20220630113338

Styrelsen för

AstraZeneca Pharmaceuticals AB

Org nr 556023-0657

får härmed avge

Årsredovisning

för räkenskapsåret 1 januari - 31 december 2021

Innehåll:	sida
Förvaltningsberättelse	2
Balansräkning	3
Rapport över förändringar i eget kapital	3
Noter med redovisningsprinciper och bokslutskommentarer	4
Underskrifter	6

Undertecknad styrelseledamot i AstraZeneca Pharmaceuticals Aktiebolag intygar härmed, dels att denna kopia av årsredovisningen överensstämmer med originalet, dels att balansräkningen har fastställts på årsstämma den 28 juni 2022. Årsstämman beslöt tillika att godkänna styrelsens förslag till vinstdisposition.

Södertälje, den 28 juni 2022

Yvonne Bertlin

Namnförtydligande: Yvonne Bertlin

Förvaltningsberättelse

Allmänt om verksamheten
Bolaget har sitt säte i Södertälje och är dotterbolag till AstraZeneca AB (org.nr. 556011-7482, med säte i Södertälje).

Bolagets syfte är att vara moderbolag för AstraZeneca Pharma Ltd, Indien.

Bolaget har under året inte haft några anställda, ej heller utbetalat några löner eller andra ersättningar.

Väsentliga händelser under räkenskapsåret
Under innevarande räkenskapsår, har samtliga intäkter och kostnader överförts till AstraZeneca AB i enlighet med det kommissionärsavtal som finns mellan bolagen.

Förväntad framtida utveckling samt väsentliga risker och osäkerhetsfaktorer
Dotterbolagsinnehav
En stor andel av tillgångarna i AstraZeneca Pharmaceuticals AB utgörs av aktier i dotterbolag. Händelser i dotterbolagen kan utgöra en viss risk för bolagets resultat och finansiella ställning.

Flerårsöversikt

	2021-12-31	*2020-12-31*	*2019-12-31*	*2018-12-31*	*2017-12-31*
Soliditet	100%	100%	100%	100%	100%

Förslag till disposition beträffande bolagets vinst
Styrelsen föreslår att till förfogande stående vinstmedel, kronor 994 346 948, disponeras enligt följande:

Balanseras i ny räkning	994 346 948
Summa	994 346 948

Vad beträffar företagets ställning i övrigt, hänvisas till efterföljande balansräkning med tillhörande bokslutskommentarer.

Balansräkning

Belopp i kr	*Not*	*2021-12-31*	*2020-12-31*
TILLGÅNGAR			
Anläggningstillgångar			
Finansiella anläggningstillgångar			
Andelar i koncernföretag	2	310 020 008	310 020 008
Andelar i intresseföretag	3	100	100
Fordringar hos koncernföretag	4	685 521 045	685 521 166
Andra långfristiga fordringar		5 122	5 122
Summa finansiella anläggningstillgångar		995 546 275	995 546 396
Summa anläggningstillgångar		995 546 275	995 546 396
Omsättningstillgångar			
Kortfristiga fordringar			
Övriga fordringar		646	552
		646	552
Kassa och bank		27	–
Summa omsättningstillgångar		673	552
SUMMA TILLGÅNGAR		995 546 948	995 546 948
EGET KAPITAL OCH SKULDER			
Eget kapital			
Bundet eget kapital			
Aktiekapital		1 000 000	1 000 000
Reservfond		200 000	200 000
Summa bundet eget kapital		1 200 000	1 200 000
Fritt eget kapital			
Balanserad vinst		994 346 948	994 346 948
Årets resultat		0	0
Summa fritt eget kapital		994 346 948	994 346 948
Summa eget kapital		995 546 948	995 546 948
SUMMA EGET KAPITAL OCH SKULDER		995 546 948	995 546 948

Rapport över förändring eget kapital

2020-12-31	Bundet eget kapital				Fritt eget kapital	
	Aktiekapital	*Uppskriv-ningsfond*	*Reservfond*	*Över-kursfond*	*Bal.res. inkl årets resultat*	*Summa eget kapital*
Ingående balans	1 000 000	–	200 000	–	994 346 948	995 546 948
Årets resultat					–	–
Summa	1 000 000	–	200 000	–	994 346 948	995 546 948
Vid årets utgång	1 000 000	–	200 000	–	994 346 948	995 546 948

2021-12-31	Bundet eget kapital				Fritt eget kapital	
	Aktiekapital	*Uppskriv-ningsfond*	*Reservfond*	*Över-kursfond*	*Bal.res. inkl årets resultat*	*Summa eget kapital*
Ingående balans	1 000 000	–	200 000	–	994 346 948	995 546 948
Årets resultat					–	–
Summa	1 000 000	–	200 000	–	994 346 948	995 546 948
Vid årets utgång	1 000 000	–	200 000	–	994 346 948	995 546 948

Noter med redovisningsprinciper och bokslutskommentarer

Belopp i kr om inget annat anges

Not 1 Redovisningsprinciper och bokslutskommentarer

Allmänna redovisningsprinciper
Årsredovisningen har upprättats i enlighet med Årsredovisningslagen och Bokföringsnämndens allmänna råd BFNAR 2012:1 Årsredovisning och koncernredovisning (K3).

Värderingsprinciper m m
Tillgångar och skulder har värderats till anskaffningsvärden om inget annat anges nedan.

Nedskrivningar - materiella och immateriella anläggningstillgångar samt andelar i koncernföretag
Vid varje balansdag bedöms om det finns någon indikation på att en tillgångs värde är lägre än dess redovisade värde. Om en sådan indikation finns, beräknas tillgångens återvinningsvärde.

Återvinningsvärdet är det högsta av verkligt värde med avdrag för försäljningskostnader och nyttjandevärde. Vid beräkning av nyttjandevärdet beräknas nuvärdet av de framtida kassaflöden som tillgången väntas ge upphov till i den löpande verksamheten samt när den avyttras eller utrangeras. Den diskonteringsränta som används är före skatt och återspeglar marknadsmässiga bedömningar av pengars tidsvärde och de risker som avser tillgången. En tidigare nedskrivning återförs endast om de skäl som låg till grund för beräkningen av återvinningsvärdet vid den senaste nedskrivningen har förändrats.

Fordringar
Fordringar har efter individuell värdering upptagits till belopp varmed de beräknas inflyta.

Revisionsarvode
Revisionsarvodet bärs av AstraZeneca AB.

Not 2 Andelar i koncernföretag

	2021-12-31	2020-12-31
Ackumulerade anskaffningsvärden		
Vid årets början	310 020 008	310 020 008
Bokfört värde vid årets slut	310 020 008	310 020 008

			Redovisat värde	
Dotterföretag / Org nr / Säte	*Antal andelar*	*Andel i %*	*2021-12-31*	*2020-12-31*
AstraZeneca Pharma Ltd, Indien	15 750 000	75,0	310 019 684	310 019 684
AstraZeneca India Private Ltd, Indien	10	<0,01	324	324
			310 020 008	310 020 008

Not 3 Andelar i intresseföretag

	2021-12-31	2020-12-31
Ackumulerade anskaffningsvärden		
Vid årets början	100	100
Bokfört värde vid årets slut	100	100

Not 4 Fordringar hos koncernföretag

	2021-12-31	2020-12-31
Vid årets början	685 521 166	685 521 366
Avgående fordringar	-121	-200
Bokfört värde vid årets slut	685 521 045	685 521 166
Varav:		
AstraZeneca AB	685 521 045	685 521 166

Not 5 Koncernuppgifter

Företaget som utgör moderföretag för en koncern med dotterföretag enligt not 2, upprättar ej koncernredovisning med hänvisning till reglerna i 7 kap. 2 § ÅRL. Det utländska moderföretagets årsredovisning finns att tillgå hos AstraZeneca AB.

Moderföretag i den största koncernen som AstraZeneca Pharmaceuticals AB är dotterföretag till och där koncernredovisning upprättas är AstraZeneca PLC. i Cambridge, med org.nr. 2723 534.

Not 6 Nyckeltalsdefinitioner

Soliditet: (Totalt eget kapital + 79,4 % av obeskattade reserver) / Totala tillgångar

Södertälje den 16 jun. 2022

Yvonne Bertlin
Ordförande

Katarina Ageborg

James Fox

Vår revisionsberättelse har lämnats den 16 juni 2022

PricewaterhouseCoopers AB

Johan Engstam
Auktoriserad revisor

Revisionsberättelse

Till bolagsstämman i AstraZeneca Pharmaceuticals Aktiebolag, org.nr 556023-0657

Rapport om årsredovisningen

Uttalanden

Vi har utfört en revision av årsredovisningen för AstraZeneca Pharmaceuticals Aktiebolag för år 2021.

Enligt vår uppfattning har årsredovisningen upprättats i enlighet med årsredovisningslagen och ger en i alla väsentliga avseenden rättvisande bild av AstraZeneca Pharmaceuticals Aktiebolags finansiella ställning per den 31 december 2021 och av dess finansiella resultat för året enligt årsredovisningslagen. Förvaltningsberättelsen är förenlig med årsredovisningens övriga delar.

Vi tillstyrker därför att bolagsstämman fastställer balansräkningen.

Grund för uttalanden

Vi har utfört revisionen enligt International Standards on Auditing (ISA) och god revisionssed i Sverige. Vårt ansvar enligt dessa standarder beskrivs närmare i avsnittet Revisorns ansvar. Vi är oberoende i förhållande till AstraZeneca Pharmaceuticals Aktiebolag enligt god revisorssed i Sverige och har i övrigt fullgjort vårt yrkesetiska ansvar enligt dessa krav.

Vi anser att de revisionsbevis vi har inhämtat är tillräckliga och ändamålsenliga som grund för våra uttalanden.

Styrelsens ansvar

Det är styrelsen som har ansvaret för att årsredovisningen upprättas och att den ger en rättvisande bild enligt årsredovisningslagen. Styrelsen ansvarar även för den interna kontroll som de bedömer är nödvändig för att upprätta en årsredovisning som inte innehåller några väsentliga felaktigheter, vare sig dessa beror på oegentligheter eller misstag.

Vid upprättandet av årsredovisningen ansvarar styrelsen för bedömningen av bolagets förmåga att fortsätta verksamheten. De upplyser, när så är tillämpligt, om förhållanden som kan påverka förmågan att fortsätta verksamheten och att använda antagandet om fortsatt drift. Antagandet om fortsatt drift tillämpas dock inte om styrelsen avser att likvidera bolaget, upphöra med verksamheten eller inte har något realistiskt alternativ till att göra något av detta.

Revisorns ansvar

Våra mål är att uppnå en rimlig grad av säkerhet om huruvida årsredovisningen som helhet inte innehåller några väsentliga felaktigheter, vare sig dessa beror på oegentligheter eller misstag, och att lämna en revisionsberättelse som innehåller våra uttalanden. Rimlig säkerhet är en hög grad av säkerhet, men är ingen garanti för att en revision som utförs enligt ISA och god revisionssed i Sverige alltid kommer att upptäcka en väsentlig felaktighet om en sådan finns. Felaktigheter kan uppstå på grund av oegentligheter eller misstag och anses vara väsentliga om de enskilt eller tillsammans rimligen kan förväntas påverka de ekonomiska beslut som användare fattar med grund i årsredovisningen.

En ytterligare beskrivning av vårt ansvar för revisionen av årsredovisningen finns på Revisorsinspektionens webbplats: www.revisorsinspektionen.se/revisornsansvar. Denna beskrivning är en del av revisionsberättelsen.

Rapport om andra krav enligt lagar och andra författningar

Uttalanden

Utöver vår revision av årsredovisningen har vi även utfört en revision av styrelsens förvaltning för AstraZeneca Pharmaceuticals Aktiebolag för år 2021 samt av förslaget till dispositioner beträffande bolagets vinst eller förlust.

Vi tillstyrker att bolagsstämman disponerar vinsten enligt förslaget i förvaltningsberättelsen och beviljar styrelsens ledamöter ansvarsfrihet för räkenskapsåret.

Grund för uttalanden

Vi har utfört revisionen enligt god revisionssed i Sverige. Vårt ansvar enligt denna beskrivs närmare i avsnittet Revisorns ansvar. Vi är oberoende i förhållande till AstraZeneca Pharmaceuticals Aktiebolag enligt god revisorssed i Sverige och har i övrigt fullgjort vårt yrkesetiska ansvar enligt dessa krav.

Vi anser att de revisionsbevis vi har inhämtat är tillräckliga och ändamålsenliga som grund för våra uttalanden.

Styrelsens ansvar

Det är styrelsen som har ansvaret för förslaget till dispositioner beträffande bolagets vinst eller förlust. Vid förslag till utdelning innefattar detta bland annat en bedömning av om utdelningen är försvarlig med hänsyn till de krav som bolagets verksamhetsart, omfattning och risker ställer på storleken av bolagets egna kapital, konsolideringsbehov, likviditet och ställning i övrigt.

Styrelsen ansvarar för bolagets organisation och förvaltningen av bolagets angelägenheter. Detta innefattar bland annat att fortlöpande bedöma bolagets ekonomiska situation, och att tillse att bolagets organisation är utformad så att bokföringen, medelsförvaltningen och bolagets ekonomiska angelägenheter i övrigt kontrolleras på ett betryggande sätt.

Revisorns ansvar

Vårt mål beträffande revisionen av förvaltningen, och därmed vårt uttalande om ansvarsfrihet, är att inhämta revisionsbevis för att med en rimlig grad av säkerhet kunna bedöma om någon styrelseledamot i något väsentligt avseende:

- företagit någon åtgärd eller gjort sig skyldig till någon försummelse som kan föranleda ersättningsskyldighet mot bolaget
- på något annat sätt handlat i strid med aktiebolagslagen, årsredovisningslagen eller bolagsordningen.

Vårt mål beträffande revisionen av förslaget till dispositioner av bolagets vinst eller förlust, och därmed vårt uttalande om detta, är att med rimlig grad av säkerhet bedöma om förslaget är förenligt med aktiebolagslagen.

Rimlig säkerhet är en hög grad av säkerhet, men ingen garanti för att en revision som utförs enligt god revisionssed i Sverige alltid kommer att upptäcka åtgärder eller försummelser som kan föranleda ersättningsskyldighet mot bolaget, eller att ett förslag till dispositioner av bolagets vinst eller förlust inte är förenligt med aktiebolagslagen.

En ytterligare beskrivning av vårt ansvar för revisionen av förvaltningen finns på Revisorsinspektionens webbplats: www.revisorsinspektionen.se/revisornsansvar. Denna beskrivning är en del av revisionsberättelsen.

Stockholm den 16 juni 2022

PricewaterhouseCoopers AB

Johan Engstam
Auktoriserad revisor

AstraZeneca

What science can do

AstraZeneca Annual Report and Form 20-F Information 2020

Company name: AstraZeneca PLC
Company number: 2723534

WEDNESDAY

AB6QCRYG

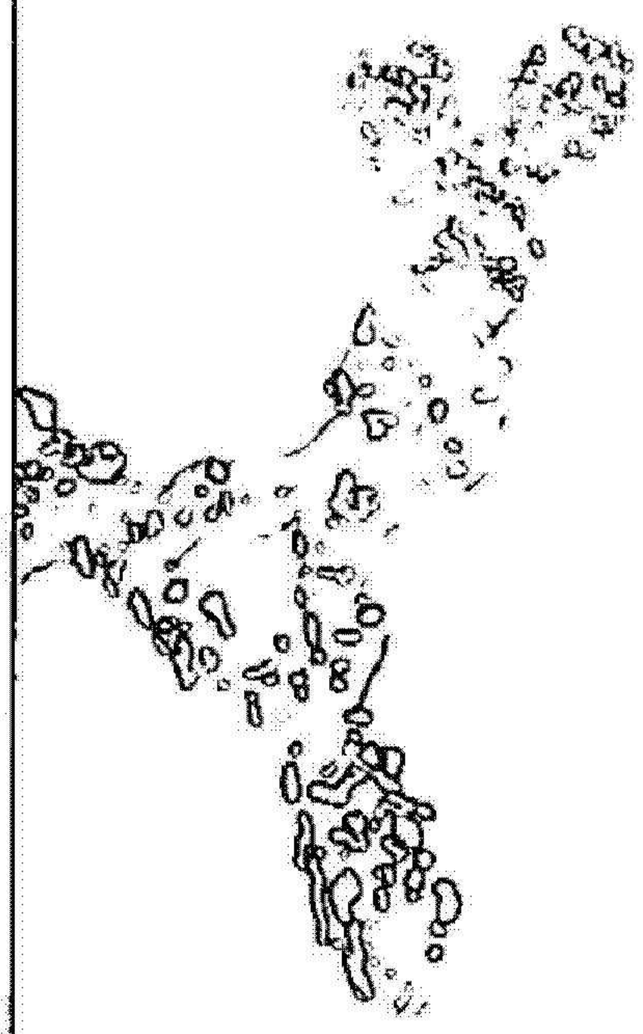
A08 22/06/2022 #186

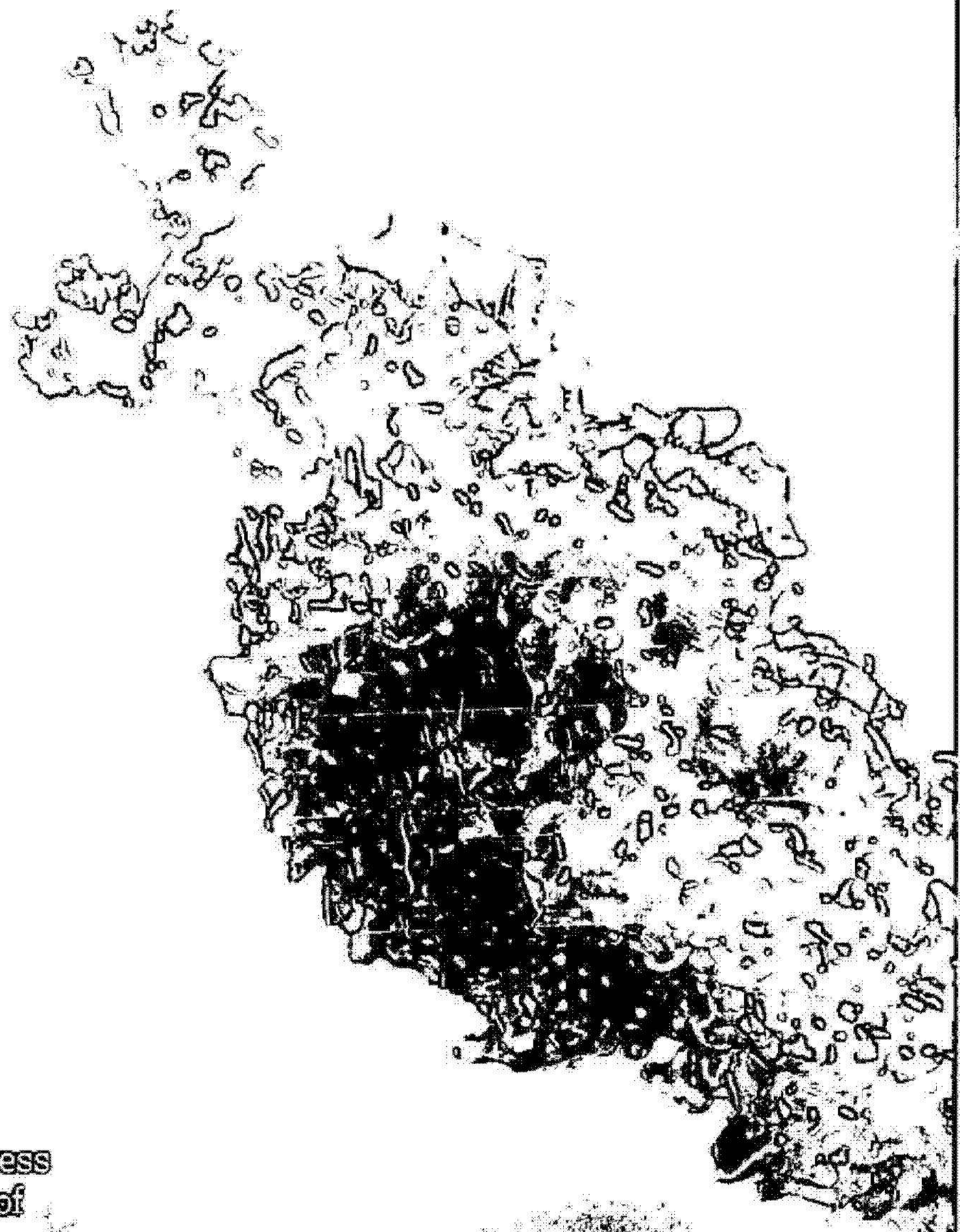
COMPANIES HOUSE

Welcome

We are a global, science-led, patient-focused pharmaceutical company. We are tireless in seeking to realise the potential of...

