AstraZeneca PLC
12 November 2021 07:00 GMT

Year to date and Q3 2021 results

AstraZeneca reinforces its scientific leadership through exceptional pipeline delivery and the addition of Alexion in the quarter

- Total Revenue in the year to date, including Alexion from 21 July 2021, was $25,406m, representing growth of 32% (28% at CER). Total Revenue in the third quarter increased by 50% (48% at CER) to $9,866m
- Excluding the pandemic COVID-19 vaccine, Total Revenue increased 21% (17% at CER) in the year to date to $23,187m, and by 34% (32% at CER) in the quarter to $8,816m
- Eight positive Phase III results since June, with potential to change standard of care in several diseases
- Alexion integration progressing well, creating new opportunities in rare diseases
- Operating Expenses in the quarter reflected the addition of Alexion, as well increased R&D expenses across multiple programs, investment in our COVID-19 medicines, and increased SG&A from pre-launch activities following successful pipeline delivery
- Earnings guidance for the full year is unchanged

In the year to date, AstraZeneca delivered double-digit revenue growth from its Oncology, CVRM[1] and R&I[2] medicines, and established its Rare Disease capability with the acquisition of Alexion Pharmaceuticals Inc. (Alexion). Rare disease is a high-growth area with rapid innovation and significant unmet medical need.

Since June, AstraZeneca has made significant progress with its late-stage pipeline, reporting eight positive Phase III trial results and the approval of *Saphnelo* (anifrolumab) in the US for the treatment of systemic lupus erythematosus, and *Ultomiris* in the EU for children and adolescents with paroxysmal nocturnal haemoglobinuria. *Enhertu* received a Breakthrough Therapy Designation from the US FDA[3] following ground-breaking results from the DESTINY-Breast03 trial. The Company also announced positive results for *Lynparza* in prostate cancer, *Imfinzi* plus tremelimumab in liver cancer, *Imfinzi* in biliary tract cancer, PT027 in asthma, ALXN1840 in Wilson disease, and AZD7442 in COVID-19 prophylaxis and treatment.

Pascal Soriot, Chief Executive Officer, commented:

"AstraZeneca's scientific leadership continues to provide strong revenue growth and exceptional pipeline delivery, with eight positive late-stage readouts across seven medicines since June, including our long acting antibody combination showing promise in both prevention and treatment of COVID-19. The addition of Alexion furthers our commitment to bring transformative therapies to patients around the world, and I am proud of our colleagues' ongoing dedication and focus.

Our broad portfolio of medicines and diversified geographic exposure provides a robust platform for long-term sustainable growth. Following accelerated investment in upcoming launches after positive data flow, we expect a solid finish to the year and our earnings guidance is unchanged."

Table 1: Revenue and EPS summary

	YTD 2021			Q3 2021		
	$m	**Actual % Change**	**CER[4] % change**	**$m**	**Actual % Change**	**CER % change**
- Product Sales	25,043	33	29	9,741	49	47
- Collaboration Revenue	363	10	10	125	n/m	n/m
Total Revenue	25,406	32	28	9,866	50	48
- Less pandemic COVID-19 vaccine[5]	2,219	n/m[6]	n/m	1,050	n/m	n/m
Total Revenue ex-pandemic vaccine[7]	*23,187*	*21*	*17*	*8,816*	*34*	*32*
Reported[8] EPS[9]	$0.33	(80)	(65)	$(1.10)	n/m	n/m
Core[10] EPS	$3.59	22	23	$1.08	14	15
Impact of pandemic vaccine on EPS	*$(0.03)*	*n/m*	*n/m*	*$0.01*	*n/m*	*n/m*

Key elements of Total Revenue performance in the year-to-date included:

- An increase in Product Sales of 33% (29% at CER) to $25,043m
- The first contribution from Rare Disease, which generated $1,311m of revenue in the period following completion of the Alexion acquisition on 21 July 2021
- Oncology growth of 19% (16% at CER) to $9,744m, CVRM growth of 14% (10% at CER) to $6,028m and R&I growth of 16% (12% at CER) to $4,456m
- An increase in Emerging Markets revenue of 33% (28% at CER) to $8,618m. In China, revenue increased 17% (8% CER) to $4,699m in the year to date and by 10% (2% CER) in the quarter. China revenues in the year to date were impacted by pricing pressure associated with NRDL[11] and VBP[12] programmes.
- *Tagrisso*'s sequential quarterly performance in China was impacted by inventory phasing and stock compensation relating to NRDL changes in March. In future periods, volume growth from increased patient access is expected to compensate for the lower NRDL price
- Revenue in ex-China Emerging Markets increased 60% in the year to date to $3,919m. Excluding vaccine revenue of $1,139m, revenue in ex-China Emerging Markets increased by 13% in the year to date (14% at CER) to $2,780m and by 30% in the quarter to $1,018m, driven by Oncology medicines and *Farxiga*
- In the US, Total Revenue increased by 29% to $8,305m and in Europe by 40% (31% at CER) to $5,178m, including pandemic COVID-19 vaccine revenue of $736m

Guidance

The Company provides further details on its FY 2021 guidance at CER.

Total revenue excluding the COVID-19 vaccine is expected to grow by a low-twenties percentage, in line with prior guidance. Including vaccine revenues in Q4 2021, revenue is expected to grow by a mid-to-high twenties percentage.

Growth in Core EPS[13] to $5.05 to $5.40, in line with prior guidance.

Prior guidance excluded the revenue and profit impact of sales of the pandemic vaccine. The Company is now expecting to progressively transition the vaccine to modest profitability as new orders are received. COVID-19 vaccine sales in Q4 2021 are expected to be a blend of the original pandemic agreements and new orders, with the large majority coming from pandemic agreements. The limited profit contribution from the vaccine in Q4 2021 is expected to offset costs relating to the Company's long acting antibody combination (AZD7442), resulting in no change to Core EPS guidance. Core Tax Rate guidance is unchanged at 18-22%.

In general, AstraZeneca continues to recognise the heightened risks and uncertainties from the effects of COVID-19. Variations in performance between quarters can be expected to continue.

The Company is unable to provide guidance on a Reported basis because AstraZeneca cannot reliably forecast material elements of the Reported result, including any fair value adjustments arising on acquisition-related liabilities, intangible asset impairment charges and legal-settlement provisions. Please refer to the cautionary statements section regarding forward-looking statements at the end of this announcement.

Currency impact

If foreign-exchange rates for October to December 2021 were to remain at the average of rates seen in the year to date, it is anticipated that there would be a low single-digit favourable impact on Total Revenue and an immaterial impact on Core EPS versus CER data. The Company's foreign-exchange rate sensitivity analysis is contained within the operating and financial review.

Financial summary

- Variances across periods are based on a comparison of the Group's performance in the year to date and the quarter, including Alexion from 21 July 2021, with the Group's performance in the comparative prior periods, which do not include Alexion. Pro forma total revenue growth rates have been presented only for Q3 2021 Rare Disease and its constituent medicines, and do not impact any Group totals
- Total Revenue, comprising Product Sales and Collaboration Revenue, increased by 32% in the year to date (28% at CER) to $25,406m. Total Revenue included $2,219m from the pandemic COVID-19 vaccine
- Reported Gross Profit[14] Margin in the year to date declined eleven percentage points to 68.8%; Core Gross Profit Margin declined six percentage points in the year to date to 74.1%, predominantly reflecting the equitable supply, at no profit to AstraZeneca, of the pandemic COVID-19 vaccine, together with an increasing impact from profit-sharing arrangements (primarily *Lynparza* and roxadustat) and the impact of the NRDL and VBP programmes in China. These effects were partially offset by the contribution of Alexion from 21 July 2021, a higher proportion of Oncology sales, and increasing patient access in China. Reported Gross Profit Margin was also impacted by $1,044m due to the unwind of the fair value adjustment to Alexion inventories at the date of acquisition. Variations in gross margin performance between periods can be expected to continue
- Reported Total Operating Expense increased in the year to date by 39% (34% at CER) to $17,591m. Core Total Operating Expense increased by 24% (20% at CER) to $13,649m and represented 54% of Total Revenue (YTD 2020: 57%)
- Reported R&D Expense increased in the year to date by 67% (63% at CER) to $7,152m including an impairment charge of $1,172m recognised in the quarter on an intangible asset related to the acquisition of Ardea Biosciences, Inc. in 2012, following the decision to discontinue the development of verinurad. Core R&D Expense increased in the year to date by 34% (30% at CER) to $5,591m with increases in both Reported and Core R&D Expense reflecting the Company's continued investment in its COVID-19 vaccine and AZD7442, investment in several late-stage Oncology trials and the advancement of a number of Phase II clinical development programmes in BioPharmaceuticals
- Reported SG&A Expense increased in the year to date by 25% (21% at CER) to $10,117m and includes the increased amortisation of intangible assets related to the Alexion acquisition. Core SG&A Expense increased by 19% (14% at CER) to $7,736m, reflecting the addition of Alexion SG&A expenses from 21 July 2021, investment in Oncology-medicine launches, the launch of several new BioPharmaceuticals medicines, particularly in the US, AstraZeneca's further expansion in Emerging Markets, and the existing infrastructure base in China
- Reported and Core Other Operating Income and Expense[15] increased in the year to date by 51% (50% at CER) to $1,345m and $1,346m respectively, and included $776m income from the divestment of AstraZeneca's 26.7% share of Viela Bio, Inc. (Viela) in March 2021
- The Reported Operating Profit Margin declined fourteen percentage points (thirteen at CER) to 5.3%, reflecting the aforementioned intangible impairments and other factors. The Core Operating Profit Margin declined two percentage points (one percentage point at CER) in the year to date to 26.0% driven by the aforementioned increase in R&D and SG&A expenses
- Reported EPS in the year to date declined 80% (65% at CER) to $0.33. Core EPS increased by 22% (23% at CER) to $3.59. Reported and Core EPS were adversely affected by $0.03 due to the pandemic COVID-19 vaccine

Table 2: Select Medicines Total Revenue performance

Further details of the individual medicine performances are provided in the Total Revenue section.

		YTD 2021			Q3 2021		
		$m	Actual % change	CER % change	$m	Actual % change	CER % change
Tagrisso	Oncology	3,701	17	13	1,247	8	7
Imfinzi		1,778	20	17	618	16	15
Lynparza		1,719	21	18	588	27	25
Calquence		843	n/m	n/m	354	n/m	n/m
Enhertu		147	n/m	n/m	57	n/m	n/m
Farxiga	CVRM	2,156	57	51	797	51	48
Brilinta		1,124	(9)	(11)	375	(3)	(4)
Bydureon		293	(10)	(11)	95	(13)	(13)
roxadustat		148	n/m	n/m	56	n/m	n/m
Lokelma		122	n/m	n/m	49	n/m	n/m
Symbicort	R&I	2,047	-	(3)	676	13	11
Fasenra		901	35	32	322	34	33
Pulmicort		714	14	7	217	44	36
Breztri		130	n/m	n/m	47	n/m	n/m
Soliris[16]	Rare Disease[16]	798	n/m	n/m	798	*(3)*	*(2)*
Ultomiris[16]		297	n/m	n/m	297	*31*	*31*
Strensiq[16]		159	n/m	n/m	159	*7*	*8*
Pandemic COVID-19 vaccine	COVID-19	2,219	n/m	n/m	1,050	n/m	n/m

Table 3: Regional Total Revenue performance

Further details of the regional performances are provided in the Regional Total Revenue section.

	YTD 2021				Q3 2021		
	$m	% of total	Actual % change	CER % change	$m	Actual % change	CER % change
Emerging Markets	8,618	34	33	28	3,159	48	42
US	8,305	33	29	29	3,471	53	53
Europe	5,178	20	40	31	1,918	52	49
Established RoW	3,305	13	28	24	1,318	45	46
Total	25,406	100	32	28	9,866	50	48

Total Revenue from Emerging Markets increased 33% (28% CER) to $8,618m, of which $1,139m came from the pandemic COVID-19 vaccine. Excluding the COVID-19 vaccine, Total Revenue from Emerging Markets increased by 16% (10% at CER) in the year to date to $7,479m.

Corporate and business development

In 2019, Caelum Biosciences (Caelum) and Alexion entered into a collaboration to develop CAEL-101 for light chain amyloidosis, whereby Alexion acquired a minority equity interest and an exclusive option to acquire the remaining equity in Caelum. AstraZeneca has treated Caelum as a subsidiary from the date of acquisition of Alexion, reflecting a non-controlling interest of $150m. On 5 October 2021, the Group completed the acquisition of the remaining shares of Caelum and paid its shareholders the option exercise price of $150m, with the potential for additional payments of up to $350m upon achievement of regulatory and commercial milestones.

In November 2021, AstraZeneca agreed to transfer its global rights to *Eklira*, known as *Tudorza* in the US, and *Duaklir* to Covis Pharma Group for $270m payable on completion, which is expected in the fourth quarter of 2021. Covis Pharma Group will also cover certain ongoing development costs related to the medicines. The income arising from the upfront payment will be fully offset by a charge for derecognition of the associated intangible asset and therefore no Other Operating Income will be recognised in AstraZeneca's financial statements.

Sustainability summary

a) Access to healthcare

In the third quarter of 2021, the Company delivered approximately 67 million doses of its pandemic COVID-19 vaccine through COVAX[17]. As of 30 September 2021, the Company and its sublicensee Serum Institute of India Pvt. Ltd. (SII) have delivered more than 145 million doses with COVAX to over 125 countries, approximately half of all COVAX supply. The majority of the doses have gone to low and middle-income countries. Globally, AstraZeneca and its sub-licensing partners have released more than 1.5 billion vaccine doses as of the 30 September 2021, for supply in over 170 countries.

b) Environmental protection

On 3 November 2021, at the 26th UN Climate Change Conference (COP26), HRH The Prince of Wales named AstraZeneca as one of the first holders of the Terra Carta Seal, in recognition of the company's efforts to lead and accelerate action for a more sustainable future. In addition, Pascal Soriot was recognised as the Champion of the new Sustainable Markets Initiative (SMI) Health System Taskforce, which was launched at COP26 with HRH The Prince of Wales and with health systems leaders, with the shared ambition to accelerate the delivery of net zero, sustainable healthcare.

A more extensive sustainability update is provided later in this announcement.

Notes

The following notes refer to pages one to five.

1. Cardiovascular, Renal & Metabolism
2. Respiratory & Immunology
3. US Food and Drug Administration
4. 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.
5. The pandemic COVID-19 vaccine Total Revenue includes $83m of Collaboration Revenue of which $80m is receivable from the Serum Institute of India Pvt. Ltd. (SII) with an equivalent charge included within Other Operating Income and Expense in relation to consequent obligations under the license agreement with Oxford University Innovation (OUI).
6. Not meaningful.
7. *Total Revenue ex-pandemic vaccine* is a non-GAAP measure, which excludes the revenue impact from sales of the pandemic COVID-19 vaccine during the pandemic period to help facilitate a comparison to guidance.
8. Reported financial measures are the financial results presented in accordance with UK-adopted International Accounting Standards and EU-adopted International Financial Reporting Standards (IFRSs), and IFRS as issued by the International Accounting Standards Board (IASB).
9. Earnings per share.
10. Core financial measures. These are non-GAAP financial measures because, unlike Reported performance, they cannot be derived directly from the information in the Group's Financial Statements. See the Operating and financial review for a definition of Core financial measures and a reconciliation of Core to Reported financial measures.
11. China's National Reimbursement Drug List.
12. Volume-based procurement.
13. The calculation of Core EPS for guidance is based on 1,418 million weighted average number of shares outstanding during 2021. The number of shares in issue as of the close of the Alexion acquisition was 1,549 million.
14. Gross Profit is defined as Total Revenue minus Cost of Sales. The calculation of Reported and Core Gross Profit Margin excludes the impact of Collaboration Revenue and any associated costs, thereby reflecting the underlying performance of Product Sales.
15. Where AstraZeneca does not retain a significant ongoing interest in medicines or potential new medicines, income from divestments is reported within Reported and Core Other Operating Income and Expense in the Company's financial statements.
16. Growth rates on Rare Disease medicines have been calculated on a pro forma basis by comparing post-acquisition revenues from 21 July 2021 with the corresponding prior year pre-acquisition Q3 revenues previously published by Alexion adjusted pro rata to match the post-acquisition period. Pro forma Total Revenue growth rates have been presented only for Q3 2021 Rare Disease area and constituent medicines, and do not impact any Group totals.
17. COVID-19 Vaccines Global Access (COVAX) is a coalition co-led by CEPI, the Coalition for Epidemic Preparedness Innovations, Gavi, the Vaccine Alliance (Gavi), and the WHO. It is the only global initiative bringing governments and manufacturers together to ensure that safe and effective COVID-19 vaccines are available worldwide to both higher-income and lower-income countries.

Upcoming pipeline news

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

Table 4: Pipeline highlights

	Medicine	Indication / Trial	Event
Regulatory approvals or other regulatory actions	*Forxiga*	CKD[18]	Approval (EU, JP)
	roxadustat	Anaemia in CKD	Complete response letter from the US FDA
	Saphnelo	SLE[19]	Approval (US, JP)
	Ultomiris	PNH[20]	Approval (paediatric) (EU)
Regulatory submissions acceptance and/or submissions	*Tagrisso*	EGFRm[21] NSCLC[22] (adjuvant)	Regulatory submission (JP)
	Enhertu	HER2+[23] breast cancer (2nd-line)	RTOR[24] regulatory submission (US)
	Enhertu	HER2+ breast cancer (2nd-line)	Regulatory submission (EU)
	Enhertu	HER2+ gastric cancer (2nd-line)	Regulatory submission (EU)
	AZD7442	COVID-19 prophylaxis	EUA[25] regulatory submission (US)
Major Phase III data readouts or other significant developments	*Imfinzi*	Biliary tract cancer (1st-line) (TOPAZ-1)	Phase III primary endpoint met
	Imfinzi + tremelimumab	Liver cancer (1st-line) (HIMALAYA)	Phase III primary endpoint met
	Lynparza	mCRPC[26] (1st-line) (PROpel)	Phase III primary endpoint met
	Enhertu	HER2+ breast cancer (2nd-line) (DESTINY-Breast03)	Phase III primary endpoint met
	Enhertu	HER2+ breast cancer (2nd-line) (DESTINY-Breast03)	Breakthrough Therapy Designation (US)
	Fasenra	EG[27]	Orphan Drug Designation (US)
	Fasenra	EG +/- EGE	Fast Track Designation (US)
	Fasenra	Eosinophilic gastroenteritis	Orphan Drug Designation (US)
	tezepelumab	EoE[28]	Orphan Drug Designation (US)
	PT027	Asthma (MANDALA, DENALI)	Phase III primary endpoints met
	Ultomiris	ALS[29] (CHAMPION)	Phase III trial stopped for futility
	ALXN1840	Wilson disease (FoCus)	Phase III primary endpoint met
	AZD7442	COVID-19 prophylaxis (PROVENT)	Phase III primary endpoint met
	AZD7442	COVID-19 treatment (TACKLE)	Phase III primary endpoint met

[18] Chronic kidney disease.

[19] Systemic lupus erythematosus.

[20] Paroxysmal nocturnal haemoglobinuria.

[21] Epidermal growth factor receptor mutation.

[22] Non-small cell lung cancer.

[23] Human epidermal growth factor receptor 2 positive.

[24] Real Time Oncology Review.

[25] Emergency Use Authorization.

[26] Metastatic castration-resistant prostate cancer.

[27] Eosinophilic gastritis.

[28] Eosinophilic oesophagitis.

[29] Amyotrophic lateral sclerosis.

Table 5: Pipeline anticipated major news flow

Timing	Medicine	Indication / Trial	Event
Q4 2021	*Imfinzi* + tremelimumab	NSCLC (1st-Line)	Regulatory submission
	Lynparza	BRCAm HER2-negative breast cancer (adjuvant)	Regulatory submission
	Lynparza	mCRPC (1st-line)	Regulatory submission
	Enhertu	HER2+ breast cancer (2nd-line)	Regulatory submission
	Ultomiris	s.c[30] formulation in PNH and aHUS[31]	Regulatory submission
	Ultomiris	gMG[32]	Regulatory submission
	AZD2816	COVID-19 (variants of concern)	Data readout
	AZD7442	COVID-19 outpatient treatment (TACKLE)	EUA regulatory submission (US),
	AZD7442	COVID-19 pre-exposure prophylaxis (PROVENT)	EUA regulatory decision (US) CMA regulatory decision (EU) Regulatory decision (JP)
H1 2022	*Imfinzi*	NSCLC (unresectable, Stage III) (PACIFIC-2)	Data readout
	Imfinzi	NSCLC (1st-line) (PEARL)	Data readout
	Imfinzi	Cervical cancer (CALLA)	Data readout
	Imfinzi	Biliary tract cancer	Regulatory submission
	Imfinzi +/- tremelimumab	Liver cancer (1st-line)	Regulatory submission
	Enhertu	HER2-low breast cancer (DESTINY-Breast04)	Data readout, regulatory submission
	Calquence	CLL[33]	Regulatory submission (JP)
	Koselugo	NF1[34]	Regulatory submission (JP, CN)
	Forxiga	CKD	Regulatory decision (CN)
	Farxiga	HFpEF[35] (DELIVER)	Data readout, regulatory submission
	Brilique	Stroke	Regulatory decision (EU, CN)
	Fasenra	Nasal polyps	Regulatory decision (US)
	Saphnelo	SLE	Regulatory decision (EU)
	tezepelumab	Asthma	Regulatory decision (US, EU, JP)
	PT027	Asthma	Regulatory submission (US)
	Ultomiris	NMOSD[36]	Data readout
	nirsevimab	RSV[37]	Regulatory submission
	Vaxzevria	COVID-19	Regulatory submission (US)

[30] Subcutaneous injection.

[31] Atypical haemolytic uraemic syndrome.

[32] Generalised myasthenia gravis.

[33] Chronic lymphocytic leukaemia.

[34] Neurofibromatosis type 1.

[35] Heart failure with preserved ejection fraction.

[36] Neuromyelitis optica spectrum disorder.

[37] Respiratory syncytial virus.

	Tagrisso	EGFRm NSCLC (adjuvant)	Regulatory decision (JP)
	Imfinzi	LS-SCLC[38] (ADRIATIC)	Data readout
	Imfinzi	NSCLC (unresectable, Stage III)	Regulatory submission
	Imfinzi	NSCLC (1st-line)	Regulatory submission
	Imfinzi	Cervical cancer	Regulatory submission
	Imfinzi	Locoregional liver cancer (EMERALD-1)	Data readout, regulatory submission
	Enhertu	HER2+ breast cancer (3rd-line) (DESTINY-Breast02)	Data readout, regulatory submission
H2 2022	*Enhertu*	HER2+ gastric cancer (2nd-line)	Regulatory decision (EU)
	Fasenra	HES[39] (NATRON)	Data readout
	Fasenra	EoE (MESSINA)	Data readout, regulatory submission
	Fasenra	Chronic spontaneous urticaria (ARROYO)	Data readout
	Fasenra	Atopic dermatitis (HILLIER)	Data readout
	ALXN1840	Wilson disease	Regulatory submission
	Ultomiris	NMOSD	Regulatory submission
	danicopan (ALXN2040)	PNH-EVH[40]	Data readout
	acoramidis (ALXN2060)	ATTR-CM[41]	Data readout, regulatory submission

Conference call

A conference call and webcast for investors and analysts will begin at 11:45 GMT. Details can be accessed via astrazeneca.com.

Reporting calendar

The Company intends to publish its full-year and fourth-quarter results on Thursday 10 February 2022.

AstraZeneca

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

Contacts

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

[38] Limited-stage small cell lung cancer.

[39] Hyper-eosinophilic syndrome: a group of rare blood disorders.

[40] Paroxysmal nocturnal haemoglobinuria with extravascular haemolysis

[41] Transthyretin amyloid cardiomyopathy.

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List of tables

Operating and financial review

All narrative on growth and results in this section is based on actual exchange rates, and financial figures are in US$ millions ($m), unless stated otherwise. The performance shown in this announcement covers the nine-month period to 30 September 2021 ('the year to date' or 'YTD 2021') and the three-month period to 30 September 2021 ('the quarter', 'the third quarter' or 'Q3 2021') compared to the nine-month period to 30 September 2020 (YTD 2020) and the three-month period to 30 September 2020 (Q3 2020) respectively, unless stated otherwise.

Following the acquisition of Alexion, the Group has made a number of changes to presented performance:

- A new disease area, Rare Disease, presents the performance of medicines acquired with Alexion
- The Group has ceased reporting New Medicines as a performance metric (*Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Enhertu*, *Koselugo, Farxiga*, *Brilinta*, *Lokelma*, roxadustat, *Fasenra*, *Bevespi* and *Breztri*). In line with practice these medicines will be reported within their respective disease areas
- The Group has ceased reporting New CVRM as a performance metric (*Brilinta*, Renal and Diabetes medicines). In line with practice these medicines will be reported within the CVRM disease area

Comparative performance relating to previous reporting periods will be presented in line with the new presentation. This approach is representative of the strategic priorities of the enlarged Group.

