core financial measures are provided on page 68 of the Annual Report and Form 20-F Information 2017. Reference should be made to the reconciliation of Core to Reported financial information and the Reconciliation of Reported to Core Financial Measures tables included in the Financial Performance section of this announcement.

EBITDA is defined as Reported Profit Before Tax after adding back Net Finance Expense, results from Joint Ventures and Associates and charges for Depreciation, Amortisation and Impairment. Reference should be made to the Reconciliation of Reported Profit Before Tax to EBITDA included in the Financial Performance section of this announcement.

Net Debt is defined as interest-bearing loans and borrowings net of cash and cash equivalents, other investments and net derivative financial instruments. Reference should be made to Note 3 'Net Debt' included in the Notes to the Condensed Financial Information section of this announcement. Ongoing Externalisation Revenue is defined as Externalisation Revenue excluding Initial Externalisation Revenue (which is defined as Externalisation Revenue that is recognised at the date of completion of an agreement or transaction, in respect of upfront consideration). Ongoing Externalisation Revenue comprises, among other items, royalties, milestone revenue and profit-sharing income. Reference should be made to the Breakdown of Externalisation Revenue table in this Operating and Financial Review.

The Company strongly encourages investors and analysts not to rely on any single financial measure, but to review AstraZeneca's financial statements, including the notes thereto and other available Company reports, carefully and in their entirety.

Due to rounding, the sum of a number of percentages may not agree to totals.

Table 1: Total Revenue

	FY 2018			Q4 2018		
	$m	% change		$m	% change	
		Actual	CER		Actual	CER
Product Sales	21,049	4	4	5,768	5	8
Externalisation Revenue	1,041	(55)	(55)	649	n/m	n/m
Total Revenue	**22,090**	**(2)**	**(2)**	**6,417**	**11**	**14**

Table 2: Product Sales

	FY 2018				Q4 2018			
	$m	% of total	% change		$m	% of total	% change	
			Actual	CER			Actual	CER
Oncology	6,028	29	50	49	1,767	31	58	61
New CVRM	4,004	19	12	12	1,103	19	8	11
Respiratory	4,911	23	4	3	1,362	24	2	5
Other	6,106	29	(22)	(23)	1,536	27	(24)	(21)
Total	**21,049**	**100**	**4**	**4**	**5,768**	**100**	**5**	**8**

Table 3: Top-ten medicines
The top-ten medicines in the year by Product Sales are shown in the table below:

Medicine	Therapy Area	$m	% of Total Product Sales
Symbicort	Respiratory	2,561	12
Tagrisso	Oncology	1,860	9
Nexium	Other	1,702	8
Crestor	CVRM	1,433	7
Farxiga	CVRM	1,391	7
Brilinta	CVRM	1,321	6
Pulmicort	Respiratory	1,286	6
Faslodex	Oncology	1,028	5
Zoladex	Oncology	752	4
Seloken/Toprol-XL	CVRM	712	3
Total		**14,046**	**67**

Table 4: Breakdown of Externalisation Revenue
Ongoing Externalisation Revenue of $929m represented 89% of total Externalisation Revenue in the year (FY 2017: $821m, 35%). A breakdown of Externalisation Revenue is shown below:

	FY 2018				Q4 2018			
	$m	% of total	% change Actual	% change CER	$m	% of total	% change Actual	% change CER
Initial Externalisation Revenue	**112**	**11**	**(93)**	**(93)**	**-**	**-**	**n/m**	**n/m**
Royalties	49	5	(54)	(54)	11	2	45	41
Milestones/Other[18]	880	84	24	23	638	98	n/m	n/m
Ongoing Externalisation Revenue	**929**	**89**	**14**	**13**	**649**	**100**	**n/m**	**n/m**
Total Externalisation Revenue	**1,041**	**100**	**(55)**	**(55)**	**649**	**100**	**n/m**	**n/m**

Table 5: Initial Externalisation Revenue
A breakdown of Initial Externalisation Revenue in the year is shown below:

Medicine	Party	Region	$m
Crestor	Almirall, S.A.	Spain	61
Other			51
Total			**112**

Table 6: Ongoing Externalisation Revenue
A breakdown of Ongoing Externalisation Revenue in the year is shown below:

Medicine	Party	Region	$m
Lynparza	MSD - milestone revenue (regulatory)	Global	140
Lynparza	MSD - milestone revenue (sales-related)	Global	250
Lynparza	MSD - milestone revenue (option payment)	Global	400
Other			139
Total			**929**

[18] May include, *inter alia*, option income and profit-sharing income.

Table 7: Externalised and divested medicines
Several AstraZeneca medicines were externalised or divested in FY 2018, thus adversely impacting the Product Sales performance:

Completion	Medicine	Region	FY 2018[19] $m	FY 2017 $m	Adverse Impact on FY 2018 Product Sales $m	%
January 2018	*Crestor*	Spain	7	74	(67)	
June 2018	*Seroquel XR* and *Seroquel* IR	UK, China and other countries	109	148	(39)	
September 2018	*Atacand*	Europe	70	86	(16)	
November 2018	*Nexium* and *Vimovo*	Europe, Global	235	248	(13)	
	Total		**421**	**556**	**(135)**	**2%**

[19] FY 2018 Product Sales here comprise sales made prior to completion, plus sales to collaborators under manufacturing and supply agreements following completion.

Product Sales

The performance of new and legacy medicines is shown below, with a geographical split shown in Notes 7 & 8.

Table 8: FY 2018 therapy area and medicine performance

Therapy Area	Medicine	FY 2018			
		$m	% of total	% change Actual	% change CER
Oncology	*Tagrisso*	1,860	9	95	93
	Lynparza	647	3	n/m	n/m
	Imfinzi	633	3	n/m	n/m
	Iressa	518	2	(2)	(4)
	Calquence	62	-	n/m	n/m
	LEGACY:				
	Faslodex	1,028	5	9	9
	Zoladex	752	4	2	2
	Arimidex	212	1	(2)	(3)
	Casodex	201	1	(7)	(8)
	Others	115	1	1	(1)
	Total Oncology	**6,028**	**29**	**50**	**49**
CVRM	*Farxiga*	1,391	7	30	30
	Brilinta	1,321	6	22	21
	Bydureon	584	3	2	1
	Onglyza	543	3	(11)	(11)
	Byetta	126	1	(28)	(28)
	Symlin	34	-	(29)	(29)
	LEGACY:				
	Crestor	1,433	7	(39)	(40)
	Seloken/Toprol-XL	712	3	2	4
	Atacand	260	1	(13)	(12)
	Others	306	1	(11)	(12)
	Total CVRM	**6,710**	**32**	**(8)**	**(8)**

Therapy Area	Medicine	FY 2018			
		$m	% of total	% change Actual	% change CER
Respiratory	*Symbicort*	2,561	12	(9)	(10)
	Pulmicort	1,286	6	9	8
	Fasenra	297	1	n/m	n/m
	Daliresp/*Daxas*	189	1	(5)	(5)
	Tudorza/*Eklira*	110	1	(27)	(29)
	Duaklir	95	-	20	14
	Bevespi	33	-	n/m	n/m
	Others	340	2	20	18
	Total Respiratory	**4,911**	**23**	**4**	**3**
Other	*Nexium*	1,702	8	(13)	(14)
	Synagis	665	3	(3)	(3)
	Seroquel XR/IR	361	2	(29)	(31)
	Losec/*Prilosec*	272	1	-	(2)
	FluMist/*Fluenz*	110	1	41	44
	Movantik/*Moventig*	109	1	(11)	(11)
	Others	181	1	(66)	(67)
	Total Other	**3,400**	**16**	**(18)**	**(19)**
	Total Product Sales	**21,049**	**100**	**4**	**4**

Specialty-care medicines comprise all Oncology medicines and *Fasenra*. At 30% of Product Sales, specialty-care medicine sales increased by 57% in the year (56% at CER) to $6,325m (FY 2017: $4,025m).

Table 9: Q4 2018 therapy area and medicine performance

Therapy Area	Medicine	Q4 2018			
		$m	% of total	% change	
				Actual	CER
Oncology	*Tagrisso*	594	10	95	98
	Lynparza	209	4	n/m	n/m
	Imfinzi	262	5	n/m	n/m
	Iressa	112	2	(14)	(11)
	Calquence	24	-	n/m	n/m
	LEGACY:				
	Faslodex	269	5	13	16
	Zoladex	182	3	(3)	3
	Arimidex	46	1	(19)	(16)
	Casodex	46	1	(15)	(13)
	Others	23	-	(21)	(17)
	Total Oncology	**1,767**	**31**	**58**	**61**
CVRM	*Farxiga*	397	7	20	24
	Brilinta	376	7	26	29
	Bydureon	138	2	(6)	(5)
	Onglyza	148	3	(18)	(15)
	Byetta	32	1	(33)	(31)
	Symlin	10	-	(23)	(23)
	LEGACY:				
	Crestor	353	6	(41)	(38)
	Seloken/Toprol-XL	160	3	(5)	4
	Atacand	58	1	(21)	(14)
	Others	75	1	(12)	(8)
	Total CVRM	**1,747**	**30**	**(10)**	**(6)**

Therapy Area	Medicine	Q4 2018			
		$m	% of total	% change Actual	% change CER
Respiratory	*Symbicort*	636	11	(15)	(13)
	Pulmicort	389	7	5	9
	Fasenra	125	2	n/m	n/m
	Daliresp/Daxas	54	1	2	4
	Tudorza/Eklira	19	-	(55)	(55)
	Duaklir	22	-	(4)	-
	Bevespi	10	-	25	25
	Others	107	2	26	32
	Total Respiratory	**1,362**	**24**	**2**	**5**
Other	*Nexium*	390	7	(9)	(6)
	Synagis	251	4	7	7
	FluMist/Fluenz	75	1	29	33
	Losec/Prilosec	60	1	(13)	(9)
	Seroquel XR/IR	56	1	(65)	(64)
	Movantik/Moventig	25	-	(17)	(17)
	Others	35	1	(70)	(68)
	Total Other	**892**	**15**	**(18)**	**(17)**
	Total Product Sales	**5,768**	**100**	**5**	**8**

Product Sales summary

Oncology

Product Sales of $6,028m in the year; an increase of 50% (49% at CER). Oncology Product Sales represented 29% of total Product Sales, up from 20% in FY 2017.

Lung cancer

Tagrisso

In the 2nd-line setting, *Tagrisso* has been approved and launched in over 80 countries, including the US, in Europe, Japan and China for patients with EGFR T790M-mutated NSCLC. By the end of the period, *Tagrisso* had been approved in more than c.60 countries including the US, in Europe and Japan for the 1st-line treatment of patients with EGFRm NSCLC; a number of additional regulatory reviews are also underway.

Product Sales of $1,860m in the year represented growth of 95% (93% at CER), partly driven by increased testing rates and the aforementioned approvals in the 1st-line setting. Continued growth was also delivered in the 2nd-line indication in other countries, including in Europe and Emerging Markets. *Tagrisso* became AstraZeneca's second-largest selling medicine and largest-selling Oncology medicine in the year.

Sales in the US increased by 115% to $869m, with sequential growth in the quarter of 21% to $289m; *Tagrisso* was established as the SoC in the 1st-line setting. A high level of penetration was achieved following the April 2018 approval in that setting.

Within Emerging Markets, *Tagrisso* sales increased by 157% in the year (159% at CER) to $347m, with notable growth in China, where the medicine was approved in March 2017 in the 2nd-line setting. Q4 2018 sales of *Tagrisso* in Emerging Markets declined sequentially from $107m to $81m, reflecting the addition of *Tagrisso* to the NRDL with effect from January 2019. The Asia-Pacific region has a relatively high prevalence of lung-cancer patients with an EGFR mutation, namely c.30-40% of lung-cancer patients, contrasting with c.10-15% in the Western hemisphere.

In Europe, sales of $314m in the year represented growth of 68% (61% at CER), driven by further growth in testing rates, positive reimbursement decisions and strong levels of demand in the 2nd-line setting. Sales in Europe increased sequentially by 11% (12% at CER) to $92m in Q4 2018 as the medicine reached more patients, with the benefit felt from the EU regulatory approval in June 2018 for the 1st-line treatment of patients with EGFRm NSCLC. *Tagrisso* was subsequently launched in a number of countries in this setting, including in France and Germany, where *Tagrisso* is listed as the preferred 1st-line tyrosine kinase inhibitor in local guidelines; reimbursement negotiations are underway elsewhere, with reimbursement decisions expected later in 2019.

Sales of *Tagrisso* in Japan increased by 45% in the year (43% at CER) to $317m, reflecting increasing use as a 1st-line treatment, following approval in this setting in the third quarter. Focused activities to maximise testing and utilisation rates in the 2nd-line setting also supported the growth in Product Sales.

Imfinzi

Imfinzi is approved in more than c.40 countries, including the US, in Europe and Japan, for the treatment of patients with unresectable, Stage III NSCLC whose disease has not progressed following platinum-based chemotherapy and radiation therapy (CRT). It is also approved for the 2nd-line treatment of patients with locally-advanced or metastatic urothelial carcinoma (bladder cancer) in a number of countries, including the US.

Global Product Sales of *Imfinzi* amounted to $633m in the year (Q4 2018: $262m), of which $564m of sales emanated from the US, mostly for the treatment of unresectable, Stage III NSCLC. $35m of sales in Japan and $27m of sales in Europe in FY 2018 followed recent approvals and launches; time was taken to achieve reimbursement decisions in many markets. Additional regulatory approvals are expected in due course and subsequent launches will follow anticipated reimbursement decisions.

Iressa
Product Sales of $518m in the year; a decline of 2% (4% at CER).

Emerging Markets sales increased by 14% (12% at CER) to $286m; *Iressa* entered the NRDL in China in 2017 and was included in the China 4+7 pilot tender scheme during the year. Given the growing use of *Tagrisso*, sales of *Iressa* declined by 33% to $26m in the US and declined by 3% (8% at CER) to $109m in Europe.

Lynparza

By the end of the period, *Lynparza* was approved in over 60 countries for the treatment of ovarian cancer. Launches in the treatment of breast cancer took place in the US and Japan in 2018 and the indication is under regulatory review in Europe.

Product Sales of *Lynparza* amounted to $647m, an increase of 118% (116% at CER). The strong performance was geographically spread, with ongoing launches in the Established Rest of World (ROW) and Emerging Markets. Ongoing MSD co-promotion efforts also contributed to sales.

US sales increased by 145% in the year to $345m, driven by increased demand that reflected continued growth in the treatment with *Lynparza* of patients suffering from ovarian or breast cancer. In December 2018, *Lynparza* was approved by the US FDA as a 1st-line maintenance treatment of patients with *BRCA*m ovarian cancer and remained the leading US medicine in the poly ADP ribose polymerase (PARP)-inhibitor class in the year, as measured by total prescription volumes and in both ovarian and breast cancer.

Sales in Europe increased by 46% in the year (41% at CER) to $190m, driven by increasing levels of reimbursement and *BRCA* testing rates. The Company also rolled out a number of launches in a broad, 2nd-line, maintenance ovarian-cancer indication, regardless of *BRCA* status. In the first half of the year, the Company announced that the EMA had approved the use of *Lynparza* tablets (300mg twice daily) as a treatment for the same patient population.

Following the initial launch in April 2018, Japan sales of *Lynparza* in the year as a treatment for 2nd-line maintenance ovarian cancer amounted to $48m. In July 2018, an additional approval was granted as a targeted chemotherapy-sparing treatment for *BRCA*m, metastatic breast cancer; a respective launch followed thereafter.

Emerging Markets sales of $51m in the year reflected the approval of *Lynparza* as a 2nd-line maintenance treatment of patients with ovarian cancer by the China National Medical Products Administration (NMPA), resulting in the subsequent launch of *Lynparza* in China, the first PARP inhibitor to be approved in the country.

Haematology and other Oncology medicines

Calquence
Product Sales of $62m in the year; *Calquence* was approved and launched in the US in October 2017. The medicine delivered a promising performance in the year, with more than one third of new patients now treated in the 2nd line with *Calquence* in the approved indication of mantle cell lymphoma (MCL). At the end of 2018, the first regulatory approvals outside the US for the treatment of patients with MCL were granted in Brazil and the United Arab Emirates, with launches expected to benefit patients in 2019.

Legacy: *Faslodex*
Product Sales of $1,028m in the year; an increase of 9%, reflecting volume growth. *Faslodex* achieved blockbuster status in the year, namely sales of more than $1bn.

Emerging Markets sales of *Faslodex* increased by 34% in the year (41% at CER) to $154m. US sales increased by 9% to $537m, highlighting a continued strong uptake of the combination with the CDK4/6 class, medicines approved for the treatment of hormone-receptor-positive breast cancer.

Europe sales declined by 14% in the year (19% at CER) to $221m, reflecting the impact of generic entrants in certain countries. In June 2017, a label extension, based upon the FALCON trial in the 1st-line setting, was approved in Japan, where sales increased by 51% in the year (49% at CER) to $109m, despite the impact of the biennial price cut, implemented in April 2018.

Legacy: *Zoladex*
Product Sales of $752m in the year; an increase of 2%.

Emerging Markets sales of *Zoladex* increased by 16% in the year (18% at CER) to $409m. Sales in Europe declined by 6% (10% at CER) to $133m. In the Established ROW region, sales declined by 11% (12% at CER) to $202m, driven by the effects of increased competition. In March 2017, the Company completed an agreement with TerSera Therapeutics LLC for the sale of the commercial rights to *Zoladex* in the US and Canada.

CVRM
Total CVRM sales, which included *Crestor* and other legacy medicines, declined by 8% to $6,710m. Total CVRM sales comprised 32% of total Product Sales in the year, down from 36% in FY 2017. New CVRM sales increased by 12% in the year to $4,004m, reflecting the strong performances of *Farxiga* and *Brilinta*.

Diabetes

Farxiga
Product Sales of $1,391m in the year; an increase of 30%.

Emerging Markets sales of *Forxiga* increased by 45% in the year (52% at CER) to $336m, reflecting ongoing launches, improved levels of patient access and strong performances in key markets such as Brazil. In 2017, *Forxiga* became the first SGLT2-inhibitor medicine to be approved in China; since the subsequent launch, the medicine has seen growing levels of access.

US sales increased by 21% in the year to $591m. The performance in the first half of 2018 was favourably impacted by the Company's changes to affordability programmes at the end of H1 2017. Despite slowing growth in the US, the SGLT2 class continued to be underpinned by growing evidence around cardiovascular (CV) benefits.

Sales in Europe increased by 30% in the year (24% at CER) to $315m. In Japan, sales increased by 42% (40% to CER) to $75m. Ono Pharmaceutical Co., Ltd, collaborating with AstraZeneca, records in-market sales in Japan.

Bydureon
Product Sales of $584m in the year; an increase of 2% (1% at CER).

Sales in the US increased by 4% in the year to $475m. This illustrated a continued encouraging performance from the launch of *Bydureon BCise*. Favourable sales volumes were driven by continued growth in the glucagon-like peptide-1 class, at the expense of insulin, for more-advanced type-2 diabetes patients. *Bydureon* sales in Europe declined by 8% (13% at CER) to $81m. In August 2018, the Company announced that *Bydureon BCise* had been approved by the EMA.

Q4 2018 global sales of *Bydureon* declined by 6% (5% at CER) to $138m, reflecting ongoing production constraints.

Onglyza
Product Sales of $543m in the year, a decline of 11%.

The performance reflected adverse pressures on the dipeptidyl peptidase-4 (DPP-4) class and an acceleration of ongoing diabetes-market dynamics, where patients are moving to medicines and classes of medicines with proven CV benefits. Given the significant future potential of *Farxiga*, the Company continues to prioritise commercial support over *Onglyza*.

Sales in Emerging Markets increased by 32% in the year (34% at CER) to $172m; this partly reflected the full-year effect of entry onto the NRDL in China in 2017. Sales in Europe declined by 14% (18% at CER) to $89m, highlighting the broader trend of a shift away from the DPP-4 class.

Other CVRM medicines

Brilinta
Product Sales of $1,321m in the year; an increase of 22% (21% at CER). Total *Brilinta* sales increased by 26% in Q4 2018 (29% at CER) to $376m.

Emerging Markets sales of *Brilinta* increased by 46% in the year (48% at CER) to $326m, bolstered by the entry onto the NRDL in China in 2017. US sales of *Brilinta*, at $588m, represented an increase of 16%. The performance, underlined by volume growth, was driven primarily by an increase in the number of patients initiated on *Brilinta* in hospitals and a lengthening in the average-weighted duration of treatment, reflecting the impact of growing 90-day prescriptions. Furthermore, *Brilinta* continued to deliver increasing levels of market share during the period. US sales increased by 15% in the quarter to $177m.

Sales of *Brilique* in Europe increased by 18% in the year (13% at CER) to $348m, highlighting increased HRPMI-penetration levels across a number of markets.