...what science can do.





In this Annual Report we report on the progress we made in 2021 in pushing the boundaries of science to deliver life-changing medicines.

Our Strategic Report
How our disease areas, also known as therapy areas, and business performed in delivering our strategic priorities in 2021.

See our Strategic Report from page 2

Our Financial Statements and Additional Information
Detailed information on our finances, as well as information for shareholders and readers of this Annual Report.

See our Financial Statements from page 123 and Additional Information from page 210

Our Corporate Governance Report
How we are managed and take decisions, including our report on Directors' remuneration.

See our Corporate Governance Report from page 71

Our Supplements
Detailed information on our Development Pipeline, Patent Expiries and Key Marketed Products and Risk.

See our website, www.astrazeneca.com/annualreport2021

Front cover and inside front cover images:
Unlocking the potential of the complement system.

The dysregulation of the complement system, an essential part of the immune system, is a key driver of many devastating diseases. Targeting and inhibiting the complement system before it can trigger tissue damage or destruction can help restore balance.

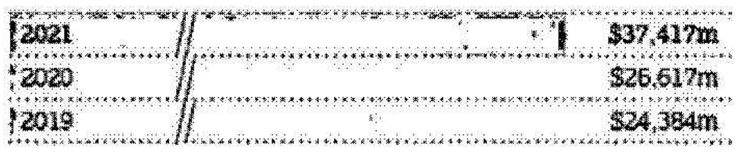
We are committed to continue unlocking the potential of the complement system to discover new life-changing therapies for even more patients.

Use of terms:
In this Annual Report, unless the context otherwise requires, 'AstraZeneca', 'the Group', 'we', 'us' and 'our' refer to AstraZeneca PLC and its consolidated entities.

Contents

Financial highlights

Total Revenue*
Up 41% at actual rate of exchange to $37,417 million (up 38% at CER), comprising Product Sales of $36,541 million (up 41%; 38% at CER) and Collaboration Revenue of $876 million (up 20%; 20% at CER)



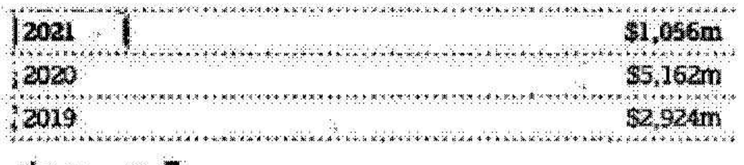
$37.4bn

Net cash flow from operating activities
Up 24% at actual rate of exchange to $5,963 million



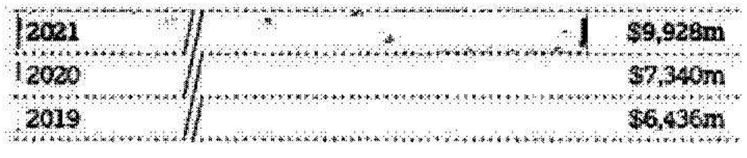
$6.0bn

Reported operating profit
Down 80% at actual rate of exchange to $1,056 million (down 70% at CER)



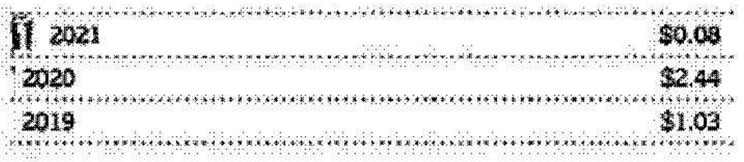
$1.1bn

Core operating profit
Up 35% at actual rate of exchange to $9,928 million (up 41% at CER)



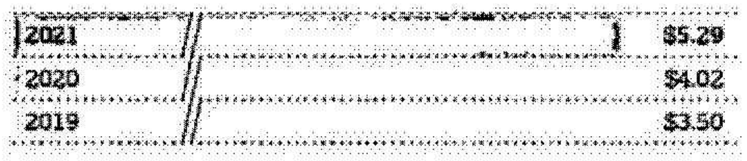
$9.9bn

Reported EPS
Down 97% at actual rate of exchange to $0.08 (down 84% at CER)



$0.08

Core EPS
Up 32% at actual rate of exchange to $5.29 (up 37% at CER)



$5.29

// Denotes a scale break. Throughout this Annual Report, all bar chart scales start from zero. We use a scale break where charts of a different magnitude, but the same unit of measurement, are presented alongside each other.

For more information in relation to the inclusion of Reported performance, Core financial measures and constant exchange rate (CER) growth rates as used in this Annual Report, see the Financial Review from page 52 and for more information on the reconciliation between Reported and Core performance, see the Reconciliation of Reported to Core results in the Financial Review on page 56.

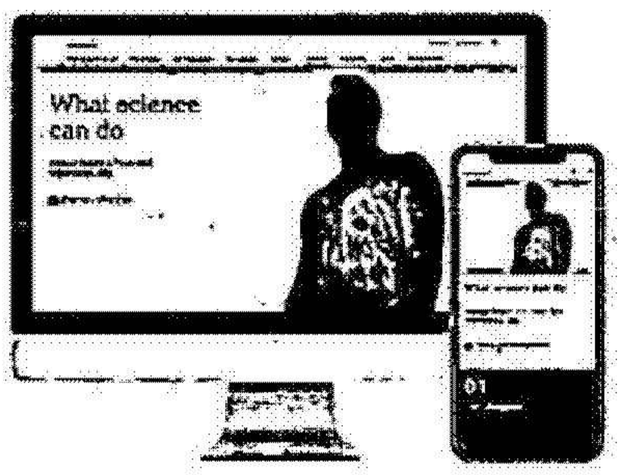
* As detailed from page 139. Total Revenue consists of Product Sales and Collaboration Revenue.

Key

For more information within this Annual Report

For more information, see www.astrazeneca.com

BV Denotes sustainability information independently assured by Bureau Veritas



This Annual Report is also available on our website. www.astrazeneca.com/annualreport2021.

Strategic Report
AstraZeneca at a Glance 2
Chair's Statement 4
Chief Executive Officer's Review 5
Healthcare in a Changing World 7
Business Model and Life-cycle of a Medicine 10
Our Strategy and Key Performance Indicators 12
Disease Area Review 16
> Oncology 16
> BioPharmaceuticals 19
– Cardiovascular, Renal & Metabolism 20
– Respiratory & Immunology 22
> Rare Disease 24
> Other Medicines and COVID-19 27
Business Review 30
Risk Overview 46
Financial Review 52

Corporate Governance
Chair's Introduction 72
Corporate Governance Overview 73
Board of Directors 74
Senior Executive Team 76
Corporate Governance Report 77
Nomination and Governance Committee Report 86
Science Committee Report 88
Sustainability Committee Report 89
Audit Committee Report 90
Directors' Remuneration Report 98

Financial Statements
Preparation of the Financial Statements and Directors' Responsibilities 126
Auditors' Report 127
Consolidated Statements 134
Group Accounting Policies 138
Notes to the Group Financial Statements 145
Group Subsidiaries and Holdings 197
Company Statements 202
Company Accounting Policies 204
Notes to the Company Financial Statements 206
Group Financial Record 209

Additional Information
Shareholder information 211
Directors' report 213
Sustainability supplementary information 216
Task force on Climate-related Financial Disclosures Statement 217
Trade Marks 223
Glossary 224
Cautionary statement regarding forward-looking statements 228

AstraZeneca at a Glance

Inspired by our Values and what science can do, we are focused on accelerating the delivery of life-changing medicines that create enduring value for patients and society.

Our strategic priorities

Our Strategy and Key Performance Indicators, see from page 12.

Our priorities reflect how we are working to deliver our growth through innovation strategy and achieve our Purpose of pushing the boundaries of science to deliver life-changing medicines.

1. Accelerate Innovative Science
2. Deliver Growth and Therapy Area Leadership
3. Be a Great Place to Work

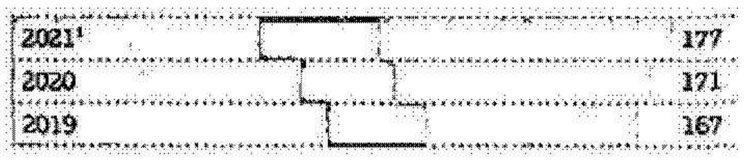
Science and innovation-led

Research & Development, see from page 32.

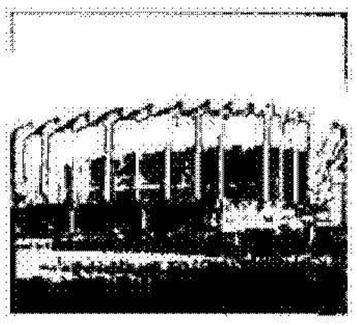
Development Pipeline Supplement, see www.astrazeneca.com/annualreport2021.

Distinctive R&D capabilities
We use our distinctive scientific capabilities to deliver a pipeline of life-changing medicines.

177
projects in our development pipeline



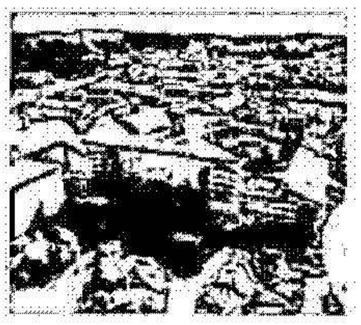
Global R&D centres



Cambridge, UK



Gaithersburg, MD, US



Gothenburg, Sweden

Other R&D centres and offices
South San Francisco, CA, US
New York, NY, US
New Haven, CT, US
Boston, MA, US
Alderley Park and Macclesfield, UK
Shanghai, China
Osaka, Japan

A diversified portfolio with broad coverage across primary, specialty care and rare disease (Product Sales)

Disease Area Review, see from page 16 and Research & Development, see from page 32.

Oncology
We are leading a revolution in oncology to redefine cancer care.

$13,048m
36% of total
2020: $10,850m
2019: $8,667m
Sales growth of 20% (18% at CER)

BioPharmaceuticals
Creating a life without limits for billions of people living with chronic diseases.

Cardiovascular, Renal & Metabolism
$8,020m
22% of total
2020: $7,096m
2019: $6,906m
Sales growth of 13% (10% at CER)

Respiratory & Immunology
$6,034m
17% of total
2020: $5,357m
2019: $5,391m
Sales growth of 13% (9% at CER)

Rare Disease
Transforming the lives of people affected by rare diseases and devastating conditions.

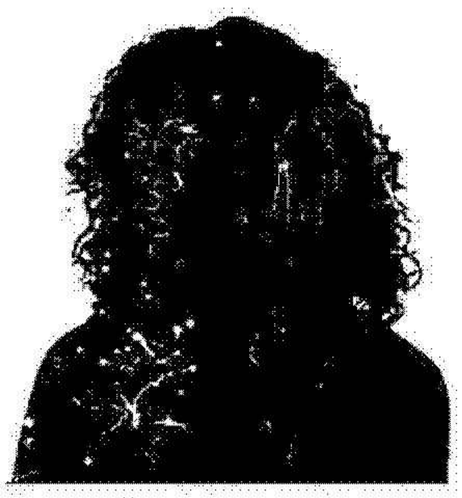
$3,070m
8% of total
Revenue includes Alexion sales from 21 July 2021

Other Medicines
We have medicines and vaccines in other disease areas that have an important impact for patients.

$2,367m
6% of total
2020: $2,585m
2019: $2,601m
Sales decline of 8% (10% at CER)

COVID-19
Helping to change the course of the pandemic with our vaccine and a long-acting antibody.

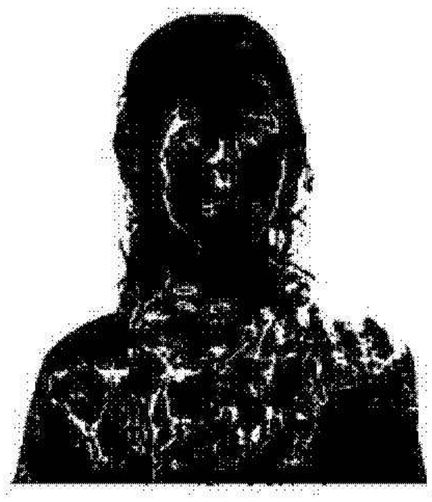
$4,002m
11% of total
2020: $2m



Oncology. See from page 16.



BioPharmaceuticals. See from page 19.

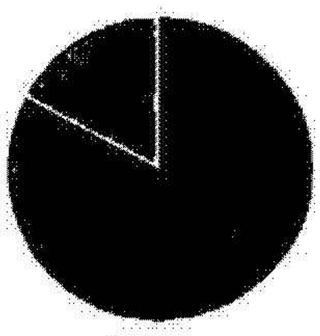


Rare Disease. See from page 24.

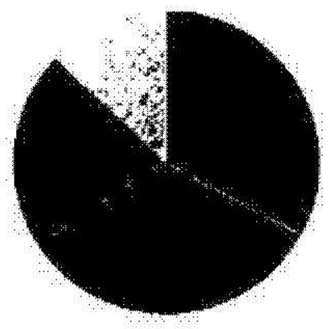
Global strength, with balanced presence across regions (Product Sales)

Our Commercial Regions, see from page 36.

Product Sales by Disease Area



Product Sales by reporting region



Commitment to our people
A focus on inclusion and diversity, as well as lifelong learning and development.

People, see from page 41.

83,100
employees
2020: 76,100
2019: 70,600

48.1%
of our senior roles are filled by women

87%
of employees believe strongly in AstraZeneca's future direction and key priorities

78%
of employees believe there is effective collaboration between teams

Commitment to society
We recognise the interconnection between our business, the needs of society and the limitations of our planet. We are harnessing the power of science and innovation to deliver a positive impact to society, healthcare systems and the environment through actions for the long term.

Sustainability, see from page 44.

Priority
1
Access to healthcare
Increasing access to life-saving treatments, promoting prevention, and strengthening global healthcare resilience and sustainability.

Priority
2
Environmental protection
Accelerating the delivery of net-zero healthcare, managing our environmental impact, and investing in nature and biodiversity.

Priority
3
Ethics and transparency
Ensuring ethical, open and inclusive behaviour across our organisation and value chain.

84%
of employees say they understand their contributions to our sustainability priorities.

access to medicine index
7th overall

CDP
A List for Climate Change and Water Security

Member of Dow Jones Sustainability Indices
In Collaboration with RobecoSAM
World and Europe constituent

GLOBAL100
Global 100 Most Sustainable Corporations in the World 2021

Capital allocation priorities
After providing for reinvestment in the business, supporting the progressive dividend policy and maintaining a strong, investment-grade credit rating, we keep under review potential investment in value-enhancing opportunities.

Financial Review, see from page 52.

Dividends
$3,856m
2020: $3,572m
2019: $3,592m

R&D expenditure (Reported)
$9,736m
2020: $5,991m
2019: $6,059m

Credit rating (Standard & Poor's)
A-
Long term:
Stable outlook

Credit rating (Moody's)
A3
Long term:
Negative outlook

Chair's Statement

We continued on our strong growth trajectory in 2021 and have confidence in our prospects for future growth and cash generation.

"Reflecting this increased confidence, the Board has approved an increase in the annualised dividend."



$2.87

Full-year dividend of $2.87 per share (2020: $2.80)

Continuing the successful implementation of AstraZeneca's 'growth through innovation' strategy in 2021 ensured we were able to deliver for patients around the world and, thereby, our shareholders. More broadly, I am proud of the role we are playing in contributing to the health of society and the planet. I am grateful to Pascal, Senior Executive Team members and everyone in AstraZeneca, whose efforts made this all possible.

A landmark year

2021 was a landmark year for the Company as we continued on our strong growth trajectory, with industry-leading R&D productivity, thirteen blockbuster medicines and the acquisition of Alexion. We also delivered on our promise of broad and equitable access to our COVID-19 vaccine. The positive news from our pipeline, including FDA emergency use authorisation of *Evusheld* and the approval of *Tezspire*, support the outlook for 2022.

Reflecting increased confidence in future growth and cash generation, the Board intends to increase the annualised dividend by $0.10 to $2.90, and has approved a second interim dividend for 2021 of $1.97, payable in March 2022. This results in a total dividend declared for 2021 of $2.87.

Alexion acquisition

Our positive outlook also stems, in part, from our transformative acquisition of Alexion which completed in July. We are already seeing the benefits across AstraZeneca in terms of scientific collaboration and expanding our Rare Disease business which is accelerating delivery of our strategy.

Our new Chief Financial Officer, Aradhana Sarin joined the Board in August from Alexion. Aradhana is a talented successor to Marc Dunoyer who stood down from the Board to become Chief Executive Officer, Alexion and Chief Strategy Officer, AstraZeneca. I am grateful to Marc for his significant contribution and the Board is pleased he is staying on as a member of the Senior Executive Team (SET).

Also in August and following the Alexion acquisition, we welcomed Andreas Rummelt to the Board as a Non-Executive Director. As a former member of the Board of Alexion, he has deep knowledge of its rare diseases business and extensive experience of the pharmaceutical industry including technical R&D, manufacturing and quality assurance expertise.

Meeting global challenges

With the efforts that many, including AstraZeneca, are making to overcome COVID-19, it's time to plan for a world beyond the pandemic. I believe there are lessons we can learn about how business, academia and government, by working together, can overcome major global challenges such as the climate crisis and the provision of sustainable healthcare.

The pandemic is also reinforcing the fact that companies succeed best when they are truly part of society, when they are driven by their purpose: a purpose that is sustained by the profit we make and our returns to you, our shareholders. This is at the heart of how AstraZeneca operates and why I am so proud of our relentless pursuit of the delivery of life-saving medicines and our wider contribution to society and the planet.

Succession planning

I will have served as a Director for ten years by April 2022. Typically, non-executive directors would step down after nine years' tenure, in line with UK corporate governance best practice. Last year, the Board asked me to seek re-election at the AGM to lead the Board's oversight of completion of the acquisition of Alexion. Again this year, your Board believes it would be in the best interests of shareholders for me to serve as Chair for one further year, to facilitate succession planning and the transition to a new Chair, and has asked me to seek re-election at the AGM in April 2022. I am honoured and happy to accept the Board's request again, mindful of my intention to retire from the Board at the end of the AGM in 2023.