Core financial measures, EBITDA, Net Debt, Initial Collaboration Revenue and Ongoing Collaboration Revenue are non-GAAP financial measures because they cannot be derived directly from the Group's Interim Financial Statements. Management believes that these non-GAAP financial measures, when provided in combination with Reported results, provide investors and analysts with helpful supplementary information to understand better the financial performance and position of the Group 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 restructuring programmes, which includes charges that relate to the impact of restructuring programmes on capitalised IT assets
- Other specified items, principally acquisition-related costs, which include fair-value adjustments and the imputed finance charge relating to contingent consideration on business combinations and legal settlements

Details on the nature of Core financial measures are provided on page 84 of the Annual Report and Form 20-F Information 2020. Following the Alexion acquisition and in line with its policies, the Group will exclude the following acquisition-related items in the current and future periods from its Core results:

- The Group recognised significant additional intangible assets reflecting the fair value of acquired launched medicines and medicines in development. Future amortisation charges on these assets will be excluded from the Group's Core results, similar to the treatment of other intangible assets
- The fair value of inventory acquired on completion was significantly higher than historical cost. The adjustment to increase the inventory to fair value is held in inventory until the product is sold, at which time it is released to the Income Statement in Cost of Sales. This results in a lower gross margin in the first turn of inventory and this temporary effect, which is expected over approximately 18 months post acquisition in line with revenues, will be excluded from the Group's Core results
- The fair value of replacement employee share awards is higher than both the value of the Alexion awards the employees were originally granted and the expected value of future awards to those employees. As a result, the Group will recognise an inflated expense during the remaining vesting period of these awards. This temporary increase in operating expenses, when compared with the expected expense based on the grant-date value, will be excluded from the Group's Core results
- Other acquisition-related items to be excluded from the Group's Core results include professional fees, retention bonuses included in the acquisition agreement and the effect of unwinding other acquisition-related fair value adjustments over time

Further details of these costs are included in Note 5, Acquisition of Alexion. All the amounts above are presented in the 'Acquisition of Alexion' column on the Reconciliation of Core to Reported Financial Measures, except for intangible asset amortisation, which is presented in the 'Intangible Asset Amortisation & Impairments' column.

Reference should be made to the Reconciliation of Reported to Core financial measures table included in the financial performance section in this announcement.

Total Revenue ex-pandemic vaccine is a non-GAAP financial measure introduced in the first quarter of 2021 to enable management to explain the financial impact of the pandemic COVID-19 vaccine on the Group's Total Revenue.

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 in this announcement.

Net Debt is defined as Interest-bearing loans and borrowings and Lease liabilities, 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 Interim Financial Statements in this announcement.

Ongoing Collaboration Revenue is defined as Collaboration Revenue excluding Initial Collaboration Revenue (which is defined as Collaboration Revenue that is recognised at the date of completion of an agreement or transaction, in respect of upfront consideration). Ongoing Collaboration Revenue comprises, among other items, royalties, milestone revenue and profit-sharing income. Reference should be made to the Collaboration 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 dollar values and percentages may not agree to totals.

Total Revenue

The performance of the Company's medicines is shown below, with more details available from Note 8.

Table 6: Total Revenue by disease area

	YTD 2021				Q3 2021			
	$m	% of total	Actual % change	CER % Change	$m	% of total	Actual % change	CER % change
Oncology	9,744	38	19	16	3,383	34	18	17
CVRM	6,028	24	14	10	2,086	21	16	13
R&I	4,456	18	16	12	1,486	15	28	25
Rare Disease[16]	1,311	5	n/m	n/m	1,311	13	*5*	*6*
Other medicines	1,648	6	(13)	(16)	550	6	(27)	(28)
COVID-19	2,219	9	n/m	n/m	1,050	11	n/m	n/m
Total Revenue	**25,406**	**100**	**32**	**28**	**9,866**	**100**	**50**	**48**
- Less pandemic COVID-19 vaccine	2,219	9	n/m	n/m	1,050	11	n/m	n/m
Total Revenue ex-pandemic vaccine	23,187	91	21	17	8,816	89	34	32

Table 7: Disease area and medicine performance

	YTD 2021				Q3 2021			
	$m	% of total	Actual % change	CER % change	$m	% of total	Actual % change	CER % change
Oncology	**9,593**	**38**	**21**	**17**	**3,326**	**34**	**18**	**16**
- *Tagrisso*	3,701	15	17	13	1,247	13	8	7
- *Imfinzi*	1,778	7	20	17	618	6	16	15
- *Lynparza*	1,719	7	34	31	588	6	27	25
- *Calquence*	843	3	n/m	n/m	354	4	n/m	n/m
- *Koselugo*	74	-	n/m	n/m	26	-	n/m	n/m
- *Enhertu*	10	-	n/m	n/m	5	-	n/m	n/m
- *Orpathys*	10	-	n/m	n/m	10	-	n/m	n/m
- *Zoladex*	716	3	7	1	250	3	9	5
- *Faslodex*	329	1	(27)	(29)	103	1	(26)	(27)
- *Iressa*	149	1	(26)	(31)	41	-	(23)	(29)
- *Casodex*	120	-	(9)	(15)	38	-	(13)	(18)
- *Arimidex*	106	-	(29)	(31)	33	-	(20)	(20)
- Others	38	-	-	(2)	13	-	2	1
BioPharmaceuticals: CVRM	**6,017**	**24**	**15**	**10**	**2,082**	**21**	**16**	**13**
- *Farxiga*	2,152	8	57	51	796	8	51	48
- *Brilinta*	1,124	4	(9)	(11)	375	4	(3)	(4)
- *Bydureon*	293	1	(10)	(11)	95	1	(13)	(13)
- *Onglyza*	284	1	(22)	(25)	84	1	(23)	(25)
- *Byetta*	45	-	(10)	(10)	13	-	(11)	(6)
- Other diabetes	43	-	24	20	14	-	24	26
- roxadustat	144	1	n/m	n/m	55	1	n/m	n/m
- *Lokelma*	122	-	n/m	n/m	49	-	n/m	n/m
- *Crestor*	837	3	(5)	(9)	298	3	(1)	(4)
- *Seloken/Toprol-XL*	749	3	21	14	234	2	4	(2)
- *Atacand*	76	-	(58)	(58)	19	-	(65)	(65)
- Others	148	1	2	(3)	50	1	29	23

BioPharmaceuticals: R&I	**4,444**	**17**	**16**	**12**	**1,483**	**15**	**28**	**25**
- *Symbicort*	2,047	8	-	(3)	676	7	13	11
- *Fasenra*	901	4	35	32	322	3	34	33
- *Pulmicort*	714	3	14	7	217	2	44	36
- *Daliresp*	168	1	3	3	54	1	(5)	(6)
- *Breztri*	130	1	n/m	n/m	47	-	n/m	n/m
- *Bevespi*	39	-	8	7	13	-	(9)	(10)
- *Saphnelo*	1	-	n/m	n/m	1	-	n/m	n/m
- Others	444	2	62	53	153	2	70	64
Rare Disease[16]	**1,311**	**5**	**n/m**	**n/m**	**1,311**	**13**	***5***	***6***
- *Soliris*[16]	798	3	n/m	n/m	798	8	*(3)*	*(2)*
- *Ultomiris*[16]	297	1	n/m	n/m	297	3	*31*	*31*
- *Strensiq*[16]	159	1	n/m	n/m	159	2	*7*	*8*
- *Andexxa*[16]	29	-	n/m	n/m	29	-	*(6)*	*(5)*
- *Kanuma*[16]	28	-	n/m	n/m	28	-	*26*	*26*
Other medicines	**1,542**	**6**	**(17)**	**(19)**	**539**	**5**	**(27)**	**(27)**
- *Nexium*	999	4	(10)	(13)	259	3	(35)	(36)
- *Synagis*	170	1	(42)	(41)	122	1	3	5
- *Losec/Prilosec*	138	1	(4)	(10)	38	-	(16)	(21)
- *FluMist*	75	-	(35)	(37)	72	1	(37)	(39)
- *Seroquel XR*/IR	74	-	(25)	(24)	24	-	(32)	(30)
- Others	86	-	(2)	(6)	24	-	23	20
COVID-19	**2,136**	**8**	**n/m**	**n/m**	**1,000**	**10**	**n/m**	**n/m**
Pandemic COVID-19 vaccine	2,136	8	n/m	n/m	1,000	10	n/m	n/m
Product Sales	**25,043**	**99**	**33**	**29**	**9,741**	**99**	**49**	**47**
Collaboration Revenue	**363**	**1**	**10**	**10**	**125**	**1**	**n/m**	**n/m**
Total Revenue	**25,406**	**100**	**32**	**28**	**9,866**	**100**	**50**	**48**
Total Revenue ex-pandemic vaccine	23,187	91	21	17	8,816	89	34	32

Table 8: Collaboration Revenue

	YTD 2021				Q3 2021			
	$m	**% of total**	**Actual % change**	**CER % change**	**$m**	**% of total**	**Actual % change**	**CER % change**
Enhertu: share of gross profits	134	37	n/m	n/m	51	41	95	95
roxadustat: share of gross profits	4	1	(78)	(80)	1	1	(83)	(84)
Other Collaboration Revenue	225	62	(9)	(10)	73	58	n/m	n/m
Total	**363**	**100**	**10**	**10**	**125**	**100**	**n/m**	**n/m**

Other Collaboration Revenue included contributions from *Movantik*, *Zoladex*, *Eklira, Duaklir, Forxiga*, *Nexium* OTC[39] and other royalties. In addition, Other Collaboration Revenue also included $80m receivable from SII for the pandemic COVID-19 vaccine; an equivalent charge has been included within Other Operating Income and Expense in relation to consequent obligations under the license agreement with Oxford University Innovation (OUI). Initial Collaboration Revenue of $75m was recorded in the year to date following the agreement to out-license the authorised generic rights to *Nexium* in Japan.

[39] Over the counter.

Total Revenue summary

Oncology

Total Revenue of $9,744m in the year to date; an increase of 19% (16% at CER). Oncology represented 38% of overall Total Revenue (YTD 2020: 43%).

Tagrisso

Tagrisso has received regulatory approval in 64 countries, including the US, China, and in the EU, for use as an adjuvant treatment of EGFRm NSCLC patients, with 13 reimbursements granted so far. This expands upon the patient benefit from use in the 1st-line treatment of patients with EGFRm NSCLC with regulatory approval in 91 countries, including the US, China, in the EU and Japan. To date, 47 reimbursements have been granted in this setting, with further decisions anticipated. These developments followed *Tagrisso*'s regulatory approval in 91 countries, including the US, China, in the EU and Japan, to treat patients with EGFR T790M[40] NSCLC, an indication in which 67 reimbursements have been granted.

Total Revenue, entirely comprising Product Sales, amounted to $3,701m in the year to date and represented growth of 17% (13% at CER). Sales in Q3 increased 8% (7% at CER) to $1,247m.

Sales in the US increased by 13% in the year to date to $1,294m and increased 5% to $441m in Q3. Performance in Q3 was impacted by the cumulative effect of lower levels of lung cancer diagnosis and biomarker testing during the COVID-19 pandemic. This was partially offset by increased use of *Tagrisso* for the adjuvant treatment of Stage IB to IIIA EGFRm NSCLC patients following the US Food and Drug Administration (FDA) approval in 2020. Current levels of diagnosis, biomarker testing and treatment of NSCLC continue to improve, but remain below pre-COVID levels.

Tagrisso sales in Emerging Markets increased by 6% in the year to date (1% at CER) to $1,012m; the performance was impacted by the admission of the medicine to the China NRDL in March 2021 for the 1st-line setting and the renewal in the 2nd-line setting. During the year to date, additional demand from increased patient access in China has not yet completely offset the NRDL price reduction which came into effect in March 2021. Emerging Markets sales of $315m in Q3 represented a decline of 11% (15% at CER) driven by lower sales in China, partially offset by growth in ex-China Emerging Markets. In Q3 2021, sales in China were lower than the prior quarter, with the phasing of inventory movements around the aforementioned NRDL changes more than offsetting the continued benefit of volume increases from expansion into 1st-line treatment. Sales in Japan increased by 9% (8% at CER) to $568m in the year to date. In Europe, sales of $727m in the year to date represented an increase of 45% (35% at CER), driven by greater adoption in the 1st-line setting, as more reimbursements were granted.

Imfinzi

Imfinzi has received regulatory approval in 74 countries, including the US, China, in the EU, and Japan, with 35 reimbursements granted, to treat patients with unresectable Stage III NSCLC, whose disease has not progressed following platinum-based CRT[41]. *Imfinzi* has also been approved to treat ES-SCLC[42] patients in 63 countries, with nine reimbursements granted.

Total Revenue, entirely comprising Product Sales, amounted to $1,778m in the year to date and represented growth of 20% (17% at CER); the performance reflected the increased use of *Imfinzi* to treat patients with ES-SCLC. US sales increased by 3% to $916m, despite the continued COVID-19 related decrease in lung cancer diagnoses. In Japan, growth of 34% (33% at CER) represented sales of $257m. Europe sales increased by 37% (27% at CER) to $347m, reflecting a growing number of reimbursements in the region. Sales in Emerging Markets increased to $211m, representing a growth of 87% (77% at CER) following recent regulatory approvals and launches, including in China.

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

[41] Chemoradiation therapy.

[42] Extensive stage non-small cell lung cancer.

Lynparza

Lynparza has received regulatory approval in 86 countries for the treatment of ovarian cancer; it has also been approved in 84 countries for the treatment of metastatic breast cancer, and in 68 countries for the treatment of pancreatic cancer. *Lynparza* has received regulatory approval in 70 countries for the 2nd-line treatment of certain prostate-cancer patients.

Total Revenue, entirely comprising Product Sales in the year to date, amounted to $1,719m, reflecting growth of 21% (18% at CER) benefiting from further launches across multiple cancer types globally. US Product Sales increased by 26% to $793m, predominantly due to growth in 2nd-line HRRm mCRPC and 1st-line HRD+[43] ovarian cancer. *Lynparza* is the leading medicine in the PARP[44] inhibitor class globally across four tumour types, as measured by total prescription volumes. Product Sales in Europe increased by 47% (36% at CER) to $456m, reflecting additional reimbursements and increasing BRCAm-testing rates, as well as successful 1st-line BRCAm ovarian and 2nd-line HRRm[45] prostate cancer launches.

Sales in Japan amounted to $145m, representing growth of 22%. Emerging Markets Product Sales were $282m, up by 44% (40% at CER); in Q3 sales increased 28% (23% at CER) to $96m. In China, *Lynparza* was admitted to the NRDL as a 1st-line treatment for BRCAm[46] ovarian cancer patients with effect from March 2021.

Enhertu

Total Revenue, predominately comprising Collaboration Revenue, increased by 134% in the year to date to $147m. Global in-market sales, excluding Japan, amounted to $293m in the year to date. In Japan, AstraZeneca receives a mid-single-digit percentage royalty on sales made by Daiichi Sankyo Company Limited (Daiichi Sankyo). US in-market sales, recorded by Daiichi Sankyo, amounted to $253m in the year to date and $92m in the quarter.

Calquence

Calquence has received regulatory approvals for the treatment patients with CLL in 70 countries and in 34 countries for the treatment of patients with R/R mantle cell lymphoma with reimbursement obtained in 20 and 13 countries, respectively.

Total Revenue, entirely comprising Product Sales, amounted to $843m in the year to date and represented growth of 148% (146% at CER). US sales increased by 124% in the year to date to $752m, representing the majority of sales, with the performance benefitting from increased market share. In Europe, Product Sales of $69m (YTD 2020: $nil) reflected the ongoing launch of the medicine.

Koselugo

Total Revenue, predominately comprising Product Sales in the US, amounted to $74m (YTD 2020: $20m) in the year to date, following its launch in the second quarter of 2020 to treat the rare disease NF1[47] in paediatric patients aged two years and older who have symptomatic, inoperable plexiform neurofibromas.

Orpathys

In June 2021, AstraZeneca and HUTCHMED's *Orpathys* was granted conditional approval in China to treat patients with NSCLC with MET exon 14 skipping[48] alterations that have progressed following prior systemic therapy or are unable to receive chemotherapy. Total Revenue entirely comprising Product Sales was $10m (YTD 2020: $nil).

Zoladex

Total Revenue, predominantly comprising Product Sales, amounted to $729m in the year to date and represented an increase of 2% (a decline of 3% at CER).

Emerging Markets sales of *Zoladex* increased by 9% (3% at CER) to $465m. Sales in Europe increased by 7% (declined by 1% at CER) to $112m while, in the Established RoW region, sales declined by 5% (8% at CER) to $128m.

[43] Homologous recombination.

[44] Poly ADP ribose polymerase.

[45] Homologous recombination repair gene mutation.

[46] A breast cancer gene mutation.

[47] Neurofibromatosis type 1.

[48] A targetable gene alteration found in NSCLC.

Faslodex

Total Revenue, entirely comprising Product Sales, amounted to $329m in the year to date and represented a decline of 27% (29% at CER) due to increasing competition from several generic versions of the medicine.

Emerging Markets sales decreased by 14% (17% at CER) to $122m, while US sales declined by 47% to $24m; in Europe, sales fell by 45% (49% at CER) to $93m. In Japan, sales increased 2% (1% at CER) to $87m.

Iressa

Total Revenue, entirely comprising Product Sales, amounted to $149m in the year to date and represented a decline of 26% (31% at CER). Emerging Markets sales fell by 25% (30% at CER) to $122m.

BioPharmaceuticals: CVRM

Total Revenue increased by 14% in the year to date (10% at CER) to $6,028m and represented 24% of Total Revenue (YTD 2020: 27%), reflecting the strong performance of *Farxiga* in the period.

Farxiga

Total Revenue, predominantly comprising Product Sales, amounted to $2,156m in the year to date and represented growth of 57% (51% at CER). The performance of *Farxiga* benefitted from growth in the SGLT2[49] inhibitor class in many regions, with volume share increasing faster than the overall market in most major regions.

Emerging Markets sales increased by 80% (74% at CER) to $877m in the year to date, still benefitting from the addition of *Forxiga* to the China NRDL in 2020. The initial price impact has been more than offset by increased access for patients. *Forxiga*'s NRDL status is due for renegotiation in the fourth quarter of 2021.

In the US, sales increased by 31% in the year to date to $504m, reflecting the benefit of the regulatory approval in May 2020 for HFrEF and more recently the approval for the treatment of CKD which was obtained in May 2021. Both approvals include patients with and without T2D[50].

Sales in Europe increased by 61% (50% at CER) to $584m in the year to date. The performance reflected SGLT2 inhibitor class growth, the beneficial addition of CV outcomes trial data to the label, the HFrEF regulatory approval in November 2020, and CKD approval in August 2021. In Japan, sales to collaborator Ono Pharmaceutical Co., Ltd, which records in-market sales, increased by 40% (39% at CER) to $108m.

Brilinta

Total Revenue, entirely comprising Product Sales, amounted to $1,124m in the year to date, representing a decrease of 9% (11% at CER). Emerging Markets sales declined by 35% (37% at CER) to $256m, reflecting the implementation of China's VBP programme, resulting in significantly lower market access for the medicine, and a mandatory price cut. In the US, sales increased by 4% to $558m partly reflecting the recent launch of *Brilinta* as a treatment to reduce the risk of stroke in patients following an acute ischaemic stroke or high-risk transient ischaemic attack. Sales of *Brilique* in Europe increased by 2% (declined by 5% at CER) to $263m. The overall performance in the year to date continued to be adversely impacted by fewer elective procedures due to the effects of COVID-19.

Onglyza

Total Revenue, entirely comprising Product Sales, amounted to $284m in the year to date and represented a decline of 22% (25% at CER). Sales in Emerging Markets decreased by 2% (6% at CER) to $151m. US sales of *Onglyza* fell by 53% in the year to $62m as the DPP-4[51] inhibitor class continues to decline, whereas in Europe sales increased by 10% (2% at CER) to $47m.

[49] Sodium-glucose co-transporter-2.

[50] Type-2 diabetes.

[51] An enzyme that destroys the hormone incretin.

Bydureon

Total Revenue, entirely comprising Product Sales, amounted to $293m in the year to date, representing a decline of 10% (11% at CER). US sales decreased by 12% in the year to date to $243m following the withdrawal of the dual-chamber pen and lower demand for the *Bydureon BCise* auto-injector device. Sales in Europe increased by 12% (4% at CER) to $43m; the performance reflected the growth of the overall glucagon-like peptide-1 receptor class.

Lokelma

Total Revenue, entirely comprising Product Sales, amounted to $122m in the year to date, representing an increase of 153% (151% at CER). Sales in the US increased by 119% to $82m, reflecting the growth in the potassium binder class. *Lokelma* continued to be the branded market share leader.

Sales in Japan increased to $28m in the year to date (YTD 2020: $5m) despite Ryotanki, a regulation that restricts prescriptions to two weeks' supply in the first year of launch. The restriction lifted in June 2021 and no longer applies. During the period, expansion in Europe continued with launches in several new markets; sales amounted to $8m (YTD 2020: $3m).

Roxadustat

Total Revenue in China, predominantly comprising Product Sales, amounted to $148m in the year to date (YTD 2020: $19m). From January 2021, AstraZeneca started recognising the overwhelming majority of China revenue as Product Sales following an amendment in July 2020 to the existing licence agreement with FibroGen, Inc. (FibroGen).

Crestor

Total Revenue, primarily comprising Product Sales, amounted to $838m in the year to date and represented a decline of 5% (9% at CER).

In Emerging Markets, sales increased by 7% (2% at CER) to $597m, despite the adverse impact of China's VBP programme. US sales declined by 17% to $59m, whereas in Europe, revenue decreased by 54% (57% at CER) in the year to date to $45m following the February 2021 divestment of European rights in more than 30 countries to Grünenthal GmbH (Grünenthal). In Japan, where AstraZeneca collaborates with Shionogi Co., Ltd, sales declined by 10% to $109m.

BioPharmaceuticals: Respiratory & Immunology

Total Revenue, which included Ongoing Collaboration Revenue of $12m from *Duaklir*, *Eklira* and other medicines, increased by 16% in the year to date (12% at CER) to $4,456m and represented 18% of Total Revenue (YTD 2020: 20%). Due to the adverse effect of COVID-19 on *Pulmicort* sales in the first nine months of 2020, the year-on-year comparison was favourably impacted.

Symbicort

Total Revenue, entirely comprising Product Sales, was stable at $2,047m in the year to date (a decline of 3% at CER). *Symbicort* remains the global market-volume and value leader within the ICS[52] / LABA[53] class. Growth in the global ICS/LABA class has been limited, due to the continued impact of COVID-19 on the prevalence and diagnosis rates of respiratory diseases, lower levels of respiratory symptoms, and reduced use of medicines.

In the US, sales increased by 6% in the year to date to $804m. The positive performance benefitted from early signs of a recovery in the ICS/LABA market and a stable market share, offset by managed markets.

Emerging Markets sales increased by 8% (4% at CER) to $457m, following several additional approvals of *Symbicort* as a medicine to treat patients with asthma on an as-needed basis, and despite COVID-19 related pressures on class growth. In Europe, sales decreased by 4% (11% at CER) in the year to date to $499m. Sales in Japan declined by 34% (35% at CER) to $95m in the year to date due to the ongoing adverse impact of generic competition and a contracting ICS/LABA market.

[52] Inhaled corticosteroid.

[53] Long-acting beta-agonist.

Pulmicort

Total Revenue, entirely comprising Product Sales, amounted to $714m in the year to date and represented an increase of 14% (7% at CER).

Emerging Markets, where *Pulmicort* sales increased by 20% (13% at CER) in the year to date to $578m, represented 81% of the global total. *Pulmicort* was included in the latest round of VBP announced in June 2021, which will result in significantly lower market access and a mandatory price reduction for the medicine in future periods. Implementation of the programme for *Pulmicort*, began after the end of Q3 2021, in October 2021.

Sales in the US decreased by 1% in the year to date to $53m due to managed markets. Europe sales decreased by 10% (17% at CER) to $49m. In Japan, sales decreased by 25% in the year to date to $17m following increasing generic competition.

Fasenra

Total Revenue, entirely comprising Product Sales, increased by 35% (32% at CER) in the year to date to $901m. Sales in the US increased by 31% in the year to date to $555m due to a partial recovery of the severe asthma biologic market. In Europe, sales increased by 51% (40% at CER) in the year to date to $211m; the performance primarily due to growth in new patient starts. Sales in Emerging Markets increased 55% (52% at CER) to $15m.

Daliresp

Total Revenue, entirely comprising Product Sales, amounted to $168m in the year to date and represented an increase of 3%. US sales increased by 9% to $153m.

Breztri

Breztri has received regulatory approval in 36 countries, including the US, in the EU, China, and Japan, to treat patients with COPD; further regulatory reviews are ongoing. *Breztri* has achieved reimbursement in 14 countries.