Lokelma
Lokelma's launch programme recently began in Scandinavia. It was approved in the EU in 2018 for the treatment of hyperkalaemia, a serious condition characterised by elevated potassium levels in the blood associated with CV, renal and metabolic diseases; launches will commence in major European markets in due course.

In the US, where *Lokelma* was approved in 2018, the Company has market-preparation processes underway in order to secure coverage across commercial and Medicare Part D plans. AstraZeneca has also actioned procedures to ensure inclusion on hospital formularies so that patients have adequate access to *Lokelma* when it is anticipated to become broadly available in the second half of 2019.

Legacy: *Crestor*
Product Sales of $1,433m in the year; a decline of 39% (40% at CER).

Sales in China increased by 22% in the year (19% at CER) to $456m, a result of underlying demand. Market growth in statin usage, AstraZeneca's commercial strength in China and the Company's successful strategy of broader coverage in China also continued to impact sales favourably.

During the period, however, the results of the first round of negotiation from the aforementioned 4+7 scheme were announced, with *Crestor* being unsuccessful; the decision is anticipated to have an adverse impact on sales of *Crestor* in China.

US sales declined by 54% in the year to $170m, underlining the ongoing impact of the entry of multiple *Crestor* generic medicines in 2016. In Europe, sales declined by 70% (71% at CER) to $203m, reflecting a similar impact that began in 2017.

In Japan, where AstraZeneca collaborates with Shionogi Co. Ltd, sales declined by 66% in the year (67% at CER) to $166m, reflecting the impact of the entry of multiple *Crestor* competitors in the market in the final quarter of 2017; AstraZeneca expects this impact to recede significantly in 2019. The decline also reflected actions by the Japanese government to focus further on incentives to increase the adoption of generic medicines.

Respiratory

Product Sales of $4,911m in the year; an increase of 4% (3% at CER). Respiratory Product Sales represented 23% of total Product Sales, unchanged vs. FY 2017.

Symbicort
Product Sales of $2,561m in the year; a decline of 9% (10% at CER).

Symbicort continued to lead the global market by volume within the inhaled corticosteroid / long-acting beta agonist (LABA) class.

Emerging Markets sales of *Symbicort* increased by 13% in the year (14% at CER) to $495m. In contrast, US sales declined by 22% to $862m, reflecting continued pricing pressure, the timing of government buying and the

impact of managed-market rebates. The performance was in line with expectations, with challenging pricing pressure expected to continue.

In Europe, sales declined by 6% in the year (10% at CER) to $773m; the performance partly reflected the level of price competition from other branded and *Symbicort*-analogue medicines, plus government pricing interventions. *Symbicort*, however, continued to retain its class-leadership position and stabilise its volume market share in the class, with volume growth achieved in a number of markets.

In Japan, sales increased by 1% in the year (stable at CER) to $207m, despite the impact of the aforementioned biennial price cut. In January 2019, AstraZeneca and Astellas Pharma Co. Ltd (Astellas) announced that the sale and distribution of *Symbicort*, conducted by Astellas in Japan, was to be transferred to AstraZeneca and that the co-promotion conducted by Astellas and AstraZeneca will be terminated on 30 July 2019. The Company will solely distribute and promote the medicine in Japan from 31 July 2019.

Pulmicort
Product Sales of $1,286m in the year; an increase of 9% (8% at CER).

Emerging Markets, where sales increased by 18% in the year (17% at CER) to $995m, represented 77% of global sales of *Pulmicort*. China, making up the overwhelming majority of *Pulmicort* sales in Emerging Markets, delivered a particularly strong performance, supported by higher demand and strong underlying volume growth, underpinned by the impact of AstraZeneca's contribution to increasing numbers of nebulisation centres.

Sales in the US and Europe declined by 26% to $116m and by 2% (8% at CER) to $90m in the year, respectively, a consequence of the medicine's legacy status.

Fasenra
Product Sales of $297m in the year (Q4 2018: $125m).

In November 2017, the Company was granted approval for *Fasenra* in the US as a treatment of patients with severe, eosinophilic asthma; the approval was followed immediately by the launch of the medicine and US sales amounted to $218m in the year. New-to-brand prescription data showed that *Fasenra* was the preferred IL-5 biologic medicine for the treatment of severe asthma at the end of the period, despite being third to market.

In Europe and Japan, AstraZeneca was granted regulatory approval in January 2018 on a similar basis to that in the US. In Europe, sales totalled $32m in the year, predominately reflecting strong sales in Germany. Sales in Japan amounted to $45m in the year, following its launch in the second quarter; *Fasenra* is already leading the class by value share in Japan.

Daliresp/Daxas
Product Sales of $189m in the year; a decline of 5%.

US sales, representing 82% of the global total, declined by 7% to $155m, driven by the impact of low market growth and payer pressures. It is the only oral, selective, long-acting inhibitor of phosphodiesterase-4, an inflammatory enzyme associated with COPD. Sales in Europe increased by 8% (4% at CER) to $28m.

Tudorza/Eklira
Product Sales of $110m in the year; a decline of 27% (29% at CER).

Sales in the US declined by 62% to $25m, reflecting the impact of federal purchases. In March 2017, AstraZeneca announced that it had entered a strategic collaboration with Circassia Pharmaceuticals plc (Circassia) for the development and commercialisation of *Tudorza* in the US, where AstraZeneca records Product Sales. As part of the collaboration agreement, Circassia had the opportunity to exercise an option to sub-licence the commercial rights to *Tudorza* in the US by paying $25m. The option was exercised in Q4 2018 and completed in Q1 2019.

Sales in Europe increased by 1% in the year (a decline of 3% at CER) to $74m, impacted by the deterioration of the long-acting muscarinic antagonist (LAMA) monotherapy class.

Duaklir
Product Sales of $95m in the year; an increase of 20% (14% at CER).

Duaklir, the Company's first inhaled dual bronchodilator medicine, is now available for patients in over 25 countries, with almost all sales emanating from Europe. Germany and the UK accounted for over half of all European sales in the year. The global LAMA/LABA class continued to grow in the period, albeit below expectations.

Bevespi
Product Sales increased by 106% in the year to $33m.

Launched in the US in Q1 2017, *Bevespi* saw prescriptions in the period track in line with other LAMA/LABA launches; the class in the US, however, continued to grow more slowly than anticipated previously. *Bevespi* was the first medicine launched using the Company's proprietary *Aerosphere* Delivery Technology.

Other (medicines outside the main therapy areas)

Product Sales of $3,400m; a decline of 18% (19% at CER). Other Product Sales represented 16% of total Product Sales, down from 21% in 2017.

Nexium
Product Sales of $1,702m in the year; a decline of 13% (14% at CER).

Emerging Markets sales increased by 1% in the year to $690m, while sales in the US declined by 39% to $306m. In Europe, sales declined by 5% (10% at CER) at $235m. In October 2018, AstraZeneca announced that it had agreed to divest the prescription medicine rights to *Nexium* in Europe to Grünenthal. In Japan, where AstraZeneca collaborates with Daiichi Sankyo Company, Ltd, sales declined by 8% (9% at CER) to $405m.

Synagis
Product Sales of $665m in the year; a decline of 3%.

US sales declined by 9% to $287m and continued to be impacted by the prevailing guidelines from the American Academy of Pediatrics Committee on Infectious Diseases. Product Sales to AbbVie Inc., responsible for the commercialisation of *Synagis* in over 80 countries outside the US, increased by 2% to $377m.

In January 2019, the Company completed an agreement with Swedish Orphan Biovitrum AB (Sobi) for the sale and licence of the rights to *Synagis* in the US.

Seroquel XR and *Seroquel* IR
Product Sales of $361m in the year; a decline of 29% (31% at CER).

Sales of *Seroquel XR* in the US declined by 58% to $73m, reflecting the ongoing impact of generic-medicine competition. Sales of *Seroquel XR* in Europe declined by 21% (24% at CER) to $62m, highlighting a similar impact. In May 2018, the Company announced that it had entered into an agreement with Luye Pharma Group, Ltd. (Luye Pharma) for the sale and licence of the rights to *Seroquel XR* and *Seroquel* IR in the UK, China and other markets. Sales of *Seroquel* IR declined by 7% in the year (8% at CER) to $167m.

FluMist/*Fluenz*
Product Sales of $110m in the year; an increase of 41% (44% at CER). *FluMist* returned to the US market in Q3 2018 in time for the 2018-2019 influenza season, where sales amounted to $15m in the year. Sales of *Fluenz* in Europe increased by 20% (22% at CER) in the year to $91m.

Regional Product Sales

Table 10: Regional Product Sales

	FY 2018				Q4 2018			
	$m	% of total	% change Actual	% change CER	$m	% of total	% change Actual	% change CER
Emerging Markets[20]	6,891	33	12	13	1,766	31	8	16
China	*3,795*	*18*	*28*	*25*	*948*	*16*	*17*	*22*
Ex-China	*3,096*	*15*	*(3)*	*1*	*818*	*14*	*-*	*10*
US	6,876	33	11	11	2,037	35	15	15
Europe	4,459	21	(6)	(10)	1,173	20	(9)	(7)
Established ROW	2,823	13	(8)	(9)	792	14	-	1
Japan	*2,004*	*10*	*(9)*	*(11)*	*588*	*10*	*4*	*5*
Canada	*489*	*2*	*1*	*-*	*131*	*2*	*-*	*4*
Other Established ROW	*330*	*2*	*(15)*	*(14)*	*73*	*1*	*(27)*	*(22)*
Total	**21,049**	**100**	**4**	**4**	**5,768**	**100**	**5**	**8**

Table 11: Regional Product Sales, Emerging Markets

Product Sales of $6,891m in the year, an increase of 12% (13% at CER). Q4 2018 sales of $1,766m represented an increase of 8% (16% at CER) and continued the strong double-digit growth seen in prior periods. The new medicines represented 15% of Emerging Market's sales in the year, up from 10% in FY 2017.

	FY 2018				Q4 2018			
	$m	% of total	% change Actual	% change CER	$m	% of total	% change Actual	% change CER
Oncology	1,528	22	36	37	355	20	19	30
CVRM	2,695	39	14	15	691	39	12	21
Respiratory	1,644	24	18	18	497	28	17	25
Other	1,024	15	(19)	(19)	223	13	(23)	(21)
Total	**6,891**	**100**	**12**	**13**	**1,766**	**100**	**8**	**16**

China sales, comprising 55% of total Emerging Markets sales, increased by 28% in the year (25% at CER) to $3,795m and by 17% (22% at CER) in the quarter to $948m. New medicines delivered particularly encouraging sales growth, supported by strong performances from *Pulmicort*, *Seloken*, *Crestor*, *Nexium* and *Symbicort*. New medicines represented 11% of China sales in the year, up from 7% in 2017.

[20] Emerging Markets comprises all remaining Rest of World markets, including Brazil, China, India, Mexico, Russia and Turkey.

Table 12: Regional Product Sales, US

Product Sales of $6,876m; an increase of 11%. Q4 2018 sales increased by 15% to $2,037m. New medicines represented 48% of US Product Sales in the year, up from 26% in FY 2017. The performance during the period reflected, in particular, the success of the new Oncology medicines, including *Tagrisso*, *Imfinzi* and *Lynparza*, plus the strong performance of *Fasenra* in Respiratory.

	FY 2018			Q4 2018		
	$m	% of total	% change	$m	% of total	% change
Oncology	2,412	35	n/m	792	39	134
CVRM	2,206	32	(7)	604	30	(14)
Respiratory	1,416	21	(6)	386	19	(6)
Other	842	12	(28)	255	12	(20)
Total	**6,876**	**100**	**11**	**2,037**	**100**	**15**

Table 13: Regional Product Sales, Europe

Product Sales of $4,459m in the year; a decline of 6% (10% at CER), reflecting the impact of the entry of generic *Crestor* medicines in various European markets in 2017 and continued competitive and price pressures. Excluding sales of *Crestor*, Europe sales increased by 4% (stable at CER) to $4,256m. *Crestor* sales in Europe declined by 70% in the year (71% at CER) to $203m and represented 5% of Europe sales. New medicines delivered an encouraging performance in the year, representing 28% of Europe Product Sales, up from 18% in FY 2017.

	FY 2018				Q4 2018			
	$m	% of total	% change		$m	% of total	% change	
			Actual	CER			Actual	CER
Oncology	1,053	24	19	14	287	25	19	21
CVRM	1,230	27	(26)	(29)	295	25	(28)	(26)
Respiratory	1,229	28	1	(4)	307	26	(9)	(7)
Other	947	21	(5)	(8)	284	24	(6)	(3)
Total	**4,459**	**100**	**(6)**	**(10)**	**1,173**	**100**	**(9)**	**(7)**

Table 14: Regional Product Sales, Established ROW
Product Sales of $2,823m; a decline of 8% (9% at CER). New medicines represented 24% of Established ROW sales in the year, up from 13% in 2017. The performance during the period reflected, in particular, the success of *Tagrisso* and *Forxiga*.

	FY 2018				Q4 2018			
	$m	% of total	% change		$m	% of total	% change	
			Actual	CER			Actual	CER
Oncology	1,035	37	16	14	333	42	38	38
CVRM	579	21	(33)	(34)	157	20	(24)	(22)
Respiratory	622	22	5	4	172	22	6	8
Other	587	21	(19)	(20)	130	16	(29)	(27)
Total	**2,823**	**100**	**(8)**	**(9)**	**792**	**100**	**-**	**1**

Japan, comprising 71% of total Established ROW sales, declined by 9% (11% at CER) to $2,004m (Q4 2018 sales increased by 4% (5% at CER) to $588m). The impact of the entry of generic *Crestor* medicines was felt faster than expected; the biennial price reduction also adversely affected sales in the year. Excluding sales of *Crestor*, Japan sales increased by 7% (5% at CER) to $1,838m. *Crestor* sales in Japan declined by 66% (67% at CER) to $166m and represented 8% of Japan sales in the year. Sales of *Tagrisso* in Japan increased by 45% in the year (43% at CER) to $317m, reflecting increasing use as a 1st-line treatment, following approval in this setting in the third quarter. Focused activities to maximise testing and utilisation rates in the 2nd-line indication also supported the growth in Product Sales.

Financial performance

Table 15: FY 2018 Reported Profit and Loss

	Reported			
	FY 2018 $m	FY 2017 $m	% change Actual	% change CER
Product Sales	21,049	20,152	4	4
Externalisation Revenue	1,041	2,313	(55)	(55)
Total Revenue	22,090	22,465	(2)	(2)
Cost of Sales	(4,936)	(4,318)	14	13
Gross Profit	17,154	18,147	(5)	(6)
Gross Margin[21]	*76.6%*	*79.6%*	*-3*	*-3*
Distribution Expense	(331)	(310)	7	6
% Total Revenue	*1.5%*	*1.4%*	-	-
R&D Expense	(5,932)	(5,757)	3	3
% Total Revenue	*26.9%*	*25.6%*	*-1*	*-1*
SG&A Expense	(10,031)	(10,233)	(2)	(3)
% Total Revenue	*45.4%*	*45.5%*	-	-
Other Operating Income and Expense	2,527	1,830	38	38
% Total Revenue	*11.4%*	*8.1%*	*+3*	*+3*
Operating Profit	3,387	3,677	(8)	(7)
% Total Revenue	*15.3%*	*16.4%*	*-1*	*-1*
Net Finance Expense	(1,281)	(1,395)	(8)	2
Joint Ventures and Associates	(113)	(55)	n/m	n/m
Profit Before Tax	1,993	2,227	(10)	(14)
Taxation	57	641		
Tax Rate	(3)%	(29)%		
Profit After Tax	2,050	2,868	(29)	(30)
Earnings Per Share	$1.70	$2.37	(28)	(29)

[21] Gross Margin, as a percentage of Product Sales, reflects Gross Profit derived from Product Sales, divided by Product Sales. FY 2018 Cost of Sales included $nil of costs relating to externalisation activities (FY 2017: $198m), which are excluded from the calculation of Gross Margin. Movements in Gross Margin are expressed in percentage points.

Table 16: Q4 2018 Reported Profit and Loss

	Reported			
	Q4 2018 $m	Q4 2017 $m	% change Actual	% change CER
Product Sales	5,768	5,487	5	8
Externalisation Revenue	649	290	n/m	n/m
Total Revenue	6,417	5,777	11	14
Cost of Sales	(1,637)	(1,225)	34	37
Gross Profit	4,780	4,552	5	8
Gross Margin[22]	*71.6%*	*77.6%*	*-6*	*-6*
Distribution Expense	(93)	(85)	10	16
% Total Revenue	*1.5%*	*1.5%*	-	-
R&D Expense	(2,012)	(1,551)	30	33
% Total Revenue	*31.4%*	*26.8%*	*-4*	*-4*
SG&A Expense	(2,600)	(3,078)	(16)	(12)
% Total Revenue	*40.5%*	*53.3%*	*+13*	*+12*
Other Operating Income & Expense	1,002	848	18	19
% Total Revenue	*15.6%*	*14.7%*	*+1*	*+1*
Operating Profit	1,077	686	57	54
% Total Revenue	*16.8%*	*11.9%*	*+5*	*+4*
Net Finance Expense	(311)	(267)	17	24
Joint Ventures and Associates	(36)	(12)	n/m	n/m
Profit Before Tax	730	407	79	69
Taxation	279	854		
Tax Rate	(38)%	(210)%		
Profit After Tax	1,009	1,261	(20)	(22)
Earnings Per Share	$0.82	$1.03	(21)	(22)

[22] Gross Margin, as a percentage of Product Sales, reflects Gross Profit derived from Product Sales, divided by Product Sales. Q4 2018 Cost of Sales included $nil of costs relating to externalisation activities (Q4 2017: $2m income), which are excluded from the calculation of Gross Margin. Movements in Gross Margin are expressed in percentage points.

Table 17: Reconciliation of Reported Profit Before Tax to EBITDA[23]

	FY 2018 $m	FY 2017 $m	% change	
			Actual	CER
Reported Profit Before Tax	1,993	2,227	(10)	(14)
Net Finance Expense	1,281	1,395	(8)	2
Joint Ventures and Associates	113	55	n/m	n/m
Depreciation, Amortisation and Impairment	3,753	3,036	24	24
EBITDA	7,140	6,713	6	7

Table 18: FY 2018 Reconciliation of Reported to Core financial measures

	Reported $m	Restructuring $m	Intangible Asset Amortisation & Impairments $m	Diabetes Alliance $m	Other[24] $m	Core[25] $m	Core % change	
							Actual	CER
Gross Profit	17,154	432	187	-	-	17,773	(4)	(4)
Gross Margin[26]	*76.6%*	-	-	-	-	*79.5%*	*-2*	*-2*
Distribution Expense	(331)	-	-	-	-	(331)	7	6
R&D Expense	(5,932)	94	572	-	-	(5,266)	(3)	(3)
SG&A Expense	(10,031)	181	1,582	(60)	(323)	(8,651)	10	9
Other Operating Income & Expense	2,527	(10)	4	-	(374)	2,147	10	10
Operating Profit	3,387	697	2,345	(60)	(697)	5,672	(17)	(17)
% Total Revenue	*15.3%*	-	-	-	-	*25.7%*	*-5*	*-5*
Net Finance Expense	(1,281)	-	-	337	208	(736)	13	11
Taxation	57	(146)	(487)	(73)	109	(540)	(37)	(36)
Earnings Per Share	$1.70	$0.43	$1.47	$0.16	$(0.30)	$3.46	(19)	(19)

[23] EBITDA is a non-GAAP financial measure. See above for the definition of EBITDA.
[24] Other adjustments include fair-value adjustments relating to contingent consideration on business combinations (see Note 4), discount unwind on acquisition-related liabilities (see Note 4) and provision movements related to certain legal matters (see Note 5).
[25] Each of the measures in the Core column in the above table are non-GAAP financial measures. See the Operating and Financial Review for related definitions.
[26] Gross Margin, as a percentage of Product Sales, reflects Gross Profit derived from Product Sales, divided by Product Sales. FY 2018 Cost of Sales included $nil of costs relating to externalisation activities (FY 2017: $198m), which are excluded from the calculation of Gross Margin. Movements in Gross Margin are expressed in percentage points.