Succession planning for the role of Chair has continued to be a focus of the Nomination and Governance Committee's work during 2021, with a search that is proceeding well led by Philip Broadley, senior independent Non-Executive Director, as noted in the Committee's report from page 86.

Meeting again

In November, it was a pleasure to be able to meet in person to celebrate the unveiling of our Discovery Centre in Cambridge, UK with HRH The Prince of Wales and guests from across business, academia and government. While much can be achieved by working and meeting virtually, there is also value in being able to meet in person. For the first time in two years, we are planning to hold this year's AGM in person and I look forward to meeting as many of you there as possible.



Leif Johansson
Chair

Chief Executive Officer's Review

2021 was another remarkable year for AstraZeneca in delivering for patients and one in which we played a leading role in changing the course of the pandemic.

"In July, we completed our landmark acquisition of Alexion which established our rare disease capability."



$37.4bn

Total Revenue[1] (2020: $26.6bn)

22

Regulatory approvals and authorisations in major markets

In 2021, despite the ongoing challenge of the COVID-19 pandemic, AstraZeneca continued to advance delivery of our strategy – supplying our medicines to patients, as well as launching new ones and expanding into new indications. It was also an outstanding year for our pipeline in progressing the next wave of science and delivering trial results that have the potential to redefine care.

During the year, we welcomed our colleagues from Alexion to the Group. With their expertise in rare diseases, not only is our science base and drive for growth strengthened, but also, more importantly, our ability to make a difference to patients around the world. At the same time, we contributed to the health of society and the planet, notably in our efforts to tackle the biggest public health crisis of our lifetime and reduce our carbon footprint. All of this was underpinned by an organisation living our Values, leading change and transforming the way we work.

I can only touch on a few of our achievements in this Review but, taken together, our efforts ensured we continued to deliver for shareholders in 2021. Total Revenue grew by 41% (38% at CER) to $37,417 million, including COVID-19 vaccine revenues. Excluding COVID-19 revenue, growth was 26% (23% at CER) and was well balanced across our disease areas. We saw double-digit growth in all major regions, including Emerging Markets despite some headwinds in China. We also achieved 14 positive Phase III readouts across nine medicines during the year, and 22 regulatory approvals and authorisations in major markets including five new molecular entities (NME).

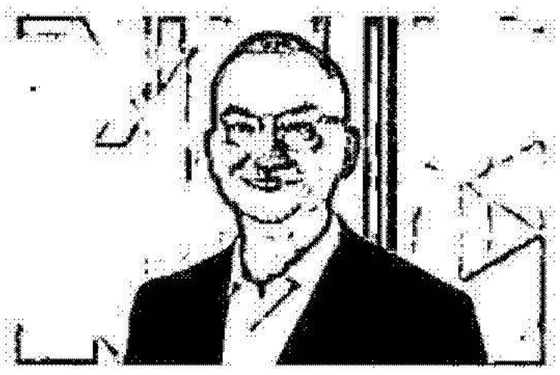
José Baselga: a visionary leader

2021 began, however, on a very sad note with the untimely death of José Baselga, my colleague and friend. José was a brilliant scientist, legendary oncologist and visionary leader. He had a passion for what he did and was always chasing the next and best therapies. He transformed AstraZeneca's Oncology R&D and accelerated our innovative science – one of the drivers behind our success.

During his brilliant career, José changed the landscape of cancer treatment and thousands of patients have benefited. It was José's passion and determination when he was at AstraZeneca that drove the development of our pipeline and the recruitment of many incredibly talented scientists.

One of the medicines José championed is *Enhertu*. Unprecedented results from our DESTINY trials during 2021 more than justify his passion for this unique medicine. The trials both confirm *Enhertu*'s potential as a new treatment for HER2-positive breast cancer and open the door to its potential use in earlier lines of treatment and other HER2 expressing tumours.

Together with patients around the world, all of us at AstraZeneca owe José a debt of gratitude and we will continue to build on his legacy.



José Baselga
1959-2021,
Executive Vice-President,
Oncology R&D

[1] Total Revenue consists of Product Sales and Collaboration Revenue

Chief Executive Officer's Review *continued*

A vaccine for the world

Patients have also benefited from *Vaxzevria*, our COVID-19 vaccine, which was first approved for emergency supply in the UK at the end of 2020. Together with our global partners, we supplied about 2.5 billion vaccine doses to more than 180 countries during the year. Of these, approximately two-thirds went to low- and lower-middle-income countries, and more than 247 million were delivered to 130 countries through the COVAX Facility in 2021. It is estimated that *Vaxzevria* has so far helped prevent 50 million cases of COVID-19, five million hospitalisations, and helped save more than one million lives. It was an honour to have this achievement recognised when we jointly received the 2021 Roy Vagelos Pro Bono Humanum Award for Global Health Equity at the Prix Galien USA Awards Ceremony.

Vaccines are not easy to manufacture and scaling up supply brought challenges. Nevertheless, I am proud of the speed with which we were able to build twelve regional supply chains around the world, relying on our own manufacturing capacity, and sharing our know-how with more than 20 collaborators.

For the future, we remain committed to providing broad and equitable global access to our vaccine.

In addition to delivering our vaccine to the world, our teams rapidly progressed the development of *Evusheld*, a long-acting antibody (LAAB) combination against COVID-19. It was the first LAAB combination to demonstrate benefit in both preventing and treating COVID-19 and received Emergency Use Authorization from the FDA in December 2021. This authorisation, which has been followed by similar authorisations in other countries, underlines the potential of *Evusheld* to make a significant difference for people most in need.

Alexion: AstraZeneca Rare Disease

In July, we completed our landmark acquisition of Alexion which established our rare disease capability. Rare diseases represent a significant unmet medical need and we believe Alexion's innovative complement-biology platform and robust pipeline will continue to pioneer the discovery and development of medicines for these often devastating conditions. It represents a high-growth opportunity and we are already starting to see the delivery of this potential with *Ultomiris* and the other medicines in the Alexion portfolio, supported by developments such as the acquisition of Caelum Biosciences and their potentially first-in-class mAb for the treatment of amyloid light-chain (AL) amyloidosis.

Moreover, the rest of AstraZeneca can benefit from applying Alexion's complement-biology platform across our broader early stage pipeline and Alexion's R&D team can take advantage of the research capabilities available at AstraZeneca to discover new treatments for rare diseases. Patients will also benefit from the opportunity to make existing and future rare disease medicines available in many countries where AstraZeneca already has a strong presence, such as China, where we have established a Rare Disease Unit.

Bridges are already being built between Alexion and the rest of AstraZeneca as we deliver on the full potential of this exciting addition to our range of capabilities.

Addressing the challenge of climate change

In addition to understanding what science can do for patients, AstraZeneca's team understands the part we need to play in securing the future of the planet. We recognise that the climate crisis is a public health emergency for which there is no vaccine, and no one is immune. As part of our efforts, we are a founding partner of HRH The Prince of Wales' Sustainable Markets Initiative (SMI), a global 'coalition of the willing' who share the vision around the need to accelerate global progress towards a sustainable future. As part of that coalition, we called for coordinated, accelerated action to tackle climate change ahead of the G7 Leaders' Summit in Cornwall, UK in June.

Those efforts continued in November at the 26th UN Climate Change Conference in Glasgow, UK, when I was proud to launch the SMI Health Systems Taskforce as its Champion. Our ambition is to accelerate the delivery of net-zero, patient-centric healthcare.

Unveiling our Discovery Centre

Also in November, it was a privilege to host HRH The Prince of Wales to unveil our Discovery Centre (DISC) in Cambridge, UK. A state-of-the-art R&D facility, DISC can accommodate more than 2,200 research scientists and is built to the world's highest environmental standards.

DISC is designed to foster collaboration and develop the next generation of science leaders. By accelerating AstraZeneca's industry-leading levels of productivity, it can drive the next wave of scientific innovation and power the next stage of our growth.

Working for inclusion and diversity

The next wave of innovation will only come from organisations that are both diverse and inclusive. While there is always room for improvement, I am proud of the progress we have made, particularly in ensuring gender balance in our leadership teams.

I was therefore delighted when Susan Galbraith and Aradhana Sarin joined the Senior Executive Team during the year. Susan was appointed in June to lead Oncology R&D in succession to José. She is an outstanding oncologist and leader with a track record of delivering breakthrough science and medicines that have transformed care and improved the lives of patients.

Aradhana assumed the role of Chief Financial Officer in August following the completion of the Alexion acquisition. She has more than 20 years of professional experience spanning operating roles at Alexion and advisory roles at global financial institutions. Marc Dunoyer, our previous CFO, has taken over as Alexion's CEO and I'd like to pay tribute to him for his tremendous achievements since he joined AstraZeneca, and thank him personally for his outstanding support, which continues in his role as Chief Strategy Officer.

Indeed, I would like to close by thanking everyone at AstraZeneca. Without their continuing and tireless contributions, none of our many achievements in 2021 would have been possible and, with them, I have every confidence in delivering the next chapter in our success.



Pascal Soriot
Chief Executive Officer



The Terra Carta Seal recognises global corporations that are demonstrating their commitment to, and momentum towards, the creation of genuinely sustainable markets

For more information on our strategy, see Our Strategy and Key Performance Indicators from page 12

Healthcare in a Changing World

Healthcare systems are having to meet increasing demand, a task made more challenging by the ongoing impact of COVID-19.



The continued growth of the healthcare sector presents us with both challenges and opportunities that require us to adapt, innovate and build trust.

Our sector's traditional focus on treatment is shifting towards prevention and early intervention. Meanwhile, social, economic and political challenges remain in meeting unmet medical need.

Impact of global trends

Global trends continue to increase the demand for healthcare. The COVID-19 pandemic has highlighted challenges and accelerated healthcare innovation and change.

Global economic recovery followed by slowdown

Following a strong rebound in 2021, the global economy is entering a pronounced slowdown amid fresh threats from COVID-19 variants and a rise in inflation, debt, and income inequality that could endanger the recovery in emerging and developing economies. Global growth is expected to decelerate markedly from 5.5% in 2021 as pent-up demand dissipates and as fiscal and monetary support is unwound across the world. This will coincide with a widening divergence in growth rates between advanced economies and emerging and developing economies.
(Source: World Bank)

4.1%
Global GDP is forecast to grow by 4.1% in 2022, slowing further to 3.2% in 2023.
(Source: World Bank)

-4%
By 2023, output in emerging and developing economies will remain 4% below its pre-pandemic trend.
(Source: World Bank)

Growing and ageing populations

People worldwide are living longer. By 2030, one in six people will be aged 60 years or over. Between 2015 and 2050, the world's population of people aged above 60 will nearly double to 2.1 billion. While this shift in distribution towards older ages started in high-income countries, it is now low- and middle-income countries that are experiencing the greatest change. By 2050, two thirds of the world's population over 60 years will live in low- and middle-income countries.
(Source: WHO)

1bn
There are now more than one billion people worldwide aged 60 and over. Most of them live in low- and middle-income countries.
(Source: WHO)

426m
The number of people aged 80 or older is expected to triple between 2020 and 2050 to reach 426 million.
(Source: WHO)

Increasing burden of chronic disease

Non-communicable diseases (NCDs) kill 41 million people each year, equivalent to 71% of all deaths globally. NCDs disproportionately affect people in low- and middle-income countries where more than three quarters of global NCD deaths occur.

People of all age groups, regions and countries are affected by NCDs. The risk factors contributing to NCDs include diet, smoking and lack of exercise.
(Source: WHO)

77%
77% of all NCD deaths are in low- and middle-income countries.
(Source: WHO)

15m
More than 15 million people aged 30–69 years die from NCDs every year. 85% of these 'premature' deaths occur in low- and middle-income countries. This compares with some 5.7 million people who have died from COVID-19 since the start of the pandemic.
(Sources: WHO and Johns Hopkins)

Healthcare in a Changing World *continued*

Growing importance of digital in healthcare

Data management in healthcare is moving beyond storing data, to focusing on extracting insights on population health management and value-based care to improve health outcomes and personalised healthcare.

Innovations in technology are allowing people to monitor their own health and become active participants in managing their healthcare. For example, Internet of Things (IoT) applications and technologies are influencing patient engagement strategies and improving patient interactions with healthcare systems.

$427bn

The digital health market exceeded $141.8 billion in 2020 and is estimated to grow to more than $426.8 billion by 2027.
(Source: Global Market Insights)

38x

The use of telehealth has increased 38 times from pre-COVID-19 levels.
(Source: McKinsey)

The health impact of climate change

Climate change affects many determinants of health: clean air, safe drinking water, sufficient food and secure shelter. For example, extreme high air temperatures raise the levels of pollutants in the air that exacerbate cardiovascular and respiratory diseases.

Increasingly variable rainfall patterns are likely to affect the supply of fresh water. This can compromise hygiene and increase the risk of diarrhoeal disease, which kills over 500,000 children below the age of five every year.
(Source: WHO)

250,000

Between 2030 and 2050, climate change is expected to cause approximately 250,000 additional deaths per year from malnutrition, malaria, diarrhoea and heat stress.
(Source: WHO)

Up to $4bn

The direct damage costs to health (excluding costs in health-determining sectors such as agriculture, water and sanitation), is estimated to be between $2-4 billion per year by 2030.
(Source: WHO)

Continued impact of COVID-19

The COVID-19 pandemic has driven changes in health system spending that impact access to medicines. For example, where hospital beds were scarce, payers reallocated resources and prioritised treatments that could help keep patients out of hospital.

The pandemic also demonstrated that when needed, healthcare systems can move quickly to grant rapid access to innovative new medicines, such as the COVID-19 vaccines.

94%

94% of countries reported one or more disruptions to essential healthcare services one year into the pandemic.
(Source: WHO)

While demographic and other changes are driving an increased demand for healthcare, continued advances in science and digital technologies are driving innovation and improvements in healthcare. One example of this is the speed of vaccines development in response to the COVID-19 pandemic. At the same time, risks remain. For instance, increasing demand is putting pressure on healthcare budgets, exacerbated by the impact of the pandemic, leading to downward pressure on pricing. We also face regulatory challenges and the loss of exclusivity and genericisation.

The pharmaceutical industry has historically faced challenges in building and maintaining its reputation and the trust of its stakeholders, as a result of improper sales and marketing practices by some companies. However, the sector has the opportunity to increase public confidence by delivering on transparent commitments to ethical practices and good governance. Initially, the rapid response and mobilisation of resources to develop a vaccine in response to COVID-19 contributed to an increase in trust in scientific and medical institutions, including the pharmaceutical industry. However, the widespread sharing of inaccurate or selective information has undermined confidence in scientific data, and trust has, in part, fallen away.

More generally, to be successful, pharmaceutical companies will need to be able to respond to the pressures and demands made on them by patients and caregivers, health authorities, payers, policymakers and others.

These risks are explored further in the Risk Overview from page 48 and Pricing and value of our medicines from page 35.

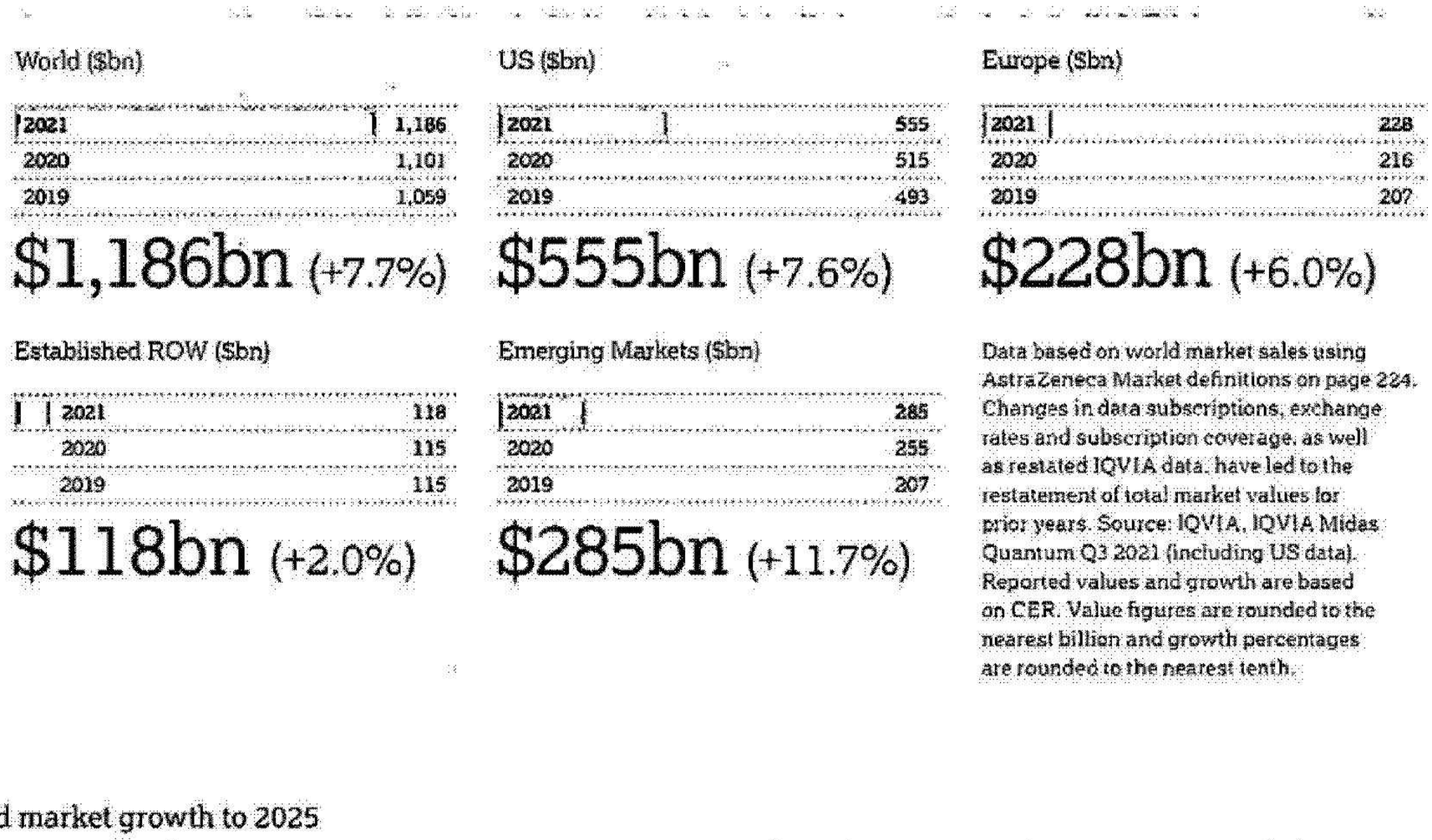
AstraZeneca's response to the trends we face is explored further in Strategy and Key Performance Indicators from page 12.

A growing pharmaceutical sector

As a result of increased demand for healthcare, the pharmaceutical sector continues to grow. Global pharmaceutical sales grew by 7.7% in 2021. Global healthcare spending is projected to increase at an annual rate of 4.8% from 2020 to 2025.