Total Revenue, entirely comprising Product Sales, amounted to $130m in the year to date (YTD 2020: $21m). Sales in the US amounted to $68m (YTD 2020: $3m), following encouraging market share growth in the fixed-dose triple market. Emerging Markets sales amounted to $40m in the year to date (YTD 2020: $14m), with the performance benefitting from inclusion of the medicine into China's NRDL in March 2021, which has significantly increased the number of patients with access to *Breztri* in China. Sales in Japan amounted to $17m (YTD 2020: $4m). In Europe, under the name *Trixeo*, sales amounted to $4m in the year to date (YTD 2020: $nil).

Saphnelo (anifrolumab)

Saphnelo has received regulatory approval in the US and Japan to treat SLE; further regulatory reviews are ongoing.

Total Revenue, entirely comprising Product Sales in the US, amounted to $1m in the year to date.

Rare Disease

Total Revenue recorded post-acquisition from 21 July 2021, entirely comprising Product Sales, amounted to $1,311m representing a pro rata increase of 5% (6% at CER) in Q3 2021. Pro forma pro rata growth rates on Rare Disease medicines for Q3 2021 have been calculated by comparing post-acquisition revenues from 21 July 2021 with the corresponding prior year pre-acquisition Q3 revenues previously published by Alexion, adjusted pro rata to match the post-acquisition period.

Soliris

Total Revenue amounted to $798m. This represented a pro rata decline on a pro forma basis of 3% (2% at CER) in Q3 2021.

In the US, Total Revenue amounted to $460m, representing a pro forma pro rata increase of 4% in Q3 2021. Sales benefitted from growing use in neurology indications, including gMG and NMOSD, offset by patient conversion to *Ultomiris* in PNH and aHUS.

Outside the US, Total Revenue amounted to $338m. Performance during the period was driven by underlying growth in neurology indications, gMG and NMOSD, and impacted by the successful conversion to *Ultomiris,* which offers patients a lower average annual treatment cost, and a more convenient dosing schedule with every eight week dosing versus *Soliris's* every two week regimen.

Ultomiris

Total Revenue amounted to $297m, representing a pro rata increase of 31% in Q3 2021. In the US, Total Revenue amounted to $167m, representing a pro rata increase of 25% in Q3 2021. Outside the US, Total Revenue amounted to $130m. Performance was driven by strong conversion from *Soliris* in PNH and aHUS, as well as new country launches in the quarter. Quarter on quarter variability can be expected due to the every eight week dosing schedule.

Strensiq

Total Revenue amounted to $159m, representing a pro forma pro rata increase of 7% (8% at CER) in Q3 2021.

In the US, Total Revenue amounted $124m, representing pro forma pro rata growth of 6%. This was driven by underlying volume gains, partly offset by a one-time true-up payment.

Other medicines (outside the main disease areas)

Total Revenue, primarily comprising Product Sales, amounted to $1,648m in the year to date, a decrease of 13% (16% at CER). This does not include revenue from the COVID-19 vaccine, which is covered in the COVID-19 commentary. Other medicines Total Revenue represented 6% of overall Total Revenue (YTD 2020: 10%).

Nexium

Total Revenue, predominantly comprising Product Sales, declined by 4% (7% at CER) in the year to date to $1,091m. Revenue in Emerging Markets increased by 3% (declined 1% at CER) in the year to date to $576m, reflecting the impact of the inclusion of *Nexium* (oral) in China's VBP programme in February 2021 resulting in significantly lower market access and a mandatory price reduction. *Nexium* (i.v.) was included in the fifth round of VBP with implementation occurring after the end of Q3 2021, in October.

In Japan, where AstraZeneca collaborates with Daiichi Sankyo, Total Revenue declined by 5% (6% at CER) in the year to date to $306m. In Q3 2021, Total Revenue in Japan declined 63% (62% at CER) to $44m reflecting phasing of orders from Daiichi Sankyo ahead of the previously announced conclusion of the joint sales promotion by the two companies. From 15 September 2021, AstraZeneca was solely responsible for marketing, distributing, and promoting *Nexium* in Japan. Total Revenue in the US declined by 19% to $115m, and in Europe, it decreased by 24% (30% at CER) to $47m.

Synagis

Total Revenue, entirely comprising Product Sales, decreased by 42% (41% at CER) in the year to date to $170m. Sales in the quarter increased by 3% (5% at CER) to $122m.

Sales in Europe declined by 67% in the year to date to $81m. This performance reflected the phasing of orders from AbbVie Inc. (AbbVie) prior to the expiry of the ex-US commercial rights agreement between AstraZeneca and AbbVie on 30 June 2021 and changes as a result of the reversion of ex-US rights to AstraZeneca thereafter. Prior to the expiry of the agreement on 30 June 2021, sales made to AbbVie were reported in Europe. During the quarter, AstraZeneca began recording revenues in regions that had been covered by the aforementioned agreement including in Q3, sales in Emerging Markets of $15m (Q3 2020: $nil), sales in Europe of $38m (Q3 2020: $97m) and sales in Established Rest of World of $53m (Q3 2020: $nil).

FluMist

Total Revenue, entirely comprising of Product Sales, declined 35% (37% at CER) to $75m in the year to date due to a one-off supplemental order in the US in 2020 causing an unfavourable comparison to the prior year. Sales in the US declined by 65% to $23m as a result. Sales in Europe in the year to date increased 5% (1% at CER) to $51m.

COVID-19

Pandemic COVID-19 vaccine

Total Revenue, predominantly comprised of Product Sales, amounted to $2,219m in the year to date reflecting the delivery of c. 580m doses worldwide by AstraZeneca[54]. Sales in Europe were $736m, Emerging Markets sales were $1,139m, and in Established RoW sales amounted to $344m.

Regional Total Revenue

A geographical split of Product Sales is shown in Note 8.

Table 9: Regional Total Revenue

	YTD 2021				Q3 2021		
	$m	% of total	Actual % change	CER % change	$m	Actual % change	CER % change
Emerging Markets	**8,618**	**34**	**33**	**28**	**3,159**	**48**	**42**
- China	*4,699*	*18*	*17*	*8*	*1,490*	*10*	*2*
- Ex-China	*3,919*	*15*	*60*	*60*	*1,669*	*113*	*112*
US	**8,305**	**33**	**29**	**29**	**3,471**	**53**	**53**
Europe	**5,178**	**20**	**40**	**31**	**1,918**	**52**	**49**
Established RoW	**3,305**	**13**	**28**	**24**	**1,318**	**45**	**46**
- Japan	*2,360*	*9*	*24*	*24*	*946*	*41*	*46*
- Canada	*536*	*2*	*17*	*8*	*205*	*28*	*19*
- Other Established RoW	*409*	*2*	*81*	*61*	*167*	*n/m*	*99*
Total	**25,406**	**100**	**32**	**28**	**9,866**	**50**	**48**

Table 10: Emerging Markets Total Revenue disease-area performance

	YTD 2021				Q3 2021		
	$m	% of total	Actual % change	CER % change	$m	Actual % change	CER % change
Oncology	2,438	28	9	4	812	5	-
CVRM	2,916	34	19	14	992	20	14
R&I	1,305	15	24	17	420	44	35
Rare Disease[16]	65	1	n/m	n/m	65	*(34)*	*(31)*
Other medicines	755	9	4	-	219	(9)	(12)
COVID-19	1,139	13	n/m	n/m	651	n/m	n/m
Total	**8,618**	**100**	**33**	**28**	**3,159**	**48**	**42**

[54] Total doses supplied to the end of September by AstraZeneca and its sub-licensees, including SII, amounted to 1.5bn.

Table 11: Ex-China Emerging Markets Total Revenue

	YTD 2021			Q3 2021		
	$m	Actual % change	CER % change	$m	Actual % change	CER % change
Ex-China Emerging Markets	3,919	60	60	1,669	113	112
- Russia	308	30	36	127	n/m	n/m
- Brazil	450	91	98	169	n/m	n/m
- Ex-Brazil Latin America	665	n/m	n/m	341	n/m	n/m
- Ex-China Asia Pacific	1,634	82	77	709	n/m	n/m
- Middle East and Africa	862	12	15	323	36	38

China Total Revenue comprised 55% of Emerging Markets Total Revenue (YTD 2020: 62%) and increased by 17% (8% at CER) in the year to date to $4,699m.

Ex-China Emerging Markets Total Revenue, primarily comprising Product Sales, increased by 60% in the year to date to $3,919m. Excluding the COVID-19 vaccine, Total Revenue increased by 13% (14% at CER) to $2,780m in the year to date and by 30% in the quarter to $1,019m.

Financial performance

Table 12: Reported Profit and Loss - YTD 2021

	YTD 2021 $m	YTD 2020 $m	Actual % change	CER % change
Total Revenue	**25,406**	**19,207**	**32**	**28**
- Product Sales	25,043	18,879	33	29
- Collaboration Revenue	363	328	10	10
Cost of Sales	(7,812)	(3,774)	n/m	99
Gross Profit	**17,594**	**15,433**	**14**	**11**
Gross Profit Margin	*68.8%*	*80.0%*	*-11*	*-11*
Distribution Expense	(322)	(290)	11	5
% Total Revenue	*1.3%*	*1.5%*	-	-
R&D Expense	(7,152)	(4,272)	67	63
% Total Revenue	*28.2%*	*22.2%*	*-6*	*-6*
SG&A Expense	(10,117)	(8,084)	25	21
% Total Revenue	*39.8%*	*42.1%*	*+2*	*+2*
Other Operating Income & Expense	1,345	888	51	50
% Total Revenue	*5.3%*	*4.6%*	*+1*	*+1*
Operating Profit	**1,348**	**3,675**	**(63)**	**(57)**
Operating Margin	*5.3%*	*19.1%*	*-14*	*-13*
Net Finance Expense	(922)	(905)	2	-
Joint Ventures and Associates	(55)	(21)	n/m	n/m
Profit Before Tax	**371**	**2,749**	**(86)**	**(77)**
Taxation	90	(610)	n/m	n/m
Tax Rate	-24%	22%		
Profit After Tax	**461**	**2,139**	**(78)**	**(63)**
Earnings per share	**$0.33**	**$1.66**	**(80)**	**(65)**

Table 13: Reported Profit and Loss - Q3 2021

	Q3 2021 $m	Q3 2020 $m	Actual % change	CER % change
Total Revenue	**9,866**	**6,578**	**50**	**48**
- Product Sales	9,741	6,520	49	47
- Collaboration Revenue	125	58	n/m	n/m
Cost of Sales	(3,757)	(1,370)	n/m	n/m
Gross Profit	**6,109**	**5,208**	**17**	**16**
Gross Profit Margin	*61.4%*	*79.0%*	*-18*	*-18*
Distribution Expense	(120)	(99)	21	18
% Total Revenue	*1.2%*	*1.5%*	-	-
R&D Expense	(3,610)	(1,495)	n/m	n/m
% Total Revenue	*36.6%*	*22.7%*	*-14*	*-14*
SG&A Expense	(4,090)	(2,730)	50	47
% Total Revenue	*41.5%*	*41.5%*	-	-
Other Operating Income & Expense	37	287	(87)	(87)
% Total Revenue	*0.4%*	*4.4%*	*-4*	*-4*
Operating (Loss)/Profit	**(1,674)**	**1,171**	**n/m**	**n/m**
Operating Margin	*-17.0%*	*17.8%*	*-35*	*-35*
Net Finance Expense	(320)	(317)	1	(1)
Joint Ventures and Associates	(7)	(1)	n/m	n/m
(Loss)/Profit Before Tax	**(2,001)**	**853**	**n/m**	**n/m**
Taxation	350	(202)	n/m	n/m
Tax Rate	-18%	24%		
(Loss)/Profit After Tax	**(1,651)**	**651**	**n/m**	**n/m**
(Loss)/Earnings per share	**$(1.10)**	**$0.49**	**n/m**	**n/m**

Table 14: Reconciliation of Reported Profit Before Tax to EBITDA - YTD 2021

	YTD 2021 $m	YTD 2020 $m	Actual % change	CER % change
Reported Profit Before Tax	**371**	**2,749**	**(86)**	**(77)**
Net Finance Expense	922	905	2	-
Joint Venture and Associates	55	21	n/m	n/m
Depreciation, Amortisation and Impairment	4,338	2,352	84	77
EBITDA	**5,686**	**6,027**	**(6)**	**(6)**

EBITDA of $5,686m in the year to date (YTD 2020: $6,027m) has been negatively impacted by the $1,044m (YTD 2020: $nil) unwind of inventory fair value uplift recognised on acquisition of Alexion. The unwind of inventory fair value is expected to depress EBITDA over approximately 18 months post-acquisition in line with revenues.

Table 15: Reconciliation of Reported (Loss)/Profit Before Tax to EBITDA - Q3 2021

	Q3 2021 $m	Q3 2020 $m	Actual % change	CER % change
Reported (Loss)/Profit Before Tax	**(2,001)**	**853**	**n/m**	**n/m**
Net Finance Expense	320	317	1	(1)
Joint Venture and Associates	7	1	n/m	n/m
Depreciation, Amortisation and Impairment	2,788	801	n/m	n/m
EBITDA	**1,114**	**1,972**	**(43)**	**(45)**

EBITDA of $1,114m in the quarter to date (Q3 2020: $1,972m) has been negatively impacted by the $1,044m (YTD 2020: $nil) unwind of inventory fair value uplift recognised on acquisition of Alexion. The unwind of inventory fair value is expected to depress EBITDA over approximately 18 months post-acquisition in line with revenues.

Table 16: Reconciliation of Reported to Core financial measures - YTD 2021

YTD 2021	Reported	Restructuring	Intangible Asset Amortisation & Impairments	Acquisition of Alexion[55]	Other[56]	Core[57]	Core % change	
	$m	$m	$m	$m	$m	$m	Actual	CER
Gross Profit	17,594	221	47	1,049	2	18,913	22	19
Gross Profit Margin	*68.8%*					*74.1%*	*-6*	*-6*
Distribution Expense	(322)	-	-	-	-	(322)	11	5
R&D Expense	(7,152)	155	1,395	10	1	(5,591)	34	30
SG&A Expense	(10,117)	172	1,977	166	66	(7,736)	19	14
Total Operating Expense	(17,591)	327	3,372	176	67	(13,649)	24	20
Other Operating Income & Expense	1,345	-	1	-	-	1,346	51	50
Operating Profit	1,348	548	3,420	1,225	69	6,610	21	23
Operating Margin	*5.3%*					*26.0%*	*-2*	*-1*
Net Finance Expense	(922)	-	-	-	294	(628)	9	10
Taxation	90	(93)	(697)	(242)	(55)	(997)	(2)	(1)
EPS	$0.33	$0.33	$1.99	$0.72	$0.22	$3.59	22	23

[55] In Q3 2021 following the acquisition of Alexion, a new column has been introduced to present acquisition-related non-core items, primarily unwind of fair value uplift on inventories and acquisition costs.

[56] In previous quarters a separate column had been included for items pertaining to the Diabetes Alliance between AstraZeneca and Bristol-Myers Squibb Company (BMS). From Q3 2021, this column has been removed with amounts now presented in the Intangible Asset Amortisation & Impairments and the Other column as applicable.

[57] Core financial measures are adjusted to exclude certain items. For more information on the Reported to Core financial adjustments, please refer to the introduction to the operating and financial review.

Table 17: Reconciliation of Reported to Core financial measures - Q3 2021

Q3 2021	Reported	Restructuring	Intangible Asset Amortisation & Impairments	Acquisition of Alexion[55]	Other[56]	Core[57]	Core % change	
	$m	$m	$m	$m	$m	$m	Actual	CER
Gross Profit	6,109	208	14	1,049	2	7,382	41	39
Gross Profit Margin	*61.4%*					*74.5%*	*-5*	*-5*
Distribution Expense	(120)	-	-	-	-	(120)	21	18
R&D Expense	(3,610)	123	1,324	10	1	(2,152)	48	46
SG&A Expense	(4,090)	97	1,013	124	(10)	(2,866)	32	29
Total Operating Expense	(7,820)	220	2,337	134	(9)	(5,138)	38	35
Other Operating Income & Expense	37	-	-	-	-	37	(87)	(87)
Operating (Loss)/Profit	(1,674)	428	2,351	1,183	(7)	2,281	27	28
Operating Margin	*-17.0%*					*23.1%*	*-4*	*-4*
Net Finance Expense	(320)	-	-	-	101	(219)	5	4
Taxation	350	(69)	(468)	(242)	(14)	(443)	29	31
EPS	$(1.10)	$0.24	$1.26	$0.63	$0.05	$1.08	14	15

Profit and Loss summary

a) Gross Profit

Reported Gross Profit Margin in the year to date declined eleven percentage points to 68.8%; Core Gross Profit Margin declined six percentage points in the year to date to 74.1% predominantly reflecting the equitable supply, at no profit to AstraZeneca, of the pandemic COVID-19 vaccine, together with an increasing impact from profit-sharing arrangements (primarily *Lynparza* and roxadustat) and the impact of the NRDL and VBP programmes in China. These effects were partially offset by the contribution from Alexion from 21 July 2021, a higher proportion of Oncology sales, and increasing patient access in China. Reported Gross Profit Margin has also been impacted by the unwind of the fair value adjustment to Alexion inventories at the date of acquisition. The fair value uplift is expected to unwind through Reported Cost of Sales over the 18 months post-acquisition, and in Q3 2021, the impact of the fair value uplift unwind on Cost of Sales was $1,044m. Variations in gross margin performance between periods can be expected to continue.

b) Total Operating Expense

Reported Total Operating Expense increased in the year to date by 39% (34% at CER) to $17,591m. Core Total Operating Expense increased by 24% (20% at CER) to $13,649m and represented 54% of Total Revenue (YTD 2020: 57%).

Reported R&D Expense increased in the year to date by 67% (63% at CER) to $7,152m including an impairment charge of $1,172m recognised in the quarter on an intangible asset related to the acquisition of Ardea Biosciences, Inc. in 2012, following the decision to discontinue the development of verinurad. Core R&D Expense increased in the year to date by 34% (30% at CER) to $5,591m with increases in both Reported and Core R&D Expense reflecting the Company's continued investment in its COVID-19 vaccine and AZD7442, and other costs related to COVID-19, such as personal protective equipment and colleague COVID-19 testing across the Company. The increases also reflected the investment in several late-stage Oncology trials and the advancement of a number of Phase II clinical development programmes in BioPharmaceuticals, mainly in CVRM. In the year to date, grant income of $451m has been recognised, of which $281m has been offset against the US clinical trial costs for AZD1222 and $170m offset against costs for AZD7442.

Reported SG&A Expense increased in the year to date by 25% (21% at CER) to $10,117m including the increased amortisation of intangible assets related to the Alexion acquisition. Core SG&A Expense increased by 19% (14% at CER) to $7,736m, reflecting the investment in Oncology-medicine launches, the launch of several new BioPharmaceuticals medicines, particularly in the US, AstraZeneca's further expansion in Emerging Markets, and the existing infrastructure base in China.

Restructuring charges primarily comprise supply chain restructuring charges, exit costs for de-prioritised R&D projects, and severance payments.

c) Other Operating Income and Expense

Reported and Core Other Operating Income and Expense increased in the year to date by 51% (50% at CER) to $1,345m and $1,346m respectively, and included:

- Income from the divestment of AstraZeneca's 26.7% share of Viela as part of the acquisition by Horizon Therapeutics plc. AstraZeneca received cash proceeds and profit of $776m upon closing with the profit being recorded as other operating income
- $309m of income from an agreement with Grünenthal to divest commercial rights to *Crestor* in over 30 countries in Europe, except in the UK and Spain

d) Net Finance Expense

Reported Net Finance Expense increased in the year to date by 2% (stable at CER) to $922m, principally reflecting lower interest income on cash and cash equivalents driven by lower interest rates, financing costs related to the facilities and debt for the Alexion transaction, partly offset by lower discount unwind costs on acquisition-related liabilities, including the Diabetes Alliance. Core Net Finance Expense increased in the year to date by 9% (10% at CER) to $628m and was principally driven by the aforementioned lower interest income and Alexion-related financing costs.

e) Taxation

The Reported Tax Rate for the year to date was -24% (YTD 2020: 22%), and the Core Tax Rate was 17% (YTD 2020: 21%). These tax rates benefitted from the following one-off favourable impacts which arose in prior quarters:

- A non-taxable gain on the divestment of the investment in Viela Bio, Inc. (Viela); and
- A reduction of tax liabilities arising from updates to estimates of prior period tax liabilities following settlements with tax authorities partially offset by a tax charge on recalculation of UK deferred tax balances following substantive enactment of the UK Corporation Tax rate increase

Excluding these net benefits, the Core Tax Rate would have been approximately 21%. The Reported tax rate for the year to date has been impacted by the above and the level of Reported Profit Before Tax.

The net cash tax paid in the year to date was $1,198m (YTD 2020: $1,221m).

f) EPS

Reported EPS in the year to date declined 80% (65% at CER) to $0.33. Core EPS increased by 22% (23% at CER) to $3.59. Reported and Core EPS were adversely affected by $0.03 due to the pandemic COVID-19 vaccine.

Table 18: Cash Flow Summary

	YTD 2021 $m	YTD 2020 $m	Change $m
Reported Operating Profit	1,348	3,675	(2,327)
Depreciation, Amortisation and Impairment	4,338	2,352	1,986
Decrease/(increase) in Working Capital and Short-term Provisions	2,063	(255)	2,318
Gains on Disposal of Intangible Assets	(371)	(535)	164
Gains on Disposal of Investments in Associates and Joint Ventures	(776)	-	(776)
Non-Cash and Other Movements	(337)	(498)	161
Interest Paid	(522)	(517)	(5)
Taxation Paid	(1,198)	(1,221)	23
Net Cash Inflow from Operating Activities	**4,545**	**3,001**	**1,544**
Net Cash (Outflow)/Inflow before Financing Activities	**(5,600)**	**2,578**	**(8,178)**
Net Cash Inflow from Financing Activities	**4,700**	**7**	**4,693**

The increase in Net Cash Inflow from Operating Activities of $1,544m was primarily driven by the decrease in working capital, of which $497m related to the movement in pandemic COVID-19 vaccine working capital balances within trade and other payables, trade and other receivables and inventories in the year to date, with the key movement being a $298m increase in vaccine contract liabilities to $1,914m as at 30 September 2021.

The decrease in Net Cash (Outflow)/Inflow before Financing activities of $8,178m is principally due to the Alexion acquisition, specifically the upfront payment of $13,349m, less cash and cash equivalents acquired of $4,086m, and $203m of payments upon vesting of employee share awards. This decrease is partially offset by the aforementioned improvement in Net Cash Inflow from Operating Activities.

Capital Expenditure

Capital Expenditure amounted to $768m in the year to date (YTD 2020: $598m). This included investment in the new AstraZeneca R&D centre on the Biomedical Campus in Cambridge, UK, to which a number of colleagues have begun relocation.

The Company anticipates an increase in Capital Expenditure, partly driven by an expansion in its capacity for growth across several limited-sized projects.

Table 19: Net Debt summary

	At 30 Sep 2021 $m	At 31 Dec 2020 $m	At 30 Sep 2020 $m
Cash and cash equivalents	7,067	7,832	8,072
Other investments	82	160	374
Cash and investments	**7,149**	**7,992**	**8,446**
Overdrafts and short-term borrowings	(605)	(658)	(1,216)
Lease liabilities	(962)	(681)	(666)
Current instalments of loans	(2,139)	(1,536)	(2,186)
Non-current instalments of loans	(28,206)	(17,505)	(18,271)
Interest-bearing loans and borrowings (Gross Debt)	**(31,912)**	**(20,380)**	**(22,339)**
Net derivatives	90	278	131
Net Debt	**(24,673)**	**(12,110)**	**(13,762)**

Net Debt increased by $12,563m in the nine months to $24,673m primarily due to financing the Alexion acquisition. Details of the committed undrawn bank facilities are disclosed within the going concern section of Note 1. Details in regards to the funding of the Alexion acquisition are provided within Note 5.

In July 2021, following the acquisition of Alexion, S&P Global Ratings upgraded AstraZeneca's long-term credit rating to A-. Other than this, there were no changes to the Company's solicited credit ratings during the nine months to 30 September 2021. At 30 September 2021, the Company's solicited credit ratings from S&P were A- (long term) and A-2 (short term) and from Moody's were A3 (long term) and P-2 (short term).

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. The Company's capital allocation priorities include investing in the business and pipeline, maintaining a strong, investment-grade credit rating, potential value-enhancing business development opportunities, and supporting the progressive dividend policy.

Summarised financial information for guarantee of securities of subsidiaries

AstraZeneca Finance LLC ("AstraZeneca Finance") is the issuer of 0.700% Notes due 2024, 1.200% Notes due 2026, 1.750% Notes due 2028 and 2.250% Notes due 2031 (the "AstraZeneca Finance Notes"). Each series of AstraZeneca Finance Notes has been fully and unconditionally guaranteed by AstraZeneca PLC. AstraZeneca Finance is 100% owned by AstraZeneca PLC and each of the guarantees by AstraZeneca PLC is full and unconditional and joint and several.