Table 19: Q4 2018 Reconciliation of Reported to Core financial measures

	Reported	Restructuring	Intangible Asset Amortisation & Impairments	Diabetes Alliance	Other[27]	Core[28]	Core % change	
	$m	$m	$m	$m	$m	$m	Actual	CER
Gross Profit	4,780	355	48	-	-	5,183	11	14
Gross Margin[29]	*71.6%*	-	-	-	-	*78.6%*	*(1)*	*(1)*
Distribution Expense	(93)	-	-	-	-	(93)	10	16
R&D Expense	(2,012)	(1)	547	-	-	(1,466)	1	3
SG&A Expense	(2,600)	71	515	(380)	(42)	(2,436)	12	15
Other Operating Income & Expense	1,002	1	1	-	-	1,004	18	18
Operating Profit	1,077	426	1,111	(380)	(42)	2,192	23	23
% Total Revenue	*16.8%*	-	-	-	-	*34.2%*	*3*	*3*
Net Finance Expense	(311)	-	-	84	52	(175)	43	41
Taxation	279	(89)	(238)	47	5	4	n/m	n/m
Earnings Per Share	$0.82	$0.26	$0.69	$(0.20)	$0.01	$1.58	22	22

Profit and Loss Commentary

Gross Profit

Reported Gross Profit declined by 5% in the year (6% at CER) to $17,154m; Core Gross Profit declined by 4% to $17,773m. The declines primarily reflected the lower level of Externalisation Revenue; there was also an adverse impact from an increase in the Cost of Sales.

The calculation of Reported and Core Gross Margin excludes the impact of Externalisation Revenue, thereby reflecting the underlying performance of Product Sales. The Reported Gross Margin declined by three percentage points in the year to 76.6%; the Core Gross Margin declined by two percentage points to 79.5%. The movements were a result of the favourable impact of manufacturing variances realised in 2017, the inclusion of the profit share on the collaboration with MSD, as well as the effect of losses of exclusivity on *Crestor* sales in Europe and Japan, partly offset by the growing favourable impact of Oncology sales.

Designed to drive further efficiencies in the operations network, the Company recently decided to close two biologic-medicine manufacturing sites in Colorado, US. Associated with the closures, the Company expects to incur $0.4bn of one-time restructuring charges, the majority of which would be non-cash expenses; $0.3bn of

[27] Other adjustments include fair-value adjustments relating to contingent consideration on business combinations (see Note 4), discount unwind on acquisition-related liabilities (see Note 4) and provision movements related to certain legal matters (see Note 5).
[28] Each of the measures in the Core column in the above table are non-GAAP financial measures. See the Operating and Financial Review for related definitions.
[29] Gross Margin, as a percentage of Product Sales, reflects Gross Profit derived from Product Sales, divided by Product Sales. Q4 2018 Cost of Sales included $nil of costs relating to externalisation activities (Q4 2017: $2m income), which are excluded from the calculation of Gross Margin. Movements in Gross Margin are expressed in percentage points.

these charges were recognised in FY 2018 as a result of impairments of site-related assets and inventory, impacting the Reported Gross Margin.

Operating Expenses: R&D

Reported R&D Expenses increased by 3% in the year to $5,932m. Targeted investment in the Company's pipeline of medicines is a consistent priority; AstraZeneca, however, is continuing to focus on resource prioritisation, productivity improvements across every therapy area, simplification and improved development processes, all helping to deliver cost reductions. Importantly, high levels of activity remained unchanged in the year.

Highlights of the progress made include:

- Moving late-stage-execution roles to lower-cost locations
- Reducing supply waste
- Optimising protocols, including a review of the number of procedures, countries involved and in-sourcing a larger proportion of clinical trials

Reported R&D Expenses contained Intangible Asset Impairment charges of $532m (FY 2017: $101m), including a $470m charge in respect of MEDI0680, a programmed cell death-1 protein monoclonal antibody, or anti PD-1; the charge reflected the assessed future potential of the antibody.

Core R&D Expenses declined by 3% in the year to $5,266m, reflecting the aforementioned productivity improvements. Core R&D Expenses represented 24% of Total Revenue.

Operating Expenses: SG&A

Reported SG&A Expenses declined by 2% in the year (3% at CER) to $10,031m, primarily due to the movement in the valuation of contingent-consideration liabilities arising on business combinations. Investment focused on commercial and medical-affairs support for launches and extensions of the new medicines. These included *Lynparza*, *Tagrisso*, *Imfinzi*, *Calquence* and *Fasenra*; additional investment was also added to support sales growth in China. Intangible Asset Amortisation and Impairment charges of $1,582m (FY 2017: $1,469m), recorded within Reported SG&A Expenses, partly reflected the impact of recent regulatory approvals granted for acquired medicines.

Core SG&A Expenses increased by 10% in the year (9% at CER) to $8,651m, reflecting the aforementioned investments. Core SG&A Expenses represented 39% of Total Revenue.

Other Operating Income and Expense

Where AstraZeneca does not retain a significant ongoing interest in medicines or potential new medicines, income from divestments is reported within Other Operating Income and Expense in the Company's financial statements. Reported Other Operating Income and Expense increased by 38% in the year to $2,527m and included:

- $695m, reflecting an agreement with Grünenthal for the prescription medicine rights to *Nexium* in Europe. Within the same agreement, an additional $33m reflected the sale of the global rights (excluding the US and Japan) to *Vimovo*. The agreement completed in Q4 2018

- $527m, reflecting an agreement with Luye Pharma for the rights to *Seroquel XR* and *Seroquel* IR in the UK, China and other international markets

- $346m, resulting from a legal settlement

- $210m, reflecting an agreement with Cheplapharm Arzneimittel GmbH for the commercial rights to *Atacand* and *Atacand Plus* in Europe

- $172m, reflecting a milestone payment under an agreement with Aspen Global Incorporated, part of the Aspen Group, for the commercialisation rights to anaesthetic medicines in markets outside the US

- $139m, reflecting an agreement with Covis Pharma B.V. (Covis Pharma) for the rights to *Alvesco*, *Omnaris* and *Zetonna*. The agreement completed in Q4 2018

- $63m, representing a gain on the spin-out of six potential new medicines from the Company's early-stage inflammation and autoimmunity programme into an independent biotech company, as announced in February 2018

Core Other Operating Income and Expense increased by 10% in the year to $2,147m, with the difference to Reported Other Operating Income and Expense reflecting the aforementioned legal settlement.

Operating Profit
Reported Operating Profit declined by 8% in the year (7% at CER) to $3,387m, partly driven by the declines in Total Revenue and the Reported Gross Margin. Restructuring costs declined to $697m in the year (FY 2017: $807m). The Reported Operating Profit margin declined by one percentage point in the year to 15% of Total Revenue. Core Operating Profit declined by 17% in the year to $5,672m; the Core Operating Profit margin declined by five percentage points to 26% of Total Revenue.

Net Finance Expense
Reported Net Finance Expense declined by 8% in the year (an increase of 2% at CER) to $1,281m. The effect of higher Net Debt and an adverse movement in the fair value of bonds and derivative instruments was offset by lower levels of discount unwind on Acerta Pharma B.V. (Acerta Pharma) liabilities and an adverse foreign-exchange impact in the comparative period. Excluding the discount-unwind on acquisition-related liabilities and the adverse foreign exchange impact in the comparative period, Core Net Finance Expense increased by 13% in the year (11% at CER) to $736m.

Profit Before Tax
Reported Profit Before Tax declined by 10% in the year (14% at CER) to $1,993m, reflecting the lower level of Externalisation Revenue, the lower Reported Gross Margin and the increase in Reported R&D Expenses.

Taxation
The Reported Tax Rate of (3)% and the Core Tax Rate in the year of 11% was impacted by a favourable adjustment of $245m to deferred taxes, reflecting the recently-announced reduction in the Dutch corporate income-tax rate, without which the Core Tax Rate would have been 16%. There was also a reduction of $188m in tax provisions and a $52m deferred tax benefit from the Swedish corporate income-tax rate reduction. Excluding these impacts, both the Reported and Core Tax Rates would have been 21%. The net cash tax paid for the year was $537m, representing 27% of Reported Profit Before Tax.

The Reported and Core Tax Rates for the comparative period were (29)% and 4% respectively. The Reported Tax Rate included $617m of adjustments to deferred taxes, in line with the reduced US federal income-tax rate from 35% to 21%. This was excluded from the Core Tax Rate. The Reported and Core Tax Rates reflected a $321m benefit driven by reductions in tax provisions, return to provision adjustments, recognition of previously-unrecognised tax losses and UK Patent-Box profits. The Reported Tax Rate also included a benefit from non-taxable remeasurements of acquisition-related liabilities. Excluding these benefits, the Reported and Core Tax Rates for the comparative period would have been 22%. The cash tax paid for the comparative period was $454m, which was 20% of Reported Profit Before Tax.

Earnings Per Share (EPS)
Reported EPS of $1.70 in the year represented a decline of 28% (29% at CER). The performance reflected a decline in Total Revenue and the Reported Gross Margin. Core EPS declined by 19% to $3.46, reflecting declines in Total Revenue and the Core Gross Margin, as well as an increase in Core SG&A Expenses.

Dividend Per Share
The Board reaffirms its commitment to the progressive dividend policy; a second interim dividend of $1.90 per share (146.8 pence, 17.46 SEK) has been declared, taking the unchanged full-year dividend per share to $2.80 (215.2 pence, 25.38 SEK). Dividend payments are normally paid as follows:

- First interim dividend - announced with half-year and second-quarter results and paid in September
- Second interim dividend - announced with full-year and fourth-quarter results and paid in March

The record date for the second interim dividend for 2018, payable on 27 March 2019, will be 1 March 2019. The ex-dividend date will be 28 February 2019. The record date for the first interim dividend for 2019, payable on 9 September 2019, will be 9 August 2019. The ex-dividend date will be 8 August 2019.

Table 20: Cash Flow

	FY 2018 $m	FY 2017 $m	Change $m
Reported Operating Profit	3,387	3,677	(290)
Depreciation, Amortisation and Impairment	3,753	3,036	717
Increase in Working Capital and Short-Term Provisions	(639)	(50)	(589)
Gains on Disposal of Intangible Assets	(1,885)	(1,518)	(367)
Non-Cash and Other Movements	(785)	(415)	(370)
Interest Paid	(676)	(698)	22
Tax Paid	(537)	(454)	(83)
Net Cash Inflow from Operating Activities	**2,618**	**3,578**	**(960)**
Net Cash Inflow/(Outflow) from Investing Activities	**963**	**(2,328)**	**3,291**
Net Cash Outflows from Financing Activities	**(2,044)**	**(2,936)**	**892**

The Company delivered a net cash inflow from operating activities of $2,618m in the year, compared with an inflow of $3,578m in FY 2017, partly reflecting the increase in the movement of working-capital and short-term provisions impacted by the reduction of provisions related to legal settlements, as well as launch support for new medicines.

Net cash inflows from investing activities were $963m, compared with outflows of $2,328m in FY 2017. The difference partly reflected the payment of deferred consideration in relation to Acerta Pharma in FY 2017 of $1,450m, as well as the movement in short-term investments and fixed deposits. Disposals of intangible assets amounted to $2,338m in the year vs. $1,376m in FY 2017. The cash payment of contingent consideration, in respect of the Bristol-Myers Squibb share of the global Diabetes alliance, amounted to $349m in the year.

Net cash outflows from financing activities were $2,044m in the year, compared to outflows of $2,936m vs. FY 2017; the difference reflected new long-term loans and the repayment of loans in the earlier period.

Capital Expenditure

Capital expenditure amounted to $1,043m in the year, compared to $1,326m in FY 2017. This included the investment in the new global headquarters in Cambridge, UK, as well as strategic biotech manufacturing capacity in Sweden.

Table 21: Debt and capital structure

	At 31 Dec 2018 $m	At 31 Dec 2017 $m
Cash and Cash Equivalents	4,831	3,324
Other Investments	895	1,300
Cash and Investments	**5,726**	**4,624**
Overdrafts and Short-Term Borrowings	(755)	(845)
Finance Leases	-	(5)
Current Instalments of Loans	(999)	(1,397)
Loans Due After One Year	(17,359)	(15,560)
Interest-Bearing Loans and Borrowings (Gross Debt)	**(19,113)**	**(17,807)**
Net Derivatives	384	504
Net Debt	**(13,003)**	**(12,679)**

Capital allocation
The Board's aim is to continue to strike a balance between the interests of the business, financial creditors and the Company's shareholders. After providing for investment in the business, supporting the progressive dividend policy and maintaining a strong, investment-grade credit rating, the Board will keep under review potential investment in immediately earnings-accretive, value-enhancing opportunities.

Foreign exchange

The Group's transactional currency exposures on working-capital balances, which typically extend for up to three months, are hedged where practicable using forward foreign-exchange contracts against the individual Group Companies' reporting currency. In addition, the Group's external dividend payments, paid principally in pounds sterling and Swedish krona, are fully hedged from announcement to payment date. Foreign-exchange gains and losses on forward contracts for transactional hedging are taken to profit.

Table 22: Currency sensitivities

The Company provides the following currency-sensitivity information:

		Average Exchange Rates vs. USD			Annual Impact Of 5% Strengthening in Exchange Rate vs. USD ($m)[30]	
Currency	**Primary Relevance**	**FY 2018[31]**	**YTD 2019[32]**	**% change**	**Product Sales**	**Core Operating Profit**
CNY	Product Sales	6.62	6.80	-3	+221	+126
EUR	Product Sales	0.85	0.88	-3	+145	+66
JPY	Product Sales	110.45	108.87	+1	+114	+74
Other[33]					+216	+105
GBP	Operating Expenses	0.75	0.78	-4	+26	-72
SEK	Operating Expenses	8.69	8.98	-3	+4	-73

[30] Based on best prevailing assumptions around currency profiles.
[31] Based on average daily spot rates between 1 January and 31 December 2018.
[32] Based on average daily spot rates between 1 January and 31 January 2019.
[33] Other currencies include AUD, BRL, CAD, KRW and RUB.

Corporate and business development

a) *Nexium* divestment in the EU and *Vimovo* divestment in ex.US/Japan markets

In November 2018, AstraZeneca completed an agreement to divest the prescription medicine rights to *Nexium* in Europe, as well as the global rights (excluding the US and Japan) to *Vimovo,* to Grünenthal. Under the terms of the agreement, AstraZeneca received payments of $700m for *Nexium* and $115m for *Vimovo*. The upfront payments, net of an appropriate derecognition of an intangible asset related to *Vimovo*, were reported within Other Operating Income and Expense in the Company's financial statements in Q4 2018 as $728m.

AstraZeneca will continue to commercialise *Nexium* in all markets outside Europe, where the Company retains the rights. The transaction did not include the transfer of any AstraZeneca employees or facilities. AstraZeneca did not retain any ownership rights to *Vimovo* globally.

b) Divestment of global rights to *Alvesco, Omnaris* and *Zetonna*

In December 2018, AstraZeneca completed an agreement with Covis Pharma to sell its rights to the medicines *Alvesco*, used for the treatment of persistent asthma, and *Omnaris* and *Zetonna*, used for the treatment of nasal symptoms associated with rhinitis. The rights covered markets outside the US and the US royalties for the medicines. The transaction did not include the transfer of any AstraZeneca employees or facilities.

Under the terms of the agreement, AstraZeneca received a payment of $350m from Covis Pharma. As AstraZeneca will not maintain a significant ongoing interest in the medicines, the upfront payment, net of an appropriate derecognition of an intangible asset, was reported as Other Operating Income and Expense in the Company's financial statements in Q4 2018 as $139m.

c) *Synagis* divestment in the US

In November 2018, AstraZeneca agreed to sell US rights to *Synagis*, used for the prevention of serious lower respiratory tract infection caused by respiratory syncytial virus, to Sobi, which will commercialise *Synagis* in the US; around 130 AstraZeneca employees transferred to Sobi as part of the transaction.

Sobi will also have the right to participate in AstraZeneca's share of US profits and losses related to potential new medicine MEDI8897, intended to treat patients with lower respiratory tract infection. The Company will continue to develop MEDI8897 in collaboration with Sanofi Pasteur, the vaccines division of Sanofi S.A.

Upon completion of the agreement in January 2019, AstraZeneca received upfront consideration including cash of $966m and ordinary shares of Sobi with an initial fair market value of c.$600m. This equated to an ownership interest of 8%, based on the relevant Sobi share price. AstraZeneca has undertaken not to sell the shares received as consideration for a period of 12 months following the closing date of the transaction.

AstraZeneca will also receive up to $470m in sales-related payments for *Synagis*, a $175m milestone following the submission of the Biologics License Application (BLA) for MEDI8897; potential net payments of approximately $110m on achievement of other MEDI8897 profit and development-related milestones; and a total of $60m in non-contingent payments for MEDI8897 during 2019-2021. Under the agreement, Sobi will have the right to participate in payments that may be received by AstraZeneca from the US profits or losses for MEDI8897.

d) AstraZeneca strengthened Oncology development and commercialisation collaboration with Innate Pharma

In October 2018, the Company announced a new multi-term agreement with Innate Pharma, building on an existing collaboration. The extension enriched AstraZeneca's immuno-oncology (IO) portfolio with pre-clinical and clinical potential new medicines. AstraZeneca obtained full oncology rights to the first-in-class humanised anti-NKG2A antibody, monalizumab. AstraZeneca also gained option rights to IPH5201, an antibody targeting CD39, as well as four preclinical molecules from Innate Pharma's pipeline. Innate Pharma licenced the US and EU commercial rights to recently US FDA-approved *Lumoxiti* for hairy cell leukaemia; *Lumoxiti* was launched in the US in Q4 2018.

AstraZeneca recorded $50m upfront for *Lumoxiti* in Q4 2018 and derecognised the related intangible asset, resulting in net income of $6m that was recorded as Other Operating Income and Expense. The Company anticipates receipt of up to $25m for future commercial and regulatory milestones, in consideration for its intellectual property and clinical and manufacturing development of the medicine. AstraZeneca will pay Innate Pharma $100m in the first quarter of 2019 for the expansion of the monalizumab collaboration, reflected by a recognition of an intangible asset in Q4 2018. Further, AstraZeneca paid Innate Pharma $50m upfront for the

development collaboration and option for further co-development and co-commercialisation of IPH5201, with recognition of a related intangible asset in Q4 2018.

AstraZeneca also paid Innate Pharma $20m upfront for an exclusive licence to option the aforementioned four molecules, treated as prepaid R&D Expenses. These options can be exercised before the molecules reach clinical development, triggering an option exercise fee in addition to milestones and royalties. Innate Pharma will have the potential for co-promotion and profit sharing in the EU, dependent on future progress. AstraZeneca also acquired a 9.8% equity stake in Innate Pharma, in line with the agreement, through the issuance of 6,260,500 new shares to AstraZeneca at €10/share (€62.6m). A non-current asset investment was recognised in relation to Innate Pharma in Q4 2018, reflecting the transaction. The premium paid on purchase of the shares over the quoted price was capitalised in Q4 2018 as part of the cost of the acquisition of IPH5201.

e) Organisational changes

As AstraZeneca recently entered a new phase in its strategic development, the Company announced in January 2019 organisational changes to enhance scientific innovation and commercial success.

The new structure takes R&D functions from discovery to late-stage development down to two, Oncology and BioPharma. The new Oncology R&D function will be led by a world-renowned expert in the field, José Baselga and the BioPharma R&D function will be led by Mene Pangalos, who was previously responsible for the Company's Innovative Medicines and Early Development Biotech Unit.

The same approach has been applied to the majority of the Company's commercial operations. The commercial unit for Oncology will continue to be led by Dave Fredrickson and the commercial unit for BioPharma will be led by Ruud Dobber, most recently responsible for the Company's commercial operations in North America. The Emerging Markets commercial unit remains under the leadership of Leon Wang.

The goals of the reorganisation are to:

- Further increase focus on the Company's main therapy areas
- Integrate R&D functions for agile decision making and more flexible resource allocation
- Increase collaboration between the R&D and commercial functions

The R&D and commercial functions will each be represented on the Senior Executive Team of AstraZeneca and report to Chief Executive Officer (CEO), Pascal Soriot. The functions will also share common basic biology and science platforms as well as medicine supply, manufacturing and IT infrastructure to improve efficiency. These resources will continue to be allocated on a Company-wide basis, according to the overall therapy-area considerations and strategy.

Prior to the changes, Bahija Jallal, Executive Vice President, MedImmune and Mark Mallon, Executive Vice President, Global Products and Portfolio Strategy, Global Medical Affairs & Corporate Affairs left AstraZeneca in January 2019. Sean Bohen, Executive Vice President, Global Medicines Development & Chief Medical Officer will provide interim leadership for Global Medicines Development and remain at AstraZeneca as Chief Medical Officer during the transitional period to support implementation of the new structure. A new Chief Medical Officer is expected to be appointed in due course.

Sustainability

AstraZeneca's sustainability ambition has three priority areas[34], aligned with the Company's purpose and business strategy:

- Access to healthcare
- Environmental protection
- Ethics and transparency

Recent developments and progress against the priorities are reported below:

a) Access to Healthcare

The Company was recognised in the 2018 *Access to Medicine Index*, which analysed 20 of the world's largest research-based pharmaceutical companies as to how they make medicines, vaccines and diagnostics more accessible in low and middle-income countries. It described AstraZeneca as maintaining a strong performance in the year. Retaining a top-10 position, the report praised the Company's innovation and the progress made against pricing commitments since the 2016 report. In particular, it noted the positive application of advanced methods for determining prices for different population subsets. It also highlighted the innovative practices used in the Dunga Beach pilot project in Kenya, that aims to reduce air pollution and improve respiratory health.