Global pharmaceutical sales

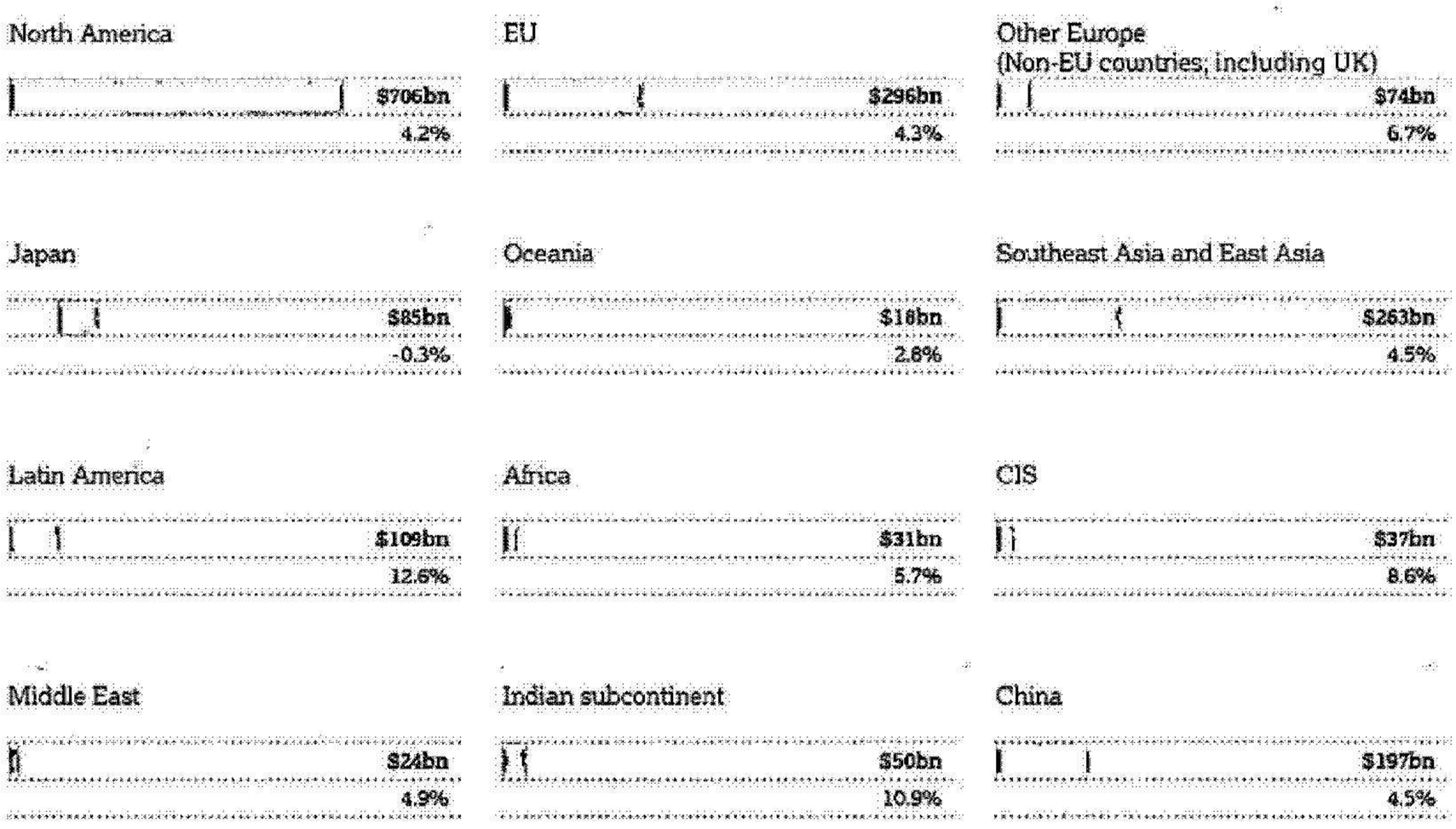
In 2021, Established Markets saw an average revenue increase of 6.4% and Emerging Markets revenue grew at 11.9%. The US, Japan, China, Germany and France are the world's top five pharmaceutical markets by 2021 sales. In 2021, the US had 46.8% of global sales (2020: 46.8%; 2019: 46.5%).



Data based on world market sales using AstraZeneca Market definitions on page 224. Changes in data subscriptions, exchange rates and subscription coverage, as well as restated IQVIA data, have led to the restatement of total market values for prior years. Source: IQVIA, IQVIA Midas Quantum Q3 2021 (including US data). Reported values and growth are based on CER. Value figures are rounded to the nearest billion and growth percentages are rounded to the nearest tenth.

Estimated pharmaceutical sales and market growth to 2025

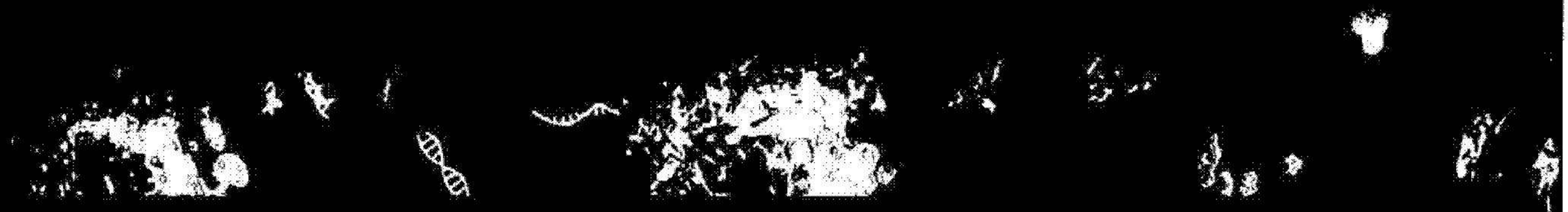
We expect developing markets, including Africa, the Commonwealth of Independent States (CIS), the Indian subcontinent and Latin America, to fuel pharmaceutical growth. Market growth in China is expected to remain below historical levels at a compound annual growth rate of 4.5%. This is due to the continued slowdown of the major hospital sector.



Estimated pharmaceutical sales – 2025. Data is based on ex-manufacturer prices at CER. Source: IQVIA
Estimated pharmaceutical market growth. Data is based on the compound annual growth rate from 2020 to 2025. Source: IQVIA Market Prognosis Global 2021 to 2025

Business Model and Life-cycle of a Medicine

We invest resources to create financial and non-financial value, bringing benefits to our patients, our world and our business.



Why AstraZeneca?

We are a global pharmaceutical business with a science-led and patient-focused value proposition committed to excellence in the research, development and commercialisation of prescription medicines.

Who we are

Inspired by our Values and what science can do, we are focused on accelerating the delivery of life-changing medicines that create enduring value for patients and society.

We are committed to operating in a way that recognises the interconnection between business growth, the needs of society and the limitations of our planet.

Our Purpose

We push the boundaries of science to deliver life-changing medicines.

Our Purpose underpins everything we do. It gives us a reason to come to work every day. It reminds us why we exist as a company. It helps us deliver benefits to patients and create value for shareholders.

Our Values

Our Values determine how we work together and the behaviours that drive our success. They guide our decision making and define our beliefs.

We follow the science.
Pushing the boundaries of science and working creatively with partners and collaborators.

We put patients first.
Striving to understand patients' needs and considering them in every decision we take.

We play to win.
Building high-performing, inclusive and diverse teams and making the right choices to win.

We do the right thing.
Employing high ethical standards when carrying out all aspects of our business globally.

We are entrepreneurial.
Acting with urgency, bravery, resilience and taking smart risks.

Our Culture

Our Culture is defined by our shared Values and Purpose. Accompanying this, our commitment to sustainability, performing as an enterprise team, lifelong learning, and inclusion and diversity makes us a great place to work.

Business Review, see from page 30.

What we do to create financial value

Our business activities span the entire life-cycle of a medicine.

Investment

We invest in the discovery, development, manufacturing and commercialisation of our pipeline of innovative prescription medicines.

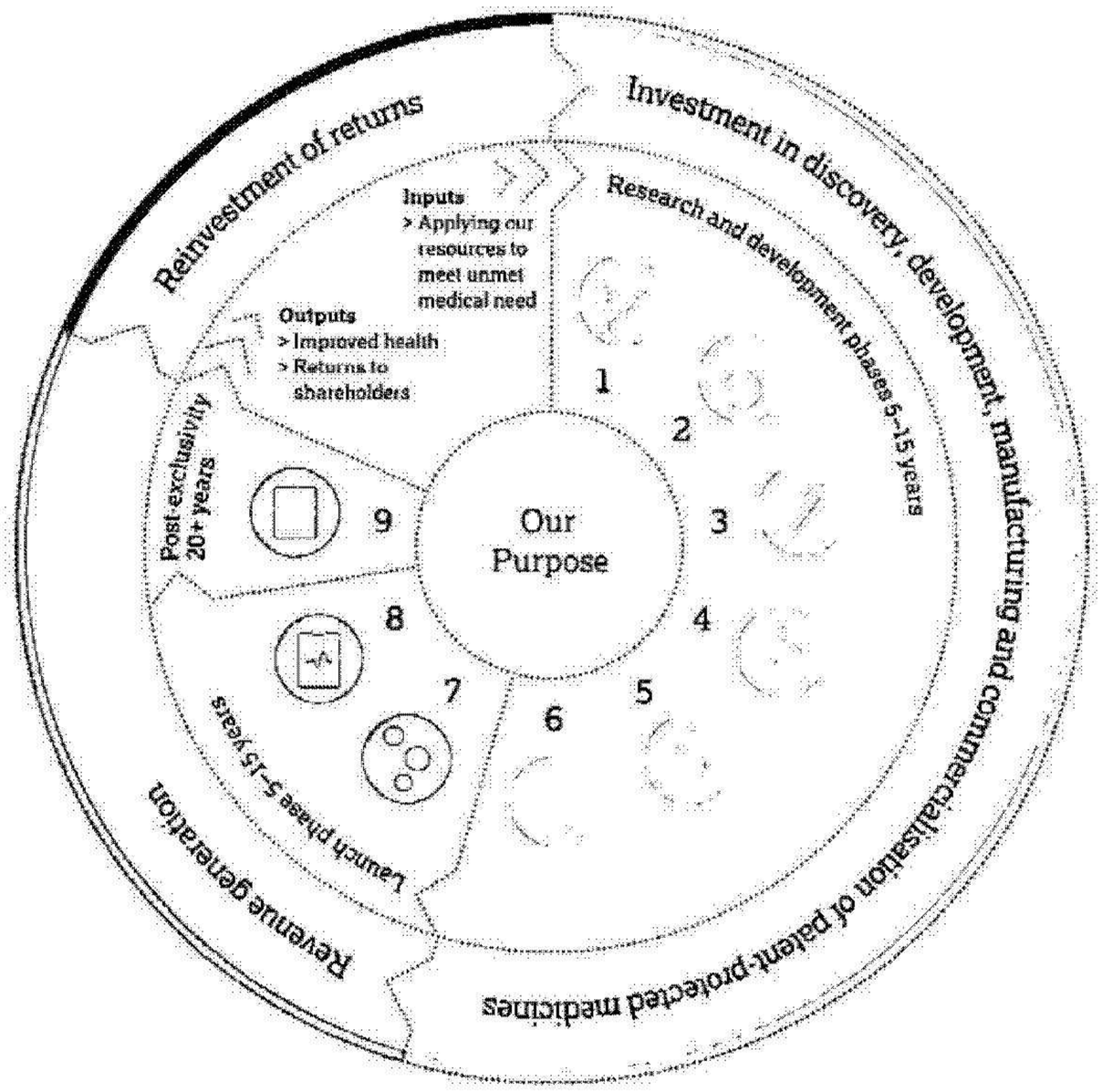
Revenue generation

We generate revenue from Product Sales of our existing medicines and new medicine launches, as well as from our collaboration activities. Our focus is on creating medicines that facilitate profitable future revenue generation, while bringing benefits to patients.

Reinvestment

We reinvest in developing the next generation of innovative medicines and in our business to provide the platform for future sources of revenue in the face of losses of key patents.

We also assess opportunities to invest in value-enhancing additions to our portfolio.



Life-cycle of a medicine

Research and development phases – duration: 5–15 years

1. Undertake scientific research to identify potential new medicines.
2. Pre-clinical studies in laboratory and animals to understand if the potential medicine is safe to introduce into humans.
3. Phase I trials with small groups of healthy human volunteers (small molecules) or patients (biologics) to understand how the potential medicine is absorbed into the body, distributed and excreted.
4. Phase II trials on small- to medium-sized groups of patients to test effectiveness and tolerability of the medicine and determine optimal dose.
5. Phase III trials in a larger group of patients to gather information about effectiveness and safety of the medicine and evaluate the overall benefit/risk profile.
6. Seek regulatory approvals for manufacturing, marketing and selling the medicine.

Launch phase – duration: 5–15 years

7. Launch new medicine while continuously monitoring, recording and analysing reported side effects.
8. Post-launch research and development to further understand the benefit/risk profile of the medicine and life-cycle management activities to understand its full potential.

Post-exclusivity – duration: 20+ years

9. Patent expiry and generic medicine entry.

What does our business model require to be successful?

A talented and diverse workforce
We need to acquire, retain and develop a talented and diverse workforce.

48.1%
of our senior roles are filled by women

A leadership position in science
We need to achieve scientific leadership if we are to deliver life-changing medicines.

$9.7bn
invested in our science in 2021

Understand our stakeholders
We need to understand the factors and issues that are most important to the many different groups of stakeholders with whom we interact.

>118,000
healthcare practitioner enquiries responded to

Effective collaborations
Business development, specifically partnering, supplements and strengthens our pipeline and our efforts to achieve scientific leadership.

>1,000
collaborations worldwide

Commercialisation skills
We need a strong global commercial presence and skilled people to ensure that our medicines are available when needed and that patients have access to them.

>130
countries where we sell our products

Intellectual property
For our investments to be viable, we seek to protect new medicines from being copied for a reasonable period of time through patent protection.

>90
countries where we obtained patent protection

A robust supply chain
We need a supply of high-quality medicines, whether from our own operations or our spend on the purchase of goods, services and active pharmaceutical ingredients.

$22.2bn
spent with suppliers

Financial strength
We need to be financially strong, including having access to equity and debt financing, to bear the financial risk of investing in the life-cycle of a medicine both internally and through acquisitions.

$6.0bn
net cash flow from operating activities

>100m

Our main Disease Area medicines impact more than 100 million patient lives annually. In addition, AstraZeneca and our global partners released for supply some 2.5 billion *Vaxzevria/Covishield* vaccine doses in 2021.

How we add value

Improved health
Continuous scientific innovation is vital to achieving sustainable healthcare, which creates value by:

- Improving health outcomes and transforming the lives of patients who use our medicines.
- Enabling healthcare systems to reduce costs and increase efficiency.
- Improving access to healthcare and healthcare infrastructure.
- Helping develop the communities in which we operate through local employment and partnering.

Financial value
Revenue from our Product Sales and collaboration activities generates cash flow, which helps us:

- Fund our investment in science and the business to drive long-term value.
- Follow our progressive dividend policy.
- Meet our debt service obligations.

Our Strategy and Key Performance Indicators

Our acquisition of Alexion enables us to capitalise on new opportunities, strengths and synergies as we seek to accelerate delivery of our strategy.



Our strategy is straightforward. We:

- Are science and innovation led
- Are focused on our chosen disease areas: Oncology; BioPharmaceuticals (comprising Cardiovascular, Renal & Metabolism (CVRM) and Respiratory & Immunology (R&I)); and Rare Disease
- Have a diversified portfolio with broad coverage across primary, specialty care and rare disease
- Have global strength with balanced presence across regions
- Have a commitment to people and society

We have three priorities designed to deliver our strategy:

1. Accelerate Innovative Science
2. Deliver Growth and Therapy Area Leadership
3. Be a Great Place to Work

Achieve Group Financial Targets

For more information, see Financial Review from page 52.

Effective delivery of our strategic priorities will help us achieve our financial targets. Our 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, balancing opportunities for growth with an appropriate level of cover.

Our KPIs and remuneration

Our KPIs are aligned to our strategic priorities and are the indicators against which we measure our productivity and success.

A number of the KPIs used in this section are used to measure the remuneration of Executive Directors and allow us to disclose aggregated targets without disclosing sensitive commercial information at the individual KPI level. Any variances between the KPI and values used in determining remuneration are explained in the Directors' Remuneration Report from page 98. Other indicators used are now included in the Business Review from page 30.

From 2021, a metric focusing on the delivery of our Ambition Zero Carbon commitments is included in our executive incentive arrangements, which underlines the importance we place on eliminating our Scope 1 and Scope 2 greenhouse gas emissions by 2025.

For more information, see the Directors' Remuneration Report from page 98.

KPI key

● Used for remuneration of Executive Directors

Achieve Group Financial Targets

Key Performance Indicators

Cash generation is a key driver of long-term shareholder returns and facilitates reinvestment in our pipeline, which is critical for delivering new medicines and future value.

Earnings per share (EPS) is an important profitability metric and a key driver of shareholder value.

For more information on our Core measures, see the Financial Review from page 52.

For details of how Achieve Group Financial Targets are considered when calculating the annual bonus, see page 108.

Net cash flow from operating activities

$5,963m ●

2021	**$5,963m**
2020	$4,799m
2019	$2,969m

Actual growth
2021 +24%
2020 -62%
2019 +13%

Reported EPS

$0.08

2021	**$0.08**
2020	$2.44
2019	$1.03

Actual growth	CER growth
2021 -97%	**2021 -84%**
2020 -137%	2020 -142%
2019 -40%	2019 -44%

Core EPS

$5.29 ●

2021	**$5.29**
2020	$4.02
2019	$3.50

Actual growth	CER growth
2021 +32%	**2021 +37%**
2020 +15%	2020 +18%
2019 +1%	2019 0%

Accelerate Innovative Science

Our prioritised initiatives

Accelerating the next wave of new molecular entities (NMEs) and building our capabilities in immunology and rare diseases.

Pursuing the next wave of disruptive R&D platforms with new scientific modalities, such as ProTACs epigenetics, oligonucleotides, antibody drug conjugates and cell therapies, as well as new technologies such as OMICs and knowledge graphs.

Driving R&D productivity through clinical trial excellence and the use of digital health, artificial intelligence (AI), data-enabled R&D that provide new insights, accelerated processes and an improved patient experience.

How our strategy responds to global trends

To ensure we are able to respond to the increasing burden of chronic disease and incorporate advances in science and digital technologies, we are:

- Developing an R&D culture of inspiring people with curious minds, harnessing data and technology, working seamlessly and inclusively, and always learning from patients.
- Focusing on innovative science, a range of drug modalities, emerging drug platforms and new technologies in our chosen disease areas.
- Driving R&D productivity by focusing on quality rather than quantity at all stages of drug discovery and development, and strengthening our ability to match targeted medicines to patients who need them most.
- Transforming our science and leveraging technology, including the provision of enhanced data and clinical insights, as well as digital and AI approaches.
- Collaborating with academia, governments, industry, and scientific and patient organisations to access the best science and patient insights.
- Seeking to attract the brightest minds and creating an environment where science can thrive.

"We seek to attract the brightest minds and create an environment where science can thrive."

How we progressed in 2021

Our science

- Achieved 49 regulatory events: 27 NME and major life-cycle management (LCM) submissions and 22 approvals in major markets (US, EU, China and Japan)
- Secured 32 pipeline progression events: 9 NME Phase II starts/progressions and 23 NME and major LCM Phase III investment decision
- Our pipeline includes 177 projects, of which 161 are in the clinical phase of development.
- At the end of the year, we had 16 NME projects in pivotal trials or under regulatory review covering 16 indications (2020: 10).
- 18 projects were discontinued.

Our sustainability

- We embed practices into the product portfolio to drive equitable access to healthcare, including digital health, clinical trial diversity, patient centricity, investing in rare diseases, open innovation and intellectual property sharing.