The AstraZeneca Finance Notes are senior unsecured obligations of AstraZeneca Finance and rank equally with all of AstraZeneca Finance's existing and future senior unsecured and unsubordinated indebtedness. The guarantee by AstraZeneca PLC of the AstraZeneca Finance Notes is the senior unsecured obligation of AstraZeneca PLC and ranks equally with all of AstraZeneca PLC's existing and future senior unsecured and unsubordinated indebtedness. Each guarantee by AstraZeneca PLC is effectively subordinated to any secured indebtedness of AstraZeneca PLC to the extent of the value of the assets securing such indebtedness. The AstraZeneca Finance Notes are structurally subordinated to indebtedness and other liabilities of the subsidiaries of AstraZeneca PLC, none of which guarantee the AstraZeneca Finance Notes.

AstraZeneca PLC manages substantially all of its operations through divisions, branches and/or investments in subsidiaries and affiliates. Accordingly, the ability of AstraZeneca PLC to service its debt and guarantee obligations is also dependent upon the earnings of its subsidiaries, affiliates, branches and divisions, whether by dividends, distributions, loans or otherwise.

Please refer to the consolidated financial statements of AstraZeneca PLC in our Annual Report on Form 20-F and reports on Form 6-K with our quarterly financial results as filed or furnished with the SEC for further financial information regarding AstraZeneca PLC and its consolidated subsidiaries. For further details, terms and conditions of the AstraZeneca Finance Notes please refer to AstraZeneca PLC's Form 6-K furnished to the SEC on 28 May 2021.

Pursuant to Rule 13-01 and Rule 3-10 of Regulation S-X under the Securities Act of 1933, as amended (the "Securities Act"), we present below the summary financial information for AstraZeneca PLC, as Guarantor, excluding its consolidated subsidiaries, and AstraZeneca Finance, as the issuer, excluding its consolidated subsidiaries. The following summary financial information of AstraZeneca PLC and AstraZeneca Finance is presented on a combined basis and transactions between the combining entities have been eliminated. Financial information for non-guarantor entities has been excluded. Intercompany balances and transactions between the obligor group and the non-obligor subsidiaries are presented on separate lines.

Table 20: Obligor group summarised Statement of Comprehensive income

	YTD 2021 $m	FY 2020 $m	YTD 2020 $m
Total revenue	-	-	-
Gross profit	-	-	-
Operating loss	(131)	(45)	(1)
Loss for the period	(553)	(663)	(463)
Transactions with subsidiaries that are not issuers or guarantors	5,731	2,637	484

Table 21: Obligor group summarised Statement of Financial position information

	At 30 Sep 2021 $m	At 31 Dec 2020 $m	At 30 Sep 2020 $m
Current assets	12	26	1
Non-current assets	-	4	-
Current liabilities	(2,347)	(1,720)	(961)
Non-current liabilities	(25,721)	(17,161)	(17,913)
Amounts due from subsidiaries that are not issuers or guarantors	12,137	7,011	6,484
Amounts due to subsidiaries that are not issuers or guarantors	(299)	(290)	(295)

Foreign exchange

The Company'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 companies' reporting currency. Foreign-exchange gains and losses on forward contracts for transactional hedging are taken to profit or loss. In addition, the Company's external dividend payments, paid principally in pounds sterling and Swedish krona, are fully hedged from announcement to payment date.

Table 22: Currency sensitivities

The Company provides the following currency-sensitivity information:

		Average Exchange Rates versus USD			Annual Impact of 5% Strengthening in Exchange Rate versus USD ($m)[58]	
Currency	**Primary Relevance**	**FY 2020[59]**	**YTD 2021[60]**	**% change**	**Product Sales**	**Core Operating Profit**
CNY	Product Sales	6.90	6.44	7	312	186
EUR	Product Sales	0.88	0.84	5	214	75
JPY	Product Sales	106.74	108.52	(2)	154	102
Other[61]					250	116
GBP	Operating Expense	0.78	0.72	7	35	(81)
SEK	Operating Expense	9.20	8.49	8	5	(59)

[58] Based on currency assumptions disclosed in the H1 2021 results announcement.

[59] Based on average daily spot rates in FY 2020.

[60] Based on average daily spot rates from 1 January 2021 to 30 September 2021.

[61] Other currencies include AUD, BRL, CAD, KRW and RUB.

Sustainability

AstraZeneca's sustainability approach has three priority areas[62], aligned with the Company's purpose and business strategy:

- Access to healthcare
- Environmental protection
- Ethics and transparency

Recent developments and progress against the Company's priorities are reported below.

The AstraZeneca Board established a Sustainability Committee to monitor the execution of the Company's sustainability strategy, oversee communication of sustainability activities with stakeholders, and provide input to the Board and other Board Committees on sustainability matters. The members of the Committee are Nazneen Rahman, Chairman of the Committee, Sheri McCoy, Andreas Rummelt and Marcus Wallenberg.

a) Access to healthcare

In the third quarter of 2021, the Company delivered approximately 67 million doses of its pandemic COVID-19 vaccine through COVAX. As of 30 September 2021, the Company and its sublicensee SII have delivered more than 145 million doses with COVAX to over 125 countries, approximately half of all COVAX supply. The majority of the doses have gone to low and middle-income countries. Globally, AstraZeneca and its sub-licensing partners have released more than 1.5 billion vaccine doses as of the 30 September 2021, for supply in over 170 countries.

AstraZeneca launched phase two of the Partnership for Health System Sustainability and Resilience (PHSSR) policy programme, expanding into 13 new countries plus a regional hub in the Central, Eastern Europe and Baltics Area (CEEBA), building on the success of the pilot phase launched in 2020. Additional information on the pilot phase and its outcomes, please see the interim report here. The PHSSR is an ambitious global-level partnership between AstraZeneca, the World Economic Forum (WEF), the London School of Economics, and others, with the aim of delivering practical solutions to make health systems more resilient and sustainable.

On 23 September 2021, the Lung Ambition Alliance (a global coalition of AstraZeneca, Guardant Health, the International Association for the Study of Lung Cancer and the Global Lung Cancer Coalition) and WEF launched a new collaboration and held an affiliated session on lung cancer at the Sustainable Development Impact Summit, which brought together high-level non-governmental organisation representatives, healthcare leaders and industry to drive multi-sector collaboration for the elimination of lung cancer as a leading cause of premature cancer death. This partnership adds significant strength and voice to the ongoing efforts of the Lung Ambition Alliance to eliminate lung cancer as a cause of death.

AstraZeneca also contributed to an event run alongside the UN General Assembly (UNGA), on the topic of Transforming Global Health Partnerships for the Sustainable Development Goals, in collaboration with the World Health Organization. The session focused on strengthening global health systems and increasing early detection and treatment for non-communicable diseases.

The Company's Healthy Heart Africa (HHA) programme expanded into the Republic of Rwanda, and is now active in eight countries in East and West Africa. Since the programme launched in 2015, HHA has conducted over 21 million blood pressure screenings, identified over four million elevated readings, activated over 900 sites and trained over 8,500 healthcare workers and volunteers.

[62] These priorities were determined through a materiality assessment conducted in 2018 with a broad range of 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 align with the United Nations Sustainable Development Goals (SDG), and, in particular, SDG three for 'Good Health'.

The Company's Young Health Programme (YHP), in collaboration with Plan International UK and various public sector bodies, reached almost 400,000 young people with health information, including a new health education module on nutrition released in partnership with UNICEF. To date, the UNICEF modules released in 2021 have reached almost two million young people. The YHP received more than 1,000 applications for its One Young World Scholarship, which strives to identify the most impactful young leaders from every country in the world, from which 15 scholars will be selected to attend a youth leadership summit in Tokyo in May 2022.

b) Environmental protection

AstraZeneca marked World Water Week from 23-27 August, including participating in a panel hosted by the Climate Disclosure Standards Board, with a case study on assessing and disclosing water risk and work done in preparation for the company's Task Force on Climate Disclosure Framework (TCFD) 2020 Report.

Aligned with Climate Week 2021 and the UNGA, AstraZeneca contributed to global dialogue at the WEF SDI Summit, by publishing a blog by Chief Executive Officer Pascal Soriot on 21 September on "Urgency, Innovation and Partnership: applying lessons from COVID-19 to tackle the climate crisis".

AstraZeneca reinforced its commitment to the 1t.org Trillion Trees Corporate Alliance, a cross-industry forest conservation and restoration coalition led by WEF, as one of 20 global companies making an initial pledge to conserve, restore and grow more than 2.5 billion trees in over 50 countries by 2030. Our AZ Forest programme recognises the strong connection between a healthy planet and healthy people, as well as the value of nature-based solutions to mitigating the negative impacts of climate change, part of our broader Ambition Zero Carbon strategy.

On 28 October 2021, the Science Based Targets initiative announced that AstraZeneca is one of the first seven companies worldwide, and the only pharmaceutical company, to have their science-based, net zero targets verified as in line with their new Net Zero Standard.

On 3 November 2021, at the 26th UN Climate Change Conference (COP26), HRH The Prince of Wales named AstraZeneca as one of the first holders of the Terra Carta Seal, in recognition of the company's efforts to lead and accelerate action for a more sustainable future. In addition, Pascal Soriot was recognised as the Champion of the new Sustainable Markets Initiative (SMI) Health System Taskforce, which was launched at COP26 with HRH The Prince of Wales and with health systems leaders, with the shared ambition to accelerate the delivery of net zero, sustainable healthcare.

On 4 November 2021, at COP26, it was announced that AstraZeneca is one of 10 leading pharmaceutical companies to be part of the Energize programme, a collaboration to encourage suppliers to purchase renewable energy at scale, in support of climate action and the decarbonisation of the pharmaceutical value chain.

c) Ethics and transparency

AstraZeneca has launched a Materiality Assessment survey inviting internal and external stakeholders to contribute to shaping the future of sustainability at the Company. The results of the Assessment will help AstraZeneca to prioritise issues where it can have the most positive impacts on patients, healthcare systems, the environment and society. The Company will use the results to update the previous Materiality Assessment carried out in 2018 and review the overall sustainability strategy and priorities.

For more details on AstraZeneca's sustainability ambition, approach and targets, please refer to the latest Sustainability Report 2020 and Sustainability Data Summary 2020. Additional information is available within AstraZeneca's analyst interactive reporting centre or alternatively at astrazeneca.com/sustainability.

Research and development

A comprehensive breakdown of AstraZeneca's pipeline of medicines in human trials can be found in the latest clinical-trials appendix, available on astrazeneca.com/investor-relations.html. Highlights of the Company's late-stage pipeline development since the prior results announcement are discussed below.

Table 23: Late-stage pipeline

New molecular entities and major lifecycle events for medicines in Phase III trials or under regulatory review	28	**Oncology** - *Tagrisso* – NSCLC - *Imfinzi* – multiple cancers - *Lynparza* – multiple cancers - *Enhertu* – multiple cancers - *Calquence* – blood cancers - *Orpathys* – NSCLC - tremelimumab – multiple cancers - capivasertib – breast, prostate cancer - monalizumab – head & neck cancer - camizestrant – breast cancer - datopotamab deruxtecan – lung cancer **CVRM** - *Farxiga* – multiple indications - roxadustat – anaemia in MDS - *Lokelma* – hyperkalaemia in CKD **Respiratory & Immunology** - *Fasenra* – multiple indications - *Breztri* – asthma - tezepelumab – multiple indications - PT027 – asthma - *Saphnelo* (anifrolumab) – SLE - brazikumab – inflammatory bowel disease **Rare Disease** - *Ultomiris* – multiple indications - ALXN1840 – Wilson disease - CAEL-101 – AL amyloidosis - acoramidis (ALXN2060) – ATTR-CM - danicopan (ALXN2040) – PNH with EVH **Other** - nirsevimab - RSV **COVID-19** - *Vaxzevria* - AZD7442
Total projects in clinical development	159	
Total projects in total pipeline	175	

Oncology

In September 2021, AstraZeneca presented new data across its diverse portfolio of cancer medicines at the International Association for the Study of Lung Cancer (IASLC) 2021 World Conference on Lung Cancer (WCLC) and the 2021 European Society for Medical Oncology (ESMO) Congress. Fourteen approved and potential new medicines were featured across more than 100 abstracts at the two meetings. Across both WCLC and ESMO, AstraZeneca medicines featured in 25 oral presentations including a Presidential Symposium at each congress.

Tagrisso

Table 24: Key *Tagrisso* Phase III trials

Trial (population)	Design	Timeline	Status
NeoADAURA (neo-adjuvant EGFRm NSCLC)	Placebo or *Tagrisso*	FPCD[63]: Q1 2021 First data anticipated: 2022+	Recruitment ongoing
ADAURA (adjuvant EGFRm NSCLC)	Placebo or *Tagrisso*	FPCD: Q4 2015 LPCD[64]: Q1 2019	Trial unblinded early due to overwhelming efficacy Regulatory approval (US, EU, CN)
LAURA (locally advanced, unresectable EGFRm NSCLC)	Placebo or *Tagrisso*	FPCD: Q4 2018 First data anticipated: 2022+	Recruitment ongoing
FLAURA2 (EGFRm NSCLC, 1st-line)	*Tagrisso* or *Tagrisso* + platinum-based chemotherapy doublet	FPCD: Q4 2019 First data anticipated: 2022+	Recruitment ongoing

Imfinzi

At WCLC 2021, positive results from the POSEIDON Phase III trial were presented during a Presidential Symposium. *Imfinzi* plus tremelimumab demonstrated statistically significant and clinically meaningful improvement in OS[65] and PFS[66] compared to chemotherapy alone in the 1st-line treatment of patients with Stage IV (metastatic) NSCLC. Patients treated with tremelimumab in addition to *Imfinzi* and chemotherapy experienced a 23% reduction in the risk of death versus a range of chemotherapy options (HR[67] 0.77; 95% CI[68] 0.65-0.92; p=0.00304) with a median OS of 14.0 months versus 11.7 months. An estimated 33% of patients were alive at two years versus 22% for chemotherapy. The combination also reduced the risk of disease progression or death by 28% compared to chemotherapy alone (HR 0.72; 95% CI 0.60-0.86; p=0.00031) with a median PFS of 6.2 months versus 4.8 months, respectively.

At ESMO 2021, positive results from the COAST Phase II trial were presented. Oleclumab, an anti-CD73 monoclonal antibody, or monalizumab, an anti-NKG2A monoclonal antibody, in combination with *Imfinzi* improved PFS and ORR[69] compared to *Imfinzi* alone in patients with unresectable, Stage III NSCLC who had not progressed after cCRT[70]. After a median follow-up of 11.5 months, *Imfinzi* plus oleclumab reduced the risk of disease progression or death by 56% (HR of 0.44; 95% CI 0.26-0.75), and *Imfinzi* in combination with monalizumab by 35% (HR of 0.65; 95% CI 0.49-0.85), when compared to *Imfinzi* alone. The 10-month PFS rate was 64.8% for *Imfinzi* plus oleclumab and 72.7% for *Imfinzi* plus monalizumab, versus 39.2% with *Imfinzi* alone.

[63] First patient commenced dosing.
[64] Last patient commenced dosing.
[65] Overall survival.
[66] Progression-free survival.
[67] Hazard ratio.
[68] Confidence interval.
[69] Objective Response Rate.
[70] Concurrent chemoradiation therapy.

During the period, AstraZeneca announced the HIMALAYA Phase III trial for *Imfinzi* plus tremelimumab in 1st-line treatment of unresectable hepatocellular carcinoma, the most common type of liver cancer, had met its primary endpoint. A single, high priming dose of tremelimumab added to *Imfinzi* demonstrated a statistically significant and clinically meaningful OS benefit versus sorafenib as a 1st-line treatment for patients not eligible for localised treatment. This novel dose and schedule of tremelimumab, an anti-CTLA4 antibody, and *Imfinzi* is called the STRIDE regimen (Single Tremelimumab Regular Interval Durvalumab). The combination demonstrated a favourable safety profile, and the addition of tremelimumab to *Imfinzi* did not increase severe hepatic toxicity.

During the period, AstraZeneca announced that the TOPAZ-1 Phase III trial evaluating the use of *Imfinzi* in combination with standard of care chemotherapy in 1st-line advanced biliary tract cancer, had met its primary endpoint. At a predefined interim analysis, the Independent Data Monitoring Committee concluded that the trial met the primary endpoint by demonstrating an improvement in overall survival in patients treated with *Imfinzi* plus chemotherapy versus chemotherapy alone. The combination also demonstrated an improvement in progression-free survival and overall response rate which were key secondary endpoints. *Imfinzi* plus chemotherapy was well tolerated, had a similar safety profile versus the comparator arm and did not increase the discontinuation rate due to adverse events compared to chemotherapy alone.

Table 25: Key *Imfinzi* Phase III trials in lung cancer

Trial (population)	Design	Timeline	Status
AEGEAN (neo-adjuvant NSCLC)	SoC[71] chemotherapy +/- *Imfinzi*, followed by surgery, followed by placebo or *Imfinzi*	FPCD: Q1 2019 First data anticipated: 2022+	Recruitment ongoing
ADJUVANT BR.31[72] (Stage IB-IIIA resected NSCLC)	Placebo or *Imfinzi*	FPCD: Q1 2015 LPCD: Q1 2020 First data anticipated: 2022+	Recruitment completed
MERMAID-1 (Stage II-III resected NSCLC)	SoC chemotherapy +/- *Imfinzi*	FPCD: Q3 2020 First data anticipated: 2022+	Recruitment ongoing
MERMAID-2 (Stage II-III NSCLC with minimal residual disease)	Placebo or *Imfinzi*	FPCD: Q3 2021 First data anticipated: 2022+	Recruitment ongoing
PACIFIC-2 (Stage III unresectable locally advanced NSCLC (concurrent CRT))	Placebo or *Imfinzi*	FPCD: Q2 2018 LPCD: Q3 2019 First data anticipated: H2 2021	Recruitment completed
ADRIATIC (LS-SCLC)	cCRT, followed by placebo or *Imfinzi* or *Imfinzi* + tremelimumab	FPCD: Q4 2018 LPCD: Q3 2021 First data anticipated: H2 2022	Recruitment completed
PEARL (Stage IV NSCLC, 1st-line)	SoC chemotherapy or *Imfinzi*	FPCD: Q1 2017 LPCD: Q1 2019 First data anticipated: H1 2022	Recruitment completed
POSEIDON (Stage IV NSCLC, 1st-line)	SoC chemotherapy or SoC + *Imfinzi* or SoC + *Imfinzi* + tremelimumab	FPCD: Q2 2017 LPCD: Q4 2018	PFS primary endpoint met; OS primary endpoint met for *Imfinzi* + tremelimumab

[71] Standard of Care.

[72] Conducted by the Canadian Cancer Trials Group.

Table 26: Key *Imfinzi* Phase III trials in tumour types other than lung cancer

Trial (population)	Design	Timeline	Status
POTOMAC (non-muscle invasive bladder cancer)	SoC BCG[73] +/- *Imfinzi*	FPCD: Q4 2018 LPCD: Q4 2020 First data anticipated: 2022+	Recruitment completed
NIAGARA (muscle-invasive bladder cancer)	Neo-adjuvant cisplatin and gemcitabine SoC chemotherapy or SoC + *Imfinzi*, followed by adjuvant placebo or *Imfinzi*	FPCD: Q4 2018 LPCD: Q3 2021 First data anticipated: 2022+	Recruitment completed
EMERALD-1 (locoregional HCC[74])	TACE[75] followed by placebo or TACE + *Imfinzi*, followed by *Imfinzi* + bevacizumab or TACE + *Imfinzi* followed by *Imfinzi*	FPCD: Q1 2019 LPCD: Q3 2021 First data anticipated: H2 2022	Recruitment completed
EMERALD-2 (locoregional HCC at high risk of recurrence after surgery or radiofrequency ablation)	Adjuvant *Imfinzi* or *Imfinzi* + bevacizumab	FPCD: Q2 2019 First data anticipated: 2022+	Recruitment ongoing
CALLA (locally advanced cervical cancer)	CRT +/- *Imfinzi*, followed by placebo or *Imfinzi*	FPCD: Q1 2019 LPCD: Q4 2020 First data anticipated: H1 2022	Recruitment completed
MATTERHORN (resectable gastric and gastroesophageal cancer)	Neoadjuvant *Imfinzi* + FLOT[76] chemotherapy +/- adjuvant *Imfinzi*	FPCD: Q4 2020 First data anticipated: 2022+	Recruitment ongoing
KUNLUN (locally advanced, unresectable oesophageal squamous cell carcinoma)	Definitive CRT or CRT +/- *Imfinzi*	FPCD: Q4 2020 First data anticipated: 2022+	Recruitment ongoing
NILE (Stage IV cisplatin chemotherapy- eligible bladder cancer, 1st-line)	SoC chemotherapy or SoC + *Imfinzi* or SoC + *Imfinzi* + tremelimumab	FPCD: Q4 2018 LPCD: Q2 2021 First data anticipated: 2022+	Recruitment completed
VOLGA (Muscle invasive bladder cancer ineligible to cisplatin)	SoC cystectomy or *Imfinzi* + tremelimumab + enfortumab vedotin or *Imfinzi* + enfortumab vedotin	FPCD: Q4 2021 First data anticipated: 2022+	Recruitment ongoing
HIMALAYA (Stage IV unresectable HCC, 1st-line)	Sorafenib or *Imfinzi* or *Imfinzi* + tremelimumab	FPCD: Q4 2017 LPCD: Q4 2019	Primary endpoint met Orphan Drug Designation (US)
TOPAZ-1 (Stage IV biliary-tract cancer, 1st-line)	Gemcitabine and cisplatin SoC chemotherapy or SoC + *Imfinzi*	FPCD: Q2 2019 LPCD: Q4 2020	Primary endpoint met Orphan Drug Designation (US)

[73] Bacillus Calmette-Guerin.

[74] Hepatocellular carcinoma.

[75] Transarterial chemoembolisation.

[76] A chemotherapy regimen comprised of 5-fluorouracil, leucovorin, oxaliplatin and docetaxel.

Lynparza

In September 2021, the Company announced that the PROpel Phase III trial for *Lynparza* in combination with abiraterone in 1st-line mCRPC in men with or without homologous recombination repair gene mutations, had met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in radiographic PFS versus standard-of-care abiraterone.

During the period, the National Comprehensive Cancer Network guidelines were updated to recommend *Lynparza* for the adjuvant treatment of BRCAm, high risk, HER2-negative early breast cancer based on the results of the Phase III OlympiA trial.

Table 27: Key *Lynparza* Phase III trials

Trial (population)	Design	Timeline	Status
OlympiA (adjuvant BRCAm[77] breast cancer)	Placebo or *Lynparza*	FPCD: Q2 2014 LPCD: Q2 2019	Primary endpoint met
MONO-OLA1 (BRCAwt[78] advanced ovarian cancer 1L maintenance)	Placebo or *Lynparza*	FPCD: Q3 2021 First data anticipated: 2022+	Recruitment ongoing
DuO-O (advanced ovarian cancer, 1st-line)	Chemotherapy + bevacizumab or chemotherapy + bevacizumab + *Imfinzi* +/- *Lynparza* maintenance	FPCD: Q1 2019 First data anticipated: 2022+	Recruitment ongoing
DuO-E (advanced endometrial cancer, 1st-line)	Chemotherapy or chemotherapy + *Imfinzi* + *Imfinzi* maintenance or chemotherapy + *Imfinzi* followed by *Imfinzi* + *Lynparza* maintenance	FPCD: Q2 2020 First data anticipated: 2022+	Recruitment ongoing
PROpel (Stage IV, castration-resistant prostate cancer)	Abiraterone or abiraterone + *Lynparza*	FPCD: Q4 2018	Primary endpoint met

[77] A mutation of the BRCA1 or BRCA2 gene

[78] Unmutated BRCA genes (wild type)

Enhertu

In August 2021, AstraZeneca announced that the *Enhertu* the AstraZeneca and Daiichi Sankyo Company, Limited (Daiichi Sankyo) HER2-directed ADC[79] Phase III DESTINY-Breast03 trial in HER2-positive metastatic breast cancer met the primary endpoint. The results were presented at a Presidential Symposium at ESMO 2021 and showed that *Enhertu* reduced the risk of disease progression or death compared to T-DM1 by 72% (HR 0.28; 95% CI 0.22-0.37; p<0.0001). There was a strong trend towards improved OS with *Enhertu* (HR 0.56; 95% CI 0.36-0.86; nominal p=0.007172), however this analysis is not yet mature and is not statistically significant. A consistent PFS benefit was observed in key subgroups of patients treated with *Enhertu*, including those with a history of stable brain metastases.

The safety profile of *Enhertu* was consistent with previous clinical trials, with no new safety concerns identified and no Grade 4 or 5 treatment-related interstitial lung disease events.

In October 2021, the US FDA granted Breakthrough Therapy Designation for *Enhertu* for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens.