During the quarter, the Company saw two key areas of progress in its focus on supporting access to healthcare in Africa. Firstly, the pilot Dunga Beach programme, launched in partnership with the Cambridge Institute for Sustainability Leadership, became fully operational in the Dunga Beach region of Kisumu county in Kenya, supporting efforts to improve respiratory health by enabling the local community to process waste into clean energy. Secondly, the Company launched a new voluntary employee-giving initiative, AZHealthConnect, which enables an initial employee population of AstraZeneca's three strategic science centres - Cambridge, UK Gaithersburg, US and Gothenburg, Sweden - to support families in Kenya with health insurance. Contributions by employees are matched by AstraZeneca and are transferred anonymously to a mobile health wallet to cover annual health insurance for an African family. Developed in response to employee crowd-sourcing, the initiative aims to engage further AstraZeneca employees around the access to healthcare priority of the sustainability strategy, while empowering Africa's poorest people to take good care of their health and build a decent future for themselves and their families. The Company aims to expand the programme to more locations during 2019.

At the close of Q3 2018, AstraZeneca had reached more than 10 million people through its portfolio of Access to Healthcare programmes (Healthy Heart Africa, Phakamisa and Healthy Lung). The Company also expanded the Healthy Lung programme to the United Arab Emirates, Saudi Arabia, Oman and Mexico.

b) Environmental protection

During the period, AstraZeneca was highlighted as a global leader in sustainable water management and for its actions and strategies to manage carbon and climate change across its supply chain by environmental impact not-for-profit organisation CDP. The Company achieved a place on the CDP Water Security A List and was ranked within the top 3% on the supplier engagement leader board. The Company was also recognised for its operational action on climate. Currently awarded a B-listing, AstraZeneca is under re-evaluation upon further review from CDP for a potential upgrade to A- for climate. CDP independently assesses companies against its scoring methodology based on data disclosed about their environmental impacts, risks and opportunities. CDP publishes A-D scores across climate, water and forests for over 3,000 major companies, with the leaders celebrated on the A List.

[34] These priorities were determined, along with a set of nine foundational areas, through a materiality assessment with external and internal stakeholders, respectively. Combined, they ensure the maximum possible benefit to patients, the Company, broader society and the planet. AstraZeneca's sustainability priorities, foundations and commitments align with the United Nations Sustainable Development Goals (SDG), and, in particular, SDG three for 'Good Health'.

As part of the Company's commitment to addressing anti-microbial resistance, a paper authored by AstraZeneca with *le Page et al* was cited by the European Federation of Pharmaceutical Industries and Associations and was included in AstraZeneca's response to the EMA environmental-risk assessment concept paper to remove fish and invertebrate testing for antibiotics. The EMA released a revised guideline taking this research into account, determining that fish trials are no longer required for the development of antibiotics.

Table 23: Environmental protection targets[35]

Target	Plan year	Performance in the period
Reach 25m patients through AstraZeneca's portfolio of access programmes	2025	**On plan:** AstraZeneca has reached more than 10 million patients through its portfolio of Access to Healthcare programmes (hHF, Phakamisa and Healthy Lung Asia). The Company recently expanded the Healthy Lung programme as mentioned above
Lead the industry to manage pharmaceuticals in the environment	2025	**On plan:** ecopharmacovigilance (EPV) spatial environmental risk-map updates have been commissioned and product-specific concentration (measured vs. predicted safe) distributions are being developed. These will form the basis for a first published EPV report AstraZeneca's Pharmaceuticals in the Environment statement was published during the period
Ensure 90% of active pharmaceutical ingredient syntheses meet resource-efficiency targets at launch	2025	**Lagging:** overall reduction in H1 2018, with a 2% decline across the Company's portfolio
Develop resource-efficiency targets for biological medicines	2025	**Lagging:** positive developments on benchmarking biologics process resource efficiency data through the American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable. Behind plan on development of target creation
Develop a medicine-sustainability index and pilot approach	2019	**On plan:** project launched to develop a medicine environmental-sustainability rating system, to be piloted internally prior to external publication in 2019
Achieve Science Based Targets for greenhouse gas emissions	2025	**On plan:** AstraZeneca's Operational Green House Gas footprint declined by 4% vs. year-to-date 2015 Scope 1 -6% Scope 2 -48% Scope 3 emissions +11%[36]
100% renewable-power consumption globally by 2025; interim ambition of 100% in the US and Europe by 2020	2025	**On plan:** 60% of sites already powered by renewable energy

[35] Data reported as of 30 September 2018.
[36] Scope 3 increase was a result primarily of growing pressurised metered device inhalation (pMDI) emissions in the Respiratory-medicines platform; also due to air travel, outweighing savings made in logistics.

Target	Plan year	Performance in the period
Reduce energy consumption by 10% against a 2015 baseline	2025	**On plan:** energy consumption increased by 2% compared with 2015
Expand the number of 'green-fleet' vehicles	2025	**On plan:** a number of European locations are implementing green-fleet vehicles through their 'Green Mobility' programmes. AstraZeneca US launched the 'GoGreen' initiative and it is expected that by 2022, the Companies entire US fleet will be made up of hybrid vehicles
Maintain water usage as the business grows against a 2015 baseline	2025	**Lagging:** water use declined by 5% vs. 2015. Water audits and energy efficiency projects have driven large reductions and cost savings. A warm summer for many of AstraZeneca's key sites, however, contributed to higher than expected usage during the period
Reduce waste 10% below the 2015 baseline	2025	**On plan:** waste generated: -3% vs. 2015 Hazardous waste: -3% Non-hazardous waste: -7% An increase in hazardous waste generation offset by reductions in non-hazardous volumes. Target currently on track despite quarterly fluctuations

c) Ethics and transparency

During the period, the Company was recognised in the 2019 *Bloomberg Gender-Equality Index*, which distinguished companies committed to transparency in gender reporting and advancing women's equality. As the only major pharmaceuticals company represented in the index, the Company achieved a number of top scores and best-in-class ratings across the index categories, including for Board and CEO representation, Pipeline from Workforce to Management, as well as Education Programmes. AstraZeneca employs c.64,000 people in more than 100 countries; in 2018, women made up half of the workforce, comprising 41% the Board and five out of 14 Senior Executive Team members.

During the period, Chairman Leif Johansson signed a pledge with the European Round Table of Industrialists (ERT) calling for action to deliver inclusion and diversity best practices and outcomes across 51 companies and numerous industries. The ERT is an organisation that advocates at both the national and European level to strengthen competitiveness across the EU.

Since committing to provide greater transparency around payments to healthcare professionals (HCPs) and healthcare organisations (HCOs) at the 2018 Annual General Meeting, the Company successfully expanded disclosure activities across an additional five countries by year-end. The Company currently discloses payments to HCPs, HCOs and patient groups across 43 countries, including in Europe, the US, Japan, Australia, the Middle East, Asia Pacific and Latin America with ongoing plans to expand its payment disclosure to a further six countries over the next two years. AstraZeneca's current disclosures comprised over 95% of all such disclosures possible worldwide in Q4 2018, an increase from 93% in Q3 2018.

The completion rate for the Code of Ethics awareness, an annual training module educating and empowering all employees to make good decisions in the long-term interest of the Company, reached the target of 100% of the workforce.

Other developments

During the period, AstraZeneca was recognised by Corporate Knights as one of the world's 100 most sustainable companies. The Company was ranked 50th overall and 5th highest-ranked pharmaceutical company. Inclusion in the Global 100 placed AstraZeneca in the top 1.3% companies in the world for sustainability performance. Although performance was consistent across the assessment, the strongest areas included top-quartile performance on board and executive-gender diversity and above-average percentage of medicines (20%), with equitable pricing strategies targeting priority countries.

During the period, the Company also conducted a sustainability materiality refresh with the aim of refining the sustainability priority areas and developing a future-ready strategy. AstraZeneca worked with an independent consultancy to examine significant trends and engage internal and external stakeholders to define the environmental, social and governance issues that matter most and where most impact can be gained. The materiality assessment identified 16 priority-material issues leading to a sharpened focus - narrowing the field of issues prioritised by c.50%. This has served as a framework for the Company to develop the sustainability strategy up to 2025 and future reporting for 2019 onwards will align to these new 16 material areas under the pillars of Access to Health, Environment and Ethics.

Research and development

A comprehensive data pack comprising AstraZeneca's pipeline of medicines in human trials can be found in the clinical-trials appendix, available on astrazeneca.com. Highlights of developments in the Company's late-stage pipeline since the prior results announcement are shown below:

Table 24: Update from the late-stage pipeline

Regulatory approvals	4	- *Lynparza* - ovarian cancer (1st line) (SOLO-1): regulatory approval (US) - roxadustat - anaemia in dialysis patients: regulatory approval (CN) - *Bevespi* - COPD: regulatory approval (EU) - *Linzess* (linaclotide) (IBS-C): regulatory approval (CN)
Regulatory submissions and/or acceptances	5	- *Imfinzi* - unresectable, Stage III NSCLC: regulatory submission (CN); acceptance (OS data) (US) - *Farxiga* - type-1 diabetes: regulatory submission acceptance (US) - *Fasenra* - severe, eosinophilic asthma; self-administration: submission - acceptance (US, EU)
Major Phase III data readouts or other major developments	11	- *Tagrisso* - EGFRm NSCLC (1st line): priority review (CN) - *Imfinzi* +/- treme - NSCLC (1st line) (MYSTIC): did not meet OS primary endpoints - *Imfinzi* +/- treme - head & neck cancer (2nd line): did not meet OS primary endpoints - *Lynparza* - ovarian cancer (1st line) (SOLO-1): priority review (CN) - *Lynparza* - ovarian cancer (3rd line+): met response rate primary endpoint - *Forxiga* - type-1 diabetes: CHMP positive opinion (EU) - roxadustat - anaemia of CKD: met primary efficacy endpoints - *Fasenra* - eosinophilic granulomatosis with polyangiitis: Orphan Drug Designation (US) - *Fasenra* - hypereosinophilic syndrome: Orphan Drug Designation (US) - PT010 - COPD: priority review (CN) - MEDI8897 - lower respiratory tract infection: Breakthrough Therapy Designation (US), PRIME designation (EU)
New molecular entities and major lifecycle medicines in Phase III trials or under regulatory review	11	**Oncology** - *Tagrisso* - NSCLC[37] - *Imfinzi* - multiple cancers[37] - *Lynparza* - multiple cancers[37] - *Calquence* - blood cancers[36] - tremelimumab - multiple cancers - selumetinib - NF1[38] - savolitinib - multiple cancers **CVRM** - roxadustat - anaemia[36] **Respiratory** - PT010 - COPD[36] - tezepelumab - severe asthma **Other** (outside main therapy areas) - anifrolumab - lupus
Total projects in clinical pipeline	131	

[37] Under regulatory review. The table shown above as at today.
[38] Phase II trial data, with potential for registration.

Oncology
AstraZeneca has a deep-rooted heritage in Oncology and offers a new generation of medicines that have the potential to transform patients' lives and the Company's future. At least six Oncology medicines are expected to be launched between 2014 and 2020, of which *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence* and *Lumoxiti* are already benefitting patients. An extensive pipeline of small-molecule and biologic medicines is in development and the Company is committed to advancing Oncology medicines, primarily focused on the treatment of patients with lung, ovarian, breast and blood cancers.

In December 2018, the Company presented further evidence of its progress at the 60th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego. At the meeting the Company presented new long-term follow-up results for *Calquence* in patients with relapsed or refractory MCL and updated results of an ongoing clinical trial, assessing *Calquence* monotherapy in treatment-naïve patients with CLL. Data from recently-approved *Lumoxiti* and early pipeline data, including the preclinical activity of the novel MCL1 inhibitor AZD5991, was also presented.

At the European Society for Medical Oncology Immuno-Oncology Congress in Geneva, the Company presented the Stage IV, 1st-line NSCLC Phase III MYSTIC trial results of *Imfinzi* or *Imfinzi* + tremelimumab or SoC chemotherapy.

Lung cancer
a) *Tagrisso*
Tagrisso 40mg and 80mg once-daily oral tablets have now received approval in more than 40 countries, including the US, Japan and in Europe, for the 1st-line treatment of patients with Stage IV EGFRm NSCLC. Multiple other reviews are underway, including in China, where a decision is now expected in H1 2019 based on a priority review granted in December 2018. Approvals have been achieved in more than 80 countries, including the US, Japan, China and in Europe, for the 2nd-line treatment of patients with EGFR T790M-mutated NSCLC. *Tagrisso* is also being developed in the adjuvant setting (ADAURA trial), in the locally-advanced, unresectable setting (LAURA trial) and in combination with other treatments, including the Company's MET-inhibitor, savolitinib. During the period, the ADAURA trial achieved its last patient commenced dosing (LPCD).

b) *Imfinzi*
During the period, the Company received an acceptance from the US FDA for a supplemental BLA (sBLA) based on PACIFIC OS trial data for *Imfinzi* as a treatment of patients with unresectable, Stage III NSCLC, reflected in a Prescription Drug User Fee Act (PDUFA) date anticipated to be in Q3 2019. The Company also submitted an application to the China NMPA for the initial indication of unresectable, Stage III NSCLC. PACIFIC was the first immunotherapy trial to demonstrate a significant OS benefit in unresectable, Stage III NSCLC, reducing the risk of death by 32% (hazard ratio (HR) 0.68, 99.73% confidence interval (CI) 0.47-0.997; p=0.0025).

The Phase III MYSTIC trial was a randomised, open-label, multi-centre, global trial of *Imfinzi* monotherapy and the combination of *Imfinzi* and tremelimumab, an anti-CTLA4 antibody, versus SoC platinum-based chemotherapy in previously-untreated patients with metastatic Stage IV NSCLC. In the primary-analysis population of patients, whose tumours expressed PD-L1 on 25% or more of their cancer cells as determined by the VENTANA PD-L1 (SP263) assay, *Imfinzi* monotherapy and the combination of *Imfinzi* plus tremelimumab did not meet the primary endpoints of improving OS, compared to SoC chemotherapy.

The full MYSTIC results showed that *Imfinzi* monotherapy did demonstrate clinical activity, with an OS HR of 0.76 (97.54% CI 0.564-1.019; nominal p=0.036) in the primary-analysis population of patients whose tumours expressed PD-L1 on 25% or more of their cancer cells, but this result did not meet statistical significance. After two years of follow-up, the OS rate for treatment with *Imfinzi* monotherapy was 38.3%, vs. 22.7% with SoC. This difference was observed despite a group of patients in the SoC arm (39.5%) receiving subsequent immunotherapy, following chemotherapy treatment. The combination of *Imfinzi* plus tremelimumab did not meet the progression-free survival (PFS) primary endpoint, as announced in July 2017, or the OS primary endpoint. A summary of these data is included below.

Table 25: Summary of MYSTIC trial results

	Imfinzi **(n=163)**	**Chemotherapy (n=162)**
OS (primary endpoint) in PD-L1 ≥25%[a]		
Number of deaths (%)	108 (66.3%)	128 (79.0%)
HR (97.54% CI)[b,c]	0.76 (0.564, 1.019)	
p-value[b,d]	0.036	
Median in months (95% CI)	16.3 (12.2, 20.8)	12.9 (10.5, 15.0)
24-month OS rate	38.3%	22.7%
	Imfinzi **+ tremelimumab (n=163)**	**Chemotherapy (n=162)**
OS (primary endpoint) in PD-L1 ≥25%[a]		
Number (%) of patients with event	113 (69.3%)	128 (79.0%)
HR (98.77% CI)[b,c]	0.85 (0.611, 1.173)	
p-value[b,d]	0.202	
Median in months (95% CI)	11.9 (9.0, 17.7)	12.9 (10.5, 15.0)
24-month OS rate	35.4%	22.7%
PFS (primary endpoint) in PD-L1 ≥25%[i]		
Number (%) of patients with event	118 (72.4%)	112 (69.1%)
HR (99.5% CI)[b,c]	1.05 (0.722, 1.534)	
p-value	0.705	
Median in months (95% CI)	3.9 (2.8, 5.0)	5.4 (4.6, 5.8)
12-month PFS rate	25.8%	14.3%

[a] The data cut-off date was 4 October 2018 (OS and safety) and 1 June 2017 (PFS).
[b] Stratified by histology.
[c] Confidence interval adjusted for interim analysis.
[d] Criteria for statistical significance at the final analysis of OS was a p-value ≤ 0.0246 for *Imfinzi* vs SoC and p-value ≤ 0.0123 for *Imfinzi* + tremelimumab vs. SoC (using Lan DeMets spending function approximating O'Brien-Fleming boundary).

A prespecified exploratory analysis of blood-tumour mutational burden (bTMB) showed that high bTMB, defined as ≥16 mutations per megabase, was associated with better OS rates in patients treated with *Imfinzi* monotherapy and the *Imfinzi*-plus-tremelimumab combination. In high-bTMB patients, combination therapy reduced the risk of death by 38%, compared to SoC (HR 0.62, CI 0.451-0.855) and the monotherapy arm had an OS HR of 0.80, compared to SoC (CI 0.588-1.077). These preliminary data included 809 samples, representing 72.4% of patients. The analysis used a plasma-based TMB score, generated from a minimally-invasive diagnostic test from Guardant Health that was recently granted Breakthrough Device Designation by

the US FDA for patients with NSCLC. Additional bTMB analyses will be presented at a forthcoming medical meeting.

Based on the results from the MYSTIC trial, the Company is assessing the need to refine ongoing trials of *Imfinzi* and tremelimumab in NSCLC, including the NEPTUNE and POSEIDON Phase III trials.

Table 26: Key *Imfinzi* trials in lung cancer

Name	Phase	Population	Design	Timelines	Status
AEGEAN	III	Neo-adjuvant (before surgery) NSCLC	SoC chemotherapy +/- *Imfinzi* followed by surgery followed by placebo or *Imfinzi*	FPCD[39] Q1 2019 First data anticipated 2020	Recruitment ongoing
ADJUVANT BR.31[40]	III	Stage Ib-IIIa NSCLC	placebo or *Imfinzi*	FPCD Q1 2015 First data anticipated 2020+	Recruitment ongoing
PACIFIC	III	Unresectable, Stage III NSCLC	concurrent CRT[41] followed by placebo or *Imfinzi*	FPCD Q2 2014 LPCD Q2 2016	PFS and OS primary endpoints both met
PACIFIC-2	III	Unresectable, Stage III NSCLC	concurrent CRT concurrent with placebo or *Imfinzi* followed by placebo or *Imfinzi*	FPCD Q2 2018 First data anticipated 2020+	Recruitment ongoing
PACIFIC-4	III	Unresectable, Stage I-II NSCLC	stereotactic body radiation therapy followed by placebo or *Imfinzi*	FPCD Q1 2019 First data anticipated 2020+	Recruitment initiating
PACIFIC-5	III	Unresectable, Stage III NSCLC (Asia predominant)	sequential or concurrent CRT followed by placebo or *Imfinzi*	FPCD Q1 2019 First data anticipated 2020+	Recruitment ongoing

[39] First patient commenced dosing.
[40] Conducted by the Canadian Cancer Trials Group.
[41] Chemotherapy and radiation therapy

Name	Phase	Population	Design	Timelines	Status
ADRIATIC	III	Limited-disease stage small cell lung cancer (SCLC)	concurrent CRT followed by placebo or *Imfinzi* or *Imfinzi* + treme	FPCD Q4 2018 First data anticipated 2020+	Recruitment ongoing
PEARL	III	Stage IV, 1st-line NSCLC (Asia)	SoC chemotherapy or *Imfinzi*	FPCD Q1 2017 First data anticipated 2020	Recruitment ongoing
MYSTIC	III	Stage IV, 1st-line NSCLC	SoC chemotherapy or *Imfinzi* or *Imfinzi* + treme	FPCD Q3 2015 LPCD Q3 2016	Recruitment completed PFS and OS primary endpoints not met
NEPTUNE	III	Stage IV, 1st-line NSCLC	SoC chemotherapy or *Imfinzi* + treme	FPCD Q4 2015 LPCD Q2 2017 First data anticipated H2 2019	Recruitment completed
POSEIDON	III	Stage IV, 1st-line NSCLC	SoC chemotherapy or SoC + *Imfinzi* or SoC + *Imfinzi* + treme	FPCD Q2 2017 LPCD Q3 2018 First data anticipated H2 2019	Recruitment completed
CASPIAN	III	Extensive-disease stage SCLC	SoC chemotherapy or SoC + *Imfinzi* or SoC + *Imfinzi* + treme	FPCD Q1 2017 LPCD Q2 2018 First data anticipated H2 2019	Recruitment completed

During the period, the Company withdrew the existing sBLA with the US FDA to update the dosing regimen for all indications of *Imfinzi* to a more convenient infusion schedule of 1,500mg, fixed-dose, once every four weeks or, for patients weighing less than 30kg, a 20mg/kg dose once every four weeks. This will allow the Company to evaluate and assess additional data from recently-concluded and currently-ongoing clinical trials of *Imfinzi*.