Focus for 2022

- Strengthen R&D bridges between AstraZeneca and Alexion.
- Drive innovation opportunities in China and beyond.
- Leverage and embed digital advances across the pipeline.

For more information, see Disease Area Review from page 16 and Business Review from page 30.

Key Performance Indicators

Our science measures incentivise the development of NMEs and the maximisation of the potential of existing medicines. Pipeline progression events (Phase II NME starts/progressions and Phase III investment decisions) measure innovation and sustainability. Regulatory events (regulatory submissions and approvals) demonstrate the advancement of this innovation to patients and the value to the Group.

For more information on performance against the Group scorecard, see page 108.

Pipeline progression events

32[1] ●

2021	32[1]
2020	36[2]
2019	22[3]

[1] 26 against our Group scorecard for determining annual bonus. 2021 total includes Alexion.
[2] 25 against our Group scorecard for determining annual bonus. 17 against our Group scorecard for determining annual bonus.

Regulatory events

49[1] ●

2021	49[1]
2020	53[2]
2019	63[3]

[1] 37 against our Group scorecard for determining annual bonus. 2021 total includes Alexion.
[2] 43 against our Group scorecard for determining annual bonus.
[3] 27 against our Group scorecard for determining annual bonus.

Our Strategy and Key Performance Indicators *continued*

Deliver Growth and Therapy Area Leadership

Our prioritised initiatives

Meeting our growth and profitability goals through successful innovation and commercial excellence, as well as completing the Alexion acquisition.

Transforming healthcare delivery through a focus on:

- > Impacting and improving the whole patient experience, from disease prevention and awareness, diagnosis, treatment, post-treatment to wellness.
- > Data analytics, omnichannel and go-to-market models.
- > Innovative value strategies for pricing that focus on the outcomes our medicines deliver to patients and healthcare systems.
- > Implementing our plans for 'smart factories' and next-generation manufacturing technologies.

How our strategy responds to global trends

To ensure we are able to respond to the increasing demand for healthcare, downward pressure on prices and increasing control that people have over their own healthcare, we are:

- > Fostering a patient-focused approach and embedding patient insights across our organisation, building integrated therapy area ecosystem models and establishing 'health innovation hubs'.
- > Engaging with policymakers to support improvements in access, coverage, care delivery, quality of care and patient care outcomes.
- > Leveraging technology across prevention and awareness, diagnosis, treatment, post-treatment and wellness to deliver better patient outcomes.
- > Partnering with industry, governments and academia to find ways to bring new medicines to market more quickly and efficiently.
- > Collaborating with the funders of healthcare to increase the use of value-based pricing solutions.
- > Enabling our Emerging Markets to deliver better and broader patient access through faster submission as well as innovative and targeted equitable pricing strategies and practices.
- > Pursuing a strong patent strategy that builds robust patent estates to protect our pipeline and products while defending and enforcing patent rights.

How we progressed in 2021

Our growth and leadership

- > Total Revenue, comprising Product Sales and Collaboration Revenue, increased by 41% (38% at CER) to $37,417 million.
- > Product Sales grew by 41% (38% at CER) to $36,541 million; Collaboration Revenue increased by 20% (20% at CER) to $876 million.
- > Oncology Product Sales grew by 20% (18% at CER) to $13,048 million, while CVRM increased by 13% (10% at CER) to $8,020 million. R&I increased by 13% (9% at CER) to $6,034 million.
- > Following completion of the Alexion acquisition on 21 July 2021, Rare Disease medicines generated $3,071 million, 8% of Total Revenue, growing 8% (9% CER) on a pro forma, pro rata basis[1].
- > Total Revenue grew in Emerging Markets by 41% (36% at CER) to $12,281 million. In the US, it grew by 38% to $12,228 million and in Europe by 45% (40% at CER) to $8,050 million.

Our sustainability

- > Over 31 million people reached through our flagship access to healthcare programmes.
- > Over 11 million people reached through patient access programmes.
- > Over 199,000 healthcare workers and others trained.

Focus for 2022

- > Advance the combined AstraZeneca and Alexion pipeline.
- > Build our new Vaccines and Immune Therapies Unit on which we will be reporting separately from 2022.
- > Advance digital approaches to transform the patient experience.

For more information, see Disease Area Review from page 16 and Business Review from page 30.

[1] Growth rates on Rare Disease medicines have been calculated on a pro forma, pro rata basis by comparing post-acquisition revenues from 21 July 2021 to 31 December 2021 with the corresponding period in the prior year pre-acquisition as previously published by Alexion. Pro forma, pro rata Total Revenue growth rates have been presented for 2021 Rare Disease area and constituent medicines, and do not impact Group totals.

Key Performance Indicators

Our Total Revenue measure reflects the importance of incentivising sustainable growth in both the short and longer term.

For details of how Total Revenue is considered when calculating the annual bonus, see from page 103.

Total Revenue

$37,417m

2021	$37,417m
2020	$25,617m
2019	$24,384m

Actual growth	CER growth
2021 +41%	**2021 +38%**
2020 -9%	2020 -10%
2019 -10%	2019 -13%

Be a Great Place to Work

Our prioritised initiatives

Contributing to the enterprise and being a great place to work, with a focus on inclusion and diversity, as well as lifelong learning.

Evolving how we work and collaborate while continuing to embrace digital ways of working.

Contributing to society by improving access to healthcare, environmental protection, and ethics and transparency, as well as delivering our Ambition Zero Carbon programme.

How our strategy responds to global trends

To ensure we are able to deliver our strategy, build trust in AstraZeneca and contribute to the health of society and the planet, we are:

- Recruiting the best talent, which underpins our innovation and growth.
- Living our Values and engendering a high-performing team and lifelong learning.
- Harnessing different perspectives, talents and ideas in an inclusive way while ensuring our employees reflect the diversity of the communities we serve.
- Empowering employees through our Code of Ethics to make decisions in the best interests of the Group and society.
- Refusing to tolerate bribery or any other form of corruption.
- Contributing to society in support of the United Nations Sustainable Development Goals.
- Broadening access to sustainable healthcare solutions for life-changing treatment and prevention.
- Taking bold action on climate, recognising the interconnection between the health of people, society and our planet.

How we progressed in 2021

Our people

- We continue to invest in our people to ensure we recruit, retain and develop a talented workforce.
- In 2021, we delivered a strong performance across the key priorities of our People and Sustainability strategies.
- We continue to score highly in our Pulse surveys for questions relating to our Purpose, direction, patient centricity and employee commitment to our success.

Our sustainability

- We achieved a 'Green' rating for performance across our three sustainability pillars.
- We provided $112 million to more than 1,220 non-profit organisations across 74 countries.
- Our Scope 1 to 3 and long-term net-zero greenhouse gas emissions reduction targets were verified by the Science Based Targets initiative.
- We maintained 100% of active employees trained on our Code of Ethics, based on our Values, expected behaviours and key policy principles.

Focus for 2022

- Maintain positive employee engagement.
- Accelerate digital transformation and activities to drive productivity.
- Deliver targeted advances across sustainability priorities.

For more information, see Our People from page 41 and Sustainability from page 44.

Key Performance Indicators

Our Great Place to Work strategy is built around two priorities: Contribution to the enterprise and Contribution to society.

Our Contribution to the enterprise KPI is based on our Pulse survey measure of those employees who believe that AstraZeneca is a great place to work.

Our Contribution to society KPI is based on our Sustainability scorecard. It measures progress on annual and long-term targets across our three pillars of sustainability: Access to healthcare, Environmental protection, and Ethics and transparency.

Employee belief that AstraZeneca is a great place to work[1]

85%

2021	85%
2020	89%
2019	86%

Source: November Pulse survey for each year.

Sustainability scorecard performance[2]

83%

2021	83%
2020	93%
2019	86%

Blue
Green
Amber
Red

A Green rating = more than 75% of our categories are rated green. Each category consists of several KPIs. We have a priority grade. Achievement of 9 is Red; 9 to 10 is Amber; 11 to 12 is Green; and 13 or 14 is Blue.

Oncology

We are leading a revolution in oncology to redefine cancer care. Our ambition is to follow the science to discover, develop and deliver life-changing treatments that increase the potential for cure.

For more information, see Accelerate Innovative Science from page 31 and Deliver Growth and Therapy Area Leadership from page 35



Product Sales

$13,048m

up 20% (18% at CER)
2020: $10,850m
2019: $8,667m

2021 overview

> Performance driven by rapid and broad market penetration of our new medicines with 253 market approvals.
> *Tagrisso* (osimertinib) approved in 71 markets as an adjuvant treatment for early-stage EGFR-mutated non-small cell lung cancer (NSCLC), including in the EU and China.
> *Orpathys* (savolitinib) approved in China for certain NSCLC patients – first global regulatory approval, and *Imfinzi* (durvalumab) approved in China for extensive-stage small cell lung cancer (ES-SCLC).
> *Lynparza* (olaparib) demonstrated positive results for the adjuvant treatment of germline BRCA-mutated high-risk early breast cancer in the OlympiA trial.
> *Enhertu* (trastuzumab deruxtecan) demonstrated positive results for previously treated patients with HER2-positive metastatic breast cancer in DESTINY-Breast03.
> Positive Phase III trials expanded our footprint across genitourinary and gastrointestinal cancers.
> Initiated 22 trials across Phases I, II and III.

Unmet medical need and world market

10m

Cancer is the second leading cause of death globally with nearly 10 million people losing their lives to cancer in 2020.

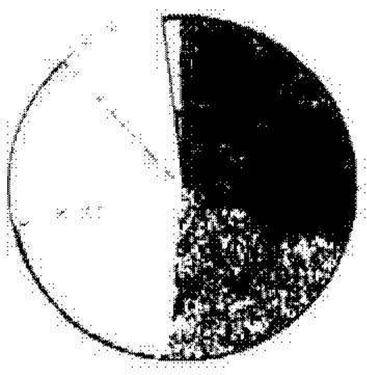
1 in 2

people will be diagnosed with some form of cancer during their lifetime. Costs associated with cancer place a heavy economic burden on societies, with an estimated global total cost of $1.16 trillion in 2010.

Disease area world market
(MAT Q3-21)

$158.6bn

Annual worldwide market value



- Small molecule targeted agents $48.6bn
- Monoclonal antibodies (mAbs) $33.3bn
- Immune checkpoint inhibitors $31.6bn
- Chemotherapy $26.3bn
- Hormonal therapies $15.6bn
- PARP inhibitors $2.6bn
- Other oncology therapies $0.4bn

Source: IQVIA
Data based on sales of specific segments within the overall disease area market.

Key marketed products

See full product information in Patent Expiries Supplement on our website, www.astrazeneca.com/annualreport2021.

Product	Disease	Total Revenue	Commentary
Tagrisso (osimertinib)	Lung cancer	$5,015m, up 16% (13% at CER)	Approved in 64 countries for the adjuvant treatment of patients with early-stage EGFR-mutated (EGFRm) NSCLC and in 91 countries for both the 1st- and 2nd-line treatment of advanced EGFRm NSCLC.
Lynparza (olaparib)	Ovarian cancer Breast cancer Pancreatic cancer Prostate cancer	$2,748m, up 23% (21% at CER)	Approved in 86 countries for the treatment of advanced ovarian cancer. It has also been approved in 84 countries for the treatment of gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer and in 68 countries for the treatment of gBRCAm metastatic pancreatic cancer. It is now approved in 70 countries for the treatment of metastatic castration-resistant prostate cancer.
Imfinzi (durvalumab)	Lung cancer Bladder cancer	$2,412m, up 18% (16% at CER)	Approved in the curative-intent setting of unresectable, Stage III NSCLC after chemoradiotherapy in 74 countries. Also approved in ES-SCLC in 63 countries and for previously treated patients with advanced bladder cancer in 17 countries.
Calquence (acalabrutinib)	Mantle cell lymphoma (MCL) Chronic lymphocytic leukaemia (CLL)	$1,238m, up 137% (136% at CER)	Approved for the treatment of CLL in 70 countries. Also approved for the treatment of patients with MCL who have received at least one prior therapy in 34 countries.
Enhertu (trastuzumab deruxtecan)	Breast cancer Gastric cancer	$214m, up 123% (123% at CER)	Approved in more than 40 countries for HER2-positive unresectable, locally advanced or metastatic breast cancer following two or more prior anti-HER2-based regimens. Approved in several countries for locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma following a prior trastuzumab-based regimen.
Koselugo (selumetinib)	Neurofibromatosis type 1 plexiform neurofibromas (PN)	$108m, up 185% (186% at CER)	Approved in the US and the EU for the treatment of paediatric patients two years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable PN.
Orpathys (savolitinib)	Lung cancer	$16m	Approved in China for the treatment of NSCLC with MET exon 14 skipping alterations.
Other products			
Zoladex (goserelin acetate implant)	Prostate cancer Breast cancer	$966m, up 3% (down 1% at CER)	
Arimidex (anastrozole)	Breast cancer	$139m, down 25% (27% at CER)	
Faslodex (fulvestrant)	Breast cancer	$431m, down 26% (27% at CER)	
Casodex/Cosudex (bicalutamide)	Prostate cancer	$143m, down 17% (21% at CER)	
Iressa (gefitinib)	Lung cancer	$163m, down 32% (35% at CER)	
Others		$50m, up 1% (down 1% at CER)	

Our strategy in Oncology

We strive to push the boundaries of science to change the practice of medicine and transform the lives of patients living with cancer. With this vision in mind, we focus on four strategic priorities:

1. Scientific platforms that work in two ways – targeting cancer cells directly and activating the immune system. We use monotherapy and combination approaches to drive deeper, more durable responses:
   a. Tumour drivers and resistance – targeting the genetic mutations and resistance mechanisms that enable cancer cells to evade treatment, survive and proliferate.
   b. DNA damage response (DDR) – targeting the DNA repair process to block cancer cells' ability to reproduce.
   c. Antibody drug conjugates (ADC) – delivering highly potent cancer-killing agents directly to cancer cells via a linker attached to a targeted antibody.
   d. Epigenetics – identifying changes in how the genome is expressed in cancer and developing drugs to target key vulnerabilities generated by these changes.
   e. Immuno-oncology (IO) – activating the body's own immune system to help fight cancer.
   f. Cell therapies – harnessing living cells to target cancer.
2. Advancing treatment in the early stages of cancer where the greatest opportunity for cure exists and building expertise and leadership in key tumour types.
3. Integrating patient-centric innovation into our programmes through partnerships that will lead to permanent changes in healthcare, including blood-based screening, computational pathology, ctDNA testing, digital health and data science/AI.
4. Delivering across our global footprint to make cancer therapies available to every eligible and appropriate patient.

Full details are given in the Development Pipeline Supplement on our website, www.astrazeneca.com/annualreport2021.

Disease Area Review
Oncology *continued*

2021 review – strategy in action
2021 saw strong growth, underpinned by positive data news flow across our late-stage pipeline assets.

Lung cancer
Scientific advances are strengthening the potential of our medicines to offer cure and long-term survivorship in lung cancer with a focus on early detection and precision medicine. We are leaders in driving a stage shift at diagnosis, through advocacy for access to lung cancer screening, biomarker testing and improved quality care.

- *Tagrisso* has been used to treat more than half a million patients worldwide with EGFR-mutated NSCLC. *Tagrisso* continues to be investigated across stages and treatment settings, and in combinations as a potential means to address tumour mechanisms of resistance.
- *Imfinzi* is being explored in combinations and beyond its established lung cancer indications in unresectable Stage III NSCLC and ES-SCLC. In 2021, we announced positive results for *Imfinzi* with tremelimumab in Stage IV NSCLC, and with novel immunotherapies oleclumab or monalizumab in unresectable Stage III NSCLC.
- *Enhertu* continued to show potential as the first HER2-directed therapy to show a strong tumour response in patients with HER2-mutant and HER2-overexpressing metastatic NSCLC with results from the DESTINY-Lung01 Phase II trial.
- Savolitinib received its first global regulatory approval in China under the brand name *Orpathys* in NSCLC patients with MET exon 14 skipping alterations. Savolitinib is an oral, potent and highly selective MET tyrosine kinase inhibitor being investigated in collaboration with HUTCHMED.
- Datopotamab deruxtecan, an anti-trophoblast cell surface antigen 2 (TROP2)-directed ADC, initiated new trials in lung cancer: TROPION-Lung08 in patients whose disease is not driven by actionable genomic alterations, and TROPION-Lung01, a Phase III head-to-head trial versus docetaxel in patients with advanced NSCLC.

Breast cancer
We are expanding into new subtypes of breast cancer and aiming to bring impactful therapies where there is more opportunity for cure.

- Full results from the OlympiA Phase III trial showed *Lynparza* reduced the risk of cancer recurrence by 42% in the adjuvant treatment of patients with germline BRCA-mutated high-risk early breast cancer.
- Full results from the head-to-head DESTINY-Breast03 Phase III trial showed *Enhertu* reduced the risk of disease progression or death by 72% in patients with HER2-positive metastatic breast cancer versus trastuzumab emtansine (T-DM1). *Enhertu* was granted Breakthrough Therapy Designation and Priority Review by the US FDA in October 2021 and January 2022 respectively, for these patients.

Blood cancers
Calquence, our next-generation Bruton's tyrosine kinase inhibitor (BTKi), is now the therapy of choice for more than 40% of patients initiating a BTKi treatment in 1st-line CLL in the US. Real world safety data is supported by the data from the ELEVATE-RR Phase III head-to-head trial in previously treated CLL, which both show less cardiovascular toxicity and fewer discontinuations due to adverse events than other commonly prescribed BTKi treatments.

Prostate cancer
It is a new era of personalised medicine in advanced prostate cancer with *Lynparza* monotherapy as a 2nd-line treatment for certain patients with advanced disease based on the PROfound Phase III trial. We are now expanding into the 1st-line setting with combinations, allowing us to reach a broad population of patients regardless of biomarker status and offering hope for people living with this aggressive disease.

- *Lynparza* in combination with standard-of-care abiraterone demonstrated a statistically significant and clinically meaningful improvement in radiographic progression-free survival versus abiraterone alone as a 1st-line treatment for patients with metastatic castration-resistant prostate cancer with or without homologous recombination repair (HRR) gene mutations in the PROpel Phase III trial.

Gastrointestinal (GI) cancers
With positive results across multiple medicines and a robust development programme, GI cancers have become a new critical area of growth.

- *Enhertu* demonstrated a clinically meaningful and durable response in patients with HER2-positive advanced gastric cancer in the DESTINY-Gastric02 Phase II trial. Additional trials are ongoing in gastric and colorectal cancers.
- Positive results from the HIMALAYA Phase III trial showed a single, high priming dose of tremelimumab added to *Imfinzi* demonstrated improved overall survival (OS) versus sorafenib in 1st-line unresectable hepatocellular carcinoma (HCC).
- Positive results from the TOPAZ-1 Phase III trial showed *Imfinzi* plus chemotherapy improved OS versus chemotherapy alone in 1st-line advanced biliary tract cancer.
- We continue to test *Imfinzi* in various combinations in other GI cancer settings.

Following completion of the Alexion acquisition, we realigned our portfolio. With effect from 1 January 2022, we moved our rare disease medicine *Koselugo* from our Oncology Business Unit to our Alexion Rare Disease Group. This realignment combines Alexion and AstraZeneca's expertise in rare diseases, in collaboration with MSD, to reach more patients impacted by the rare disease NF1.