In October 2021, updated ESMO Clinical Practice Guidelines were published in *Annals of Oncology* adding *Enhertu* as the new standard of care in 2nd-line therapy in HER2+ metastatic breast cancer.

At ESMO 2021, the Company also presented detailed results of key Phase II trials of *Enhertu* in gastric and lung cancer.

Results from the Phase II DESTINY-Gastric02 trial presented during a late-breaking mini-oral presentation showed that *Enhertu* provided a clinically meaningful and durable tumour response in patients with HER2-positive metastatic and/or unresectable gastric or GEJ[80] previously treated with a trastuzumab-containing regimen.

In the primary analysis of DESTINY-Gastric02, the first trial of *Enhertu* specifically in Western patients with HER2-positive metastatic gastric cancer or GEJ adenocarcinoma, *Enhertu* (6.4 mg/kg) demonstrated a confirmed ORR of 38% as assessed by independent central review. Three (3.8%) complete responses and 27 (34.2%) partial responses were observed in patients treated with *Enhertu*. These results were consistent with those from the registrational DESTINY-Gastric01 Phase II trial previously published in *The New England Journal of Medicine.* After a median follow-up of 5.7 months, the median DoR[81] of *Enhertu* was 8.1 months (95% CI 4.1-NE). The median progression-free survival (PFS) was 5.5 months (95% CI 4.2-7.3). An exploratory endpoint of confirmed disease control rate of 81% (95% CI; 70.6-89.0) was seen.

Results from the Phase II DESTINY-Lung01 trial presented during a late-breaking Proffered Paper session showed a robust and durable tumour response in previously treated patients with HER2-mutant (HER2m) unresectable and/or metastatic non-squamous non-small cell lung cancer.

Primary results from the HER2m cohort (cohort 2) of DESTINY-Lung01 in previously treated HER2m NSCLC demonstrated a confirmed ORR of 54.9% in patients treated with *Enhertu* (6.4 mg/kg) as assessed by independent central review. One (1.1%) complete response and 49 (53.8%) partial responses were observed. A confirmed disease control rate of 92.3% was seen with a reduction in tumour size observed in most patients. After a median follow-up of 13.1 months, the median DoR for *Enhertu* was 9.3 months. The median PFS was 8.2 months and the median OS was 17.8 months.

[79] Antibody drug conjugate.

[80] Gastroesophageal junction adenocarcinoma.

[81] Duration of response.

Table 28: Key *Enhertu* trials

Trial (population)	Design	Timeline	Status
DESTINY-Breast02-U301, Phase III (Stage IV, HER2+ breast cancer post trastuzumab emtansine)	SoC chemotherapy or *Enhertu*	FPCD: Q3 2018 LPCD: Q4 2020 First data anticipated: H2 2022	Recruitment completed
DESTINY-Breast03-U302, Phase III (Stage IV, HER2+ breast cancer, 2nd-line)	Trastuzumab emtansine or *Enhertu*	FPCD: Q3 2018 LPCD: Q2 2020	Primary endpoint met Breakthrough Therapy Designation (US)
DESTINY-Breast04, Phase III (Stage IV, HER2-low breast cancer, 2nd-line)	SoC chemotherapy or *Enhertu*	FPCD: Q4 2018 LPCD: Q4 2020 First data anticipated: H1 2022	Recruitment completed
DESTINY-Breast05, Phase III (high-risk HER2+ breast cancer, post-neoadjuvant)	Trastuzumab emtansine or *Enhertu*	FPCD Q4 2020 First data anticipated: 2022+	Recruitment ongoing
DESTINY-Breast06, Phase III (Stage IV, HER2-low breast cancer, post endocrine therapy)	SoC chemotherapy or *Enhertu*	FPCD: Q3 2020 First data anticipated: 2022+	Recruitment ongoing
DESTINY-Breast09, Phase III (Stage IV, HER2+ breast cancer, 1st-line)	SoC chemotherapy + trastuzumab + pertuzumab or *Enhertu* + pertuzumab or *Enhertu*	FPCD: Q2 2021 First data anticipated: 2022+	Recruitment ongoing
DESTINY-Gastric01, Phase II (Stage IV, HER2+ gastric cancer)	SoC chemotherapy or *Enhertu*	FPCD: Q4 2017 LPCD: Q2 2019	Primary endpoint met Breakthrough Therapy Designation (US) Regulatory approval (US, JP)
DESTINY-Gastric02, Phase II (Stage IV, HER2+ gastric cancer)	*Enhertu*	FPCD: Q4 2019 LPCD: Q4 2020	Positive data readout Recruitment completed
DESTINY-Gastric04, Phase III (Stage IV, HER2+ gastric cancer, 2nd-line)	Paclitaxel + ramucirumab or *Enhertu*	FPCD: Q2 2021 First data anticipated: 2022+	Recruitment ongoing
DESTINY-Lung04, Phase III (Stage III, HER2 mutated NSCLC, 1st-line)	SoC platinum chemotherapy, pemetrexed and pembrolizumab or *Enhertu*	Initiating First data anticipated: 2022+	Initiating

Calquence

Table 29: Key *Calquence* Phase III trials

Trial (population)	Design	Timeline	Status
ESCALADE (Diffuse large B-cell lymphoma)	SoC R-CHOP[82] +/- *Calquence*	FPCD: Q2 2020 Data anticipated: 2022+	Recruitment ongoing

Orpathys

During the period, HUTCHMED announced the initiation of the SAMETA Phase III trial of AstraZeneca and HUTCHMED's *Orpathys,* in combination with *Imfinzi* in unresectable, locally advanced or metastatic PRCC[83].

Camizestrant

Table 30: Camizestrant Phase III trials

Trial (population)	Design	Timeline	Status
SERENA-4 (ER+, HER2-, advanced breast cancer)	Palbociclib + anastrazole or albociclib + camizestrant	FPCD: Q1 2021 First data anticipated: 2022+	Recruitment ongoing
SERENA-6 (HR+, HER2-, metastatic breast cancer)	Palbociclib or abemaciclib + camizestrant, or anastrozole or letrozole + albociclib or abemaciclib	FPCD: Q3 2021 First data anticipated: 2022+	Recruitment ongoing

Datopotamab deruxtecan

Table 31: Datopotamab deruxtecan Phase III trials

Trial (population)	Design	Timeline	Status
TROPION-Lung01 (Stage IV NSCLC, 2nd-line)	SoC chemotherapy or datopotamab deruxtecan	FPCD: Q1 2021 First data anticipated: 2022+	Recruitment ongoing
TROPION-Breast01	SoC chemotherapy or datopotamab deruxtecan	Initiating First data anticipated: 2022+	Initiating

[82] A chemotherapy combination comprised of rituximab, clyclophosphamide, doxorubicin hydrochloride, vincristine and prednisolone.

[83] Papillary renal cell carcinoma.

BioPharmaceuticals - CVRM

Farxiga

During the period, *Forxiga* received regulatory approval in both the EU and in Japan for the treatment of CKD. The approvals were based on results from the DAPA-CKD Phase III trial where *Farxiga*, on top of standard of care, reduced the composite measure of worsening of renal function or risk of cardiovascular or renal death by 39%, compared to placebo in patients with CKD Stages 2-4 and elevated urinary albumin excretion.

During the period, *Forxiga* was one of two SGLT-2 inhibitors added to the European Society of Cardiology's guidelines for the treatment of chronic heart failure with reduced ejection fraction with a Class 1 recommendation.

In October, AstraZeneca voluntarily withdrew the indication for *Forxiga* 5mg in the EU for the treatment of adults with insufficiently controlled T1D[84]. The decision does not impact the indication outside of the EU and does not impact other approved *Farxiga* indications or the 10mg dose within or outside of the EU. The decision followed discussions with the EMA[85] regarding product information changes needed post-approval for *Forxiga* 5mg specific to T1D, which might cause confusion among physicians treating patients with T2D[86], HFrEF or CKD.

Table 32: Key CVRM Phase III trials

Trial (population)	Design	Timeline	Status
Brilinta			
THALES (c.11,000 patients with acute ischaemic stroke[87] or transient ischaemic attack)	Aspirin plus placebo or aspirin plus *Brilinta* 90mg BID	FPCD: Q1 2018 LPCD: Q4 2019	Primary endpoint met Regulatory approval (US)
Farxiga			
DELIVER (c.6,300 patients with HF (HFpEF) with and without T2D)	Placebo or *Farxiga* 10mg QD	FPCD: Q4 2018 LPCD: Q4 2020 First data anticipated: H1 2022	Recruitment completed Fast Track[88] designation (US)
DAPA-MI (c.6,400 patients with confirmed MI, either STEMI[89] or NSTEMI[90], within the preceding seven days)	Placebo or *Farxiga* 10mg QD	FPCD: Q4 2020 First data anticipated: 2022+	Recruitment ongoing

Roxadustat

During the period, AstraZeneca and its partner FibroGen Inc. (FibroGen) received a complete response letter from the US FDA, asking for an additional clinical trial on the safety of roxadustat in both the non-dialysis and dialysis dependent populations. AstraZeneca is working with FibroGen to evaluate next steps.

[84] Type-1 diabetes.

[85] European Medicines Agency.

[86] Type-2 diabetes.

[87] Ischaemic strokes are the most common type of stroke.

[88] A process designed to facilitate the development and expedite the review of medicines to treat serious conditions that fill an unmet medical need.

[89] ST elevation myocardial infarction

[90] Non-ST elevation myocardial infarction.

Lokelma

Table 33: Key *Lokelma* Phase III trials

Trial (population)	Design	Timeline	Status
DIALIZE (c.2,300 patients with recurrent hyperkalaemia on chronic haemodialysis)	Placebo or *Lokelma* 10mg QD for 4 weeks on non-dialysis days, thereafter adjusted monthly	FPCD: Q3 2021 First data anticipated: 2022+	Recruitment ongoing
STABILIZE-CKD (c.1,360 patients with CKD and hyperkalaemia or at risk of hyperkalaemia)	Placebo or *Lokelma* 5g QOD to 15g QD plus lisonopril or valsartan	FPCD: Q4 2021 First data anticipated: 2022+	Recruitment ongoing

BioPharmaceuticals – Respiratory & Immunology

Breztri

Table 34: Key *Breztri* Phase III trials

Trial (population)	Design	Timeline	Status
KALOS (asthma)	Budesonide/formoterol or *Breztri*	FPCD: Q1 2021 First data anticipated: 2022+	Recruitment ongoing
LOGOS (asthma)	Budesonide/formoterol or *Breztri*	FPCD: Q1 2021 First data anticipated: 2022+	Recruitment ongoing

Fasenra

During the quarter, *Fasenra* was granted Orphan Drug Designations in EGE and EG, and a Fast Track Designation for the treatment of EG with or without EGE in the US by the FDA. A Phase III trial (HUDSON) is planned for later this year. EG and EGE are rare, chronic relapsing conditions that may co-exist or be independent. These diseases have symptoms that are primarily related to eosinophilic tissue inflammation, which can cause tissue injury and remodelling of the gastrointestinal tract.

Table 35: Key *Fasenra* lifecycle management Phase III trials

Trial (population)	Design	Timeline	Status
OSTRO (severe bilateral nasal polyps)	Placebo or *Fasenra* 30mg Q8W[91] s.c.	FPCD: Q1 2018 LPCD: Q2 2019	Co-primary endpoints met
RESOLUTE (moderate to very severe COPD with a history of exacerbations and elevated peripheral blood eosinophils)	Placebo or *Fasenra* 100mg Q8W s.c.	FPCD: Q4 2019 First data anticipated: 2022+	Recruitment ongoing
MANDARA (eosinophilic granulomatosis with polyangiitis)	Mepolizumab 3x100mg Q4W[92] or *Fasenra* 30mg s.c.	FPCD: Q4 2019 First data anticipated: 2022+	Recruitment ongoing Orphan Drug Designation (US)
NATRON (HES)	Placebo or *Fasenra* 30mg Q4W s.c.	FPCD: Q3 2020 First data anticipated: H2 2022	Recruitment ongoing Orphan Drug Designation (US)
MESSINA (EoE)	Placebo or *Fasenra* 30mg Q4W s.c.	FPCD: Q4 2020 First data anticipated: H2 2022	Recruitment ongoing Orphan Drug Designation (US)
FJORD (bullous pemphigoid)	Placebo or *Fasenra* 30mg Q4W s.c.	FPCD: Q2 2021 First data anticipated: 2022+	Recruitment ongoing
MAHALE (non-cystic fibrosis bronchiectasis)	Placebo or *Fasenra* 30mg Q4W s.c.	FPCD: Q3 2021 First data anticipated: 2022+	Recruitment ongoing
HUDSON (EG/EGE)	Placebo or Fasenra 30mg Q4W s.c.	First data anticipated: 2022+	Initiating

Tezepelumab

In July 2021, tezepelumab received US regulatory submission acceptance for its Biologics License Application and was also granted Priority Review for the treatment of asthma. The PDUFA date is anticipated to be during the first quarter of 2022. In October 2021, tezepelumab was granted Orphan Drug Designation in the US by the FDA for the treatment of EoE; a Phase III trial is planned.

Table 36: Key tezepelumab Phase III trials

Trial (population)	Design	Timeline	Status
NAVIGATOR (asthma)	Placebo or tezepelumab 210mg Q4W s.c.	FPCD: Q1 2018 LPCD: Q3 2019	Primary endpoint met Breakthrough Therapy Designation (US)
WAYPOINT (chronic rhinosinusitis with nasal polyps)	Placebo or tezepelumab 210mg Q4W s.c.	FPCD: Q2 2021 First data anticipated: 2022+	Recruitment ongoing

[91] Once every eight weeks.

[92] Once every four weeks.

PT027

In September 2021, AstraZeneca and Avillion LLC, announced positive high-level results from the MANDALA and DENALI Phase III trials for PT027, a fixed-dose combination of albuterol (salbutamol) and budesonide. The trials met all primary endpoints demonstrating statistically significant benefits in patients with asthma versus PT027's individual components.

Table 37: Key PT027 Phase III trials

Trial	Design	Timeline	Status
TYREE (asthma with exercise-induced broncho constriction)	Placebo or PT027 160/180mcg, single dose	FPCD: Q1 2020 LPCD: Q3 2020	Primary endpoint met
MANDALA (asthma)	Albuterol or PT027 80/180mcg or PT027 160/180mcg (all 'as needed')	FPCD: Q4 2018 LPCD: Q1 2021	Primary endpoint met
DENALI (asthma)	Placebo or albuterol 180mcg or budesonide 160mcg or PT027 80/180mcg or PT027 160/180mcg QID	FPCD: Q2 2019 LPCD: Q2 2021	Dual primary endpoints met

Saphnelo (anifrolumab)

During the period, *Saphnelo* received regulatory approval in the US and Japan, for the treatment of SLE. The approvals were based on efficacy and safety data from the *Saphnelo* clinical development programme, which included two TULIP Phase III trials and the MUSE Phase II trial. In these trials, more patients treated with *Saphnelo* experienced a reduction in overall disease activity across organ systems, including skin and joints, and achieved sustained reduction in oral corticosteroid use compared to placebo, with both groups receiving standard therapy.

During the period, the European Medicines Agency (EMA) informed AstraZeneca that an Ad Hoc Expert Group (AHEG) meeting is planned for Q4 2021. Given the lack of new medicines submitted for approval for the treatment of SLE in the past 10 years, the AHEG meeting provides an opportunity for experts to review the clinical data available for *Saphnelo* and provide input to the EMA. The Company anticipates a regulatory decision for the EU in H1 2022.

Table 38: Key *Saphnelo* Phase III trials

Trial (population)	Design	Timeline	Status
TULIP 1 (moderate to severely active SLE)	Placebo or *Saphnelo* 150mg or 300mg i.v.[93] Q4W[94]	FPCD: Q4 2015 LPCD: Q4 2017	Primary endpoint not met Regulatory approval (US)
TULIP 2 (moderate to severely active SLE)	Placebo or *Saphnelo* 300mg i.v. Q4W	FPCD: Q4 2015 LPCD: Q4 2017	Primary endpoint met Regulatory approval (US)
TULIP-SC (moderate to severely active SLE)	Placebo or *Saphnelo* 120mg s.c. Q1W[95]	First data anticipated: 2022+	Recruitment ongoing

[93] Intravenous.

[94] Once every four weeks.

[95] Once a week.

Rare Disease

Ultomiris

In July 2021, AstraZeneca's Alexion received regulatory approval in the EU for expanded use to include children (10kg or above) and adolescents with PNH.

The approval was based on positive interim results from the Phase III clinical trial in children and adolescents that demonstrated *Ultomiris* was effective in achieving complete C5 complement inhibition through 26 weeks for the treatment of patients up to 18 years of age.

In August 2021, Alexion announced discontinuation of the CHAMPION-ALS Phase III clinical trial of *Ultomiris* in adults with ALS. The decision was based on the recommendation of the IDMC[96] following their review of data from a pre-specified interim analysis. The IDMC recommended that the trial be discontinued due to lack of efficacy. No new safety findings were observed and the data were consistent with the established safety profile of *Ultomiris*.

In September 2021, Alexion received US regulatory submission acceptance for its Biologics License Application for the subcutaneous formulation of *Ultomiris* for the treatment of PNH and aHUS[97].

Table 39: Key *Ultomiris* Phase III trials

Trial (population)	Design	Timeline	Status
NMOSD	External placebo-controlled open-label *Ultomiris* Q8W	FPCD: Q4 2019 LPCD: H1 2022 Data anticipated: 1H 2022	Recruitment completed
gMG	Placebo or *Ultomiris* Q8W	FPCD: Q1 2019 LPCD: Q2 2021	Primary endpoint met
CM-TMA[98]	Placebo or *Ultomiris* Q8W	FPCD: Q3 2021 Data anticipated: 2022+	Recruitment ongoing
HSCT-TMA[99] Adult	Placebo or *Ultomiris* Q8W	FPCD: Q4 2020 Data anticipated: 2022+	Recruitment ongoing

ALXN1840

In August 2021, positive high-level results from ALXN1840's FoCus Phase III trial for Wilson disease demonstrated statistically significant improvement in daily mean copper mobilisation from tissues, showing superiority compared with SoC treatments.

The primary endpoint measured the daily mean Area Under the Effect Curve for directly measured non-ceruloplasmin-bound copper over 48 weeks. ALXN1840 demonstrated three times greater copper mobilisation than SoC and was generally well-tolerated with most reported adverse events considered mild to moderate. No neurological worsening upon initiation of treatment was observed. Additional analyses, including individual patient-reported outcomes and clinician-reported functional assessments, are ongoing.

[96] Independent Data Monitoring Committee.

[97] Atypical haemolytic uremic syndrome.

[98] Complement-mediated thrombotic microangiopathy.

[99] Hematopoietic stem cell transplantation-associated thrombotic microangiopathy.

Andexxa

In October 2021, AstraZeneca's Alexion received a Complete Response Letter from the US FDA for its sBLA for *Andexxa* to extend the indication to include patients treated with edoxaban or enoxaparin, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. Alexion is reviewing the letter and evaluating next steps.

Other medicines (outside the main disease areas)

Nirsevimab

In September 2021, results from the Phase III MELODY trial were presented at the 2021 IDWeek Virtual Conference, demonstrating that a single dose of nirsevimab had efficacy of 74.5% (CI: 49.6-87.1) in protecting late pre-term and term infants against lower respiratory tract infection caused by RSV over an RSV season. Results from the Phase II/III MEDLEY trial presented in November 2021 at the RSV Vaccines for the World Congress showed nirsevimab had a similar safety and tolerability profile to *Synagis* (current SoC) in infants with CHD, CLD and those born pre-term.

Table 40: Key nirsevimab trials

Trial (population)	Design	Timeline	Status
MELODY (healthy late preterm and term infants)	Placebo or nirsevimab IM[100]	FPCD: Q3 2019 LPCD: Q3 2020	Primary endpoint met Breakthrough therapy designation (US, EU, CN)
MEDLEY (high-risk children)	*Synagis* or nirsevimab IM	FPCD: Q3 2019 LPCD: Q4 2020	Safety objective met

COVID-19

COVID-19 vaccines

Trial	Design	Timeline	Status
COV002 (UK), Phase II/III	MenACWY or AZD1222	FPCD: Q2 2020 LPCD: Q4 2020	Initial data readout Regulatory authorisation (EU, JP, UK)
COV003 (Brazil), Phase II/III	MenACWY or AZD1222	FPCD: Q2 2020 LPCD: Q4 2020	Initial data readout Regulatory authorisation (EU, JP, UK)
COV005 ChAdOx1 nCoV-19 ZA[101] (South Africa), Phase I/II	Placebo or AZD1222	FPCD: Q2 2020 LPCD: Q4 2020	Initial data readout
D8110C00001 (US, global), Phase III	Placebo or AZD1222	FPCD: Q3 2020 LPCD: Q1 2021	Primary endpoint met
D7220C00001 (Global), Phase II/III	AZD1222 or AZD2816	FPCD: Q2 2021 First data anticipated: Q4 2021	Recruitment ongoing

[100] Intramuscular.

[101] Conducted by University of Witwatersrand, South Africa.

AZD7442

In August 2021, AstraZeneca announced that the PROVENT Phase III trial of long-acting antibody combination AZD7442 in pre-exposure prophylaxis of COVID-19 demonstrated statistically significant reduction in the incidence of symptomatic disease. The results were presented at the aforementioned IDWeek and showed that in a trial population in which more than 75% of participants had co-morbidities, including conditions that have been reported to cause a reduced immune response to vaccination, AZD7442 reduced the risk of developing symptomatic COVID-19 by 77% compared to placebo.

In October, the Company announced positive high-level results from the TACKLE Phase III trial showed AZD7442, achieved a statistically significant reduction in severe COVID-19 or death compared to placebo in non-hospitalised patients with mild-to-moderate symptomatic COVID-19. The trial met the primary endpoint, with a 600mg dose of AZD7442 reducing the risk of developing severe COVID-19 or death (from any cause) by 50% compared to placebo in outpatients who had been symptomatic for seven days or less. In a prespecified analysis of participants who received treatment within five days of symptom onset, AZD7442 reduced the risk of developing severe COVID-19 or death (from any cause) by 67% compared to placebo.

In the period, AstraZeneca submitted an EUA request for AZD7442 to the US FDA, for the prophylaxis of symptomatic COVID-19.