***Imfinzi* as a treatment in other tumour types**

The Company continues to advance multiple monotherapy trials of *Imfinzi* and combination trials of *Imfinzi* with tremelimumab and other potential new medicines in tumour types other than lung cancer.

Imfinzi is now approved for the 2nd-line treatment of patients with locally-advanced or metastatic urothelial carcinoma (bladder cancer) in the US, Canada, Brazil, Israel, India, Australia, Hong Kong and Singapore.

During the period, AstraZeneca announced OS topline results for the Phase III EAGLE trial. EAGLE was a randomised, open-label, multi-centre trial evaluating *Imfinzi* monotherapy or *Imfinzi* in combination with tremelimumab vs. SoC chemotherapy in patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) who experienced disease progression following platinum-based chemotherapy, regardless of their PD-L1 tumour status. *Imfinzi* monotherapy and the combination of *Imfinzi* plus tremelimumab did not meet the primary endpoints of improving OS, compared to SoC chemotherapy in these hard-to-treat patients. The safety and tolerability profiles for *Imfinzi* and the combination with tremelimumab were consistent with previous experience.

Table 27: Key *Imfinzi* trials in tumour types other than lung cancer

Name	Phase	Population	Design	Timelines	Status
Stage I, II & III (non-metastatic disease)					
POTOMAC	III	Non-muscle invasive bladder cancer	SoC BCG or SoC BCG[42] + *Imfinzi*	FPCD Q3 2018 First data anticipated 2020+	Recruitment ongoing
NIAGARA	III	Muscle-invasive bladder cancer	SoC chemotherapy or SoC + *Imfinzi*	FPCD Q1 2019 First data anticipated 2020+	Recruitment ongoing
EMERALD-1	III	Locoregional hepatocellular carcinoma (liver cancer)	transarterial chemoembolisation (TACE) followed by placebo or TACE + *Imfinzi* followed by *Imfinzi* + bevacizumab or TACE + *Imfinzi* followed by *Imfinzi*	FPCD Q1 2019 First data anticipated 2020+	Recruitment ongoing
Stage IV (metastatic disease)					
DANUBE	III	Stage IV, 1st-line cisplatin chemotherapy-eligible/ineligible bladder cancer	SoC chemotherapy or *Imfinzi* or *Imfinzi* + treme	FPCD Q4 2015 LPCD Q1 2017 First data anticipated H2 2019	Recruitment completed

[42] Bacillus Calmette-Guerin.

Name	Phase	Population	Design	Timelines	Status
NILE	III	Stage IV, 1st-line cisplatin chemotherapy-eligible bladder cancer	SoC chemotherapy or SoC + *Imfinzi* or SoC + *Imfinzi* + treme	FPCD Q3 2018 First data anticipated 2020+	Recruitment ongoing
KESTREL	III	Stage IV, 1st-line HNSCC	SoC or *Imfinzi* or *Imfinzi* + treme	FPCD Q4 2015 LPCD Q1 2017 First data anticipated H1 2019	Recruitment completed
EAGLE	III	Stage IV, 2nd-line HNSCC	SoC or *Imfinzi* or *Imfinzi* + treme	FPCD Q4 2015 LPCD Q3 2017	Recruitment completed OS primary endpoints not met
HIMALAYA	III	Stage IV, 1st-line unresectable hepatocellular carcinoma	sorafenib or *Imfinzi* or *Imfinzi* + treme	FPCD Q4 2017 First data anticipated 2020+	Recruitment ongoing

***Lynparza* (multiple cancers)**
In December 2018, AstraZeneca announced that the US FDA had approved *Lynparza* for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated (g*BRCA*m or s*BRCA*m) advanced epithelial ovarian, fallopian-tube or primary peritoneal cancer who are in complete or partial response to 1st-line platinum-based chemotherapy, as detected by a US FDA-approved companion-diagnostic test. This was the first regulatory approval for a PARP inhibitor in the 1st-line maintenance setting for *BRCA*m advanced ovarian cancer, based on the positive results from the pivotal Phase III SOLO-1 trial.

During the period, the Company announced positive overall response rate (ORR) results from the randomised, open-label, controlled, Phase III SOLO-3 trial of *Lynparza* tablets in 266 patients with relapsed ovarian cancer after two or more lines of treatment, in the non-maintenance setting vs. SoC chemotherapy. This was the first PARP-inhibitor trial to demonstrate superiority over chemotherapy in ovarian cancer. The trial was conducted as a post-approval commitment in agreement with the US FDA. This was the fourth Phase III trial to demonstrate a positive result for *Lynparza*. AstraZeneca and MSD now plan to discuss these results with the US FDA.

Table 28: Key *Lynparza* trials in combination

Name	Phase	Population	Design	Timelines	Status
PAOLA-1[43]	III	Stage IV, 1st-line ovarian cancer	bevacizumab maintenance or bevacizumab + *Lynparza* maintenance	FPCD Q2 2015 LPCD Q2 2018 First data anticipated H2 2019	Recruitment completed
DuO-O	III	Stage IV, 1st-line ovarian cancer	chemotherapy + bevacizumab or chemotherapy + bevacizumab + *Imfinzi* +/- *Lynparza* maintenance	FPCD Q1 2018 First data anticipated 2020+	Recruitment ongoing
GY005[44]	II/III	Platinum resistant/refractory ovarian cancer	SoC chemotherapy or cediranib or *Lynparza* + cediranib	FPCD Q2 2016 First data anticipated 2020+	Recruitment ongoing
MEDIOLA	I/II	Advanced, 2nd-line g*BRCA*m ovarian cancer Stage IV, 1st to 3rd-line g*BRCA*m, *HER2*-negative breast cancer Stage IV, 2nd-line SCLC Stage IV, 2nd-line gastric cancer	*Lynparza* + *Imfinzi*	FPCD Q2 2016	Recruitment ongoing Initial data from lung, breast, prostate and ovarian-cancer cohorts presented in 2017 and 2018

[43] Conducted by the ARCAGY/Groupe d'Investigateurs National des Etudes des Cancers Ovariens et du sein.
[44] Conducted by the National Cancer Institute (US).

VIOLETTE	II	Stage IV, advanced, triple-negative breast cancer: -HRRm[45] (*BRCA*) -HRRm (non-*BRCA*) -Non-HRRm	*Lynparza* *Lynparza* + ATR (AZD6738) *Lynparza* + WEE1 (AZD1775)	FPCD Q2 2018 First data anticipated 2020+	Recruitment ongoing
PROpel	III	Stage IV, advanced, castration-resistant prostate cancer	abiraterone or abiraterone + *Lynparza*	FPCD Q4 2018	Recruitment ongoing
BAYOU	II	Stage IV, 1st line cis-platinum chemotherapy-ineligible urothelial bladder cancer	*Imfinzi* or *Imfinzi* + *Lynparza*	FPCD Q1 2018 First data anticipated 2020	Recruitment ongoing
DuO-L ORION	II	Stage IV, 1st-line NSCLC	SoC chemotherapy + *Imfinzi* followed by *Imfinzi* or *Imfinzi* + *Lynparza* maintenance	FPCD Q4 2018 Data anticipated 2020+	Recruitment ongoing

[45] Homologous Recombination Repair mutated.

Haematology

Table 29: Key *Calquence* trials in CLL

Name	Phase	Population	Design	Timelines	Status
ACE-CL-007 ELEVATE-TN	III	Previously-untreated CLL	chlorambucil + obinutuzumab or obinutuzumab + *Calquence* or *Calquence*	FPCD Q2 2015 Data anticipated H2 2019	Recruitment completed
ACE CL-311	III	Previously-untreated CLL	fludarabine, cyclophosphamide and rituximab or *Calquence* + venetoclax +/- obinutuzumab	Data anticipated 2020+	Initiating
ACE-CL-309	III	Relapsed/refractory CLL	bendamustine or idelalisib + rituximabor *Calquence*	FPCD Q3 2016 Data anticipated H2 2019	Recruitment completed
ACE-CL-006 ELEVATE-RR	III	Relapsed/refractory high risk CLL	ibrutinib or *Calquence*	FPCD Q2 2015 Data anticipated 2020+	Recruitment ongoing

During the period, AstraZeneca received the first approval for *Calquence* outside the US in the United Arab Emirates and Brazil. The Company also presented new, long-term follow-up results for *Calquence* in patients with relapsed or refractory MCL and updated results of an ongoing clinical trial assessing *Calquence* monotherapy in treatment-naïve patients with CLL, at the aforementioned ASH meeting.

Long-term follow-up data presented from the Phase II ACE-LY-004 trial in relapsed or refractory MCL showed sustained and clinically-meaningful responses to *Calquence* with a median follow-up of more than two years (26 months), confirming its efficacy and safety profile in this patient population. Initial data from this trial served as the basis for the accelerated approval of *Calquence* by the US FDA in October 2017.

A summary of key investigator-assessed[a] efficacy results from the open-label, single-arm clinical trial of *Calquence* in 124 adult patients with relapsed or refractory MCL is shown below:

Table 30: *Calquence* ACE-LY-004 efficacy measures

Efficacy measure	Result (n=124; 95% CI)
ORR[a] (complete response + partial response)	81% (73, 87)
Best response	
Complete response	43% (34, 52)
Partial response	38% (29, 47)
Median duration of response	26 months (17.5, not reached)
Median PFS	20 months (16.5, 27.7)

[a] Response was assessed based on the Lugano classification.

The median follow-up was 26 months, with 40% of patients remaining on treatment with *Calquence* at the time of analysis. An exploratory analysis of the trial found that an undetectable minimal-residual disease status was achieved in a sub-set of patients.

There was no new onset of atrial fibrillation, and bleeding events occurred in 33% of patients, most frequently contusion (13%) and all bleeding events but three (2%, Grade 3) were Grade 1/2 events.

Updated results of the Phase I/II ACE-CL-001 trial were presented in an oral session. In a cohort of treatment-naïve patients with CLL, long-term safety and efficacy of assessment showed high response rates with no new safety signals identified. The median time on trial was 42 months, with 89% of patients remaining on treatment with *Calquence* at the time of analysis.

Summary of key investigator-assessed[a] efficacy results from the Phase I/II open-label, single-arm ACE-CL-001 *Calquence* trial in 99 patients with CLL, evaluating the treatment-naïve cohort:

Table 31: *Calquence* ACE-CL-001 efficacy measures

Efficacy measure	Result (n=99)
ORR[a] (complete response + partial response)	97%
Complete response	5%
Partial response	92%
Median duration of response[b]	NR (range, 42.4 to NR)[c]
36-month duration of response rate (95% CI)[b,d]	98% (90, 99)
Median PFS	NR (range, 44.2 to NR)[c]
36-month PFS rate (95% CI)[d]	97% (91, 99)

[a] Response was assessed using International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2008 criteria with modification for lymphocytosis.
[b] Only responders with ≥ partial response were included in this analysis.
[c] Not reached (NR).
[d] Based on the Kaplan-Meier estimates.

Atrial fibrillation and hypertension (all grades) occurred in 6% and 17% of patients, respectively, with Grade 3 events occurring in 2% and 7% of patients, respectively. Bleeding events (all grades) occurred in 64% of patients with contusion being most common (39%). All but three (3% Grade 3) bleeding events were Grade 1/2 events and no patients discontinued due to bleeding.

Other Oncology medicines

c) Savolitinib

The Phase III SAVOIR trial of savolitinib in papillary renal-cell carcinoma is currently being reassessed, taking into account the lower likelihood of success in this trial given a recent molecular epidemiology update as well as the rapidly changing renal-cell carcinoma treatment landscape. As a result, enrolment in the SAVOIR trial has been suspended.

During the period, the SAVANNAH trial achieved its FPCD. SAVANNAH is a phase II, single arm trial assessing the efficacy of *Tagrisso* in combination with savolitinib in patients with EGFRm and MET, locally-advanced or metastatic NSCLC, who have progressed following treatment with *Tagrisso*.

CVRM

CV, renal and metabolism (CVRM) together form one of AstraZeneca's main therapy areas and a key growth drive for the Company. By following the science to understand more clearly the underlying links between the heart, kidneys and pancreas, AstraZeneca is investing in a portfolio of medicines to protect organs and improve outcomes by slowing disease progression, reducing risks and tackling co-morbidities. The Company's ambition is to modify or halt the natural course of CVRM diseases and potentially regenerate organs and restore function, by continuing to deliver transformative science that improves treatment practices and CV health for millions of patients.

At the American Heart Association Scientific Sessions in Chicago in November 2018, the Company presented, in addition to the full DECLARE trial data, twenty abstracts, including new data on the CV effects of long-term *Brilinta* use for patients with a history of heart attack (PEGASUS-TIMI 54), as well as new findings in hyperkalaemia, highlighting the Company's holistic approach to care.

a) *Farxiga* (diabetes)
The aforementioned presentation of DECLARE-TIMI 58 Phase III CV outcomes trial data showed that *Farxiga* significantly reduced hospitalisation rates for heart failure or CV death in a broad patient population with type-2 diabetes. There were fewer major adverse CV events vs. placebo, although this finding did not reach statistical significance.

During the period, the Company received an acceptance from the US FDA for *Farxiga* in patients with type-1 diabetes. The acceptance was based on Phase III data from the DEPICT (Dapagliflozin Evaluation in Patients with Inadequately Controlled Type 1 diabetes) clinical programme. The safety profile of *Farxiga* in the programme to date was consistent with its established profile in type-2 diabetes, with the exception of a higher number of diabetic ketoacidosis (DKA) events in dapagliflozin-treated patients vs. placebo in these type-1 diabetes trials. DKA is a known complication for patients with diabetes that affects those with type-1 diabetes more frequently than with type-2 diabetes.

In November 2018, the Company was granted approval by the China NMPA for two new add-on indications for *Forxiga* in China. The first was the combination therapy with metformin, the other being the combination therapy with insulin for inadequately-controlled type-2 diabetes mellitus (T2DM). This marked the first time the two combination therapies with an SGLT2 inhibitor have been approved in China. The approval of the combination therapy with metformin was based on the positive result of MB102055, a multi-centre, randomised, double-blinded, placebo-controlled, parallel-group, Phase III trial to evaluate the safety and efficacy of *Forxiga* in combination with metformin in Asian patients with type-2 diabetes who have inadequate glycaemic control on metformin alone. The trial data showed significant improvement in glycaemic control and better weight loss with *Forxiga* 5mg or 10mg added onto metformin, compared with placebo added onto metformin in patients with T2DM.

In November 2018, the European Commission approved an update of the European Study of Product Characteristics (SmPC), based on the DERIVE trial. The trial is designed to evaluate the clinical efficacy and safety of *Forxiga* in patients with type-2 diabetes and CKD stage 3A. The updates to the SmPC included a change in the posology section to allow the use of *Forxiga* by patients with type-2 diabetes mellitus and renal impairment down to, and including, CKD stage 3A. Prior to this update, *Forxiga* was the only SGLT2 inhibitor with a restriction to CKD, stages 2 and above. The removal of this restriction brings the *Forxiga* SmPC in line with the other SGLT2 inhibitors.

b) *Brilinta*
During the period, the first patient was dosed in the HESTIA3 trial. HESTIA3 is a randomised, double-blinded, multi-centre, Phase III trial assessing the effect of *Brilinta* versus placebo in reducing the rate of vaso-occlusive crises in paediatric patients with sickle cell disease (SCD). SCD is a genetic disorder that affects millions of patients worldwide, being particularly common in sub-Saharan Africa, the Middle East and India and among descendants from these regions living in the West; current treatment options are limited.

Table 32: CV outcomes trials

Major CVRM outcomes trials are highlighted in the following table:

Medicine	Trial	Mechanism	Population	Primary endpoint(s)	Timeline
Farxiga	DECLARE	SGLT2 inhibitor	c.17,000[46] patients with type-2 diabetes	Superiority for MACE[47] or superiority for the composite endpoint of CV death or hHF	Primary safety endpoint met One of two primary efficacy endpoints met
Farxiga	DAPA-HF	SGLT2 inhibitor	c.4,500 patients with heart failure (HF) and reduced ejection fraction	Time to first occurrence of CV death or hHF or an urgent HF visit	FPCD Q1 2017 LPCD Q3 2018 Data anticipated 2020
Farxiga	DELIVER	SGLT2 inhibitor	c.4,700 patients with HF and a preserved ejection fraction	Time to first occurrence of CV death or worsening heart failure	FPCD Q3 2018 Data anticipated 2020+
Farxiga	DAPA-CKD	SGLT2 inhibitor	c.4,000 patients with CKD	Time to first occurrence of ≥ 50% sustained decline in eGFR[48] or reaching ESRD[49] or CV death or renal death	FPCD Q1 2017 Data anticipated 2020
Brilinta	THEMIS	P2Y12 receptor antagonist	c.19,000 patients with type-2 diabetes and CAD without a history of MI or stroke	Composite of CV death, non-fatal MI and non-fatal stroke	FPCD Q1 2014 LPCD Q2 2016 Data anticipated H1 2019

[46] Included c.10,000 patients who had no prior index event and c.7,000 patients who had suffered an index event.
[47] Major adverse cardiovascular event.
[48] Estimated glomerular filtration rate.
[49] End-stage renal disease.

Medicine	Trial	Mechanism	Population	Primary endpoint(s)	Timeline
Brilinta	THALES	P2Y12 receptor antagonist	c.13,000 patients with acute ischaemic stroke or transient ischaemic attack	Prevention of the composite of subsequent stroke and death at 30 days	FPCD Q1 2018 Data anticipated 2020
Epanova	STRENGTH	Omega-3 carboxylic acids	c.13,000 patients with mixed dyslipidaemia/ hypertriglyceride-aemia	Time to first occurrence of CV death, non-fatal MI or non-fatal stroke	FPCD Q4 2014 LPCD Q2 2017 Data anticipated 2020

d) Roxadustat (anaemia)

During the period, AstraZeneca announced that its partner FibroGen, Inc. (FibroGen) had received formal marketing authorisation from the China NMPA for roxadustat, a first-in-class hypoxia-inducible factor prolyl hydroxylase inhibitor and new oral treatment of patients with anaemia caused by CKD that are on dialysis. The medicine can be prescribed to patients treated with haemodialysis or peritoneal dialysis. This was the first regulatory approval for roxadustat.

AstraZeneca and FibroGen expect to launch roxadustat in China during the second half of 2019, once a new manufacturing facility has been commissioned, inspected and approved.

In December 2018, the Company announced that the Phase III OLYMPUS and ROCKIES trials for roxadustat each met their primary efficacy endpoints for the treatment of patients with anaemia in CKD that are either non-dialysis-dependent or dialysis-dependent, respectively.

OLYMPUS met its primary efficacy endpoint by demonstrating a statistically-significant and clinically-meaningful improvement in mean change from baseline in haemoglobin (Hb) levels averaged over weeks 28 to 52 vs. placebo. ROCKIES met its primary efficacy endpoint, demonstrating a statistically-significant improvement in mean change from baseline in Hb levels averaged over weeks 28 to 52 vs. epoetin alfa.

The global Phase III programme consists of more than 9,000 patients in trials conducted by AstraZeneca, FibroGen and Astellas. In September 2018, Astellas announced high-level results from the Phase III ALPS trial; FibroGen and Astellas anticipate reporting high-level results from their remaining trials in due course. These trials will contribute to the combined pooled safety analysis, including MACE outcomes, anticipated during H1 2019.

Data from the Phase III OLYMPUS and ROCKIES trials, together with the efficacy and pooled safety data from the global Phase III programme, will form part of the regulatory submission package in the US and other major markets. Results from these trials will be presented at forthcoming medical meetings.

Respiratory

AstraZeneca's Respiratory focus is aimed at transforming the treatment of patients with asthma and COPD through combined inhaled therapies and biologic medicines for the unmet medical needs of specific populations and an early pipeline focused on disease modification.

The growing range of medicines includes up to four anticipated launches between 2017 and 2020; of these, *Bevespi* and *Fasenra* are already benefitting patients, with regulatory reviews for *Symbicort* as an anti-inflammatory reliever in mild asthma and PT010 in COPD underway. The capability in inhalation technology spans both pMDIs and dry-powder inhalers to serve patient needs, including the innovative *Aerosphere* Delivery Technology, a focus of AstraZeneca's future-platform development for respiratory-disease combination therapies.