Our robust pipeline across cancers
Our diverse portfolio and pipeline encompasses molecules and modalities designed to kill cancer cells preferentially, at every stage of the disease across multiple cancer types. We are expanding our discovery capabilities to explore new targets and rapidly progress the most promising programmes, including potential first- and best-in-class treatments. We are:

- Investing heavily in IO, including novel bispecific antibodies and other checkpoint inhibitors, as well as cell therapies.
- Advancing next wave DDR assets including PARP1 selective agents.
- Accelerating ADCs including our proprietary asset AZD8205 (B7H4) into the clinic.
- Exploring combinations focusing on complementary mechanisms to drive deeper treatment responses.

Full details are given in the Development Pipeline Supplement on our website, www.astrazeneca.com/annualreport2021.

BioPharmaceuticals

We want to change the lives of billions of people living with chronic diseases for the better, enabling them to live life without limits. We are addressing some of the biggest healthcare challenges facing humankind by following the science to uncover and target the drivers of the most common chronic diseases. Our ambition is to stop the progress of these often degenerative, debilitating and life-threatening conditions, achieve remission and, one day, cure them.

BioPharmaceuticals is responsible for Cardiovascular, Renal & Metabolism and Respiratory & Immunology.

For more information, see Accelerate Innovative Science from page 31 and Deliver Growth and Therapy Area Leadership from page 35.



Cardiovascular, Renal & Metabolism

Product Sales
$8,020m
up 13% (10% at CER)
2020: $7,096m
2019: $6,906m

We have a relentless focus on developing and delivering innovative, life-changing medicines and solutions for the millions of people affected by the complex spectrum of cardiovascular, renal and metabolic (CVRM) diseases – so they can live life without limits.

Respiratory & Immunology

Product Sales
$6,034m
up 13% (9% at CER)
2020: $5,357m
2019: $5,391m

Our bold ambition is to rewrite the future of respiratory and immunology conditions, evolving from pure symptom control to disease modification, remission and, one day, cure.

Disease Area Review
BioPharmaceuticals *continued*

Cardiovascular, Renal & Metabolism

Unmet medical need and world market

CVRM diseases are the leading causes of death across the globe, killing more than 20 million people each year.

Currently there are:

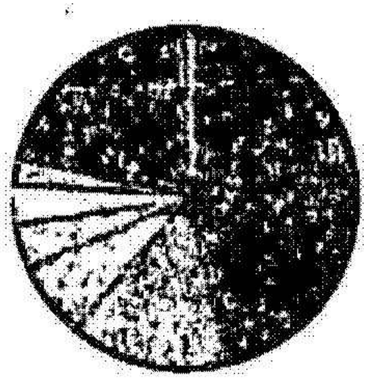
537m
people living with diabetes.

64m
people living with heart failure (HF).

840m
people living with chronic kidney disease (CKD).

Disease area world market
(MAT Q3-21)

$229.6bn
Annual worldwide market value



- Diabetes $114.2bn
- High blood pressure $37.5bn
- Abnormal levels of blood cholesterol $17.7bn
- CKD $10.4bn
- Thrombosis $7.4bn
- CKD associated $6.5bn
- Other CV $52.2bn
- Hyperkalaemia $0.6bn

AstraZeneca focuses on specific segments within this overall disease area market. Sales for CKD ($10.4 billion) and CKD-associated anaemia ($6.5 billion) fall outside the CVRM total market.

All sales for CKD-associated anaemia ($6.5 billion) fall within the CKD market and should not be double-counted.

CVRM disease area world market total excludes sales from the HIF-PHI + ESA market.

2021 overview

> *Farxiga* was the primary growth driver with chronic kidney disease (CKD) added to the label.
> *Lokelma* secured label extensions to include patients with hyperkalaemia (HK) on haemodialysis.
> Our pipeline remains strong, well balanced and grows with existing products, LCMs and multiple NMEs.

Key marketed products

See full product information in the Patent Expiries Supplement on our website, www.astrazeneca.com/annualreport2021.

Product	Disease	Total Revenue	Commentary
Farxiga/ Forxiga (dapagliflozin)	Type-2 diabetes (T2D) Type-1 diabetes (T1D) Heart failure with reduced ejection fraction (HFrEF) Chronic kidney disease (CKD)	↓ $3,005m, down 23% (23% at CER)	Approved in over 100 countries to improve glycaemic control in adult patients with T2D and for HFrEF in patients with and without T2D. First-in-class approval for CKD in patients with and without T2D in the US, EU, UK, Japan and other countries.
Brilinta/Brilique (ticagrelor)	Acute coronary syndromes (ACS)	↓ $1,472m, down 8% (10% at CER)	Approved in over 115 countries for ACS and in 80 countries for high-risk patients with history of heart attack. Approved in the US to reduce the risk of a first heart attack or stroke in high-risk patients.
Bydureon (exenatide XR injectable suspension)	Type-2 diabetes	↓ $385m, down 14% (15% at CER)	
Onglyza (saxagliptin)	Type-2 diabetes	↓ $360m, down 37% (26% at CER)	
Roxadustat	Anaemia of CKD	↑ $180m, up 493% (448% at CER)	
Lokelma (sodium zirconium cyclosilicate)	Hyperkalaemia	↑ $175m, up 130% (130% at CER)	Approved in 47 countries. Label extensions secured in 45 countries including patients on haemodialysis.
Byetta (exenatide injection)	Type-2 diabetes	↓ $55m, down 25% (24% at CER)	
Other products			
Crestor (rosuvastatin calcium)	Dyslipidaemia Hyper-cholesterolaemia	↓ $1,098m, down 7% (10% at CER)	
Seloken/Toprol-XL (metoprolol succinate)	Hypertension Heart failure Angina	↑ $953m, up 16% (11% at CER)	
Atacand/Atacand HCT/Atacand Plus (candesartan cilexetil)	Hypertension Heart failure	↓ $97m, down 60% (60% at CER)	
Others		↑ $196m, up 3% (down 2% at CER)	

Our strategy in CVRM

Our ambition is to stop, reverse and cure CVRM diseases by maximising the value of our medicines, delivering innovative solutions and advancing our pipeline to transform CVRM care. We do this by:

> Unravelling the underlying causes of these diseases by identifying novel targets linked to disease biology to create the next generation of medicines.
> Driving a precision medicine approach that enables us to develop diagnostic strategies and more effective treatments by focusing on the right patients for a specific therapy.
> Developing a pipeline that goes beyond small molecules, mAbs and peptides to include new modalities such as oligonucleotides, mRNA and cell therapy, and also seeks to drive value beyond the first indication.
> Pursuing real-world evidence programmes that improve understanding of disease epidemiology and burden, treatment effectiveness and safety, and health economics.
> Bringing medicines to market more quickly through our CVRM Clinical Trials of the Future programme.

Full details are given in the Development Pipeline Supplement on our website, www.astrazeneca.com/annualreport2021.

2021 review – strategy in action

Cardiovascular disease

With an ambition to eliminate CV residual risk and stop disease progression, we are making a difference for patients with *Brilinta* and developing a next-generation PCSK9 inhibitor. In 2021, *Brilinta* received expanded use in the US beyond cardiovascular disease to patients with mild-to-moderate stroke. Additionally, results from ALETHEIA, an observational trial in patients with a history of heart attack being treated with *Brilinta* 60mg in a real-world setting, showed bleeding rates remained low overall and reinforced the role of *Brilinta* in this patient population.

Positive Phase IIa results from the EPICCURE trial, the first clinical trial to inject naked mRNA directly into the heart of patients undergoing elective coronary artery bypass surgery, demonstrated that AZD8601 met the primary endpoint of safety and tolerability in patients with heart failure.

Phase I results for monthly administered AZD8233 demonstrated that the therapy was generally safe and well tolerated and reduced PCSK9 levels by up to 95% and LDL-C levels by more than 70% over the entire dosing interval.

Heart failure

In 2021, *Forxiga* gained another major market approval in China with continued launches in HFrEF contributing to strong growth for the brand in 2021. The large randomised DELIVER Phase III trial, evaluating *Farxiga* in heart failure with preserved ejection fraction (HFpEF), is expected to read out in the first half of 2022.

HF patients are often prescribed life-saving renin-angiotensin-aldosterone system inhibitors, which lead to elevated potassium levels. These patients have an increased risk of developing HK, a serious condition characterised by elevated potassium levels in the blood associated with cardiovascular, renal and metabolic diseases, which can be life threatening if left untreated. For the first time, a globally recognised cardiology guideline, the 2021 European Society of Cardiology-HF guidelines, listed novel K^+ binders, including *Lokelma*, as options to manage HK.

Renal diseases

CKD is a progressive disease that can eventually lead to end-stage kidney disease (ESKD), with the potential for dialysis and serious life-threatening complications. Based on last year's ground-breaking DAPA-CKD Phase III trial results, *Farxiga* was approved in the US, EU, UK and Japan for the treatment of CKD in patients with and without T2D.

Roxadustat is an oral hypoxia inducible factor prolyl hydroxylase (HIF-PH) inhibitor that has the potential to transform the lives of people living with anaemia of CKD, both on dialysis and not on dialysis. Roxadustat is the first HIF-PH inhibitor currently approved in China, Japan, Chile, South Korea and in the EU under the name *Evrenzo* for the treatment of anaemia in CKD in non-dialysis dependent (NDD) and dialysis-dependent (DD) adult patients. In the third quarter of 2021, the US Food and Drug Administration (FDA) issued a complete response letter (CRL) regarding the new drug application (NDA) for roxadustat for the treatment of anaemia of CKD, in both NDD and DD adult patients. The CRL requested an additional clinical trial on the safety of roxadustat. AstraZeneca is working with its collaborator FibroGen, and the FDA to evaluate next steps. Roxadustat is also in clinical development for anaemia associated with myelodysplastic syndrome and for chemotherapy-induced anaemia.

People living with CKD are at an increased risk of developing HK. The evidence generated from the CRYSTALIZE programme will provide insights into patient-centric management of HK with *Lokelma*, including the Phase III DIALIZE-Outcomes trial to evaluate the effect of *Lokelma* on arrhythmia-related CV outcomes in patients on chronic haemodialysis with recurrent HK. In the fourth quarter of 2021, AstraZeneca was granted Fast Track Designation in the US for the investigation of *Lokelma* in the DIALIZE-Outcomes trial. The Phase III STABILIZE CKD trial will evaluate the effect of *Lokelma* on CKD progression in patients with CKD and HK or at risk of HK.

To help address the unmet medical need in CKD, we are exploring the clinical science behind our medicines with DELIGHT, an exploratory Phase II/III trial, also part of the DapaCare programme. The trial evaluates the potential albuminuria-lowering effect of *Farxiga* in the treatment of CKD and T2D.

ZENITH-CKD, our Phase II trial of zibotentan and dapagliflozin is underway for the treatment of CKD patients, reducing mortality and delaying progression to ESKD. We will also be exploring ZiboDapa for the treatment of cirrhosis with features of portal hypertension.

Metabolism

Non-alcoholic steatohepatitis (NASH) prevalence is growing and is a major public health burden. The Phase II PROXYMO trial demonstrated that, on a background of acceptable safety, cotadutide delivers significant benefits on hepatic fat fraction and aminotransferases. It also delivers improvements in markers of inflammation and fibrosis in the target population of patients with biopsy-proven non-cirrhotic NASH with fibrosis. AZD4831, a myeloperoxidase inhibitor, has moved into NASH following strong pre-clinical data demonstrating a reduction in inflammation and fibrosis in a diet-induced NASH model.

In 2021, the indication for *Forxiga* was voluntarily removed in the EU for the treatment of adults with insufficiently controlled T1D. This decision did not impact the indication outside the EU and did not impact other approved *Forxiga* indications within or outside the EU. This decision follows discussions with the EMA regarding product information changes after approval for *Forxiga* 5mg for T1D. This was to address potential confusion among physicians treating patients with T2D, HFrEF or CKD. It was not due to any new safety or efficacy concerns in T1D or any other indication. In the EU, *Forxiga* received approval for the treatment of T2D in the paediatric population.

Beyond research

We have made a long-term investment to improve CVRM patient care through a multi-disciplinary programme called Accelerate Change Together (ACT). ACT on HF aims to improve lives by halving HF hospitalisations and improving five-year survival rates by 20% by 2024. To date, approximately 140,000 healthcare providers and 2.5 million patients have been positively impacted by the project.

ACT on CKD seeks to transform kidney health and reduce the number of patients developing kidney failure by 20% by 2025. Our efforts in 2021 resulted in 11.5 million patients being screened. ACT programmes have been implemented in more than 40 countries.

We also invest in programmes to improve patient access. These include Healthy Heart Africa, which addresses hypertension and the increasing burden of CV disease.

For more information, see page 45.

Additionally, we have formed strategic collaborations with healthcare innovators to further understand CVRM diseases, with the aim of harnessing data, new technologies and digital health to transform the lives of patients and clinical practice. This year, our digital health collaborations continued. Collaborations include:

- Eko Health and Us2.ai in HF
- RenalytixAI in CKD
- the NHS through Imperial College Health Partners (London, UK) on Discover-NOW, the Health Data Research Hub for real world evidence in T2D and HF.

Respiratory & Immunology

Unmet medical need and world market

550m
Nearly 550 million people worldwide live with chronic respiratory disease.

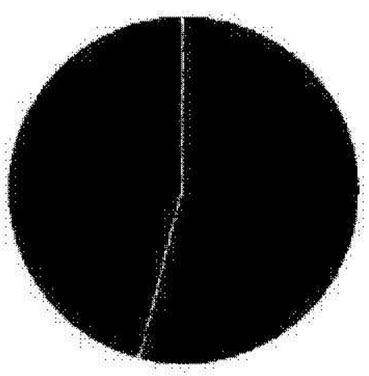
Up to 10%
of patients with asthma have severe asthma and account for approximately 50% of asthma-related costs.

1 in 10
Chronic obstructive pulmonary disease is the third leading cause of death worldwide, affecting one in 10 people over the age of 40.

5m
At least five million people worldwide have a form of lupus, yet only two new treatments for systemic lupus erythematosus (SLE) have been approved in the last 60 years.

Disease area world market
(MAT Q3-21)

$77.8bn
Annual worldwide market value



- Asthma $23.4bn
- COPD $18.7bn
- Other $35.7bn

Source: IQVIA
AstraZeneca focuses on specific segments within this overall disease area market

2021 overview

> The respiratory market has been particularly affected by COVID-19 due to respiratory physicians focusing on the pandemic, a reduction in patients attending hospital visits and self-isolation reducing exacerbation rates.
> Despite ongoing challenges created by the COVID-19 pandemic, our Product Sales grew by 13% (9% at CER). Key growth drivers were *Fasenra* (benralizumab), *Symbicort* (budesonide/formoterol) and *Breztri* (budesonide/glycopyrrolate/formoterol).
> *Tezspire* (tezepelumab) was approved for the treatment of severe asthma in the US.
> *Saphnelo* (anifrolumab) was approved for the treatment of SLE in the US, Japan and also received recommendation for approval in the EU.
> PT027 (albuterol/budesonide) demonstrated positive high-level results in two Phase III trials in asthma.

Key marketed products

See full product information in the Patent Expiries Supplement on our website, www.astrazeneca.com/annualreport2021.

Product	Disease	Total Revenue	Commentary
Symbicort (budesonide/formoterol)	Asthma COPD	$2,728m, stable at 0% (down 2% at CER)	Continued global volume and value leadership of the inhaled corticosteroid/long-acting beta2-agonist (ICS/LABA) class, decline in the EU and Established Rest of World partially offset by growth in the US and Emerging Markets. Pricing pressure is expected to continue in major territories such as the US, EU, China and Japan.
Fasenra (benralizumab)	Severe asthma	$1,256m, up 33% (31% at CER)	Achieved blockbuster status and consolidated its position as the leading novel biologic in total and new to brand prescriptions in severe asthma in key markets around the world.
Pulmicort (budesonide)	Asthma	$962m, down 3% (8% at CER)	In-hospital paediatric use of nebulised *Pulmicort* in Emerging Markets continued to be significantly affected by COVID-19 in the first half of the year and by the implementation of volume-based procurement for this formulation in China in the fourth quarter.
Daliresp/Daxas (roflumilast)	COPD	$227m, up 5% (4% at CER)	Stable sales driven by the US, where a 2021 price increase offset slightly lower demand.
Breztri (budesonide/glycopyrrolate/formoterol)	COPD	$203m, up 637% (623% at CER)	New launches across 14 countries. Sales accelerated in Japan following Ryotanki lift in the fourth quarter of 2020. Strong sales and market leadership in China following inclusion on the National Reimbursement Drug List. Strong performance in the US, exceeding competitors' total prescriptions uptake in the first six months from launch, on a time-aligned basis.
Beuespi (glycopyrrolate/formoterol)	COPD	$54m, up 12% (12% at CER)	Launched in 18 countries to date, including Italy in May 2021.
Saphnelo (anifrolumab)	SLE	$8m	First-in-class approval in the US and Japan for the treatment of moderate to severe SLE. Recommended for approval in the EU and under regulatory review for SLE in other countries worldwide.

Our strategy in Respiratory & Immunology

Our aim is to defy the natural course of disease, drive disease modification and ultimately remission, so that patients can live life without limits.

We will realise our ambition by focusing on three core areas:

> reaching more patients earlier by driving broad diagnosis and accelerating access
> slowing disease progression and driving remission by targeting core disease drivers
> achieving greater efficacy through new modalities and novel combinations.

Chronic obstructive pulmonary disease (COPD)

Our ambition is to eliminate COPD as a leading cause of death by slowing and ultimately reversing the progression of the disease. Our strategy is to:

> drive broad, early diagnosis and first-line use of the best therapies to improve patient outcomes
> modify disease through investment in therapies that repair the lung to halt structural damage and lung function decline
> strengthen our ability to monitor progression
> target our medicines through novel, enhanced diagnostics and endpoints that enable us to act earlier in the disease.

Asthma

Our ambition in asthma is to eliminate exacerbations and achieve clinical remission, even in people with the most severe asthma. We continue to advance our inhaled portfolio. This includes establishing our anti-inflammatory relievers as the backbone of care across all severities, in addition to developing novel biologics that deliver disease control and allow reduction or even elimination of background medication in severe disease. Our research pushes the boundaries of

disease control in uncontrolled severe asthma by combining precision medicines with new delivery modalities.

Immunology
Our ambition is to disrupt immunology by focusing on areas of high unmet medical need in rheumatology, gastroenterology and dermatology to drive clinical remission and eventually cure.

We have been targeting a variety of diseases where type 1 interferon plays a role with recent approvals in the treatment of SLE and pursuing programmes in cutaneous lupus erythematosus, lupus nephritis and myositis. We are also targeting diseases in gastroenterology, such as ulcerative colitis and Crohn's disease, where IL-23 and Th17 play a role.

We are also advancing immune therapies where they share common pathways or biological mechanisms (for example, eosinophilic/epithelial immune dysfunction disorders) with respiratory diseases.

Full details are given in the Development Pipeline Supplement on our website, www.astrazeneca.com/annualreport2021.

2021 review – strategy in action
Asthma
In 2021, *Symbicort* launched in China as the first dual-combination therapy approved for mild, moderate and severe disease. The anti-inflammatory reliever indication has been approved in 43 countries.

Our second anti-inflammatory reliever, PT027, is a potential first-in-class short-acting beta2-agonist (albuterol)/ICS (budesonide) rescue treatment for asthma in the US. Positive high-level results from the MANDALA and DENALI Phase III trials showed PT027 met all primary endpoints, demonstrating statistically significant benefits in patients with asthma versus individual components albuterol and budesonide.

Breztri, our triple therapy, is being studied in asthma, and recruitment in two Phase III pivotal trials, KALOS and LOGOS, is ongoing.