Table 41: Key AZD7442 Phase III trials in COVID-19

Trial	Design	Timeline	Status
PROVENT (prophylaxis)	Placebo or AZD7442 300mg i.m.[102]	FPCD: Q4 2020 LPCD: Q1 2021	Primary endpoint met
STORM CHASER (post-exposure prophylaxis)	Placebo or AZD7442 300mg i.m.	FPCD: Q4 2020 LPCD: Q1 2021	Primary endpoint not met
TACKLE (outpatient treatment)	Placebo or AZD7442 600mg i.m.	FPCD: Q1 2021 LPCD: Q3 2021	Primary endpoint met

[102] Intramuscular

Table 42: YTD 2021 - Condensed consolidated statement of comprehensive income

For the **nine months** ended 30 September	2021 $m	2020 $m
Total Revenue	25,406	19,207
Product Sales	*25,043*	*18,879*
Collaboration Revenue	*363*	*328*
Cost of Sales	(7,812)	(3,774)
Gross Profit	17,594	15,433
Distribution costs	(322)	(290)
Research and development expense	(7,152)	(4,272)
Selling, general and administrative costs	(10,117)	(8,084)
Other operating income and expense	1,345	888
Operating Profit	1,348	3,675
Finance income	42	80
Finance expense	(964)	(985)
Share of after tax losses in associates and joint ventures	(55)	(21)
Profit Before Tax	371	2,749
Taxation	90	(610)
Profit for the period	461	2,139
Other comprehensive income		
Items that will not be reclassified to profit or loss		
Remeasurement of the defined benefit pension liability	592	(191)
Net gains on equity investments measured at fair value through other comprehensive income	144	974
Fair value movements related to own credit risk on bonds designated as fair value through profit or loss	4	(1)
Tax on items that will not be reclassified to profit or loss	71	(70)
	811	712
Items that may be reclassified subsequently to profit or loss		
Foreign exchange arising on consolidation	(368)	(121)
Foreign exchange arising on designated borrowings in net investment hedges	(275)	145
Fair value movements on cash flow hedges	(103)	2
Fair value movements on cash flow hedges transferred to profit or loss	137	(115)
Fair value movements on derivatives designated in net investment hedges	22	39
Costs of hedging	(6)	10
Tax on items that may be reclassified subsequently to profit or loss	37	7
	(556)	(33)
Other comprehensive income for the period, net of tax	255	679
Total comprehensive income for the period	716	2,818
Profit attributable to:		
Owners of the Parent	459	2,184
Non-controlling interests	2	(45)
	461	2,139
Total comprehensive income attributable to:		
Owners of the Parent	714	2,864
Non-controlling interests	2	(46)
	716	2,818
Basic earnings per $0.25 Ordinary Share	$0.33	$1.66
Diluted earnings per $0.25 Ordinary Share	$0.33	$1.66
Weighted average number of Ordinary Shares in issue (millions)	1,374	1,312
Diluted weighted average number of Ordinary Shares in issue (millions)	1,382	1,313

Table 43: Q3 2021 - Condensed consolidated statement of comprehensive income

For the **quarter** ended 30 September	**2021 $m**	**2020 $m**
Total Revenue	9,866	6,578
Product Sales	*9,741*	*6,520*
Collaboration Revenue	*125*	*58*
Cost of Sales	(3,757)	(1,370)
Gross Profit	6,109	5,208
Distribution costs	(120)	(99)
Research and development expense	(3,610)	(1,495)
Selling, general and administrative costs	(4,090)	(2,730)
Other operating income and expense	37	287
Operating (Loss)/Profit	(1,674)	1,171
Finance income	15	7
Finance expense	(335)	(324)
Share of after tax losses in associates and joint ventures	(7)	(1)
(Loss)/Profit Before Tax	(2,001)	853
Taxation	350	(202)
(Loss)/Profit for the period	(1,651)	651
Other comprehensive (loss)/income		
Items that will not be reclassified to profit or loss		
Remeasurement of the defined benefit pension liability	(100)	14
Net gains/(losses) on equity investments measured at fair value through other comprehensive income	171	(95)
Fair value movements related to own credit risk on bonds designated as fair value through profit or loss	2	(7)
Tax on items that will not be reclassified to profit or loss	19	9
	92	(79)
Items that may be reclassified subsequently to profit or loss		
Foreign exchange arising on consolidation	(427)	373
Foreign exchange arising on designated borrowings in net investment hedges	(45)	162
Fair value movements on cash flow hedges	(44)	133
Fair value movements on cash flow hedges transferred to profit or loss	64	(114)
Fair value movements on derivatives designated in net investment hedges	15	(21)
Costs of hedging	(4)	6
Tax on items that may be reclassified subsequently to profit or loss	19	(22)
	(422)	517
Other comprehensive (loss)/income for the period, net of tax	(330)	438
Total comprehensive (loss)/income for the period	(1,981)	1,089
(Loss)/Profit attributable to:		
Owners of the Parent	(1,652)	648
Non-controlling interests	1	3
	(1,651)	651
Total comprehensive (loss)/income attributable to:		
Owners of the Parent	(1,982)	1,087
Non-controlling interests	1	2
	(1,981)	1,089
Basic (loss)/earnings per $0.25 Ordinary Share	$(1.10)	$0.49
Diluted (loss)/earnings per $0.25 Ordinary Share	$(1.10)	$0.49
Weighted average number of Ordinary Shares in issue (millions)	1,496	1,312
Diluted weighted average number of Ordinary Shares in issue (millions)[103]	1,496	1,313

[103] The same weighted average number of shares was used for the calculation of basic and diluted loss per share in the quarter as the effect of potentially dilutive shares outstanding was anti-dilutive

Table 44: Condensed consolidated statement of financial position

	At 30 Sep 2021 $m	At 31 Dec 2020 $m	At 30 Sep 2020 $m
Assets			
Non-current assets			
Property, plant and equipment	9,214	8,251	7,707
Right-of-use assets	948	666	653
Goodwill	20,081	11,845	11,711
Intangible assets	44,104	20,947	20,613
Investments in associates and joint ventures	39	39	42
Other investments	1,546	1,108	1,173
Derivative financial instruments	90	171	119
Other receivables	811	720	685
Deferred tax assets	3,697	3,438	3,243
	80,530	47,185	45,946
Current assets			
Inventories	10,528	4,024	3,683
Trade and other receivables	8,258	7,022	5,668
Other investments	82	160	374
Derivative financial instruments	60	142	37
Intangible assets	100	-	-
Income tax receivable	596	364	332
Cash and cash equivalents	7,067	7,832	8,072
	26,691	19,544	18,166
Total assets	107,221	66,729	64,112
Liabilities			
Current liabilities			
Interest-bearing loans and borrowings	(2,744)	(2,194)	(3,402)
Lease liabilities	(229)	(192)	(183)
Trade and other payables	(18,663)	(15,785)	(13,406)
Derivative financial instruments	(54)	(33)	(9)
Provisions	(972)	(976)	(621)
Income tax payable	(987)	(1,127)	(1,321)
	(23,649)	(20,307)	(18,942)
Non-current liabilities			
Interest-bearing loans and borrowings	(28,206)	(17,505)	(18,271)
Lease liabilities	(733)	(489)	(483)
Derivative financial instruments	(6)	(2)	(16)
Deferred tax liabilities	(6,400)	(2,918)	(2,576)
Retirement benefit obligations	(2,449)	(3,202)	(2,895)
Provisions	(726)	(584)	(854)
Other payables	(5,140)	(6,084)	(6,457)
	(43,660)	(30,784)	(31,552)
Total liabilities	(67,309)	(51,091)	(50,494)
Net assets	39,912	15,638	13,618
Equity			
Capital and reserves attributable to equity holders of the Parent			
Share capital	387	328	328
Share premium account	35,118	7,971	7,952
Other reserves	2,039	2,024	2,039
Retained earnings	2,200	5,299	1,876
	39,744	15,622	12,195
Non-controlling interests	168	16	1,423
Total equity	39,912	15,638	13,618

Table 45: Condensed consolidated statement of changes in equity

	Share capital	Share premium account	Other reserves	Retained earnings	Total attributable to owners of the parent	Non-controlling interests	Total equity
	$m	$m	$m	$m	$m	$m	$m
At 1 Jan 2020	328	7,941	2,046	2,812	13,127	1,469	14,596
Profit for the period	-	-	-	2,184	2,184	(45)	2,139
Other comprehensive income	-	-	-	680	680	(1)	679
Transfer to other reserves	-	-	(7)	7	-	-	-
Transactions with owners:							
Dividends	-	-	-	(3,669)	(3,669)	-	(3,669)
Issue of Ordinary Shares	-	11	-	-	11	-	11
Share-based payments charge for the period	-	-	-	187	187	-	187
Settlement of share plan awards	-	-	-	(325)	(325)	-	(325)
Net movement	-	11	(7)	(936)	(932)	(46)	(978)
At 30 Sep 2020	**328**	**7,952**	**2,039**	**1,876**	**12,195**	**1,423**	**13,618**
At 1 Jan 2021	**328**	**7,971**	**2,024**	**5,299**	**15,622**	**16**	**15,638**
Profit for the period	-	-	-	459	459	2	461
Other comprehensive income	-	-	-	255	255	-	255
Transfer to other reserves	-	-	15	(15)	-	-	-
Transactions with owners:							
Dividends	-	-	-	(3,884)	(3,884)	-	(3,884)
Issue of Ordinary Shares	59	27,147	-	-	27,206	-	27,206
Changes in non-controlling interest	-	-	-	-	-	150	150
Share-based payments charge for the period	-	-	-	384	384	-	384
Settlement of share plan awards	-	-	-	(811)	(811)	-	(811)
Issue of replacement share awards upon acquisition	-	-	-	513	513	-	513
Net movement	59	27,147	15	(3,099)	24,122	152	24,274
At 30 Sep 2021	**387**	**35,118**	**2,039**	**2,200**	**39,744**	**168**	**39,912**

Table 46: Condensed consolidated statement of cash flows

For the **nine months** ended 30 September	**2021 $m**	**2020 $m**
Cash flows from operating activities		
Profit Before Tax	371	2,749
Finance income and expense	922	905
Share of after tax losses of associates and joint ventures	55	21
Depreciation, amortisation and impairment	4,338	2,352
Decrease/(increase) in working capital and short-term provisions	2,063	(255)
Gains on disposal of intangible assets	(371)	(535)
Gains on disposal of investments in associates and joint ventures	(776)	-
Fair value movements on contingent consideration arising from business combinations	33	(14)
Non-cash and other movements	(370)	(484)
Cash generated from operations	6,265	4,739
Interest paid	(522)	(517)
Tax paid	(1,198)	(1,221)
Net cash inflow from operating activities	4,545	3,001
Cash flows from investing activities		
Acquisition of subsidiaries, net of cash acquired	(9,263)	-
Payments upon vesting of employee share awards attributable to business combinations	(203)	-
Payment of contingent consideration from business combinations	(470)	(663)
Purchase of property, plant and equipment	(768)	(598)
Disposal of property, plant and equipment	10	67
Purchase of intangible assets	(714)	(1,460)
Disposal of intangible assets	584	664
Purchase of non-current asset investments	(190)	(119)
Disposal of non-current asset investments	-	1,121
Movement in short-term investments, fixed deposits and other investing instruments	120	530
Payments to associates and joint ventures	(55)	(8)
Disposal of investments in associates and joint ventures	776	-
Interest received	28	43
Net cash outflow from investing activities	(10,145)	(423)
Net cash (outflow)/inflow before financing activities	(5,600)	2,578
Cash flows from financing activities		
Proceeds from issue of share capital	10	11
Repayment of loans	(2,934)	-
Issue of loans	11,942	2,968
Dividends paid	(3,856)	(3,572)
Hedge contracts relating to dividend payments	(28)	(101)
Repayment of obligations under leases	(173)	(157)
Movement in short-term borrowings	(261)	858
Net cash inflow from financing activities	4,700	7
Net (decrease)/increase in cash and cash equivalents in the period	(900)	2,585
Cash and cash equivalents at the beginning of the period	7,546	5,223
Exchange rate effects	(73)	(14)
Cash and cash equivalents at the end of the period	6,573	7,794
Cash and cash equivalents consist of:		
Cash and cash equivalents	7,067	8,072
Overdrafts	(494)	(278)
	6,573	7,794

Notes to the Interim Financial Statements

1) Basis of preparation and accounting policies

These unaudited Interim Financial Statements for the nine months ended 30 September 2021 have been prepared in accordance with International Accounting Standard 34, 'Interim Financial Reporting' (IAS 34), as issued by the International Accounting Standards Board (IASB), IAS 34 as adopted by the European Union, UK-adopted IAS 34, and the Disclosure Guidance and Transparency Rules sourcebook of the United Kingdom's Financial Conduct Authority. On 31 December 2020, EU-adopted IFRS at that date was brought into UK law and became UK-adopted international accounting standards, with future changes being subject to endorsement by the UK Endorsement Board. The Interim Financial Statements have transitioned to UK-adopted international accounting standards from financial periods beginning 1 January 2021. There was no impact or changes in accounting policies from the transition.

The unaudited Interim Financial Statements for the nine months ended 30 September 2021 include Alexion's post-acquisition results which have been consolidated into the Group's results from 21 July 2021 therefore are not entirely comparable with respective comparative periods shown. Following the acquisition of Alexion, the Group has reviewed its assessment of reportable segments under IFRS 8 'Operating Segments' and concluded that the Group continues to have one reportable segment.

The unaudited Interim Financial Statements for the nine months ended 30 September 2021 were approved by the Board of Directors for publication on 12 November 2021.

The annual financial statements of the Group for the year ended 31 December 2020 were prepared in accordance with international accounting standards in conformity with the requirements of the Companies Act 2006, International Financial Reporting Standards (IFRSs) adopted pursuant to Regulation (EC) No 1606/2002 as it applies in the EU and IFRSs as issued by the International Accounting Standards Board (IASB). Except as noted below and for the estimation of the interim income tax charge, the Interim Financial Statements have been prepared applying the accounting policies that were applied in the preparation of the Group's published consolidated financial statements for the year ended 31 December 2020.

IFRS 9 and IFRS 7

The replacement of benchmark interest rates such as LIBOR and other interbank offered rates (IBORs) is a priority for global regulators. Phase 2 amendments to IFRS 9 'Financial Instruments' and IFRS 7 'Financial Instruments: Disclosures' were issued in August 2021 and have been adopted by the Group for 2021 reporting. As at 30 September 2021, the Group had two floating rate notes, a cross currency swap and a fixed to floating USD interest rate swap that reference USD LIBOR but these instruments will either have matured or will have their last LIBOR fixings set before the relevant USD LIBORs cease publication on 30 June 2023. The group also has $4bn of term bank loans that currently reference US LIBOR but these agreements have a mandatory switch from US LIBOR to an alternative risk free rate on 30 June 2023, should the group not elect to do so before that date. In addition, arrangements are being made with other financial institutions for the transition away from IBOR to alternative rates for other existing instruments.

COVID-19

AstraZeneca has assessed the impact of the uncertainty presented by the COVID-19 pandemic on the Interim Financial Statements comprising the financial results to 30 September 2021 and the financial position as at 30 September 2021, specifically considering the impact on key judgements and significant estimates as detailed on page 180 of the Annual Report and 20-F Information 2020 along with several other areas of elevated risk during the pandemic period.

A detailed assessment has been performed, focussing on the following areas:

- recoverable value of goodwill, intangible assets and property, plant and equipment
- impact on key assumptions used to estimate contingent consideration liabilities
- key assumptions used in estimating the Group's defined benefit pension obligations
- basis for estimating clinical trial accruals
- key assumptions used in estimating rebates, chargebacks and returns for US Product Sales
- valuations of unlisted equity investments
- expected credit losses associated with changes in credit risk relating to trade and other receivables
- net realisable value of inventories
- fair value of certain financial instruments
- recoverability of deferred tax assets
- effectiveness of hedge relationships

There were no material accounting impacts identified relating to the above areas during the nine-month period ended 30 September 2021.

The Group will continue to monitor these areas of increased judgement, estimation and risk for material changes.

Going concern

The Group has considerable financial resources available. As at 30 September 2021, the Group had $11.2bn in financial resources (cash and cash-equivalent balances of $7.1bn and undrawn committed bank facilities of $4.1bn, of which $3.4bn was available until April 2024 and $0.7bn was available until November 2021, with only $3.0bn of borrowings due within one year). Additionally, as at 30 September 2021, the Group had $1.0bn of available committed facilities that had been arranged to support the acquisition of Alexion. All facilities contain no financial covenants and were undrawn at 30 September 2021.

Subsequent to 30 September 2021, the Group's $3.4bn facilities available to April 2024 have been increased to $4.9bn and the maturity date extended by one year to April 2025. These facilities can be extended in the future by a further one year at the lenders' discretion. In addition, the $0.7bn facilities available to November 2021 and the $1bn Alexion related facility have either expired or have been cancelled.

The directors have considered the impact of COVID-19 on AstraZeneca's operations and mitigations to these risks. Overall, the impact of these items would heighten certain risks, such as those relating to the delivery of the pipeline or launch of new medicines, the execution of AstraZeneca's commercial strategy, the manufacturing and supply of medicines and reliance on third-party goods and services. The Group is continuously monitoring and mitigating where possible impacts of these risks.

The Group's revenues are largely derived from sales of medicines covered by patents which provide a relatively high level of resilience and predictability to cash inflows, although government price interventions in response to budgetary constraints are expected to continue to affect adversely revenues in some of our significant markets. The Group, however, anticipates new revenue streams from both recently launched medicines and those 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.

Accordingly, the going concern basis has been adopted in these Interim Financial Statements.

Legal proceedings

The information contained in Note 6 updates the disclosures concerning legal proceedings and contingent liabilities in the Group's Annual Report and Form 20-F Information 2020.

Financial information

The comparative figures for the financial year ended 31 December 2020 are not the Group's statutory accounts for that financial year. Those accounts have been reported on by the Group's auditors and have been delivered to the registrar of companies; 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.

2) Intangible assets

In accordance with IAS 36 'Impairment of Assets', reviews for triggers at an individual asset or cash-generating-unit level were conducted, and impairment tests carried out where triggers were identified. As a result and following the Group undertaking a portfolio prioritisation of development projects, total net impairment charges of $1,492m have been recorded against intangible assets during the nine months ended 30 September 2021 (YTD 2020: $188m). Net impairment charges in respect of launched medicines and medicines in development were $121m (YTD 2020: $133m) and $1,371m (YTD 2020: $55m) respectively. Impairments recorded on products in development included an impairment charge of $1,172m recognised in the quarter on the Ardea intangible asset as a consequence of the decision to discontinue the development of verinurad.

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 27 of the Annual Report and Form 20-F Information 2020. Net Debt is a non-GAAP financial measure.

Table 47: Net Debt

	At 1 Jan 2021 $m	Cash flow $m	Acquisitions $m	Non-cash & other $m	Exchange movements $m	At 30 Sep 2021 $m
Non-current instalments of loans	(17,505)	(11,942)	(187)	1,257	171	(28,206)
Non-current instalments of leases	(489)	-	(228)	(29)	13	(733)
Total long-term debt	**(17,994)**	**(11,942)**	**(415)**	**1,228**	**184**	**(28,939)**
Current instalments of loans	(1,536)	2,934	(2,336)	(1,260)	59	(2,139)
Current instalments of leases	(192)	183	(34)	(193)	7	(229)
Bank collateral	(288)	183	-	-	-	(105)
Other short-term borrowings excluding overdrafts	(84)	78	-	-	-	(6)
Overdraft	(286)	(219)	-	-	11	(494)
Total current debt	**(2,386)**	**3,159**	**(2,370)**	**(1,453)**	**77**	**(2,973)**
Gross borrowings	**(20,380)**	**(8,783)**	**(2,785)**	**(225)**	**261**	**(31,912)**
Net derivative financial instruments	278	(16)	6	(178)	-	90
Net borrowings	**(20,102)**	**(8,799)**	**(2,779)**	**(403)**	**261**	**(31,822)**
Cash and cash equivalents	7,832	(4,767)	4,086	-	(84)	7,067
Other investments - current	160	(76)	-	-	(2)	82
Cash and investments	**7,992**	**(4,843)**	**4,086**	**-**	**(86)**	**7,149**
Net Debt	**(12,110)**	**(13,642)**	**1,307**	**(403)**	**175**	**(24,673)**

Non-cash movements in the period include fair-value adjustments under IFRS 9.

The Group has agreements with some bank counterparties whereby the parties agree to post cash collateral on financial derivatives, for the benefit of the other, equivalent to the market valuation of the derivative positions above a predetermined threshold. The carrying value of such cash collateral held by the Group was $105m (YTD 2020: $133m) and the carrying value of such cash collateral posted by the Group was $21m (YTD 2020: $7m). Cash collateral posted by the Group is presented within Cash and cash equivalents.

Other investments - non-current are included within the balance of $1,546m (31 December 2020: $1,108m) in the Condensed consolidated 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 Pharma liability of $2,416m (31 December 2020: $2,297m), $904m of which is shown in current other payables and $1,512m is shown in non-current other payables. In April 2021, AstraZeneca exercised its option to acquire the remaining 45% of shares in Acerta.

Net Debt increased by $12,563m in the nine months to $24,673m primarily due to financing the Alexion acquisition. Details of the committed undrawn bank facilities are disclosed within the going concern section of Note 1. Details in regards to the funding of the Alexion acquisition are provided within Note 5.

In July 2021, following the acquisition of Alexion, S&P Global Ratings upgraded AstraZeneca's long-term credit rating to A-. Other than this, there were no changes to the Company's solicited credit ratings during the nine months to 30 September 2021. At 30 September 2021, the Company's solicited credit ratings from S&P were A- (long term) and A-2 (short term) and from Moody's were A3 (long term) and P-2 (short term).

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, lease liabilities and interest-bearing loans and borrowings. During the nine month period ended 30 September 2021, equity investments previously categorised as Level 3 in the fair-value hierarchy (carrying value of $108m at 31 December 2020) are now categorised as Level 1 (carrying value of $128m at 30 September 2021) on availability of quoted prices in the market. There have been no other changes of significance to the categorisation or fair-value hierarchy classification of financial instruments from those detailed in the Notes to the Group Financial Statements in the Annual Report and Form 20-F Information 2020.

The Group holds certain equity investments that are categorised as Level 3 in the fair value hierarchy and for which fair value gains of $nil (Q3 2020: $63m gain) have been recognised in the nine months ended 30 September 2021. All other fair value gains and/or losses that are presented in Net gains on equity investments measured at fair value through other comprehensive income in the Condensed consolidated statement of comprehensive income for the nine months ended 30 September 2021 are Level 1 fair value measurements.

Financial instruments measured at fair value include $1,628m of other investments, $5,049m held in money-market funds, $325m of loans designated at fair value through profit or loss, $349m of loans designated in a fair-value hedge relationship and $90m of derivatives as at 30 September 2021. The total fair value of interest-bearing loans and borrowings at 30 September 2021, which have a carrying value of $31,912m in the Condensed consolidated statement of financial position, was $34,758m. 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:

Table 48: Financial instruments - contingent consideration

	2021			2020
	Diabetes alliance $m	Other $m	Total $m	Total $m
At 1 January	2,932	391	3,323	4,139
Additions through business combinations	-	324	324	-
Settlements	(460)	(10)	(470)	(663)
Revaluations	82	(49)	33	(14)
Discount unwind	148	24	172	212
At 30 September	**2,702**	**680**	**3,382**	**3,674**

Contingent consideration arising from business combinations is fair-valued using decision-tree analysis, with key inputs including the probability of success, consideration of potential delays and the expected levels of future revenues.

The contingent consideration balance relating to BMS's share of the global diabetes alliance of $2,702m (31 December 2020: $2,932m) would increase/decline by $270m with an increase/decline in sales of 10%, as compared with the current estimates.

5) Acquisition of Alexion

On 21 July 2021, AstraZeneca completed the acquisition of 100% of the issued shares of Alexion Pharmaceuticals, Inc (Alexion), based in Boston, Massachusetts, US. Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialisation of life-changing medicines.

At closing, Alexion shareholders received 2.1243 AstraZeneca American Depository Shares (ADSs) and $60 in cash for each of their Alexion shares. Unvested Alexion employee share awards were converted to equivalent AstraZeneca share awards. The fair value of the purchase consideration was $41,058m, comprising AstraZeneca ADSs of $27,196m, cash of $13,349m and replacement employee share awards of $513m.

The Group has funded the cash element of the acquisition with $8bn of new long-term debt, issued in May and June 2021, $4bn of term loans drawn in July 2021 under the $17.5bn committed bank facilities entered into in December 2020 to secure the acquisition financing, and existing cash balances. The Group cancelled the remaining $13.5bn of the facilities in June, July and October 2021. Loans and borrowings of $2.3bn acquired with Alexion were repaid in full shortly following completion of the acquisition. Changes to financing balances during the reporting period are included in Table 47 on Net Debt.

The acquisition has been accounted for as a business combination using the acquisition method of accounting in accordance with IFRS 3 'Business Combinations' and consequently the Alexion assets acquired, and liabilities assumed have been recorded by AstraZeneca at fair value, with any excess of the purchase price over the fair value of the identifiable assets and liabilities being recognised as goodwill.

Given the proximity of the completion of the transaction to the reporting date, the review and finalisation of the fair values is ongoing. On that basis, the amounts detailed below are provisional:

Table 49: Alexion acquisition fair values as of 21 July 2021

	Fair value $m
Non-current assets	
Property, plant and equipment	1,134
Right-of-use assets	264
Intangible assets	26,691
Other non-current assets	301
	28,390
Current assets	
Inventories	6,886
Trade and other receivables	2,096
Intangible assets	100
Cash and cash equivalents	4,086
	13,168
Current liabilities	
Interest-bearing loans and borrowings	(2,336)
Trade and other payables	(1,192)
Other current liabilities	(40)
	(3,568)
Non-current liabilities	
Lease liabilities	(228)
Deferred tax liabilities	(4,191)
Other non-current liabilities	(697)
	(5,116)
Total net assets acquired	**32,874**
Less: non-controlling interests	(150)
Goodwill	8,334
Total fair value of consideration	**41,058**
Less: fair value of equity consideration	(27,196)
Less: fair value of replacement employee share awards	(513)
Less: cash and cash equivalents acquired	(4,086)
Net cash outflow	**9,263**

Intangible assets principally represent intellectual property rights over launched medicines and medicines under development, which were fair valued using the multi-period excess earnings method. The estimated fair value and useful lives of intangible assets were as follows:

Table 50: Alexion Intangible asset fair values and useful lives

	Fair value $m	Useful lives Years
Launched medicines – C5 franchise (*Soliris*/*Ultomiris*)	18,355	6-15
Launched medicines – *Strensiq*, *Kanuma*, *Andexxa*	5,232	11-17
Medicines in development	2,704	Not amortised
Other intangibles	500	5-10
	26,791	

The fair value of inventory, which includes raw materials, work in progress and finished goods related to the launched medicines, was estimated at $6,886m, an uplift of $5,752m on the carrying value prior to the acquisition. The fair value adjustment relates only to work in progress and finished goods and was calculated as the estimated selling price less estimated costs to complete and sell the inventory, the associated margins on these activities and holding costs. The fair value adjustment is expected to amortise over approximately the first 18 months post-acquisition, in line with revenues.

Property, plant and equipment principally comprises the manufacturing facilities in Dublin and Athlone, Ireland and was fair valued using a cost approach. The estimated fair value of $1,134m represents an uplift of $110m over carrying value.

The estimated fair value of contingent liabilities was $76m, relating to various claims and disputes in each case where there is a possible, but not probable, future financial exposure. This amount has been included within other non-current liabilities of $697m.

The estimated fair value of trade and other receivables was $2,096m, which approximated the contractual cash flows.