AstraZeneca published data from the BORA trial in *The Lancet Respiratory Medicine* during the period. In BORA, *Fasenra* showed a safety and tolerability profile similar to that observed in the predecessor trials, with no increase in the frequencies of overall or serious adverse events. Improvements in efficacy measures observed with *Fasenra* in SIROCCO or CALIMA were maintained over the second year of treatment.

The Company also published and presented results from the Phase III KRONOS trial, which evaluated the efficacy and safety of PT010 (budesonide/glycopyrronium/formoterol) vs. dual-combination therapies *Bevespi*, *Symbicort* and PT009 in patients with moderate to very severe COPD regardless of whether or not they had an exacerbation in the prior year. PT009 is being characterised to qualify as a relevant comparator in clinical trials for PT010. The data were presented at the ERS International Congress and were published in *The Lancet Respiratory Medicine*.

a) *Bevespi* (COPD)
During the period, AstraZeneca announced that the EMA had approved *Bevespi Aerosphere* in a pMDI as a maintenance dual bronchodilator treatment to relieve symptoms in adult patients with COPD. *Bevespi Aerosphere* is the first medicine in its class to be approved by the EMA in a pMDI.

Bevespi Aerosphere is a twice-daily, fixed-dose dual bronchodilator combining glycopyrrolate, a LAMA and formoterol fumarate, a LABA. The approval was based on the Phase III PINNACLE trial programme, which evaluated the efficacy and safety of *Bevespi Aerosphere* and involved more than 5,000 patients with moderate to very-severe COPD.

Bevespi Aerosphere is also approved in the US, Canada, Australia, Turkey and Taiwan as a dual bronchodilator for the long-term maintenance treatment of airflow obstruction resulting from COPD and is under review in a number of other regions.

b) *Fasenra* (severe asthma)
In November 2018, the Company announced that the US FDA had granted ODD status for *Fasenra* for the treatment of eosinophilic granulomatosis with polyangiitis (EGPA), a rare autoimmune disease that can cause damage to multiple organs and tissues.

In January 2019, the US FDA also granted ODD status for *Fasenra* for the treatment of hypereosinophilic syndrome (HES), a group of rare, potentially fatal disorders characterised by high numbers of eosinophils in blood and tissues, which can cause progressive damage to any organ in the body.

The US FDA grants ODD status to medicines intended for the treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 patients in the US. Orphan designation qualifies the sponsor of the medicine for various development incentives of the US Orphan Drug Act.

During the period, the regulatory submissions for the addition of self-administration and an auto injector device for *Fasenra* in severe asthma were accepted in the US and the EU, based on results from the GRECO and GREGALE Phase III trials. Regulatory decisions are anticipated in H2 2019.

c) PT027 (asthma)
During the period, the first patient was recruited into the PT027 (budesonide/albuterol sulfate) clinical-development programme in asthma by our co-development partner Avillion (Bond Avillion 2 Development LP). PT027 is a potential reliever therapy medicine for asthma patients that could be used as needed in response to symptoms, regardless of background maintenance therapy. The Phase III programme includes MANDALA, an exacerbation trial and DENALI, a lung-function trial.

Other
a) MEDI8897 (lower respiratory tract infection)
Following a positive primary analysis of the Phase IIb trial of MEDI8897, a monoclonal antibody being developed for the prevention of lower respiratory tract infection caused by respiratory syncytial virus, the EMA granted MEDI8897 access to its PRIME (PRIority MEdicines) scheme and the US FDA granted Breakthrough Therapy Designation for the medicine. MEDI8897 is being developed in partnership with Sanofi Pasteur and full results of the Phase IIb trial will be presented at a forthcoming medical meeting later this year.

b) Lanabecestat (Alzheimer's disease)
In December 2018, high-level results of the AMARANTH and DAYBREAK-ALZ trials for lanabecestat, an oral beta secretase cleaving enzyme inhibitor, showed no significant disease slowing for those patients on lanabecestat treatment. These results supported the decision to discontinue the AMARANTH, AMARANTH Extension and DAYBREAK-ALZ trials following interim futility analyses in June 2018. The results indicated that the trials were unlikely to meet their primary efficacy endpoints upon completion and discontinuation was justified as no significant efficacy signal was observed in any of the Phase III trials.

c) *Linzess* (linaclotide) (IBS-C)
In January 2019, AstraZeneca announced that its partner Ironwood Pharmaceuticals, Inc. (Ironwood) had received marketing authorisation from the China NMPA for *Linzess* for the treatment of adult patients with IBS-C. *Linzess* is a first-in-class guanylate cyclase-C receptor agonist and the approval, offering an important treatment option for adult patients in China, was based on a Phase III global, multi-centre, clinical trial jointly conducted by AstraZeneca China and Ironwood in five countries, evaluating the efficacy and safety of *Linzess* in patients suffering from IBS-C.

For more details on the development pipeline, including anticipated timelines for regulatory submission/acceptances, please refer to the latest Clinical Trials Appendix available on astrazeneca.com.

Condensed consolidated statement of comprehensive income

For the **year** ended 31 December	2018 $m	2017 $m
Product Sales	21,049	20,152
Externalisation Revenue	1,041	2,313
Total Revenue	22,090	22,465
Cost of sales	(4,936)	(4,318)
Gross profit	17,154	18,147
Distribution costs	(331)	(310)
Research and development expense	(5,932)	(5,757)
Selling, general and administrative costs	(10,031)	(10,233)
Other operating income and expense	2,527	1,830
Operating profit	3,387	3,677
Finance income	138	113
Finance expense	(1,419)	(1,508)
Share of after tax losses in associates and joint ventures	(113)	(55)
Profit before tax	1,993	2,227
Taxation	57	641
Profit for the period	2,050	2,868
Other comprehensive income		
Items that will not be reclassified to profit or loss		
Remeasurement of the defined benefit pension liability	(46)	(242)
Net losses on equity investments measured at fair value through other comprehensive income	(171)	-
Fair value movements related to own credit risk on bonds designated as fair value through profit or loss	8	(9)
Tax on items that will not be reclassified to profit or loss	56	16
	(153)	(235)
Items that may be reclassified subsequently to profit or loss		
Foreign exchange arising on consolidation	(450)	536
Foreign exchange arising on designating borrowings in net investment hedges	(520)	505
Fair value movements on cash flow hedges	(37)	311
Fair value movements on cash flow hedges transferred to profit or loss	111	(315)
Fair value movements on derivatives designated in net investment hedges	(8)	(48)
Costs of hedging	(54)	-
Amortisation of loss on cash flow hedge	1	1
Net available for sale losses taken to equity	-	(83)
Tax on items that may be reclassified subsequently to profit or loss	51	(33)
	(906)	874
Other comprehensive (loss)/income for the period, net of tax	(1,059)	639
Total comprehensive income for the period	991	3,507
Profit attributable to:		
Owners of the Parent	2,155	3,001
Non-controlling interests	(105)	(133)
	2,050	2,868
Total comprehensive income attributable to:		
Owners of the Parent	1,097	3,640
Non-controlling interests	(106)	(133)
	991	3,507
Basic earnings per $0.25 Ordinary Share	$1.70	$2.37
Diluted earnings per $0.25 Ordinary Share	$1.70	$2.37
Weighted average number of Ordinary Shares in issue (millions)	1,267	1,266
Diluted weighted average number of Ordinary Shares in issue (millions)	1,267	1,267

Condensed consolidated statement of comprehensive income

For the **quarter** ended 31 December	2018 $m	2017 $m
Product Sales	5,768	5,487
Externalisation Revenue	649	290
Total Revenue	6,417	5,777
Cost of sales	(1,637)	(1,225)
Gross profit	4,780	4,552
Distribution costs	(93)	(85)
Research and development expense	(2,012)	(1,551)
Selling, general and administrative costs	(2,600)	(3,078)
Other operating income and expense	1,002	848
Operating profit	1,077	686
Finance income	26	49
Finance expense	(337)	(316)
Share of after tax losses in associates and joint ventures	(36)	(12)
Profit before tax	730	407
Taxation	279	854
Profit for the period	1,009	1,261
Other comprehensive income		
Items that will not be reclassified to profit or loss		
Remeasurement of the defined benefit pension liability	(184)	(96)
Net losses on equity investments measured at fair value through other comprehensive income	(330)	-
Fair value movements related to own credit risk on bonds designated as fair value through profit or loss	5	(9)
Tax on items that will not be reclassified to profit or loss	121	(7)
	(388)	(112)
Items that may be reclassified subsequently to profit or loss		
Foreign exchange arising on consolidation	(99)	5
Foreign exchange arising on designating borrowings in net investment hedges	(71)	(117)
Fair value movements on cash flow hedges	(42)	85
Fair value movements on cash flow hedges transferred to profit or loss	39	(34)
Fair value movements on derivatives designated in net investment hedges	(14)	(9)
Costs of hedging	(19)	-
Amortisation of loss on cash flow hedge	1	-
Net available for sale losses taken to equity	-	(47)
Tax on items that may be reclassified subsequently to profit or loss	12	92
	(193)	(25)
Other comprehensive loss for the period, net of tax	(581)	(137)
Total comprehensive income for the period	428	1,124
Profit attributable to:		
Owners of the Parent	1,034	1,301
Non-controlling interests	(25)	(40)
	1,009	1,261
Total comprehensive income attributable to:		
Owners of the Parent	453	1,164
Non-controlling interests	(25)	(40)
	428	1,124
Basic earnings per $0.25 Ordinary Share	$0.82	$1.03
Diluted earnings per $0.25 Ordinary Share	$0.82	$1.03
Weighted average number of Ordinary Shares in issue (millions)	1,267	1,266
Diluted weighted average number of Ordinary Shares in issue (millions)	1,267	1,267

Condensed consolidated statement of financial position

	At 31 Dec 2018 $m	At 31 Dec 2017 $m
ASSETS		
Non-current assets		
Property, plant and equipment	7,421	7,615
Goodwill	11,707	11,825
Intangible assets	21,959	26,188
Derivative financial instruments	157	504
Investments in associates and joint ventures	89	103
Other investments	833	933
Other receivables	515	847
Deferred tax assets	2,379	2,189
	45,060	50,204
Current assets		
Inventories	2,890	3,035
Trade and other receivables	5,574	5,009
Other investments	849	1,230
Derivative financial instruments	258	28
Income tax receivable	207	524
Cash and cash equivalents	4,831	3,324
Assets held for sale	982	-
	15,591	13,150
Total assets	60,651	63,354
LIABILITIES		
Current liabilities		
Interest-bearing loans and borrowings	(1,754)	(2,247)
Trade and other payables	(12,841)	(11,641)
Derivative financial instruments	(27)	(24)
Provisions	(506)	(1,121)
Income tax payable	(1,164)	(1,350)
	(16,292)	(16,383)
Non-current liabilities		
Interest-bearing loans and borrowings	(17,359)	(15,560)
Derivative financial instruments	(4)	(4)
Deferred tax liabilities	(3,286)	(3,995)
Retirement benefit obligations	(2,511)	(2,583)
Provisions	(385)	(347)
Other payables	(6,770)	(7,840)
	(30,315)	(30,329)
Total liabilities	(46,607)	(46,712)
Net assets	14,044	16,642
EQUITY		
Capital and reserves attributable to equity holders of the Company		
Share capital	317	317
Share premium account	4,427	4,393
Other reserves	2,041	2,029
Retained earnings	5,683	8,221
	12,468	14,960
Non-controlling interests	1,576	1,682
Total equity	14,044	16,642

Condensed consolidated statement of changes in equity

	Share capital $m	Share premium account $m	Other reserves[50] $m	Retained earnings $m	Total attributable to owners $m	Non-controlling interests $m	Total equity $m
At 1 Jan 2017	316	4,351	2,047	8,140	14,854	1,815	16,669
Profit for the period	-	-	-	3,001	3,001	(133)	2,868
Other comprehensive income	-	-	-	639	639	-	639
Transfer to other reserves	-	-	(18)	18	-	-	-
Transactions with owners:							
Dividends	-	-	-	(3,543)	(3,543)	-	(3,543)
Issue of Ordinary Shares	1	42	-	-	43	-	43
Share-based payments charge for the period	-	-	-	220	220	-	220
Settlement of share plan awards	-	-	-	(254)	(254)	-	(254)
Net movement	1	42	(18)	81	106	(133)	(27)
At 31 Dec 2017	**317**	**4,393**	**2,029**	**8,221**	**14,960**	**1,682**	**16,642**

	Share capital $m	Share premium account $m	Other reserves $m	Retained earnings $m	Total attributable to owners $m	Non-controlling interests $m	Total equity $m
At 1 Jan 2018	317	4,393	2,029	8,221	14,960	1,682	16,642
Adoption of new accounting standards[51]	-	-	-	(91)	(91)	-	(91)
Profit for the period	-	-	-	2,155	2,155	(105)	2,050
Other comprehensive loss	-	-	-	(1,058)	(1,058)	(1)	(1,059)
Transfer to other reserves	-	-	12	(12)	-	-	-
Transactions with owners:							
Dividends	-	-	-	(3,539)	(3,539)	-	(3,539)
Issue of Ordinary Shares	-	34	-	-	34	-	34
Share-based payments charge for the period	-	-	-	219	219	-	219
Settlement of share plan awards	-	-	-	(212)	(212)	-	(212)
Net movement	-	34	12	(2,538)	(2,492)	(106)	(2,598)
At 31 Dec 2018	**317**	**4,427**	**2,041**	**5,683**	**12,468**	**1,576**	**14,044**

[50] Other reserves include the capital redemption reserve and the merger reserve.
[51] The Group adopted IFRS 15 'Revenue from Contracts with Customers' from 1 January 2018. See Note 1.

Condensed consolidated statement of cash flows

For the **year** ended 31 December	2018 $m	2017 $m
Cash flows from operating activities		
Profit before tax	1,993	2,227
Finance income and expense	1,281	1,395
Share of after tax losses in associates and joint ventures	113	55
Depreciation, amortisation and impairment	3,753	3,036
Increase in working capital and short-term provisions	(639)	(50)
Gains on disposal of intangible assets	(1,885)	(1,518)
Fair value movements on contingent consideration arising from business combinations	(495)	109
Non-cash and other movements	(290)	(524)
Cash generated from operations	3,831	4,730
Interest paid	(676)	(698)
Tax paid	(537)	(454)
Net cash inflow from operating activities	2,618	3,578
Cash flows from investing activities		
Movement in short-term investments and fixed deposits	405	(345)
Purchase of property, plant and equipment	(1,043)	(1,326)
Disposal of property, plant and equipment	12	83
Purchase of intangible assets	(328)	(294)
Disposal of intangible assets	2,338	1,376
Purchase of non-current asset investments	(102)	(96)
Disposal of non-current asset investments	24	70
Payments to joint ventures	(187)	(76)
Non-contingent payments on business combinations	-	(1,450)
Payment of contingent consideration from business combinations	(349)	(434)
Interest received	193	164
Net cash inflow/(outflow) from investing activities	963	(2,328)
Net cash inflow before financing activities	3,581	1,250
Cash flows from financing activities		
Proceeds from issue of share capital	34	43
Issue of loans	2,971	1,988
Repayment of loans	(1,400)	(1,750)
Dividends paid	(3,484)	(3,519)
Hedge contracts relating to dividend payments	(67)	(20)
Repayment of obligations under finance leases	-	(14)
Movement in short-term borrowings	(98)	336
Net cash outflow from financing activities	(2,044)	(2,936)
Net increase/(decrease) in cash and cash equivalents in the period	1,537	(1,686)
Cash and cash equivalents at the beginning of the period	3,172	4,924
Exchange rate effects	(38)	(66)
Cash and cash equivalents at the end of the period	4,671	3,172
Cash and cash equivalents consist of:		
Cash and cash equivalents	4,831	3,324
Overdrafts	(160)	(152)
	4,671	3,172

Notes to the condensed financial information

1 Basis of preparation and accounting policies

The preliminary announcement for the year ended 31 December 2018 has been prepared in accordance with International Financial Reporting Standards (IFRSs) as adopted by the European Union (EU) and as issued by the International Accounting Standards Board (IASB).

The annual financial statements of the Group are prepared in accordance with IFRSs as adopted by the EU and as issued by the IASB. Except as noted below, the preliminary announcement has been prepared applying the accounting policies and presentation that were applied in the preparation of the Group's published consolidated financial statements for the year ended 31 December 2017.

IFRS 9 'Financial Instruments' is effective for accounting periods beginning on or after 1 January 2018 and replaces existing accounting standards. It is applicable to financial assets and liabilities and introduces changes to existing accounting concerning classification and measurement, impairment (introducing an expected-loss method), hedge accounting, and on the treatment of gains arising from the impact of own credit risk on the measurement of liabilities held at fair value. The Group early adopted the treatment of fair value changes arising from changes in own credit risk from 1 January 2017 and has adopted the remainder of the standard from 1 January 2018. The principal impact is that equity investments previously classified as available for sale have been re-categorised on initial application and the Group has elected to record fair value movements on certain non-current equity investments in other comprehensive income from 1 January 2018. There is no future recycling of such gains and losses to profit or loss. Fair value movements on other equity investments are recorded in profit. Given the general quality and short-term nature of the trade receivables, there is no material impact on the introduction of an expected-loss impairment method. Other changes include classifying factored receivables and investments in money market funds at fair value through profit and loss, but these changes have not had a material measurement impact. The Group's existing hedging arrangements have been assessed as compliant with the new rules.

IFRS 15 'Revenue from Contracts with Customers' is effective for accounting periods beginning on or after 1 January 2018 and replaces existing accounting standards. It provides enhanced detail on the principle of recognising revenue to reflect the transfer of goods and services to customers at a value which the Company expects to be entitled to receive. The standard also updates revenue disclosure requirements.

The standard has not had a material impact on the revenue streams from the supply of goods and associated rebates and returns provisions. The timing of the recognition of product sales and the basis for the estimates of sales deductions under IAS 18 are consistent with those adopted under IFRS 15.

The previous accounting for externalisation transactions under IAS 18 includes an analysis of the performance obligations under the arrangement and upfront revenue recognition requires the transfer of substantive rights, for example a licence to use the intellectual property and an appropriate allocation of revenue to the remaining performance obligations. While the basis for such allocation is different in IFRS 15, the impact of the adoption of the new standard on the historical allocations is not material. The licences we grant are typically rights to use the intellectual property, which does not change during the period of the licence. Those licences are generally unique and therefore the basis of allocation of revenue to performance obligations makes use of the residual approach as permitted by IFRS 15. The related sales milestones and royalties to these licences qualify for the royalty exemption available under IFRS 15 and will continue to be recognised as the underlying sales are made. Furthermore, there is no material change to the assessment of whether the performance obligations are distinct from applying the new standard.

The Group has retrospectively applied the standard from 1 January 2018 recognising the cumulative effect of initially applying the standard as an increase to trade and other payables of $133m to defer externalisation revenue previously recognised, an increase to trade and other receivables of $20m to recognise externalisation revenue previously not recognised, a total related tax adjustment of $22m and a corresponding net adjustment to the opening balance of retained earnings of $91m. There is no restatement to prior periods as permitted in the transition rules for IFRS 15. The impact of initial application in the year to 31 December 2018 as compared with the year to 31 December 2017 is the recognition of additional Externalisation Revenue of $27m in the year to 31 December 2018. Earnings per share increased by $0.02.

Legal proceedings

The information contained in Note 5 updates the disclosures concerning legal proceedings and contingent liabilities in the Group's Annual Report and Form 20-F Information 2017, the interim financial statements for the three months ended 31 March 2018, the interim financial statements for the three months ended 30 June 2018 and the interim financial statements for the three months ended 30 September 2018.

Going concern

The Group has considerable financial resources available. As at 31 December 2018 the Group has $7.1bn in financial resources (cash balances of $4.8bn and undrawn committed bank facilities of $4.1bn, of which $3.4bn is available until April 2022, $0.5bn is available until December 2020 (extendable to December 2021) and $0.2bn is available until December 2019 (extendable to December 2020), with only $1.8bn of debt due within one year). The Group's revenues are largely derived from sales of products which are covered by patents which provide a relatively high level of resilience and predictability to cash inflows, although the revenue is expected to continue to be significantly impacted by the expiry of patents over the medium term. In addition, government price interventions in response to budgetary constraints are expected to continue to

adversely affect revenues in many of the mature markets. The Group, however, anticipates new revenue streams from both recently launched medicines and products in development, and the Group has a wide diversity of customers and suppliers across different geographic areas. Consequently, the Directors believe that, overall, the Group is well placed to manage its business risks successfully.

On the basis of the above paragraph, the going concern basis has been adopted in the preliminary announcement.

Financial information

The financial information for the year contained in the preliminary announcement does not constitute statutory accounts of the Group for the years ended 31 December 2018 and 2017 but is derived from those accounts. Statutory accounts for 2017 have been delivered to the registrar of companies and those for 2018 will be delivered in due course. Those accounts have been reported on by the Group's auditors; their report was (i) unqualified, (ii) did not include a reference to any matters to which the auditors drew attention by way of emphasis without qualifying their report, and (iii) did not contain a statement under section 498(2) or (3) of the Companies Act 2006. The quarterly financial information has not been subject to audit.