Fasenra, our first respiratory biologic, is now approved in over 65 countries and has reached more than 100,000 patients with severe, eosinophilic asthma. Around half of all patients now self-administer *Fasenra*. Our patient support programme, Connect 360, increased enrolment by more than 60% in 2021.

In December 2021, *Tezspire* was approved in the US for the add-on maintenance treatment of adult and paediatric patients aged 12 years and above with severe asthma – the first and only biologic for severe asthma to be approved without phenotypic or biomarker limitations. Approval was based on results from the PATHFINDER clinical trial programme, including positive results from the Phase III NAVIGATOR trial. This followed the granting of Priority Review for *Tezspire* for the treatment of asthma by the FDA in July 2021.

COPD
In January 2022, we initiated two Phase III trials, CHERON and TITANIA, of tozorakimab (MEDI3506), an investigational, biologically differentiated mAb with dual pathway inhibition targeting IL-33 in patients with COPD.

Immunology
In the second half of 2021, *Saphnelo* was approved in the US for the treatment of adult patients with moderate to severe SLE who are receiving standard therapy. It was also approved in Japan for the treatment of adult patients with SLE who show insufficient response to currently available treatment. These approvals were based on data from the *Saphnelo* clinical development programme, including two TULIP Phase III trials and the MUSE Phase II trial. These are the first regulatory approvals for a type I interferon receptor antagonist and the only new treatment approved for SLE in more than 10 years. In December 2021, the European Medicines Agency's Committee for Medicinal Products recommended the approval of *Saphnelo* in the EU as an add-on therapy for the treatment of adult patients with moderate to severe, active autoantibody-positive SLE, despite receiving standard therapy.

Fasenra is being investigated in eight Phase II and Phase III trials in eosinophilic diseases beyond severe asthma, COPD and chronic rhinosinusitis with nasal polyps. These include atopic dermatitis, bullous pemphigoid, chronic spontaneous urticaria, eosinophilic esophagitis (EoE), eosinophilic gastritis/eosinophilic gastroenteritis (EG/EGE), eosinophilic granulomatosis with polyangiitis, hypereosinophilic syndrome and non-cystic fibrosis bronchiectasis.

In November 2021, the FDA granted *Fasenra* Orphan Drug Designations (ODDs) for the treatment of EG and EGE as well as a Fast Track Designation for EG with or without EGE. In October 2021, tezepelumab was granted an ODD by the FDA for the treatment of EoE.

Respiratory infectious diseases
Nirsevimab is the first potential immunisation to show protection against respiratory syncytial virus (RSV) in the general infant population in a Phase III trial and is being developed by AstraZeneca and Sanofi.

Positive results from the MELODY Phase III trial, reported in April 2021, showed nirsevimab met its primary endpoint of a statistically significant reduction in the incidence of medically-attended lower respiratory tract infections caused by RSV versus placebo in healthy late preterm and term infants (35 weeks or more) during their first RSV season.

Nirsevimab builds on the efficacy offered by the current standard of care, *Synagis* (palivizumab), which is indicated for high-risk infants and requires up to five monthly injections to cover a typical RSV season. In June 2021, results from the MEDLEY Phase II/III trial evaluating the safety and tolerability of nirsevimab versus *Synagis* in infants with chronic lung disease, congenital heart disease and/or prematurity, and therefore at high risk of RSV entering their first RSV season, showed a similar occurrence of treatment emergent adverse events or treatment emergent serious adverse events between the two treatments.

Early science
Compounds in early-stage development include AZD1402, an inhaled Anticalin® protein developed with our collaborator Pieris Pharmaceuticals for moderate to severe asthma and a potential first-in-class oral therapy AZD5718 FLAP, targeting a novel inflammatory endotype in asthma.

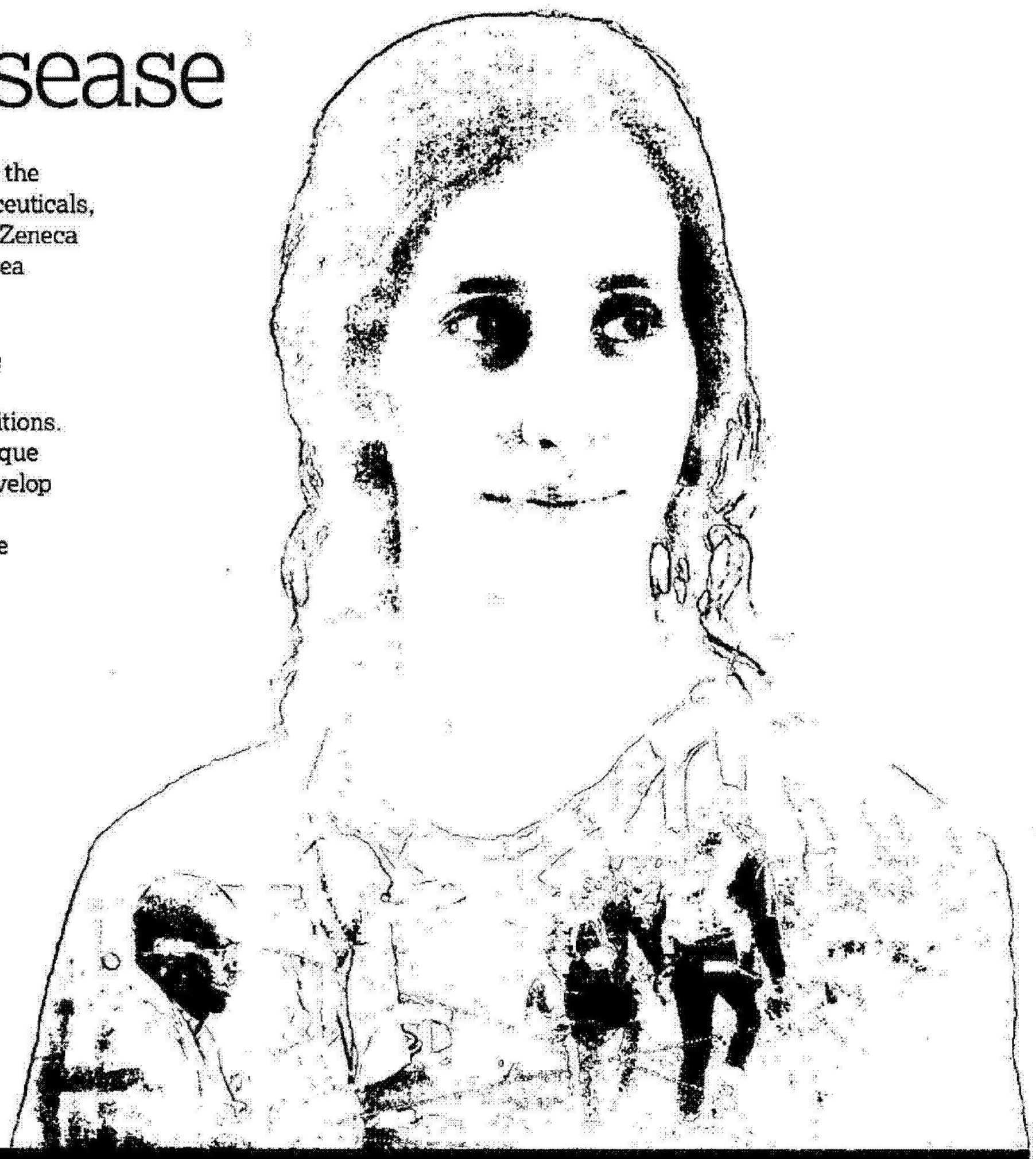
In our early research and development for immune-mediated diseases, we are focusing on those with great unmet medical need. We entered a licensing agreement with F-Star Therapeutics, Inc., for exclusive access to novel pre-clinical STING inhibitors to investigate their potential.

Rare Disease

On 21 July 2021, we completed the acquisition of Alexion Pharmaceuticals, Inc. and created Alexion, AstraZeneca Rare Disease, a new disease area within our company.

Our mission is to transform the lives of people affected by rare diseases and devastating conditions. By understanding patients' unique needs, we can research and develop innovative medicines, support access and advocate for the rare disease community.

For more information, see Accelerate Innovative Science from page 31 and Deliver Growth and Therapy Area Leadership from page 35.



Product Sales

$3,070m

Revenue includes Alexion sales from 21 July 2021.

2021 overview

> Rare Disease Total Revenue grew by 8% (9% at CER) on a pro forma, pro rata basis[1].
> In the US, sales of *Soliris* benefited from growing use in neurology indications, generalised myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD), offset by the successful conversion to *Ultomiris* in haematological indications paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uraemic syndrome (aHUS).
> Acquired Caelum Biosciences and its lead candidate CAEL-101, a potential first-in-class therapy for light chain (AL) amyloidosis.
> Reported positive Phase III results for ALXN1840 in Wilson disease.
> Reported positive Phase III results for *Ultomiris* in gMG. As a result, we filed for regulatory approval in the US, EU and Japan.
> Secured an expansion of our approval of *Ultomiris* in the US and EU to include children and adolescents with PNH.
> Discontinued CHAMPION-ALS, the global Phase III trial of *Ultomiris* in adults with amyotrophic lateral sclerosis (ALS) due to lack of efficacy in that disease.

[1] Growth rates on Rare Disease medicines have been calculated on a pro forma, pro rata basis by comparing post-acquisition revenues from 21 July 2021 to 31 December 2021 with the corresponding period in the prior year, pre-acquisition as previously published by Alexion. Pro forma, pro rata Total Revenue growth rates have been presented for 2021 Rare Disease area and constituent medicines, and do not impact Group totals.

Unmet medical need and world market

400 million
people around the world are affected by a rare disease, half of whom are children.

>7,000
rare diseases are known to exist today but only 5% have treatments.

3 in 10
children with a rare disease don't live to see their fifth birthday.

Key marketed products

See full product information in the Patent Expiries Supplement on our website, www.astrazeneca.com/annualreport2021.

Product	Disease	Total Revenue[1]	Commentary
Soliris (eculizumab)	PNH aHUS gMG NMOSD	$1,874m	> Approved in nearly 50 countries for treatment of patients with PNH, including the US, EU and Japan. > Approved in 40+ countries for treatment of aHUS, including the US, EU and Japan. > Approved in the US as treatment for gMG in adults who are anti-acetylcholine receptor antibody positive. > Approved in the EU and Japan as treatment for refractory gMG in adults who are anti-acetylcholine receptor antibody positive. > Approved in the US, EU, Canada and Japan as treatment for NMOSD in adults who are anti-aquaporin-4 antibody positive.
Ultomiris (ravulizumab)	PNH aHUS	$688m	> Approved in 35+ countries for treatment of adults with PNH, including the US, EU, Canada and Japan. > Approved in the US and EU for treatment of children and adolescents with PNH. > Approved in the US, EU and Japan for treatment of aHUS.
Strensiq (asfotase alfa)	Hypophosphatasia (HPP)	$378m	> Approved in 40+ countries, including the US, EU, Japan and Canada.
Ondexxya (andexanet alfa)/ *Andexxa* (coagulation factor Xa (recombinant), inactivated-zhzo)	Factor Xa inhibitor reversal agent	$68m	> Approved in the US under the accelerated approval pathway for adults treated with FXa inhibitors apixaban and rivaroxaban. Conditional approval in the EU for adults treated with FXa inhibitors apixaban and rivaroxaban.
Kanuma (sebelipase alfa)	Lysosomal acid lipase deficiency (LAL-D)	$62m	> Approved in 40 countries including the US, EU, Japan and Canada.

[1] Total Revenue includes Alexion sales from 21 July 2021.

Our strategy in Rare Disease

Alexion's pioneering legacy in rare diseases is rooted in being the first to translate the complex biology of the complement system into transformative medicines. By driving innovative research and development across new disease targets and modalities, we have diversified our pipeline into additional rare diseases over the last several years. Today, as part of AstraZeneca, we are building bridges across our scientific platforms with a focus on bringing more innovative medicines to people worldwide.

Following the close of the acquisition, we have evolved our rare disease strategy to focus on three core priorities:

1. **Accelerate** by creating smart and efficient strategies to speed access to our medicines for patients.
2. **Innovate** by investing in science, platforms and capabilities, including using AstraZeneca technologies and research capabilities.
3. **Reach** beyond our current geographic footprint to as many rare disease patients as possible.

2021 review – strategy in action

Complement

We have continued to grow *Ultomiris'* leadership position in our three largest markets – the US, Germany and Japan – as we establish the medicine as the standard of care (SoC) for both PNH and aHUS, two chronic and potentially life-threatening diseases that can lead to serious health complications including organ damage.

During 2021, our advancements have ensured more patients will be able to access *Ultomiris*, which offers a reduced dosing frequency compared to *Soliris*. *Ultomiris* was approved in 2021 for children and adolescents with PNH in the US and EU, expanding on its previous approvals for adults.

Additionally, with the approval of *Ultomiris* 100mg/ml in Japan and the filing of *Ultomiris* subcutaneous formulation and device combination in the US, we are making further advances to lessen the treatment burden on patients.

Neurology

Neurology is a key growth area. This is driven by our clinical development programmes as well as the increased use of *Soliris* by patients with gMG, a progressive autoimmune neuromuscular disease, and NMOSD, an autoimmune disorder of the central nervous system that affects the optic nerve and spinal cord.

We completed enrolment in the Phase III trial of *Ultomiris* in NMOSD in March 2021 and expect to have high-level results in 2022.

In July 2021, we reported the high-level results of our Phase III trial of *Ultomiris* in gMG. The trial met its primary endpoint of change from baseline in the myasthenia gravis-activities of daily living profile total score at week 26. As a result, we have filed for regulatory approval in the US, EU and Japan.

We are also exploring the ability to treat earlier-line patients with gMG with ALXN1720, an internally discovered potential third-generation C5 inhibitor. Pending successful completion of the Phase I trial, we intend to initiate a Phase III trial in gMG. We launched a Phase I programme for ALXN1820, an internally discovered bispecific anti-properdin minibody.

Disease Area Review
Rare Disease *continued*

Beyond gMG and NMOSD, we are continuing efforts to expand the use of our existing medicines into new diseases. This includes additional clinical trials of *Soliris* and *Ultomiris* in a number of disease areas where the complement pathway is thought to play a role. A full list of ongoing trials can be found within the Development Pipeline Supplement on our website, www.astrazeneca.com/annualreport2021.

We discontinued CHAMPION-ALS, the global Phase III trial of *Ultomiris* in adults with ALS in August 2021 due to lack of efficacy in that disease.

Factor D is a component of the complement alternative pathway and has a critical role in multiple complement-mediated rare diseases. Targeting Factor D can potentially address a wide range of therapeutic areas of interest including haematology, nephrology and ophthalmology.

ALXN2040 and ALXN2050 are investigational, oral, Factor D inhibitors. A Phase III trial of ALXN2040 as an add-on therapy for PNH patients with extravascular haemolysis is underway. We have initiated a Phase II trial of ALXN2050 monotherapy in PNH patients and plan to initiate proof-of-concept studies in rare renal diseases.

We have also continued to progress our efforts to expand our rare disease focus beyond complement with novel assets.

AL amyloidosis
AL amyloidosis is a rare disease in which misfolded amyloid proteins build up in organs throughout the body, including the heart and kidneys, causing significant organ damage and failure that may ultimately be fatal.

Alexion acquired Caelum Biosciences to advance and accelerate ongoing Phase III clinical development of CAEL-101, a potentially first-in-class fibril-reactive mAb for the treatment of AL amyloidosis. CAEL-101 is currently being evaluated in the Cardiac Amyloid Reaching for Extended Survival Phase III clinical programme in combination with SoC therapy in AL amyloidosis. Two parallel Phase III trials in patients with Mayo stage IIIa and stage IIIb disease, respectively, are ongoing.

Transthyretin amyloidosis (ATTR)
ATTR cardiomyopathy (ATTR-CM) is a systemic, progressive and fatal condition that leads to progressive heart failure and high rate of fatality within four years from diagnosis.

Alexion has entered into an exclusive global collaboration and licence agreement with Neurimmune AG for NI006, an investigational human mAb currently in Phase Ib development for the treatment of ATTR-CM. NI006 specifically targets misfolded transthyretin and is designed to directly address the pathology of ATTR-CM by enabling removal of amyloid fibril deposits in the heart, with the potential to treat patients with advanced ATTR-CM. The transaction is expected to close following satisfaction of customary closing conditions and regulatory clearances.

Additionally, Alexion holds an exclusive licence from Eidos Therapeutics to develop and commercialise ALXN2060 (acoramidis) in Japan. Alexion is conducting a Phase III bridging trial of ALXN2060 for patients with ATTR-CM in Japan.

Wilson disease
Wilson disease is a rare and progressive genetic condition in which the body's pathway for removing excess copper is compromised. Damage from toxic copper build-up in tissues and organs leads to liver disease, psychiatric and/or neurological symptoms.

ALXN1840, a potential new once daily, oral medicine that we are studying in Wilson disease, demonstrated approximately three times greater copper mobilisation than SoC treatments in the FoCus Phase III trial.

Hypophosphatasia (HPP)
We are progressing our next-generation alkaline phosphatase enzyme replacement therapy into clinical trials, with the intention of helping more people living with HPP. We launched a Phase I trial for ALXN1850 in adult patients with HPP.

Factor Xa bleeds
In October, Alexion received a Complete Response Letter from the FDA for its sBLA for *Andexxa*, which extended the indication to include patients treated with edoxaban or enoxaparin when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

Following completion of the Alexion acquisition, *Ondexxya*/*Andexxa* has moved to the CVRM portfolio within our BioPharmaceuticals Business Unit.

Other Medicines and COVID-19

We have medicines and vaccines in other disease areas that have an important impact for patients. As such, we are selectively active in the areas of infection, neuroscience and gastroenterology, where we follow an opportunity-driven approach and often work through collaborations.

We are working to defeat the COVID-19 pandemic. With *Vaxzevria* and *Evusheld*, we are significantly contributing to global public health.

For more information, see Accelerate Innovative Science from page 31 and Deliver Growth and Therapy Area Leadership from page 35.



Product Sales

$6,369m

up 146% (142% at CER)
2020: $2,587m
2019: $2,601m

2021 overview

> *Fluenz* Tetra/*FluMist* Quadrivalent performed strongly driven primarily by heightened focus on increased vaccination coverage as a means to further limit the healthcare burden given the ongoing COVID-19 pandemic.

> Through an agreement with Oxford University in 2020, *Vaxzevria* was developed and distributed by AstraZeneca. In 2021, AstraZeneca and our global partners released for supply more than 2.5 billion doses of COVID-19 vaccine to over 180 countries with about two thirds of these doses going to low- and lower-middle-income countries (LMICs).

Unmet medical need and world market

390m

The Johns Hopkins Disease Tracker has recorded more than 390 million confirmed cases of COVID-19 and more than 5.7 million deaths globally.

Source: Johns Hopkins COVID-19 Dashboard https://coronavirus.jhu.edu/map.html

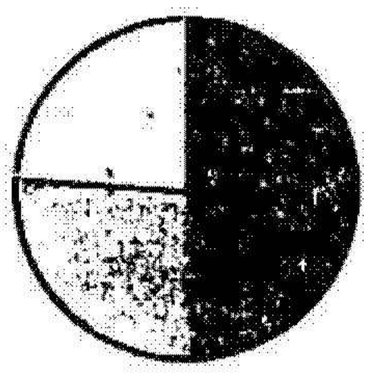
1bn

The WHO estimates that seasonal influenza may result in nearly one billion cases of influenza and 290,000 to 650,000 deaths each year due to influenza-related respiratory diseases.