The net tax position reflected an adjustment of $5,215m related to the deferred tax impact of the fair value uplifts on intangible assets, inventories, property, plant and equipment and contingent liabilities as described above.

Goodwill amounting to $8,334m was recognised on acquisition and is underpinned by a number of elements, which individually could not be quantified. Most significant amongst these is the premium attributable to a pre-existing, well positioned business in the innovation intensive, high growth rare diseases market with a highly skilled workforce and established reputation. Other important elements include the potential unidentified products that future research and development may yield and the core technological capabilities and knowledge base of the company. Goodwill is not expected to be deductible for tax purposes.

Non-controlling interests reflect Alexion's pre-existing minority equity interest in Caelum Biosciences and have been valued at $150m, the agreed exercise price for the exclusive option to acquire the remaining equity. The option was exercised on 5 October 2021.

Alexion's results have been consolidated into the Group's results from 21 July 2021. For the period from acquisition to 30 September 2021, before reflecting the fair value adjustments arising on acquisition, Alexion's total revenues were $1,311m and profit after tax was $378m. If the acquisition had taken effect at the beginning of the reporting period in which the acquisition occurred (1 January 2021), on a pro forma basis, after reflecting the fair value adjustments arising on consolidation, the total revenue of the combined Group for the nine months ended 30 September 2021 would have been $29,121m and the loss after tax would have been $904m. This pro forma information does not purport to represent the results of the combined Group that actually would have occurred had the acquisition taken place on 1 January 2021 and should not be taken to be representative of future results.

Total acquisition-related costs of $156m have been incurred by the Group, which include advisory, legal and other professional fees. These costs are presented in the Statement of Comprehensive Income within Selling, general and administrative expenses.

The terms of the acquisition include a retention bonus plan for legacy Alexion employees whereby up to $50m may be used for retention bonus awards to employees at the level of Vice President or below. These bonuses will vest and be payable 6 months after the acquisition, or earlier. In the period since acquisition, a cost of $10m has been recorded in the Statement of Comprehensive Income ($1m in Cost of Sales, $3m in Research and development expense and $6m in Selling, general and administrative costs).

Upon completion of the acquisition, all unvested Alexion employee share awards were converted into AstraZeneca restricted stock awards that continue to have, and shall be subject to, the same terms and conditions as applied in the corresponding Alexion awards immediately prior to completion. Alexion Performance Stock Plan (PSU) awards that included performance-based vesting conditions were converted using the greater of the original target level and Alexion's assessment of the level of achievement immediately prior to completion (subject to a limit of 175 per cent. for the awards granted in 2019 and a limit of 150 per cent. for the awards granted in 2020). In the period since acquisition, a cost of $147m has been recorded in the Statement of Comprehensive Income ($4m in Cost of sales, $37m in Research and development expense and $106m in Selling, general and administrative costs). Payments made upon vesting of share awards recognised as part of the consideration for the acquisition of Alexion are recognised within Investing activities in the Group's statement of cash flows.

6) 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 (IP) 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 2020 and H1 2021 results (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, the majority of claims involve highly complex issues. Often these issues are subject to substantial uncertainties and, therefore, the probability of a loss, if any, being sustained and/or an estimate of the amount of any loss is difficult to ascertain.

Unless specifically identified below that a provision has been taken, AstraZeneca considers each of the claims to represent a contingent liability and discloses information with respect to the nature and facts of the cases in accordance with IAS 37.

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, AstraZeneca records the loss absorbed or makes a provision for its best estimate of the expected loss. The position could change over time and the estimates that the Company made, and upon which the Company 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 IP.

Matters disclosed in respect of the third quarter of 2021 and to 12 November 2021

Patent litigation

Enhertu

US patent proceedings

As previously disclosed, in October 2020, Seagen Inc. (Seagen) filed a complaint against Daiichi Sankyo Company, Limited in the US District Court for the Eastern District of Texas (the Texas Court) alleging that *Enhertu* infringes US Patent No. 10,808,039 (the '039 patent). AstraZeneca Pharmaceuticals LP co-commercialises *Enhertu* with Daiichi Sankyo Inc. in the US. In July 2021, AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited intervened in the Texas action in support of Daiichi Sanyko. A claim construction hearing took place in August 2021 and a trial has been scheduled for April 2022.

On 23 December 2020, AstraZeneca and Daiichi Sankyo, Inc. filed a post -grant review petition with the US Patent and Trademark Office alleging, *inter alia*, that the '039 patent is invalid for lack of written description and enablement. In January 2021, AstraZeneca and Daiichi Sankyo, Inc filed a second post -grant review petition with the US Patent and Trademark Office extending its challenge to additional claims in the '039 patent. In June 2021, the US Patent and Trademark Office declined to institute the post grant reviews. AstraZeneca and Daiichi Sankyo have requested a rehearing of their post grant review petitions.

In August 2021, AstraZeneca Pharmaceuticals LP and Daiichi Sankyo, Inc. filed an action against Andrew Hirshfeld, acting in his official capacity as Under Secretary of Commerce, and the US Patent and Trademark Office in the US District Court for the Eastern District of Virginia seeking judicial review of the US Patent Office's discretionary authority to deny institution of post-grant review proceedings.

Faslodex

Patent proceedings outside the US

As previously disclosed, in Japan, in April 2021, AstraZeneca received notice from the Japan Patent Office that Sandoz K.K. filed a Request for Invalidation Trial to seek invalidation of the *Faslodex* formulation patent. In September 2021, AstraZeneca filed a response defending the patent. In October 2021, AstraZeneca received notice that Sun Pharma Japan Ltd. is seeking to intervene in the Sandoz K.K. Request for Invalidation.

Farxiga

US patent proceedings

As previously disclosed, in 2018, in response to Paragraph IV notices, AstraZeneca initiated ANDA litigation against Zydus Pharmaceuticals (USA) Inc. (Zydus) in the US District Court for the District of Delaware (the District Court). In May 2021, trial against Zydus proceeded in the District Court. In October 2021, the District Court issued a decision finding AstraZeneca's US Patent No. 6,515,117 as valid and infringed by Zydus's proposed ANDA product.

Patent proceedings outside the US

In Canada, in January 2021, Sandoz Canada Inc. served three Notices of Allegation on AstraZeneca alleging invalidity and/or non-infringement of all three patents listed on the Canadian Patent Register in relation to *Forxiga*. AstraZeneca commenced litigation in response. A trial date has been set for October 2022 with closing argument in December 2022.

In Canada, in February 2021, Teva Canada Limited served a Notice of Allegation on AstraZeneca alleging invalidity and/or non-infringement of all three patents listed on the Canadian Patent Register in relation to *Forxiga*. AstraZeneca commenced litigation in response. A trial date has been set for October 2022 with closing argument in December 2022.

Onglyza

Patent proceedings outside the US

In Canada, in November 2019, Sandoz Canada Inc. sent a Notice of Allegation to AstraZeneca challenging the validity of Canadian substance Patent No. 2402894 (expiry March 2021) (the '894 patent) and formulation Patent No. 2568391 (expiry May 2025) related to *Onglyza*. AstraZeneca commenced an action in response related to the '894 patent in January 2020. In October 2021, the parties reached an agreement to resolve the dispute. This matter is now concluded.

Symbicort

US Patent Proceedings

As previously disclosed, AstraZeneca is involved in ongoing ANDA litigation with Mylan Pharmaceuticals Inc. (Mylan) and Kindeva Drug Delivery L.P. (Kindeva) brought in the US District Court for the Northern District of West Virginia (the District Court). In the action, AstraZeneca alleges that the defendants' generic versions of *Symbicort*, if approved and marketed, would infringe various AstraZeneca patents. In September 2020, Mylan and Kindeva stipulated to patent infringement to the extent that the asserted patent claims are found to be valid and enforceable, but reserved the right to seek a vacatur of the stipulation if the U.S. Court of Appeals for the Federal Circuit reverses or modifies the District Court's claim construction. In March 2021, the District Court decided in favour of AstraZeneca and determined that the asserted patent claims were not invalid or unenforceable. Mylan and Kindeva appealed to the United States District Court of Appeals for the Federal Circuit. Oral argument of the appeal was held in August 2021.

Tagrisso

US patent proceedings

In September 2021, Puma Biotechnology, Inc. and Wyeth LLC filed a patent infringement lawsuit in the US District Court for the District of Delaware against AstraZeneca relating to *Tagrisso*. Neither a case schedule, nor a trial date have been set yet.

Patent proceedings outside the US

In Russia, in October 2021, AstraZeneca filed a lawsuit in the Arbitration Court of the Moscow Region against Axelpharm, LLC to prevent it from obtaining authorization to market a generic version of *Tagrisso* prior to the expiration of AstraZeneca's patents covering *Tagrisso*. The lawsuit also names the Ministry of Health of the Russian Federation as a third party. Neither a case schedule, nor a trial date have been set.

Ultomiris

US patent proceedings

In November 2018, Chugai Pharmaceutical Co., Ltd. ("Chugai") filed a lawsuit against Alexion in the Delaware District Court alleging that *Ultomiris* infringes a U.S. patent held by Chugai. Upon issuance of another U.S. patent in November 2019, Chugai filed a second lawsuit in the same court alleging that *Ultomiris* also infringes the second patent. The two lawsuits were consolidated. A trial is scheduled to occur in January 2022.

Patent proceedings outside the US

In December 2018, Chugai Pharmaceutical Co., Ltd (Chugai) filed a lawsuit in the Tokyo District Court against Alexion Pharma GK in Japan and alleges that *Ultomiris* infringes two Japanese patents held by Chugai. Chugai's complaints seek unspecified damages and certain injunctive relief. On 5 March 2020, the Supreme Court of Japan dismissed Chugai's appeal against an earlier IP High Court of Japan decision which held that one of the Chugai patents-in-suit is invalid. Subsequently, Chugai filed a correction to the claims of this patents-in-suit and Alexion has countered that the corrected claims are still invalid and not infringed. In all cases, Alexion has denied the charges and countered that the patents are neither valid nor infringed. In October 2021 the Japanese Patent Office invalidated four Chugai patents, including those asserted in the Tokyo District Court Case. Chugai has appealed the patent office decision.

Product liability litigation

Byetta/Bydureon

In the US, Amylin Pharmaceuticals, LLC (a wholly owned subsidiary of AstraZeneca) and AstraZeneca are among multiple defendants in various lawsuits filed in federal and state courts involving claims of physical injury from treatment with *Byetta* and/or *Bydureon*. The lawsuits allege several types of injuries including pancreatic cancer and thyroid cancer. A multidistrict litigation was established in the US District Court for the Southern District of California (the District Court) in regard to the alleged pancreatic cancer cases in federal courts. Further, a coordinated proceeding has been established in Superior Court in Los Angeles, California ("the California Court") in regard to the various lawsuits in California state courts. In October and December 2020, the District Court and the California Court jointly heard oral argument on renewed motions filed by Defendants seeking summary judgment and dismissal of all claims alleging pancreatic cancer. In March and April 2021, the District Court and the California Court respectively granted the Defendants' motions, and dismissed all cases alleging pancreatic cancer with prejudice. Plaintiffs have dismissed the appeal as to Amylin Pharmaceuticals, LLC and AstraZeneca. The other claims in both courts, including those alleging thyroid cancer, remain pending.

Nexium and *Losec*/*Prilosec*

US proceedings

As previously disclosed, in the US, AstraZeneca is defending various lawsuits brought in federal and state courts involving multiple plaintiffs claiming that they have been diagnosed with various injuries following treatment with proton pump inhibitors (PPIs), including *Nexium* and *Prilosec*. The vast majority of those lawsuits relate to allegations of kidney injuries. In particular, in May 2017, counsel for a group of such plaintiffs claiming that they have been diagnosed with kidney injuries filed a motion with the Judicial Panel on Multidistrict Litigation (JPML) seeking the transfer of any currently pending federal court cases as well as any similar, subsequently filed cases to a coordinated and consolidated pre-trial multidistrict litigation (MDL) proceeding. In August 2017, the JPML granted the motion and consolidated the pending federal court cases in an MDL proceeding in federal court in New Jersey for pre-trial purposes. A trial in the MDL has been rescheduled for January 2022. In addition to the MDL cases, there are cases filed in several state courts around the US; a trial in Delaware state court has been scheduled for February 2022.

In addition, AstraZeneca has been defending lawsuits involving allegations of gastric cancer following treatment with PPIs. One such claim is filed in the US District Court for the Middle District of Louisiana, where the court has rescheduled a trial for November 2022.

Canada proceedings

As previously disclosed, in Canada, in July and August 2017, AstraZeneca was served with three putative class action lawsuits. Two of the lawsuits seek authorisation to represent individual residents in Canada who allegedly suffered kidney injuries from the use of proton pump inhibitors, including *Nexium* and *Losec*. In August 2019, the third lawsuit, filed in Quebec, was dismissed.

Commercial litigation

AZD1222 Securities Litigation

As previously disclosed, in January 2021, putative securities class action lawsuits were filed in the US District Court for the Southern District of New York against AstraZeneca PLC and certain officers, on behalf of purchasers of AstraZeneca publicly traded securities during the period 21 May 2020 through 20 November 2020. The Court appointed co-lead plaintiffs in April 2021 and they filed an Amended Complaint in July 2021 on behalf of purchasers of AstraZeneca publicly traded securities during the period 15 June 2020 through 29 January 2021. The Amended Complaint alleges that defendants made materially false and misleading statements in connection with the development of AZD1222, AstraZeneca's vaccine for the prevention of COVID-19. In September 2021, AstraZeneca moved to dismiss the Amended Complaint.

Amplimmune

As previously disclosed, in the US, in June 2017, AstraZeneca was served with a lawsuit filed by the stockholders' agents for Amplimmune, Inc. (Amplimmune) in Delaware State Court that alleged, among other things, breaches of contractual obligations relating to a 2013 merger agreement between AstraZeneca and Amplimmune. A trial of the matter was held in February 2020 and post-trial oral argument was heard in August 2020. In November 2020, the Delaware Court of Chancery decided in AstraZeneca's favour and subsequently entered a Final Judgment as to all pending claims in favour of AstraZeneca. In December 2020, the plaintiffs filed an appeal to the Delaware Supreme Court. In October 2021, the Delaware Supreme Court affirmed the Delaware Court of Chancery's decision.

Shareholder Litigation – Alexion

In December 2016, putative securities class action lawsuits were filed in the US District Court for the District of Connecticut against Alexion and certain officers and directors, on behalf of purchasers of Alexion publicly traded securities during the period 30 January 2014 through 26 May 2017. The amended complaint alleges that defendants engaged in securities fraud, including by making misrepresentations and omissions in its public disclosures concerning Alexion's *Soliris* sales practices, management changes, and related investigations. In August 2021, the court issued a decision denying in part Defendants' motion to dismiss the matter.

Shareholder Litigation - Portola

In connection with Alexion's July 2020 acquisition of Portola Pharmaceuticals, Inc (Portola), Alexion assumed litigation to which Portola is a party. In January 2020, putative securities class action lawsuits were filed in the US District Court for the Northern District of California against Portola and certain officers and directors, on behalf of purchasers of Portola publicly traded securities during the period 8 January 2019 through 26 February 2020. The third amended complaint alleges that defendants made materially false and/or misleading statements or omissions about the demand for *Andexxa*, usage of *Andexxa* by hospitals and healthcare organisations, and about Portola's accounting for its return reserves. In August 2021, the court denied in part defendants' motion to dismiss the case. A trial date has been set in the matter for December 2022.

Anti-Terrorism Act Civil Lawsuit

As previously disclosed, in July 2020, the US District Court for the District of Columbia granted AstraZeneca's and certain other pharmaceutical and/or medical device companies' motion and dismissed a lawsuit filed by US nationals (or their estates, survivors, or heirs) who were killed or wounded in Iraq between 2005 and 2011, which had alleged that the defendants violated the US Anti-Terrorism Act and various state laws by selling pharmaceuticals and medical supplies to the Iraqi Ministry of Health. The plaintiffs are appealing the District Court's order dismissing the litigation. The DC Circuit Court of Appeals heard oral argument on the plaintiffs' appeal in September 2021.

Government investigations/proceedings

US 340B Litigations and Proceedings

As previously disclosed, AstraZeneca is involved in several matters relating to its policy with regard to contract pharmacy recognition under the 340B Drug Pricing Program in the US. In October and November 2020, two lawsuits, one in the US District Court for the District of Columbia and one in the US District Court for the Northern District of California, were filed by covered entities and advocacy groups against the US Department of Health and Human Services, the US Health Resources and Services Administration as well as other US government agencies and their officials. The complaints allege, among other things, that these agencies should enforce an interpretation of the governing statute for the 340B Drug Pricing Program that would require drug manufacturers participating in the program to offer their drugs for purchase at statutorily capped rates by an unlimited number of contract pharmacies. AstraZeneca has sought to intervene in the lawsuits. The case in US District Court for the District of Columbia is currently stayed pending further proceedings and the case in federal court in California has been dismissed. Administrative Dispute Resolution (ADR) proceedings have also been initiated against AstraZeneca before the US Health Resources and Services Administration.

In February 2021, AstraZeneca received a Civil Investigative Subpoena from the Attorney General's Office for the State of Vermont seeking documents and information relating to AstraZeneca's policy regarding contract pharmacy recognition under the 340B Drug Pricing Program. AstraZeneca is cooperating with the inquiry.

In addition, in January 2021, AstraZeneca filed a separate lawsuit in federal court in Delaware alleging that a recent Advisory Opinion issued by the Department of Health and Human Services violates the Administrative Procedure Act. In June 2021, the Court found in favour of AstraZeneca, invalidating the Advisory Opinion. Prior to the Court's ruling, however, in May 2021, the US government issued new and separate letters to AstraZeneca (and other companies) asserting that our contract pharmacy policy violates the 340B statute. In July 2021, AstraZeneca amended the complaint to include allegations challenging the letter sent in May. In September 2021, the US government issued a follow-up letter to AstraZeneca (and other companies) asserting that it has referred the matter to the Office of Inspector General for further review and consideration. In October 2021, oral arguments were held before the federal court in Delaware challenging the letters sent in May and September.

In September 2021, AstraZeneca was served with a class-action complaint filed in federal court in New York by Mosaic Health on behalf of a purported class. The complaint alleges that AstraZeneca conspired with Sanofi-Aventis U.S., LLC, Eli Lilly and Company, Lilly USA, LLC, and Novo Nordisk Inc to restrict access to 340B discounts through contract pharmacies.

European Commission Claim Regarding AZD1222

As previously disclosed, in April 2021 and May 2021, the European Commission (acting on behalf of the European Union and its member states) initiated two separate legal proceedings against AstraZeneca AB in the Court of First Instance in Brussels. Both proceedings related to an Advance Purchase Agreement between the parties dated 27 August 2020 (the APA) for the supply of AZD1222. The allegations include claims that AstraZeneca has failed to meet certain of its obligations under the APA and the European Commission is seeking, among other things, a Court order to compel AstraZeneca to supply a specified number of doses before the end of the second quarter of 2021. In June 2021, the Court issued a decision in the first proceeding finding that AstraZeneca did not meet its Best Reasonable Efforts obligation in the APA because AstraZeneca did not use all of the manufacturers listed in the APA to supply the member states. The Court ordered AstraZeneca to provide an additional 50 million doses of vaccine by the end of September 2021, which AstraZeneca exceeded by the end of June 2021. The Court denied the remainder of the Commission's claims and requested relief.

In September 2021, the parties reached an agreement to resolve the dispute. This matter is now concluded.

COVID-19 Vaccine Supply and Manufacturing Inquiries

As previously disclosed, in June 2021, Argentina's Federal Criminal Prosecutor's Office (the Prosecutor) contacted AstraZeneca Argentina seeking documents and electronic records in connection with a local criminal investigation relating to the public procurement and supply of *Vaxzevria* in that country. In October 2021, the Prosecutor filed a submission with the presiding court requesting dismissal of the criminal investigation. The request remains pending.

Turkish Ministry of Health Matter

In Turkey, in July 2020, the Turkish Ministry of Health initiated an investigation regarding payments to healthcare providers by Alexion Turkey and former employees and consultants. The investigation arose from Alexion's disclosure of a civil settlement with the U.S. Securities & Exchange Commission in July 2020 fully resolving the SEC's investigation into possible violations of the FCPA. Alexion neither admitted nor denied any wrongdoing in connection with the settlement but paid US$21.5 million to the SEC, consisting of amounts attributable to disgorgement, civil penalties, and pre-judgment interest. AstraZeneca is cooperating with the investigation by the Turkish agency. In September 2021, the Ministry of Health completed its draft investigation report, and referred the matter to the Ankara Public Prosecutor's Office with a recommendation for further proceedings against certain former employees.

Canadian Pricing Matter

In October 2017, Alexion filed proceedings in the Federal Court of Canada to seek judicial review of a determination by the Canadian Patented Medicine Prices Review Board that Alexion had excessively priced *Soliris* in a manner inconsistent with the Canadian pricing rules and guidelines. In its decision, the PMPRB ordered Alexion to decrease the price of *Soliris* to an upper limit based upon pricing in certain other countries and to forfeit excess revenues for the period between 2009 and 2017. In May 2019, the Federal Court dismissed Alexion's application. Alexion appealed the decision to the Canadian Federal Court of Appeal. On 29 July 2021, the Federal Court of Appeal of Canada issued its judgment allowing the appeal, reversing the PMPRB's decision and remitting the matter to the PMPRB for re-determination with costs to AstraZeneca. In September 2021, the Attorney General of Canada sought leave to appeal the decision to the Supreme Court of Canada. Pursuant to an order made by the Federal Court of Canada, as of August 2021, AstraZeneca has placed approximately US$71.4 million in escrow pending the final resolution of all appeals in this matter.

Taxation

As previously disclosed in the Annual Report and Form 20-F Information 2020, AstraZeneca faces a number of audits and reviews in jurisdictions around the world and, in some cases, is in dispute with the tax authorities. The issues under discussion are often complex and can require many years to resolve. Accruals for tax contingencies require management to make key judgements and significant estimates with respect to the ultimate outcome of current and potential future tax audits, and actual results could vary from these estimates.

The total net accrual to cover the worldwide tax exposure for transfer pricing and other international tax contingencies of $82m (31 December 2020: $287m) reflected the progress in those tax audits and reviews during the year and for those audits where AstraZeneca and tax authorities are in dispute, AstraZeneca estimates the potential for reasonably possible additional liabilities above and beyond the amount provided to be up to $25m, including associated interest (31 December 2020: $251m).

There is no material change to other tax exposures.

7) Subsequent Events

In 2019 Caelum and Alexion entered into a collaboration to develop CAEL-101 for light chain amyloidosis, whereby Alexion acquired a minority equity interest and an exclusive option to acquire the remaining equity in Caelum. AstraZeneca has treated Caelum as a subsidiary from the date of acquisition of Alexion, reflecting a non-controlling interest of $150m. On 5 October 2021, the Group completed the acquisition of the remaining shares of Caelum and paid its shareholders the option exercise price of $150m, with the potential for additional payments of up to $350m upon achievement of regulatory and commercial milestones.

In November 2021, AstraZeneca agreed to transfer its global rights to *Eklira*, known as *Tudorza* in the US, and *Duaklir* to Covis Pharma Group for $270m payable on completion, which is expected in the fourth quarter of 2021. Covis Pharma Group will also cover certain ongoing development costs related to the medicines. The income arising from the upfront payment will be fully offset by a charge for derecognition of the associated intangible asset and therefore no Other Operating Income will be recognised in AstraZeneca's financial statements.