2 Restructuring costs

Profit before tax for the year ended 31 December 2018 is stated after charging restructuring costs of $697m ($807m for the year ended 31 December 2017). These have been charged to profit as follows:

	FY 2018 $m	FY 2017 $m	Q4 2018 $m	Q4 2017 $m
Cost of sales	432	181	355	53
Research and development expense	94	201	(1)	24
Selling, general and administrative costs	181	347	71	83
Other operating income and expense	(10)	78	1	3
Total	697	807	426	163

3 Net debt

The table below provides an analysis of Net Debt and a reconciliation of net cash flow to the movement in Net Debt. The Group monitors Net Debt as part of its capital management policy as described in Note 26 of the Annual Report and Form 20-F Information 2017. Net Debt is a non-GAAP financial measure.

	At 1 Jan 2018 $m	Cash Flow $m	Non-cash & Other $m	Exchange Movements $m	At 31 Dec 2018 $m
Loans due after one year	(15,560)	(2,971)	1,006	166	(17,359)
Total long-term debt	(15,560)	(2,971)	1,006	166	(17,359)
Current instalments of loans	(1,397)	1,400	(1,002)	-	(999)
Current instalments of finance leases	(5)	-	5	-	-
Commercial paper	(180)	(31)	-	-	(211)
Bank Collateral	(513)	129	-	-	(384)
Overdraft	(152)	(19)	-	11	(160)
Total current debt	(2,247)	1,479	(997)	11	(1,754)
Gross borrowings	(17,807)	(1,492)	9	177	(19,113)
Net derivative financial instruments	504	67	(187)	-	384
Net Borrowings	(17,303)	(1,425)	(178)	177	(18,729)
Cash and cash equivalents	3,324	1,556	-	(49)	4,831
Other investments - current	1,230	(405)	24	-	849
Other investments - non-current	70	-	(24)	-	46
Cash and investments	4,624	1,151	-	(49)	5,726
Net funds / (debt)	(12,679)	(274)	(178)	128	(13,003)

Non-cash movements in the period include fair value adjustments.

Other investments - non-current are included within the balance of $833m (31 December 2017: $933m) in the Statement of Financial Position. The equivalent GAAP measure to net debt is 'liabilities arising from financing activities' which excludes the amounts for cash and overdrafts, other investments and non-financing derivatives shown above and includes the Acerta put option liability of $1,838m (31 December 2017: $1,823m) shown in non-current other payables.

4 Financial instruments

As detailed in the Group's most recent annual financial statements, the principal financial instruments consist of derivative financial instruments, other investments, trade and other receivables, cash and cash equivalents, trade and other payables, and interest-bearing loans and borrowings.

Other than changes resulting from the Group's adoption of IFRS 9 'Financial Instruments' from 1 January 2018, as detailed in Note 1, there have been no changes of significance to the categorisation or fair value hierarchy classification of our financial instruments from those detailed in the Notes to the Group Financial Statements in the Company's Annual Report and Form 20-F Information 2017.

The Group holds certain equity investments that are categorised as Level 3 in the fair value hierarchy and for which fair value losses of $1m have been recognised in the year to 31 December 2018. These are presented in Fair value gains on equity investments in the Condensed Consolidated Statement of Comprehensive Income.

Financial instruments measured at fair value include $1,682m of other investments, $671m of loans, and $384m of derivatives as at 31 December 2018. The total fair value of interest-bearing loans and borrowings at 31 December 2018 which have a carrying value of $19,113m in the Condensed Consolidated Statement of Financial Position, was $19,588m. Contingent consideration liabilities arising on business combinations have been classified under Level 3 in the fair value hierarchy and movements in fair value are shown below

	Diabetes Alliance 2018 $m	Other 2018 $m	Total 2018 $m	Total 2017 $m
At 1 January	4,477	1,057	5,534	5,457
Settlements	(349)	-	(349)	(434)
Revaluations	(482)	(13)	(495)	109
Discount unwind	337	79	416	402
At 31 December	3,983	1,123	5,106	5,534

A description of the methods and assumptions used in our valuation approach for financial instruments, and an analysis of the key sensitivities, is included in Notes 11, 12, 18 and 19 to the Financial Statements in our Annual Report on Form 20-F Information 2017.

5 Legal proceedings and contingent liabilities

AstraZeneca is involved in various legal proceedings considered typical to its business, including litigation and investigations relating to product liability, commercial disputes, infringement of intellectual property rights, the validity of certain patents, anti-trust law and sales and marketing practices. The matters discussed below constitute the more significant developments since publication of the disclosures concerning legal proceedings in the Company's Annual Report and Form 20-F Information 2017, the interim financial statements for the three months ended 31 March 2018, the interim financial statements for the three months ended 30 June 2018 and the interim financial statements for the three months ended 30 September 2018 (the Disclosures). Unless noted otherwise below or in the Disclosures, no provisions have been established in respect of the claims discussed below.

As discussed in the Disclosures, for the majority of claims in which AstraZeneca is involved it is not possible to make a reasonable estimate of the expected financial effect, if any, that will result from ultimate resolution of the proceedings. In these cases, AstraZeneca discloses information with respect only to the nature and facts of the cases, but no provision is made.

In cases that have been settled or adjudicated, or where quantifiable fines and penalties have been assessed and which are not subject to appeal, or where a loss is probable and we are able to make a reasonable estimate of the loss, we record the loss absorbed or make a provision for our best estimate of the expected loss.

The position could change over time and the estimates that we have made and upon which we have relied in calculating these provisions are inherently imprecise. There can, therefore, be no assurance that any losses that result from the outcome of any legal proceedings will not exceed the amount of the provisions that have been booked in the accounts. The major factors causing this uncertainty are described more fully in the Disclosures and herein.

AstraZeneca has full confidence in, and will vigorously defend and enforce, its intellectual property.

Matters disclosed in respect of the fourth quarter of 2018 and to 14 February 2019

Patent litigation

Imfinzi

US patent proceedings

As previously disclosed, in July 2017, Bristol-Myers Squibb, E.R. Squibb & Sons LLC, Ono Pharmaceutical Co. Limited and Tasuku Honjo filed a patent infringement action in the US District Court relating to AstraZeneca's commercialisation of *Imfinzi*. A trial has been scheduled for October 2020.

Calquence

US patent proceedings

As previously disclosed, in November 2017, Pharmacyclics LLC (Pharmacyclics, a company in the AbbVie group) filed a patent infringement lawsuit in the District Court of Delaware (the District Court) against Acerta Pharma and AstraZeneca relating to *Calquence*. A trial has been scheduled for June 2020.

In April 2018, AstraZeneca and Acerta Pharma filed a complaint in the District Court against Pharmacyclics and AbbVie, Inc. alleging that their medicine, ibrutinib, infringes a US patent owned by Acerta Pharma. In November 2018, Janssen Biotech, Inc. intervened as a defendant. A trial has been scheduled for January 2021.

Faslodex

US patent proceedings

As previously disclosed, AstraZeneca has resolved all of the patent infringement lawsuits that it filed in the US District Court for the District of New Jersey (the District Court) relating to four patents listed in the US FDA Orange Book with reference to *Faslodex* after receiving a number of Paragraph IV notices relating to multiple abbreviated new drug applications (ANDAs) seeking US FDA approval to market generic versions of *Faslodex* prior to the expiration of AstraZeneca's patents, and the District Court has entered consent judgments ending those lawsuits. In December 2018, AstraZeneca filed a new patent infringement lawsuit in the District Court relating to all four listed patents after receiving a new Paragraph IV notice relating to an ANDA seeking US FDA approval to market generic versions of *Faslodex* prior to the expiration of AstraZeneca's patents.

Patent proceedings outside the US

As previously disclosed, in May 2017, the Opposition Division of the European Patent Office (EPO) revoked European Patent No. EP 2,266,573. AstraZeneca appealed the decision and, in January 2019, the Board of Appeal of the EPO reversed the earlier and upheld the validity of the '573 patent.

Brilinta

Patent proceedings outside the US

In Canada, in October 2018, Taro Pharmaceuticals Inc. (Taro) challenged the patents listed on the Canadian Patent Register with reference to *Brilinta*. AstraZeneca commenced an infringement action against Taro in November 2018.

As previously disclosed in China, in October 2017, the Chinese Patent Office issued a decision invalidating one of AstraZeneca's Chinese substance patents relating to *Brilinta*. AstraZeneca appealed and, in December 2018, the Beijing High People's Court vacated the invalidation decision and remanded the case back to the Chinese Patent Office for further

processing in view of the Court's decision. The patent, Chinese Patent No. ZL99815926.3, is due to expire in December 2019.

Symbicort

US patent proceedings

As previously disclosed, in October 2018, AstraZeneca initiated ANDA litigation against Mylan Pharmaceuticals Inc., Mylan Laboratories Limited, Mylan Inc., and Mylan N.V. (collectively, Mylan) and, separately, against Teva Pharmaceuticals USA, Inc. (Teva) in the US District Court for the District of Delaware. In its complaints, AstraZeneca alleges that Mylan's and Teva's generic versions of *Symbicort*, if approved and marketed, would infringe AstraZeneca's US Patents Nos. 7,759,328; 8,143,239; 8,575,137; and 7,967,011. AstraZeneca also filed a similar action against Mylan in the US District Court for the Northern District of West Virginia.

In November 2018, AstraZeneca filed an amended complaint in the Teva action to add Catalent Pharma Solutions LLC (Catalent) as a party. In December 2018, Teva and Catalent responded to the amended complaint and alleged that their proposed generic product does not infringe the asserted patents and/or that the asserted patents are invalid and/or unenforceable. Teva also asserted counterclaims in which it alleged that the proposed generic product does not infringe five additional patents that AstraZeneca did not assert in its complaint, namely: US Patents Nos. 7,587,988; 8,528,545; 8,387,615; 8,616,196; and 8,875,699. In December 2018, AstraZeneca filed an amended complaint in the Mylan Delaware action to add 3M Company as a party. In January 2019, in the Mylan Delaware action, Mylan Laboratories Limited, Mylan Inc., and Mylan N.V. filed a motion to dismiss for failure to state a claim and MPI filed a motion to dismiss for improper venue.

In January 2019, MPI responded to the West Virginia complaint and alleged that its proposed generic product does not infringe the asserted patents and/or that the asserted patents are invalid and/or unenforceable. Mylan also asserted counterclaims to the asserted patents. In January 2019, in the West Virginia action, Mylan Laboratories Limited, Mylan Inc., and Mylan N.V. filed a motion to dismiss for failure to state a claim.

Movantik

US patent proceedings

In December 2018, AstraZeneca initiated ANDA litigation against Apotex Inc. and Apotex Corp. (together, Apotex), and against MSN Laboratories (MSN), in the US District Court for the District of Delaware. In each of its complaints, AstraZeneca alleges that the generic companies' versions of *Movantik*, if approved and marketed, would infringe US Patent No. 9,012,469.

Product liability litigation

Seroquel

As previously disclosed, in the US, in November 2017, AstraZeneca was named as one of several defendants in a lawsuit filed in Missouri involving one plaintiff alleging, among other things, wrongful death from treatment with *Seroquel*. This matter was resolved and is now concluded.

Commercial litigation

Toprol-XL

In October 2016, AstraZeneca completed its sale of certain assets related to the US rights to *Toprol-XL* and AstraZeneca's authorised generic metoprolol succinate product to Aralez Pharmaceuticals Trading DAC (Aralez). In August 2018, Aralez commenced voluntary insolvency proceedings and filed voluntary petitions for relief under Chapter 11 of the US Bankruptcy Code in the US Bankruptcy Court for the Southern District of New York. Aralez listed AstraZeneca as an unsecured creditor in the US Bankruptcy proceedings with a claim of $14m. AstraZeneca filed a proof of claim asserting an unsecured claim of approximately $65m. In October 2018, Aralez filed a motion in the Bankruptcy Court seeking to sell the US rights to *Toprol-XL* and its authorised generic. AstraZeneca filed an objection to the proposed sale. A hearing on the proposed sale is scheduled for 20-21 February 2019.

Government investigations/proceedings

Multi-product litigation

Litigation in Washington State

In the US, in September 2018, a lawsuit against AstraZeneca and several other defendants was unsealed in the US District Court for the Western District of Washington. The complaint alleges that the defendants violated various laws, including state and federal false claims acts, by offering clinical educator and reimbursement support programmes. In September 2018, the government moved to dismiss the lawsuit against AstraZeneca and similar lawsuits filed against other companies by relator Health Choice Alliance.

US Congressional Inquiry

In January 2019, AstraZeneca received a letter from E. Cummings, Chairman of the US House of Representatives Committee on Oversight and Reform seeking information related to pricing practices for *Crestor*. Requests were also sent to 11 other pharmaceutical manufacturers. AstraZeneca intends to cooperate with the inquiry.

6 Subsequent events

In December 2018, an internal decision was taken to close two Biologics manufacturing sites in Colorado, USA. The Group assessed the recoverable value of the site assets including property, plant and equipment and inventory, and have recorded an impairment of $252m within land and buildings and a provision against inventories of $75m at 31 December 2018. The announcement to those impacted of these closures was made subsequent to year end.

On 10 January 2019, the Company entered into a floating rate $500m committed bank-loan agreement, which was drawn in full on 4 February 2019. The loan is repayable in December 2019 although can be partially or fully repaid in advance, but in that event, is not available to be redrawn.

On 23 January 2019, AstraZeneca completed the sale of its US rights to *Synagis*, and of a right to participate in the payments from the US profits and losses for MEDI8897, to Swedish Orphan Biovitrum AB (Sobi). Under the terms of the agreement, AstraZeneca has received upfront consideration including cash of $966m and ordinary shares in Sobi with an initial fair market value of c.$600m, equating to an ownership interest of 8%. The majority of consideration is attributable to the sale of US rights to *Synagis*.

Consideration attributable to the sale of US rights to *Synagis* will be treated as Other Operating Income and Expense in 2019, net of the derecognition of $893m of the related intangible asset, which was transferred to assets held for sale on 31 December 2018.

The right to participate in payments from the US profits and losses for MEDI8897 will be treated as a financial liability at amortised cost, recognised initially at fair value. The valuation of this financial liability was not finalised at the date of this announcement. Any difference between the amount of consideration received and the fair value recognised will be recorded within Other Operating Income and Expense in FY 2019.

7 Product Sales analysis - FY 2018

The table below provides an analysis of year-on-year Product Sales, with Actual and CER growth rates reflecting year-on-year growth.

The CER information in respect of FY 2018 included in the interim financial statements has not been audited by PricewaterhouseCoopers LLP.

	World			Emerging Markets			US		Europe			Established ROW		
	FY 2018 $m	Actual %	CER %	FY 2018 $m	Actual %	CER %	FY 2018 $m	Actual %	FY 2018 $m	Actual %	CER %	FY 2018 $m	Actual %	CER %
Oncology														
Tagrisso	1,860	95	93	347	n/m	n/m	869	n/m	314	68	61	330	45	43
Lynparza	647	n/m	n/m	51	n/m	n/m	345	n/m	190	46	41	61	n/m	n/m
Imfinzi	633	n/m	n/m	6	n/m	n/m	564	n/m	27	n/m	n/m	36	n/m	n/m
Iressa	518	(2)	(4)	286	14	12	26	(33)	109	(3)	(8)	97	(23)	(25)
Calquence	62	n/m	n/m	-	-	-	62	n/m	-	-	-	-	-	-
Legacy:														
Faslodex	1,028	9	9	154	34	41	537	9	221	(14)	(19)	116	49	46
Zoladex	752	2	2	409	16	18	8	(47)	133	(6)	(10)	202	(11)	(12)
Arimidex	212	(2)	(3)	132	12	11	-	n/m	31	(9)	(9)	49	(16)	(17)
Casodex	201	(7)	(8)	113	5	2	1	n/m	20	(9)	(9)	67	(22)	(23)
Others	115	1	(1)	30	29	30	-	-	8	20	20	77	(7)	(8)
Total Oncology	**6,028**	**50**	**49**	**1,528**	**36**	**37**	**2,412**	**n/m**	**1,053**	**19**	**14**	**1,035**	**16**	**14**
CVRM														
Farxiga	1,391	30	30	336	45	52	591	21	315	30	24	149	34	34
Brilinta	1,321	22	21	326	46	48	588	16	348	18	13	59	16	16
Bydureon	584	2	1	8	(11)	(11)	475	4	81	(8)	(13)	20	5	5
Onglyza	543	(11)	(11)	172	32	34	223	(30)	89	(14)	(18)	59	4	4
Byetta	126	(28)	(28)	8	(33)	(33)	74	(35)	29	(15)	(15)	15	(6)	(6)
Symlin	34	(29)	(29)	-	-	-	34	(29)	-	-	-	-	-	-
Legacy:														
Crestor	1,433	(39)	(40)	841	7	7	170	(54)	203	(70)	(71)	219	(60)	(60)
Seloken/Toprol-XL	712	2	4	641	8	10	39	5	19	(63)	(63)	13	-	-
Atacand	260	(13)	(12)	157	(12)	(7)	13	(32)	70	(19)	(20)	20	18	18
Others	306	(11)	(12)	206	-	-	(1)	n/m	76	(17)	(20)	25	(42)	(42)
Total CVRM	**6,710**	**(8)**	**(8)**	**2,695**	**14**	**15**	**2,206**	**(7)**	**1,230**	**(26)**	**(29)**	**579**	**(33)**	**(34)**
Respiratory														
Symbicort	2,561	(9)	(10)	495	13	14	862	(22)	773	(6)	(10)	431	(3)	(4)
Pulmicort	1,286	9	8	995	18	17	116	(26)	90	(2)	(8)	85	(3)	(5)
Fasenra	297	n/m	n/m	1	n/m	n/m	218	n/m	32	n/m	n/m	46	n/m	n/m
Daliresp/Daxas	189	(5)	(5)	5	25	25	155	(7)	28	8	4	1	-	-
Tudorza/Eklira	110	(27)	(29)	1	(50)	n/m	25	(62)	74	1	(3)	10	11	11
Duaklir	95	20	14	1	n/m	n/m	-	-	91	18	12	3	50	50
Bevespi	33	n/m	n/m	-	-	-	33	n/m	-	-	-	-	-	-
Others	340	20	18	146	42	41	7	40	141	9	6	46	(2)	(2)
Total Respiratory	**4,911**	**4**	**3**	**1,644**	**18**	**18**	**1,416**	**(6)**	**1,229**	**1**	**(4)**	**622**	**5**	**4**
Other														
Nexium	1,702	(13)	(14)	690	1	1	306	(39)	235	(5)	(10)	471	(10)	(11)
Synagis	665	(3)	(3)	1	n/m	n/m	287	(9)	377	2	2	-	-	-
Seroquel XR/IR	361	(29)	(31)	118	(22)	(23)	108	(44)	107	(16)	(20)	28	(26)	(26)
Losec/Prilosec	272	-	(2)	161	15	11	7	(36)	70	(9)	(12)	34	(21)	(21)
FluMist/Fluenz	110	41	44	1	n/m	n/m	15	n/m	91	20	22	3	-	-
Movantik/Moventig	109	(11)	(11)	-	-	-	108	(10)	-	n/m	n/m	1	n/m	n/m
Others	181	(66)	(67)	53	(82)	(79)	11	(59)	67	(27)	(41)	50	(59)	(60)
Total Other	**3,400**	**(18)**	**(19)**	**1,024**	**(19)**	**(19)**	**842**	**(28)**	**947**	**(5)**	**(8)**	**587**	**(19)**	**(20)**
Total Product Sales	**21,049**	**4**	**4**	**6,891**	**12**	**13**	**6,876**	**11**	**4,459**	**(6)**	**(10)**	**2,823**	**(8)**	**(9)**

8 Product Sales analysis - Q4 2018

The table below provides an analysis of year-on-year Product Sales, with Actual and CER growth rates reflecting year-on-year growth.

The Q4 2018 information in respect of the three months ended 31 December 2018 included in the condensed financial information has not been audited by PricewaterhouseCoopers LLP.