8) Table 51: YTD 2021 - Product Sales year-on-year analysis[104]

	World			Emerging Markets			US			Europe			Established RoW		
	$m	Actual % change	CER % change	$m	Actual % change	CER % change	$m	Actual % change	$m	Actual % change	CER % change	$m	Actual % change	CER % change
Oncology	**9,593**	**21**	**17**	**2,438**	**9**	**4**	**3,871**	**26**	**1,823**	**34**	**24**	**1,461**	**16**	**14**
Tagrisso	3,701	17	13	1,012	6	1	1,294	13	727	45	35	668	16	14
Imfinzi	1,778	20	17	211	87	77	916	3	347	37	27	304	29	27
Lynparza	1,719	34	31	282	44	40	793	26	456	47	36	188	32	29
Calquence	843	n/m	n/m	12	n/m	n/m	752	n/m	69	n/m	n/m	10	n/m	n/m
Koselugo	74	n/m	n/m	-	-	-	72	n/m	2	n/m	n/m	-	-	-
Enhertu	10	n/m	n/m	8	n/m	n/m	-	-	2	n/m	n/m	-	-	-
Orpathys	10	n/m	n/m	10	n/m	n/m	-	-	-	-	-	-	-	-
Zoladex	716	7	1	465	9	3	11	80	112	7	(1)	128	(5)	(8)
Faslodex	329	(27)	(29)	122	(14)	(17)	24	(47)	93	(45)	(49)	90	(3)	(3)
Iressa	149	(26)	(31)	122	(25)	(30)	9	(13)	5	(59)	(66)	13	(24)	(23)
Casodex	120	(9)	(15)	92	(11)	(18)	-	-	2	10	10	26	(1)	(4)
Arimidex	106	(29)	(31)	80	(34)	(37)	-	-	3	23	31	23	(11)	(11)
Others	38	-	(2)	22	8	5	-	-	5	32	12	11	(19)	(17)
BioPharmaceuticals: CVRM	**6,017**	**15**	**10**	**2,912**	**20**	**15**	**1,548**	**3**	**1,108**	**23**	**15**	**449**	**6**	**1**
Farxiga	2,152	57	51	877	80	74	504	31	584	61	50	187	37	31
Brilinta	1,124	(9)	(11)	256	(35)	(37)	558	4	263	2	(5)	47	7	(3)
Bydureon	293	(10)	(11)	2	(24)	(17)	243	(12)	43	12	4	5	(28)	(36)
Onglyza	284	(22)	(25)	151	(2)	(6)	62	(53)	47	10	2	24	(29)	(34)
Byetta	45	(10)	(10)	11	33	43	20	(15)	9	(16)	(21)	5	(29)	(35)
Other diabetes	43	24	20	12	n/m	n/m	16	(20)	13	47	38	2	24	(4)
Roxadustat	144	n/m	n/m	144	n/m	n/m	-	-	-	-	-	-	-	-
Lokelma	122	n/m	n/m	3	(8)	(15)	82	n/m	8	n/m	n/m	29	n/m	n/m
Crestor	837	(5)	(9)	597	7	2	59	(17)	43	(55)	(58)	138	(12)	(14)
Seloken/Toprol-XL	749	21	14	731	23	17	1	(85)	9	(24)	(24)	8	7	(5)
Atacand	76	(58)	(58)	25	(81)	(81)	3	(55)	48	n/m	n/m	-	n/m	n/m
Others	148	2	(3)	103	10	3	-	-	41	(9)	(11)	4	(32)	(34)
BioPharmaceuticals: Respiratory & Immunology	**4,444**	**16**	**12**	**1,305**	**24**	**17**	**1,757**	**24**	**912**	**5**	**(3)**	**470**	**(5)**	**(9)**
Symbicort	2,047	-	(3)	457	8	4	804	6	499	(4)	(11)	287	(16)	(21)
Fasenra	901	35	32	15	55	52	555	31	211	51	40	120	29	24
Pulmicort	714	14	7	578	20	13	53	(1)	49	(10)	(17)	34	(16)	(20)
Daliresp	168	3	3	2	(10)	6	153	9	12	(35)	(40)	1	28	(12)
Breztri	130	n/m	n/m	40	n/m	n/m	68	n/m	4	n/m	n/m	18	n/m	n/m
Bevespi	39	8	7	3	n/m	n/m	29	(14)	7	n/m	n/m	-	-	-
Saphnelo	1	n/m	n/m	-	-	-	1	n/m	-	-	-	-	-	-
Others	444	62	53	210	72	59	94	n/m	130	(2)	(9)	10	(11)	(18)
Rare disease	**1,311**	n/m	n/m	**65**	n/m	n/m	**785**	n/m	**302**	n/m	n/m	**159**	n/m	n/m
Soliris	798	n/m	n/m	53	n/m	n/m	460	n/m	199	n/m	n/m	86	n/m	n/m
Ultomiris	297	n/m	n/m	5	n/m	n/m	167	n/m	69	n/m	n/m	56	n/m	n/m
Strensiq	159	n/m	n/m	4	n/m	n/m	124	n/m	16	n/m	n/m	15	n/m	n/m
Andexxa	29	n/m	n/m	-	n/m	n/m	20	n/m	9	n/m	n/m	-	n/m	n/m
Kanuma	28	n/m	n/m	3	n/m	n/m	14	n/m	9	n/m	n/m	2	n/m	n/m
Other medicines	**1,542**	**(17)**	**(19)**	**755**	**4**	**(1)**	**180**	**(40)**	**267**	**(38)**	**(40)**	**340**	**(13)**	**(15)**

[104] The table provides an analysis of year-on-year Product Sales, with Actual and CER growth rates reflecting year-on-year growth. Due to rounding, the sum of a number of dollar values and percentages may not agree to totals.

Nexium	999	(10)	(13)	576	2	(1)	99	(22)	47	(20)	(26)	277	(24)	(26)
Synagis	170	(42)	(41)	15	n/m	n/m	21	(54)	81	(67)	(67)	53	n/m	n/m
Losec/Prilosec	138	(4)	(10)	116	(3)	(10)	-	(96)	21	29	29	1	(85)	(87)
FluMist	75	(35)	(37)	1	n/m	n/m	23	(65)	51	5	1	-	-	-
Seroquel XR/IR	74	(25)	(24)	36	(11)	(9)	13	(42)	22	-	-	3	(78)	(75)
Others	86	(2)	(6)	11	85	79	24	(36)	45	15	9	6	12	3
COVID-19	**2,136**	**n/m**	**n/m**	**1,056**	**n/m**	**n/m**	**-**	**-**	**736**	**n/m**	**n/m**	**344**	**n/m**	**n/m**
Pandemic COVID-19 vaccine	2,136	n/m	n/m	1,056	n/m	n/m	-	-	736	n/m	n/m	344	n/m	n/m
Total Product Sales	**25,043**	**33**	**29**	**8,531**	**32**	**27**	**8,141**	**29**	**5,148**	**45**	**35**	**3,223**	**25**	**22**

9) Table 52: Q3 2021 - Product Sales year-on-year analysis[105]

			World		Emerging Markets			US		Europe			Established RoW	
		Actual	CER		Actual	CER		Actual		Actual	CER		Actual	CER
	$m	% change	% change	$m	% change	% change	$m	% change	$m	% change	% change	$m	% change	% change
Oncology	**3,326**	**18**	**16**	**812**	**5**	**-**	**1,377**	**22**	**640**	**35**	**31**	**497**	**10**	**13**
Tagrisso	1,247	8	7	315	(11)	(15)	441	5	259	46	42	232	14	17
Imfinzi	618	16	15	78	58	50	319	2	120	38	35	101	19	21
Lynparza	588	27	25	96	28	23	270	21	155	36	33	67	32	33
Calquence	354	n/m	n/m	5	n/m	n/m	308	n/m	37	n/m	n/m	4	n/m	n/m
Koselugo	26	n/m	n/m	-	-	-	25	96	1	n/m	n/m	-	-	-
Enhertu	5	n/m	n/m	4	n/m	n/m	-	-	1	n/m	n/m	-	-	-
Orpathys	10	n/m	n/m	10	n/m	n/m	-	-	-	-	-	-	-	-
Zoladex	250	9	5	169	22	15	3	n/m	38	4	1	40	(25)	(24)
Faslodex	103	(26)	(27)	42	1	(3)	8	(33)	23	(59)	(59)	30	(1)	2
Iressa	41	(23)	(29)	34	(22)	(27)	3	21	2	(34)	(52)	2	(54)	(44)
Casodex	38	(13)	(18)	28	(19)	(25)	-	(92)	1	57	34	9	12	11
Arimidex	33	(20)	(20)	24	(23)	(26)	-	-	1	20	56	8	(12)	(7)
Others	13	2	1	7	17	15	-	-	2	65	31	4	(29)	(23)
BioPharmaceuticals: CVRM	**2,082**	**16**	**13**	**991**	**21**	**15**	**561**	**9**	**381**	**22**	**20**	**149**	**(1)**	**(1)**
Farxiga	796	51	48	320	76	69	202	36	213	51	48	61	12	11
Brilinta	375	(3)	(4)	76	(25)	(28)	198	7	85	1	(1)	16	10	5
Bydureon	95	(13)	(13)	-	(60)	(37)	81	(13)	13	(3)	(2)	1	(68)	(65)
Onglyza	84	(23)	(25)	42	(22)	(26)	18	(37)	17	17	15	7	(37)	(41)
Byetta	13	(11)	(6)	3	(18)	(5)	6	1	3	9	17	1	(50)	(51)
Other diabetes	14	24	26	5	n/m	n/m	4	(32)	4	37	44	1	22	(27)
Roxadustat	55	n/m	n/m	55	n/m	n/m	-	-	-	-	-	-	-	-
Lokelma	49	n/m	n/m	1	(63)	(65)	32	n/m	3	n/m	n/m	13	n/m	n/m
Crestor	298	(1)	(4)	225	18	13	18	(30)	11	(65)	(65)	44	(18)	(17)
Seloken/Toprol-XL	234	4	(2)	227	5	-	1	(81)	3	(25)	(33)	3	15	1
Atacand	19	(65)	(65)	5	(88)	(88)	1	(52)	13	80	80	-	n/m	n/m
Others	50	29	23	32	13	6	-	-	16	60	55	2	n/m	n/m
BioPharmaceuticals: Respiratory & Immunology	**1,483**	**28**	**25**	**420**	**44**	**35**	**609**	**41**	**295**	**5**	**3**	**159**	**2**	**-**
Symbicort	676	13	11	151	14	9	274	39	155	(6)	(8)	96	(8)	(11)
Fasenra	322	34	33	7	n/m	n/m	199	32	75	45	42	41	20	19
Pulmicort	217	44	36	173	59	48	17	1	15	5	5	12	4	5

[105] The table provides an analysis of year-on-year Product Sales, with Actual and CER growth rates reflecting year-on-year growth. Due to rounding, the sum of a number of dollar values and percentages may not agree to totals. *Growth rates on Rare Disease medicines have been calculated by comparing post-acquisition revenues from 21 July 2021 with the corresponding prior year pre-acquisition Q3 revenues previously published by Alexion adjusted pro rata to match the post-acquisition period.

Daliresp	54	(5)	(6)	-	(61)	(14)	50	(3)	3	(34)	(36)	1	n/m	n/m
Breztri	47	n/m	n/m	14	n/m	n/m	25	n/m	2	n/m	n/m	6	n/m	n/m
Bevespi	13	(9)	(10)	1	68	34	9	(28)	3	n/m	n/m	-	-	-
Saphnelo	1	n/m	n/m	-	-	-	1	n/m	-	-	-	-	-	-
Others	153	70	64	74	78	66	34	n/m	42	(6)	(8)	3	1	-
Rare disease*	**1,311**	***5***	***6***	**65**	***(34)***	***(31)***	**785**	***7***	**302**	***12***	***12***	**159**	***7***	***9***
*Soliris**	798	*(3)*	*(2)*	53	*(44)*	*(40)*	460	*4*	199	*(3)*	*(3)*	86	*9*	*10*
*Ultomiris**	297	*31*	*31*	5	*n/m*	*n/m*	167	*25*	69	*78*	*77*	56	*2*	*5*
*Strensiq**	159	*7*	*8*	4	*87*	*84*	124	*6*	16	*6*	*5*	15	*8*	*11*
*Andexxa**	29	*(6)*	*(5)*	-	-	-	20	*(30)*	9	*n/m*	*n/m*	-	-	-
*Kanuma**	28	*26*	*26*	3	*n/m*	*n/m*	14	*13*	9	*16*	*16*	2	*85*	*63*
Other medicines	**539**	**(27)**	**(27)**	**219**	**(10)**	**(13)**	**80**	**(47)**	**122**	**(36)**	**(37)**	**118**	**(21)**	**(19)**
Nexium	259	(35)	(36)	156	(19)	(21)	32	(32)	11	(50)	(51)	60	(57)	(56)
Synagis	122	3	5	15	n/m	n/m	16	(36)	38	(61)	(62)	53	n/m	n/m
Losec/Prilosec	38	(16)	(21)	32	(16)	(23)	-	-	6	(9)	(9)	-	-	-
FluMist	72	(37)	(39)	-	-	-	23	(65)	49	1	(2)	-	n/m	n/m
Seroquel XR/IR	24	(32)	(30)	12	(13)	(10)	3	(66)	7	9	8	2	(69)	(64)
Others	24	23	20	4	50	39	6	33	11	3	4	3	72	41
COVID-19	**1,000**	**n/m**	**n/m**	**601**	**n/m**	**n/m**	**-**	**-**	**165**	**n/m**	**n/m**	**234**	**n/m**	**n/m**
Pandemic COVID-19 vaccine	1,000	n/m	n/m	601	n/m	n/m	-	-	165	n/m	n/m	234	n/m	n/m
Total Product Sales	**9,741**	**49**	**47**	**3,108**	**46**	**40**	**3,412**	**53**	**1,905**	**51**	**48**	**1,316**	**45**	**47**

10) Table 53: Q3 2021 - Product Sales quarterly sequential analysis[106]

		Q1 2021			Q2 2021			Q3 2021	
		Actual	CER		Actual	CER		Actual	CER
	$m	% change	% change	$m	% change	% change	$m	% change	% change
Oncology	**2,981**	**3**	**1**	**3,286**	**10**	**11**	**3,326**	**1**	**2**
Tagrisso	1,149	(1)	(3)	1,306	14	14	1,247	(5)	(4)
Imfinzi	556	-	(1)	604	9	10	618	2	3
Lynparza	543	9	8	588	8	9	588	-	1
Calquence	209	15	15	280	34	34	354	26	26
Koselugo	21	23	23	26	23	22	26	-	2
Enhertu	1	n/m	n/m	3	n/m	n/m	5	64	63
Orpathys	-	-	-	-	-	-	10	n/m	n/m
Zoladex	221	2	-	244	10	11	250	2	3
Faslodex	122	(6)	(8)	105	(14)	(12)	103	(2)	(2)
Iressa	61	(9)	(11)	47	(23)	(22)	41	(11)	(14)
Casodex	42	7	5	41	(2)	(1)	38	(7)	(8)
Arimidex	44	22	18	29	(34)	(33)	33	16	19
Others	12	(4)	(6)	13	13	11	13	(5)	(4)
BioPharmaceuticals: CVRM	**1,912**	**4**	**1**	**2,023**	**6**	**6**	**2,082**	**3**	**3**
Farxiga	624	6	4	732	17	18	796	9	9
Brilinta	374	3	1	375	-	1	375	-	1
Bydureon	103	(16)	(17)	95	(8)	(7)	95	1	2

[106] The table provides an analysis of sequential quarterly Product Sales, with Actual and CER growth rates reflecting quarter-on-quarter growth. Due to rounding, the sum of a number of dollar values and percentages may not agree to totals. † Sequential growth rates on Rare Disease medicines have been calculated by comparing post-acquisition revenues from 21 July 2021 with the prior quarter pre-acquisition Q2 revenues previously published by Alexion adjusted pro rata to match the post-acquisition period.

Onglyza	101	(3)	(6)	99	(2)	(2)	84	(15)	(15)
Byetta	16	(14)	(15)	16	(4)	(7)	13	(15)	(7)
Other diabetes	13	7	1	15	14	14	14	(9)	(4)
Roxadustat	39	n/m	n/m	51	32	32	55	7	7
Lokelma	33	16	18	39	21	21	49	25	26
Crestor	274	(8)	(9)	265	(3)	(3)	298	12	13
Seloken/Toprol-XL	250	25	21	266	6	7	234	(12)	(13)
Atacand	34	(45)	(45)	23	(35)	(32)	19	(15)	(18)
Others	51	12	10	47	(7)	(10)	50	6	7
BioPharmaceuticals: Respiratory & Immunology	**1,541**	**1**	**(1)**	**1,420**	**(8)**	**(7)**	**1,483**	**4**	**5**
Symbicort	691	2	-	680	(2)	(1)	676	(1)	-
Fasenra	260	(8)	(9)	320	23	23	322	1	1
Pulmicort	330	(10)	(13)	167	(50)	(49)	217	30	30
Daliresp	60	11	10	54	(10)	(9)	54	-	(2)
Breztri	27	n/m	n/m	56	n/m	n/m	47	(15)	(15)
Bevespi	13	7	8	13	1	3	13	(1)	(2)
Saphnelo	-	-	-	-	-	-	1	n/m	n/m
Others	160	28	25	130	(19)	(19)	153	17	19
Rare disease†	**-**	**-**	**-**	**-**	**-**	**-**	**1,311**	***(2)***	***(1)***
Soliris†	-	-	-	-	-	-	798	*(6)*	*(4)*
Ultomiris†	-	-	-	-	-	-	297	*7*	*8*
Strensiq†	-	-	-	-	-	-	159	*(2)*	*(2)*
Andexxa†	-	-	-	-	-	-	29	*5*	*6*
Kanuma†	-	-	-	-	-	-	28	*9*	*9*
Other medicines	**548**	**(25)**	**(26)**	**454**	**(17)**	**(16)**	**539**	**19**	**20**
Nexium	403	7	5	336	(17)	(15)	259	(23)	(23)
Synagis	24	(69)	(69)	24	1	1	122	n/m	n/m
Losec/Prilosec	54	39	36	46	(14)	(15)	38	(18)	(17)
FluMist	2	(99)	(99)	1	(51)	(71)	72	n/m	n/m
Seroquel XR/IR	29	51	38	21	(29)	(22)	24	17	14
Others	36	(6)	(4)	26	(28)	(32)	24	(8)	(5)
COVID-19	**275**	**n/m**	**n/m**	**862**	**n/m**	**n/m**	**1,000**	**16**	**18**
Pandemic COVID-19 vaccine	275	n/m	n/m	862	n/m	n/m	1,000	16	18
Total Product Sales	**7,257**	**4**	**1**	**8,045**	**11**	**12**	**9,741**	**21**	**22**

11) Table 54: FY 2020 - Product Sales quarterly sequential analysis[107]

	Q1 2020			Q2 2020			Q3 2020			Q4 2020		
	$m	Actual % change	CER % change	$m	Actual % change	CER % change	$m	Actual % change	CER % change	$m	Actual % change	CER % change
Oncology	**2,502**	**10**	**10**	**2,609**	**4**	**6**	**2,831**	**8**	**6**	**2,908**	**3**	**2**
Tagrisso	982	11	11	1,034	5	7	1,155	12	9	1,157	-	(1)
Imfinzi	462	9	9	492	6	8	533	8	6	555	4	3
Lynparza	397	13	13	419	5	7	464	11	8	496	7	6
Calquence	88	58	58	107	21	23	145	36	35	182	25	25
Koselugo	-	-	-	7	n/m	n/m	13	75	75	17	34	34
Zoladex	225	15	15	217	(3)	-	230	6	3	216	(6)	(7)
Faslodex	166	-	-	146	(12)	(9)	138	(5)	(8)	130	(6)	(7)
Iressa	77	(3)	(4)	70	(9)	(7)	54	(23)	(24)	67	24	19
Arimidex	50	(1)	(2)	58	17	16	42	(28)	(27)	36	(14)	(16)
Casodex	42	(2)	(3)	47	14	12	44	(7)	(8)	39	(11)	(14)
Others	13	(52)	(52)	12	(11)	(1)	13	4	3	13	2	2
BioPharmaceuticals: CVRM	**1,701**	**(5)**	**(5)**	**1,759**	**3**	**6**	**1,794**	**2**	**-**	**1,842**	**3**	**1**
Farxiga	405	(3)	(3)	443	9	13	525	19	16	586	11	10
Brilinta	408	(5)	(5)	437	7	9	385	(12)	(13)	363	(6)	(6)
Onglyza	141	8	8	115	(19)	(17)	110	(6)	(6)	105	(4)	(5)
Bydureon	100	(28)	(28)	116	16	17	109	(5)	(7)	122	12	11
Byetta	20	(24)	(24)	15	(28)	(28)	15	1	4	19	26	24
Other diabetes	13	(22)	(22)	10	(21)	(19)	11	9	6	12	11	15
Lokelma	11	42	42	17	56	58	21	22	26	28	37	28
Crestor	301	2	1	281	(7)	(4)	300	7	5	298	(1)	(4)
Seloken/Toprol-XL	177	(6)	(6)	218	23	27	225	4	3	200	(11)	(13)
Atacand	66	11	12	59	(11)	(5)	54	(9)	(12)	63	16	14
Others	59	(21)	(22)	48	(18)	(16)	39	(19)	(22)	46	18	17
BioPharmaceuticals: Respiratory & Immunology	**1,551**	**1**	**1**	**1,117**	**(28)**	**(26)**	**1,161**	**4**	**1**	**1,528**	**32**	**29**
Symbicort	790	11	11	653	(17)	(15)	599	(8)	(11)	680	13	13
Pulmicort	380	(8)	(9)	97	(74)	(73)	151	56	49	368	n/m	n/m
Fasenra	199	(3)	(3)	227	14	15	240	5	4	283	18	17
Daliresp	53	(8)	(8)	53	(1)	(3)	57	8	11	54	(4)	(6)
Bevespi	12	9	9	10	(19)	(21)	14	47	46	12	(16)	(17)
Breztri	4	n/m	n/m	7	58	64	10	45	48	6	(39)	(38)
Others	113	(16)	(17)	70	(38)	(36)	90	27	22	125	39	35
Other medicines	**557**	**(15)**	**(15)**	**563**	**1**	**4**	**734**	**30**	**27**	**733**	**-**	**(2)**
Nexium	338	(4)	(4)	377	12	14	401	6	4	377	(6)	(7)
Synagis	85	35	35	90	6	7	118	31	29	78	(34)	(33)
FluMist	-	n/m	n/m	-	n/m	n/m	116	n/m	n/m	179	55	50
Losec/Prilosec	54	18	17	45	(15)	(15)	45	-	-	39	(15)	(18)
Seroquel XR/IR	36	(12)	(12)	27	(26)	(23)	35	32	29	19	(45)	(42)
Others	44	(71)	(70)	24	(46)	(42)	19	(17)	(19)	41	n/m	n/m
Total Product Sales	**6,311**	**1**	**1**	**6,048**	**(4)**	**(2)**	**6,520**	**8**	**6**	**7,011**	**8**	**6**

[107] The table provides an analysis of sequential quarterly Product Sales, with actual and CER growth rates reflecting quarter-on-quarter growth. Due to rounding, the sum of a number of dollar values and percentages may not agree to totals.

Table 55: Collaboration Revenue

	YTD 2021 $m	YTD 2020 $m	FY 2020 $m	FY 2019 $m
Initial Collaboration Revenue				
Nexium (Japan)	75	-	-	-
Ongoing Collaboration Revenue				
Lynparza: regulatory milestones	-	135	160	60
Lynparza: sales milestones	-	-	300	450
Lynparza/*Koselugo*: option payments	-	-	-	100
Crestor (Spain)	-	-	-	39
Enhertu: share of gross profits	134	63	94	-
roxadustat: share of gross profits	4	19	30	-
Royalty income	137	47	62	62
Other Ongoing Collaboration Revenue	13	64	81	108
Total	**363**	**328**	**727**	**819**

Table 56: Other Operating Income and Expense

The table below provides an analysis of Reported Other Operating Income and Expense.

	YTD 2021 $m	YTD 2020 $m	FY 2020 $m	FY 2019 $m
Divestment of Viela Bio, Inc. shareholding	776	-	-	-
Crestor (Europe ex-UK and Spain)	309	-	-	-
Oxra and *Oxramet* (India)	40	-	-	-
Hypertension medicines (ex-US, India and Japan)	-	350	350	-
Monetisation of an asset previously licensed	-	120	120	-
brazikumab licence termination funding	77	51	107	-
Inderal, *Tenormin*, *Seloken* and *Omepral* (Japan)	-	51	51	-
Synagis (US)	-	-	-	515
Losec (ex-China, Japan, US and Mexico)	-	-	-	243
Seroquel and Seroquel XR (US, Canada, Europe and Russia)	-	-	-	213
Arimidex and *Casodex* (various countries)	-	-	-	181
Nexium (Europe) and *Vimovo* (ex-US)	-	-	54	-
Atacand	-	-	400	-
Other	143	316	446	389
Total	**1,345**	**888**	**1,528**	**1,541**

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- the risk of failure to meet regulatory or ethical requirements for medicine development or approval
- the risk of failure to obtain, defend and enforce effective IP protection and IP challenges by third parties
- the impact of competitive pressures including expiry or loss of IP rights, and generic competition
- the impact of price controls and reductions
- the impact of economic, regulatory and political pressures
- the risk of failures or delays in the quality or execution of the Group's commercial strategies
- the risk of failure to maintain supply of compliant, quality medicines
- the risk of illegal trade in the Group's medicines
- the impact of reliance on third-party goods and services
- the risk of failure in information technology, data protection or cybercrime
- the risk of failure of critical processes
- any expected gains from productivity initiatives are uncertain
- the risk of failure to attract, develop, engage and retain a diverse, talented and capable workforce, including following the completion of the Alexion transaction
- the risk of failure to adhere to applicable laws, rules and regulations
- the risk of the safety and efficacy of marketed medicines being questioned
- the risk of adverse outcome of litigation and/or governmental investigations, including relating to the Alexion transaction
- the risk of failure to adhere to increasingly stringent anti-bribery and anti-corruption legislation
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- the risk that AstraZeneca is unable to achieve the synergies and value creation contemplated by the Alexion transaction, or that AstraZeneca is unable to promptly and effectively integrate Alexion's businesses

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