	World			Emerging Markets			US		Europe			Established ROW		
	Q4 2018 $m	Actual %	CER %	Q4 2018 $m	Actual %	CER %	Q4 2018 $m	Actual %	Q4 2018 $m	Actual %	CER %	Q4 2018 $m	Actual %	CER %
Oncology														
Tagrisso	594	95	98	81	62	78	289	n/m	92	46	48	132	n/m	n/m
Lynparza	209	n/m	n/m	18	n/m	n/m	112	n/m	53	47	50	26	n/m	n/m
Imfinzi	262	n/m	n/m	2	n/m	n/m	216	n/m	18	n/m	n/m	26	n/m	n/m
Iressa	112	(14)	(11)	60	18	24	6	(50)	24	(25)	(22)	22	(37)	(37)
Calquence	24	n/m	n/m	-	-	-	24	n/m	-	-	-	-	-	-
Legacy:														
Faslodex	269	13	16	43	59	81	143	15	50	(19)	(19)	33	32	32
Zoladex	182	(3)	3	96	3	12	2	n/m	34	(8)	(5)	50	(14)	(12)
Arimidex	46	(19)	(16)	26	(21)	(18)	-	n/m	8	-	13	12	(14)	(14)
Casodex	46	(15)	(13)	23	(23)	(20)	-	n/m	5	-	-	18	(14)	(14)
Others	23	(21)	(17)	6	(14)	-	-	-	3	n/m	n/m	14	(39)	(39)
Total Oncology	**1,767**	**58**	**61**	**355**	**19**	**30**	**792**	**134**	**287**	**19**	**21**	**333**	**38**	**38**
CVRM														
Farxiga	397	20	24	94	31	42	171	14	84	18	24	48	23	28
Brilinta	376	26	29	94	92	n/m	177	15	91	11	13	14	-	-
Bydureon	138	(6)	(5)	(1)	n/m	n/m	115	-	19	(17)	(13)	5	-	-
Onglyza	148	(18)	(15)	51	38	49	61	(41)	21	(19)	(19)	15	7	14
Byetta	32	(33)	(31)	2	(33)	-	19	(42)	7	(13)	(13)	4	-	-
Symlin	10	(23)	(23)	-	-	-	10	(23)	-	-	-	-	-	-
Legacy:														
Crestor	353	(41)	(38)	210	1	7	42	(67)	44	(71)	(70)	57	(47)	(47)
Seloken/Toprol-XL	160	(5)	4	148	(5)	4	6	n/m	3	(25)	(25)	3	(40)	(40)
Atacand	58	(21)	(14)	43	-	12	2	-	8	(65)	(65)	5	-	-
Others	75	(12)	(8)	50	4	10	1	(50)	18	(22)	(22)	6	(50)	(50)
Total CVRM	**1,747**	**(10)**	**(6)**	**691**	**12**	**21**	**604**	**(14)**	**295**	**(28)**	**(26)**	**157**	**(24)**	**(22)**
Respiratory														
Symbicort	636	(15)	(13)	131	12	20	207	(28)	185	(19)	(17)	113	(4)	(2)
Pulmicort	389	5	9	307	14	20	35	(29)	22	(15)	(15)	25	(7)	(7)
Fasenra	125	n/m	n/m	1	n/m	n/m	89	n/m	15	n/m	n/m	20	n/m	n/m
Daliresp/Daxas	54	2	4	1	n/m	n/m	45	5	8	(20)	(20)	-	-	-
Tudorza/Eklira	19	(55)	(55)	-	n/m	n/m	(3)	n/m	20	11	11	2	(33)	(33)
Duaklir	22	(4)	-	-	-	-	-	-	21	(9)	(9)	1	n/m	n/m
Bevespi	10	25	25	-	-	-	10	25	-	-	-	-	-	-
Others	107	26	32	57	54	65	3	(25)	36	16	16	11	(27)	(20)
Total Respiratory	**1,362**	**2**	**5**	**497**	**17**	**25**	**386**	**(6)**	**307**	**(9)**	**(7)**	**172**	**6**	**8**
Other														
Nexium	390	(9)	(6)	166	(1)	5	57	-	56	(22)	(22)	111	(15)	(14)
Synagis	251	7	7	1	n/m	n/m	154	14	96	(3)	(3)	-	-	-
FluMist/Fluenz	75	29	33	1	n/m	n/m	-	-	71	22	26	3	n/m	n/m
Losec/Prilosec	60	(13)	(9)	30	(17)	(14)	2	-	19	(5)	5	9	(18)	(18)
*Seroquel XR/*IR	56	(65)	(64)	12	(69)	(67)	13	(84)	26	(13)	(13)	5	(44)	(44)
Movantik/Moventig	25	(17)	(17)	-	-	-	27	(7)	(2)	n/m	n/m	-	-	-
Others	35	(70)	(68)	13	(73)	(88)	2	(86)	18	(18)	9	2	(94)	(84)
Total Other	**892**	**(18)**	**(17)**	**223**	**(23)**	**(21)**	**255**	**(20)**	**284**	**(6)**	**(3)**	**130**	**(29)**	**(27)**
Total Product Sales	**5,768**	**5**	**8**	**1,766**	**8**	**16**	**2,037**	**15**	**1,173**	**(9)**	**(7)**	**792**	**-**	**1**

9 Sequential quarterly Product Sales - 2018

The table below provides an analysis of sequential quarterly Product Sales, with Actual and CER growth rates reflecting quarter-on-quarter growth.

The sequential quarterly product sales information included in the condensed financial information has not been audited by PricewaterhouseCoopers LLP.

	Q1 2018 $m	Actual %	CER %	Q2 2018 $m	Actual %	CER %	Q3 2018 $m	Actual %	CER %	Q4 2018 $m	Actual %	CER %
Oncology												
Tagrisso	338	11	10	422	25	25	506	20	23	594	17	19
Iressa	132	2	(1)	143	8	8	131	(8)	(5)	112	(15)	(13)
Lynparza	119	19	18	150	26	26	169	13	15	209	24	25
Imfinzi	62	n/m	n/m	122	98	98	187	53	52	262	40	41
Calquence	8	n/m	n/m	12	51	50	18	50	50	24	33	33
Legacy:												
Faslodex	254	7	5	247	(3)	(2)	258	4	7	269	4	5
Zoladex	184	(2)	(4)	192	4	5	194	1	6	182	(6)	(2)
Arimidex	54	(5)	(7)	57	6	6	55	(4)	-	46	(16)	(13)
Casodex	52	(4)	(6)	52	-	(2)	51	(2)	4	46	(10)	(8)
Others	27	(7)	(20)	37	37	50	28	(24)	(22)	23	(18)	13
Total Oncology	**1,230**	**10**	**8**	**1,434**	**17**	**17**	**1,597**	**11**	**14**	**1,767**	**11**	**13**
CVRM												
Farxiga	299	(10)	(11)	340	14	15	355	4	7	397	12	13
Brilinta	293	(2)	(4)	316	8	9	336	6	9	376	12	13
Onglyza	129	(28)	(29)	126	(2)	(2)	140	11	14	148	6	8
Bydureon	139	(5)	(5)	155	12	11	152	(2)	(1)	138	(9)	(9)
Byetta	31	(35)	(38)	29	(7)	(3)	34	17	17	32	(6)	(6)
Symlin	9	(31)	(31)	7	(22)	(22)	8	14	14	10	25	25
Legacy:												
Crestor	389	(35)	(36)	338	(13)	(12)	353	4	8	353	-	2
Seloken/Toprol-XL	200	19	18	173	(14)	(13)	179	3	10	160	(11)	(8)
Atacand	71	(3)	(3)	66	(8)	(8)	65	(2)	5	58	(11)	(9)
Others	85	6	4	73	(13)	(11)	73	(3)	-	75	3	3
Total CVRM	**1,645**	**(15)**	**(17)**	**1,623**	**(1)**	**-**	**1,695**	**4**	**8**	**1,747**	**3**	**5**
Respiratory												
Symbicort	634	(16)	(17)	672	6	6	619	(8)	(5)	636	3	4
Pulmicort	346	(7)	(8)	287	(17)	(17)	264	(8)	(4)	389	47	51
Daliresp/Daxas	38	(28)	(30)	45	19	22	52	16	18	54	4	4
Tudorza/Eklira	34	(19)	(21)	39	15	15	18	(54)	(59)	19	6	11
Duaklir	28	22	17	22	(22)	(19)	23	5	5	22	(4)	-
Fasenra	21	n/m	n/m	65	n/m	n/m	86	32	34	125	45	46
Bevespi	5	(38)	(38)	8	61	60	10	25	25	10	-	-
Others	75	(12)	(20)	88	17	16	70	(20)	(13)	107	53	57
Total Respiratory	**1,181**	**(11)**	**(13)**	**1,226**	**4**	**4**	**1,142**	**(7)**	**(4)**	**1,362**	**19**	**21**
Other												
Nexium	448	5	3	442	(1)	(1)	422	(5)	97	390	(8)	(7)
Synagis	224	(4)	(4)	26	(89)	(88)	164	n/m	n/m	251	53	n/m
Seroquel XR/IR	97	n/m	40	131	35	37	77	(41)	6	56	(27)	(31)
Losec/Prilosec	69	-	(4)	76	10	11	67	(12)	85	60	(10)	(8)
Movantik/Moventig	28	(7)	(7)	24	(14)	(14)	32	33	167	25	(22)	(22)
FluMist/Fluenz	-	n/m	n/m	-	n/m	n/m	35	n/m	n/m	75	n/m	n/m
Others	63	(62)	(45)	48	(25)	(26)	35	(27)	n/m	35	-	31
Total Other	**929**	**(15)**	**(16)**	**747**	**(20)**	**(20)**	**832**	**12**	**15**	**892**	**7**	**22**
Total Product Sales	**4,985**	**(9)**	**(11)**	**5,030**	**1**	**1**	**5,266**	**5**	**8**	**5,768**	**10**	**13**

10 Sequential quarterly Product Sales - 2017

The table below provides an analysis of sequential quarterly Product Sales, with Actual and CER growth rates reflecting quarter-on-quarter growth.

The sequential quarterly product sales information included in the condensed financial information has not been audited by PricewaterhouseCoopers LLP.

	Q1 2017 $m	Actual %	CER %	Q2 2017 $m	Actual %	CER %	Q3 2017 $m	Actual %	CER %	Q4 2017 $m	Actual %	CER %
Oncology												
Tagrisso	171	16	19	232	36	34	248	7	5	304	23	22
Iressa	124	5	8	137	10	9	137	-	(1)	130	(5)	(6)
Lynparza	57	(8)	(6)	59	4	2	81	37	33	100	23	22
Imfinzi	-	-	-	1	n/m	n/m	-	-	-	18	n/m	n/m
Calquence	-	-	-	-	-	-	-	-	-	3	n/m	n/m
Legacy:												
Faslodex	214	(4)	(3)	248	16	15	241	(3)	(5)	238	(1)	(1)
Zoladex	185	(21)	(12)	178	(4)	(5)	185	4	2	187	1	1
Casodex	56	(7)	(2)	54	(4)	(3)	51	(6)	(9)	54	6	6
Arimidex	52	(9)	(7)	54	4	4	54	-	(2)	57	6	6
Others	26	(10)	(3)	30	15	7	29	(3)	(3)	29	-	3
Total Oncology	**885**	**(5)**	**-**	**993**	**12**	**11**	**1,026**	**3**	**1**	**1,120**	**9**	**9**
CVRM												
Farxiga	207	(13)	(13)	250	21	20	285	14	11	332	16	16
Brilinta	224	(5)	(4)	272	21	20	284	4	3	299	5	5
Onglyza	154	3	3	150	(3)	(3)	127	(15)	(17)	180	42	42
Bydureon	153	8	8	146	(5)	(5)	128	(12)	(14)	147	15	15
Byetta	46	(16)	(16)	43	(7)	(7)	39	(9)	(9)	48	23	23
Symlin	14	-	-	11	(21)	(21)	10	(9)	(9)	13	30	30
Qtern	-	-	-	-	-	-	-	-	-	5	n/m	n/m
Legacy:												
Crestor	631	-	3	560	(11)	(12)	580	4	2	594	2	2
Seloken/Toprol-XL	186	4	6	181	(3)	(4)	160	(12)	(14)	168	5	4
Atacand	75	(7)	(6)	72	(4)	(5)	80	11	8	73	(9)	(6)
Others	89	3	12	90	1	(3)	80	(11)	(12)	80	-	(4)
Total CVRM	**1,779**	**(2)**	**-**	**1,775**	**-**	**(1)**	**1,773**	**-**	**(2)**	**1,939**	**9**	**9**
Respiratory												
Symbicort	677	(9)	(7)	706	4	3	668	(5)	(7)	752	13	12
Pulmicort	337	17	19	226	(33)	(33)	242	7	5	371	53	51
Daliresp/Daxas	44	7	10	48	9	9	53	10	8	53	-	(2)
Tudorza/Eklira	37	3	6	34	(8)	(8)	37	9	6	42	14	14
Duaklir	19	-	-	16	(16)	(15)	21	31	18	23	10	10
Bevespi	1	(67)	(50)	3	n/m	n/m	4	33	33	8	100	100
Others	66	(20)	(19)	66	-	(4)	67	2	4	85	27	30
Total Respiratory	**1,181**	**(2)**	**(1)**	**1,099**	**(7)**	**(8)**	**1,092**	**(1)**	**(3)**	**1,334**	**22**	**21**
Other												
Nexium	461	(6)	(4)	595	29	28	469	(21)	(22)	427	(9)	(9)
Synagis	230	(24)	(24)	70	(70)	(70)	153	n/m	n/m	234	53	53
Seroquel XR/IR	104	(36)	(35)	135	30	30	113	(16)	(16)	156	38	36
Losec/Prilosec	68	15	18	68	-	(3)	66	(3)	(6)	69	5	5
Movantik/Moventig	30	15	15	32	7	7	30	(6)	(6)	30	-	-
FluMist/Fluenz	-	n/m	n/m	-	-	-	20	n/m	n/m	58	190	175
Others	105	(48)	44	173	65	n/m	140	(19)	(21)	120	(14)	(15)
Total Other	**998**	**(24)**	**(22)**	**1,073**	**8**	**7**	**991**	**(8)**	**(9)**	**1,094**	**10**	**10**
Total Product Sales	**4,843**	**(8)**	**(6)**	**4,940**	**2**	**1**	**4,882**	**(1)**	**(3)**	**5,487**	**12**	**12**

11 Sequential quarterly Product Sales - 2016

The table below provides an analysis of sequential quarterly Product Sales, with Actual and CER growth rates reflecting quarter-on-quarter growth.

The sequential quarterly product sales information included in the condensed financial information has not been audited by PricewaterhouseCoopers LLP.

	Q1 2016 $m	Actual %	CER %	Q2 2016 $m	Actual %	CER %	Q3 2016 $m	Actual %	CER %	Q4 2016 $m	Actual %	CER %
Oncology												
Iressa	135	5	5	135	-	(2)	125	(7)	(8)	118	(6)	(4)
Tagrisso	51	183	200	92	80	82	133	45	44	147	11	11
Lynparza	44	22	22	54	23	23	58	7	7	62	7	9
Legacy:												
Faslodex	190	3	3	211	11	9	207	(2)	(2)	222	7	9
Zoladex	178	(10)	(8)	204	15	8	199	(2)	(2)	235	18	11
Arimidex	57	(5)	(5)	62	9	7	56	(10)	(13)	57	2	5
Casodex	62	(2)	(6)	63	2	-	62	(2)	(5)	60	(3)	(2)
Others	21	(22)	(22)	27	29	12	27	-	4	29	7	-
Total Oncology	**738**	**3**	**3**	**848**	**15**	**12**	**867**	**2**	**2**	**930**	**7**	**7**
CVRM												
Farxiga	165	9	10	211	28	26	220	4	4	239	9	9
Brilinta	181	4	5	214	18	16	208	(3)	(2)	236	13	15
Onglyza	211	10	12	191	(9)	(11)	169	(12)	(11)	149	(12)	(11)
Bydureon	135	(13)	(16)	156	16	14	145	(7)	(6)	142	(2)	(1)
Byetta	62	(14)	(14)	76	23	21	61	(20)	(19)	55	(10)	(10)
Symlin	5	(64)	(64)	10	n/m	n/m	11	10	10	14	27	27
Legacy:												
Crestor	1,156	(13)	(13)	926	(20)	(21)	688	(26)	(26)	631	(8)	(7)
Seloken/Toprol-XL	185	16	11	189	2	-	185	(2)	(2)	178	(4)	(2)
Atacand	71	(17)	(15)	89	25	22	74	(17)	(19)	81	9	14
Others	121	(9)	(16)	106	(12)	(11)	84	(21)	(19)	86	2	-
Total CVRM	**2,292**	**(7)**	**(7)**	**2,168**	**(5)**	**(7)**	**1,845**	**(15)**	**(15)**	**1,811**	**(2)**	**(1)**
Respiratory												
Symbicort	749	(13)	(12)	803	7	6	697	(13)	(13)	740	6	8
Pulmicort	310	13	14	239	(23)	(23)	224	(6)	(6)	288	29	31
Daliresp/Daxas	31	(3)	(3)	40	29	29	42	5	5	41	(2)	(2)
Tudorza/Eklira	39	(17)	(17)	48	23	21	47	(2)	-	36	(23)	(23)
Duaklir	13	8	8	17	31	31	14	(18)	(18)	19	36	43
Bevespi	-	-	-	-	-	-	-	-	-	3	n/m	n/m
Others	65	-	(3)	79	22	18	86	9	12	83	(3)	1
Total Respiratory	**1,207**	**(6)**	**(6)**	**1,226**	**2**	**1**	**1,110**	**(9)**	**(9)**	**1,210**	**9**	**10**
Other												
Nexium	463	(18)	(18)	562	21	20	516	(8)	(9)	491	(5)	(4)
Seroquel XR/IR	286	(6)	(6)	283	(1)	(2)	236	(17)	(16)	162	(31)	(32)
Synagis	244	(11)	(11)	27	(89)	(89)	104	n/m	n/m	302	n/m	n/m
Losec/Prilosec	75	(3)	(4)	70	(7)	(9)	72	3	4	59	(18)	(17)
Movantik/Moventig	17	13	13	23	35	35	25	9	9	26	4	4
FluMist/Fluenz	5	(97)	(97)	6	20	20	26	n/m	n/m	67	n/m	n/m
Others	238	n/m	(31)	256	8	(87)	224	(13)	(19)	202	(10)	n/m
Total Other	**1,328**	**(24)**	**(22)**	**1,227**	**(8)**	**(9)**	**1,203**	**(2)**	**(3)**	**1,309**	**9**	**10**
Total Product Sales	**5,565**	**(10)**	**(10)**	**5,469**	**(2)**	**(3)**	**5,025**	**(8)**	**(8)**	**5,260**	**5**	**6**

Shareholder information

Announcement of first quarter 2019 results and Annual General Meeting	26 April 2019
Announcement of first half and second quarter 2019 results	25 July 2019
Announcement of nine months and third quarter 2019 results	24 October 2019

Future dividends will normally be paid as follows:

First interim	Announced with half-year and second-quarter results and paid in September
Second interim	Announced with full-year and fourth-quarter results and paid in March

The record date for the second interim dividend for 2018, payable on 27 March 2019, will be 1 March 2019. The ex-dividend date will be 28 February 2019. The record date for the first interim dividend for 2019, payable on 9 September 2019, will be 9 August 2019. The ex-dividend date will be 8 August 2019.

Information on or accessible through AstraZeneca's websites, including astrazeneca.com, does not form part of and is not incorporated into this announcement.

Addresses for correspondence

Registered Office	**Registrar and Transfer Office**	**Swedish Central Securities Depository**	**US Depositary**
1 Francis Crick Avenue Cambridge Biomedical Campus Cambridge CB2 0AA UK	Equiniti Limited Aspect House Spencer Road Lancing West Sussex BN99 6DA UK	Euroclear Sweden AB PO Box 191 SE-101 23 Stockholm Sweden	Citibank Shareholder Services PO Box 43077 Providence RI 02940-3077 USA
Tel: +44 (0)20 3749 5000	Tel (Freephone in UK): 0800 389 1580 Tel (outside UK): +44 (0)121 415 7033	Tel: +46 (0)8 402 9000	Tel: (toll free in the US) +1 (888) 697 8018 Tel: (outside the US) +1 (781) 575 4555 citibank@shareholders-online.com

Cautionary statements regarding forward-looking statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement:

This document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; effects of patent litigation in respect of IP rights; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure of outsourcing; the risks associated with manufacturing biologics; the risk that R&D will not yield new products that achieve commercial success; the risk of delay to new product launches; the risk that new products do not perform as we expect; the risk that strategic alliances and acquisitions, including licensing and collaborations, will be unsuccessful; the risks from pressures resulting from generic competition; the impact of competition, price controls and price reductions; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the difficulties of obtaining and maintaining regulatory approvals for products; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; the risk of failure of critical processes affecting business continuity; economic, regulatory and political pressures to limit or reduce the cost of our products; failure to achieve strategic priorities or to meet targets, expectations, guidance or indications; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; the risk of substantial product liability claims; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; taxation risks; exchange rate fluctuations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the risk of misuse of social medial platforms and new technology; and the risk of failure of information technology and cybercrime. Nothing in this document, or any related presentation / webcast, should be construed as a profit forecast.