Disease area world market (MAT Q3-21)

$31.1bn

Annual worldwide market value



- Gastrointestinal $15.4bn
- Infection $8.3bn
- Vaccines $7.4bn

Source: IQVIA.
AstraZeneca focuses on specific segments within this overall disease area market.

Key marketed products

See full product information in the Patent Expiries Supplement on our website, www.astrazeneca.com/annualreport2021.

Product	Disease	Total Revenue	Commentary
Other Medicines			
Infection			
Synagis (palivizumab)	RSV	$410m, up 10% (13% at CER)	Commercial rights to *Synagis* outside the US reverted back to AstraZeneca on 1 July 2021. Agreement with Sobi for rights to *Synagis* in US unaffected.
Fluenz Tetra/ *FluMist* Quadrivalent (live attenuated influenza vaccine)	Influenza	$253m, down 14% (17% at CER)	Approved in the US, EU, Canada, Israel and Hong Kong. Daiichi Sankyo holds rights to *FluMist* Quadrivalent in Japan.
Neuroscience			
Seroquel IR/ *Seroquel XR* (quetiapine fumarate)	Schizophrenia Bipolar disease	$92m, down 21% (20% at CER)	Divested rights in Europe and Russia in October 2019 and in the US and Canada in December 2019 to Cheplapharm. Luye Pharma holds rights to *Seroquel* and *Seroquel XR* in the UK, China and other international markets. There is an agreement in place with Astellas with respect to the rights to *Seroquel* and *Seroquel XR* in Japan.
Gastroenterology			
Nexium (esomeprazole)	Proton pump inhibitor to treat acid-related diseases	$1,424m, down 7% (8% at CER)	Divested European rights to Grünenthal in October 2018.
Losec/ *Prilosec* (omeprazole)	Proton pump inhibitor to treat acid-related diseases	$180m, down 2% (7% at CER)	In October 2019, divested global commercial rights, excluding China, Japan, the US and Mexico to Cheplapharm.
COVID-19			
Vaxzevria (ChAdOx1-S [Recombinant])	COVID-19	$3,981m	Through an agreement with Oxford University in 2020, *Vaxzevria* was developed and distributed by AstraZeneca. More than 2.5 billion doses have been released for supply to over 180 countries.
Evusheld (tixagevimab co-packaged with cilgavimab)	COVID-19	$135m	The first long-acting antibody combination to demonstrate benefit in both prevention and treatment of COVID-19. *Evusheld* is authorised for emergency use for the prevention of COVID-19 in the US and several other countries.

Our strategy in Other Disease Areas

Our approach in these other disease areas looks to maximise revenue of on-market medicines, divest medicines where this enhances shareholder value and advance the novel medicine pipeline with collaborations where appropriate, while preserving a financial stake in the most promising assets.

For 2022, we will be reporting separately on our new Vaccines and Immune Therapies Unit. This will incorporate revenues from *Vaxzevria*, *Evusheld*, *FluMist*, *Synagis* and nirsevimab. For 2021, these are all included in the Other Medicines and COVID-19 Disease Area.

Full details are given in the Development Pipeline Supplement on our website, www.astrazeneca.com/annualreport2021.

2021 review – strategy in action

Infection

Seasonal influenza is a serious public health problem that causes severe illness and death in high-risk populations. *Fluenz* Tetra/*FluMist* Quadrivalent continues to be licensed in multiple markets, including the US, Canada, EU, Israel and Hong Kong, and it remains a central part of the UK and Finnish paediatric national influenza vaccination programmes.

For the 2020 to 2021 flu season, nine million children in the UK were offered *Fluenz* Tetra as part of the UK's national immunisation programme. In addition, we participated in both the US Centers for Disease Control and Prevention Vaccine for Children programme and Vaccine for Adult programme. These are federally funded programmes that ensure under or uninsured children and adults have access to vaccines at little or no cost. We also have an ongoing agreement with the WHO to donate and supply stock at reduced prices in the event of an influenza pandemic.

Respiratory syncytial virus (RSV) is a common seasonal virus and the most prevalent cause of lower respiratory tract infection among infants and young children. Since its initial approval in 1998, *Synagis* has become the global standard of care for RSV prevention and helps protect at-risk babies against RSV. The lifting of public health measures to combat COVID-19, including national and local lockdowns, has led to out-of-season surges of RSV, creating increased demand for preventive options like *Synagis*. These COVID-19 impacts varied across markets.

The commercial rights to the sale and distribution of *Synagis* in more than 80 countries outside the US reverted back to AstraZeneca on 1 July 2021, following the end of our agreement with AbbVie. Our agreement with Sobi for the rights to *Synagis* in the US was unaffected by this reversion.

Neuroscience

We are progressing MEDI7352, a bispecific molecule that targets nerve growth factor and tumour necrosis factor alpha, in both painful diabetic neuropathy in Phase II and osteoarthritis pain in Phase IIb. Also in Phase I are MEDI0618, an anti-PAR2 (protease activated receptor 2) mAb being developed for osteoarthritis pain and migraine and AZD4041, a selective orexin 1 receptor antagonist being developed for opioid use disorder. This has been awarded a grant from the US National Institute on Drug Abuse to progress clinical development.

We continue our collaboration with Takeda on MEDI1341 for Parkinson's disease and multiple system atrophy, which is in Phase I.

We have a collaboration with Eli Lilly on MEDI1814, an antibody selective for amyloid beta 1-42 that has completed Phase I as a potential disease-modifying treatment for Alzheimer's disease.

COVID-19

Vaxzevria

Vaxzevria (ChAdOx1-S [Recombinant], formerly AZD1222) was co-invented by the University of Oxford. Through a landmark agreement in 2020 *Vaxzevria* was developed and distributed by AstraZeneca. Under a sub-license agreement with AstraZeneca, the vaccine is manufactured and supplied by the Serum Institute of India under the name *Covishield*.

Vaxzevria received its first approval for emergency use in December 2020 and it has now been granted a conditional marketing or emergency use authorisation in 93 countries worldwide, including an Emergency Use Listing from the WHO in February 2021, which accelerated access in more than 140 countries through the COVAX Facility.

In just over a year, AstraZeneca built more than 12 regional supply chains around the world, relying on our own manufacturing capacity, and sharing our know-how with more than 20 partners. In 2021, AstraZeneca and our global partners released for supply 2.5 billion vaccine doses to over 180 countries. Approximately two thirds of these went to LMICs, and more than 247 million doses have been delivered to 130 countries through the COVAX Facility in 2021.

The European Commission initiated legal proceedings against AstraZeneca in April 2021 in relation to the Advance Purchase Agreement for the COVID-19 vaccine. The parties reached a settlement in September 2021 which brought these proceedings to an end.

Vaxzevria is effective against all severities of COVID-19 from symptomatic to severe disease and hospitalisation, and is generally well tolerated, according to clinical studies and real-world evidence from tens of millions of people globally. Over the course of 2021, the vaccine is estimated to have helped prevent 50 million COVID-19 cases, five million hospitalisations, and helped save more than one million lives.

The SARS-CoV-2 virus which causes COVID-19 has changed over time with the emergence of new variants including Alpha, Beta, Gamma, Delta and Omicron. Data from clinical studies and real-world evidence demonstrate the effectiveness of two doses of *Vaxzevria* against Alpha, Beta, Gamma and Delta.

Vaxzevria has also shown an increased immune response to the Alpha, Beta, Gamma, Delta and Omicron variants when used as a third dose booster, after either two doses of *Vaxzevria*, of an mRNA vaccine or of CoronaVac (Sinovac Biotech Ltd.). *Vaxzevria* is already approved as a homologous third dose booster in several countries.

Regulators around the world have confirmed that *Vaxzevria* has a favourable benefit-risk profile. Incidents of thrombosis with thrombocytopenia (TTS) are very rare and lower than in those diagnosed with COVID-19, and following a second dose of *Vaxzevria* are comparable to the background rate in an unvaccinated population. Early diagnosis allows appropriate treatment of these very rare events.

In 2021, the majority of vaccine product sales and doses delivered related to pandemic contracts. AstraZeneca will continue to supply the vaccine around the world in 2022. We have moved to an affordable pricing approach that enables us to maintain broad global access. This includes a tiered pricing approach aligned to Gross National Income per capita, a widely recognised model used by developers of medicines and vaccines. We remain committed to supplying the vaccine at no profit in low-income countries, in line with our agreement with Oxford University.

In the first half of 2021, AstraZeneca initiated development of the AZD2816 COVID-19 vaccine to address the Beta variant. In February 2022, we reported the positive interim results of the Phase II/III trial (D7220C00001) and additional analysis, which demonstrated that AZD2816 generated a similar immune response to *Vaxzevria* against variants, including Omicron. Given these data, the low circulation of the Beta variant and the substantial body of evidence supporting *Vaxzevria* against current variants, we discontinued the AZD2816 development programme and will continue to focus on the supply of *Vaxzevria* around the world.

Evusheld

AstraZeneca's response to the pandemic also included the development of *Evusheld* (tixagevimab co-packaged with cilgavimab, formerly AZD7442), a long-acting antibody (LAAB) combination against the virus.

Evusheld is the first LAAB combination to demonstrate benefit in both prevention and treatment of COVID-19, as well as the first antibody therapy to have shown a high level of protection against symptomatic COVID-19 in a pre-exposure prevention setting, as demonstrated in the PROVENT prevention Phase III trial in August 2021.

Evusheld retains in vitro neutralising activity against the Omicron variant at a level that may continue to provide protection to patients, according to consistent data across multiple independent preclinical studies, making it one of only two antibody therapies authorised for use that showed neutralising activity against Omicron and against all other tested variants to date. In vitro activity does not always correlate with clinical efficacy. AstraZeneca is continuing to collect further data to better understand the implications of these data in clinical practice.

Evusheld received Emergency Use Authorization (EUA) from the FDA in December 2021 for the pre-exposure prophylaxis (prevention) of COVID-19 in people with moderate to severe immune compromise due to a medical condition or immunosuppressive medications and who may not mount an adequate immune response to COVID-19 vaccination, as well as those individuals for whom COVID-19 vaccination is not recommended. In 2021, AstraZeneca agreed to supply the US Government with 700,000 *Evusheld* doses, and in January 2022 the US Government announced that it had agreed to purchase 500,000 additional doses. *Evusheld* is also authorised for emergency use for prevention of COVID-19 in several other countries, including France.

Business Review

Our business is organised to deliver our strategic priorities sustainably, supporting scientific innovation and commercial success.

Our business

Our business is organised to deliver our growth through innovation strategy and our three strategic priorities. Our R&D and Commercial functions have been organised to accelerate decision making and the launches of new medicines across our main disease areas.

Full details are provided in the Financial Review from page 52.

Accelerate Innovative Science

To drive our science, we have disease area-focused R&D organisations that are responsible for discovery through to late-stage development – one each for Oncology, BioPharmaceuticals (CVRM and R&I) and Rare Disease. A separate Vaccines and Immune Therapies Unit has been created for 2022.

These enable us to follow the science by accelerating promising early-stage assets and life-cycle management programmes in our pipeline and also provide new opportunities for combinations.

Deliver Growth and Therapy Area Leadership

Our growth is delivered by our Commercial teams, which comprised around 46,380 employees at the end of 2021. We have an active presence in some 90 countries and sold our products in more than 130 countries in 2021. In most markets, we sell our medicines through wholly owned local marketing companies. We also sell through distributors and local representative offices. We market our products largely to primary care and specialty care physicians.

Two commercial units, one for Oncology and one for BioPharmaceuticals, align product strategy and commercial delivery across our US and Europe-Canada regions.

Our International region has commercial responsibility for Emerging Markets, including China, as well as Australia and New Zealand. Japan reports separately.

Our Operations function plays a key role in developing, manufacturing, testing and delivering our medicines to our customers.

Our Rare Disease group, in addition to R&D, also manages the commercial and operations functions for our rare diseases portfolio in our Established Markets.

Be a Great Place to Work

For the benefit of our employees and our business, we want AstraZeneca to be a great place to work. We are building and developing capabilities and a strong leadership pipeline. We value diversity and aim to attract, retain and develop talented employees who thrive in a vibrant, high-performing culture with a passion for people development.

For the benefit of society, we want to be valued and trusted by our stakeholders as a sustainable source of great medicines over the long term. We are committed to operating in a way that recognises the interconnection between business growth, the needs of society and the limitations of our planet.

Our sustainability approach

Our ambition is to harness the power of science and innovation in ways that have a positive impact on society, patients, healthcare systems and the environment, through actions for the long term.

Sustainability strategy

In 2021, we refreshed our sustainability strategy by conducting a materiality assessment. The assessment shows which topics are most important to AstraZeneca and our stakeholders, helping us to focus for maximum positive impact. The assessment resulted in nine focus areas where we can make the most meaningful impact, grouped under three interconnected priorities:

- **Access to healthcare:** we are working towards a future where all people have access to sustainable healthcare solutions for life-changing treatment. We are increasing equitable access to medicines, promoting disease prevention and strengthening healthcare system resilience worldwide.
- **Environmental protection:** we aim to minimise our environmental impact across all our activities and products. We are increasingly circular – designing out waste and pollution, keeping products and materials in use to maximise resource efficiency. We are adopting nature-based solutions to protect, sustainably manage and restore natural and modified ecosystems that address societal challenges, such as the impact of the climate crisis, and support biodiversity.

- **Ethics and transparency:** we seek to create positive societal impact and embed ethical behaviour in all our business activities, markets and value chain. We do this by promoting ethical, transparent and inclusive policies, both within AstraZeneca as well as across all our partners and suppliers.

Our sustainability approach is centred around three principles:

- **Systems thinking:** we recognise that our globalised world binds us together in a dynamic, complex network of relationships. We look for opportunities that offer synergies and address systemic issues.
- **Long-term perspective:** we acknowledge there are no quick fixes so we must be proactive and think long term. We anticipate, avoid or address unintended impacts, monitoring changes over time and building resilience.
- **Creating the conditions for lasting sustainability:** we apply science to go beyond preventing and addressing any impacts from our activities to improve the environment.

We know that acting sustainably is at the core of our licence to operate as a company. Sustainability is an engine for innovation that helps to future-proof our business against risk and opens up new opportunities in support of our strategic objectives. We continue to embed sustainability within AstraZeneca in an integrated manner, which recognises that every scientific or business decision we make must be aligned with our sustainability objectives and commitments.

Governance

Our Board and our Senior Executive Team (SET) review our internal sustainability scorecard quarterly. In 2021, the Board established a Sustainability Committee to monitor the execution of our sustainability strategy, oversee communication of our sustainability activities with stakeholders, and provide input to the Board and other Board Committees on sustainability matters.

Benchmarking and assurance

We contribute to several key global environmental, social and governance (ESG) performance evaluations, recognising the value of independent third-party assessment and insights. Our performance is also assessed independently based on the information and data we make publicly available.

Bureau Veritas has provided independent external assurance to a limited level for the sustainability information contained within this Annual Report and Form 20-F. Assurance is in accordance with the International Standard on Assurance Engagements (ISAE) 3000 (Revised) and ISAE 3410 Assurance Engagements on Greenhouse Gas Statements.

For more information, see Sustainability supplementary information on page 216 and the letter of assurance available on www.astrazeneca.com/sustainability.

Accelerate Innovative Science

We are using our distinctive scientific capabilities to deliver a pipeline of life-changing medicines.

Our performance in 2021

- Invested $9.7 billion in our R&D.
- With the completion of the Alexion acquisition, we gained an innovative complement-biology platform and robust rare disease pipeline.
- First major approvals were granted for five NMEs: *Vaxzevria*, *Orpathys*, *Saphnelo*, *Evusheld* and *Tezspire*.
- 177 projects in our pipeline, of which 161 are in the clinical phase of development.
- 15 NME projects in pivotal trials or under regulatory review (2020: 10).
- R&D productivity increased to 23% in 2021 versus an industry average of 14%.
- We published 169 manuscripts in 'high-impact' journals.
- At the end of 2021, 30% of our early pipeline comprised new drug modalities.
- Shared anonymised individual patient-level data from 165 clinical studies with 64 unique research teams.
- We unveiled our global R&D Discovery Centre in Cambridge, UK.

Performance indicators

By measuring both Phase II and Phase III pipeline progressions, we are focused on both near-term and longer-term delivery. Phase II NME starts ensure the ongoing robustness and future stability of the pipeline (and reflect the outcome of nearer-term strategic investment decisions). Phase III investments measure assets that will deliver nearer-term value (and reflect the outcome of longer-term strategic investment decisions). Submissions and approvals metrics demonstrate the advancement of this innovation through filing and approval in our four major markets (US, EU, China and Japan).

NME Phase II starts/progressions

9

2021	9
2020	8
2019	6

NME and major LCM submissions

27

2021	27
2020	24
2019	35

NME and major LCM Phase III investment decisions

23

2021	23
2020	28
2019	14

NME and major LCM approvals

22

2021	22
2020	29
2019	28

Research & Development

Our ambition is to transform the lives of patients with improved outcomes and a better quality of life, through more effective treatment and prevention, ultimately working towards a cure for some of the world's most complex diseases.

Throughout 2021, we continued to progress our science, guided by our 5R framework (right target, right patient, right tissue, right safety, right commercial potential) and focusing on the three key areas of science, as below. This was bolstered by the addition of Alexion's complement expertise and innovative technology platforms.

Our R&D productivity, defined as progressing from candidate drug nomination to Phase III completion, increased to 23% in 2021 versus an industry average of 14%. Our scientists published 871 manuscripts with 169 in 'high-impact' peer-reviewed journals, each with an impact factor exceeding 15 (Thomson Reuters 5yr IF score). The increase in high impact from 123 in 2020 continues to reflect the quality and drive to share our science.

Enhancing our understanding of disease

We are advancing our understanding of disease biology to uncover novel drivers and insights into the diseases we aim to treat, hope to prevent and, in the future, even cure. Selecting the right target remains one of the most important decisions in the drug discovery process and our continued investments into multiple approaches in this area are delivering to our pipeline. 2021 developments included:

- Making progress towards our ambition to analyse two million genomes by 2026. Our Centre for Genomics Research has already analysed more than 800,000 exomes/genomes or five petabytes of genomic data, highlighting novel and important contributions of rare genetic variants to some of the most common diseases. This was reflected in a *Nature* publication reporting the largest exome-wide genotype-phenotype data set from nearly 300,000 UK Biobank participants.
- Adding the first AI-derived targets to our portfolio, as part of our collaboration with BenevolentAI. Combining artificial and human intelligence is helping us find previously unexplored patterns and draw better, faster conclusions.
- Driving deeper disease understanding and progressing two new targets in Oncology, the outcome of more than 290 CRISPR screens conducted by the AstraZeneca-Cancer Research UK Functional Genomics Centre.
- Becoming the co-lead of an international consortium (PERSIST-SEQ) that will employ single-cell sequencing to explore mechanisms of resistance to cancer treatment. Experts from 15 universities and biotechnology and pharmaceutical companies aim to characterise five million individual cancer cells over five years. Thereafter, data will be publicly available to aid cancer research.
- Collaborating with Tempus on the use of artificial intelligence to analyse real world data. The aim is to deepen our understanding of complex tumour biology to more accurately predict how new treatments may help specific patient populations, and to accelerate clinical trials.
- Furthering our investment in cell therapy research by progressing our first armoured CAR-T programme into development, initially in hepatocellular carcinoma and progressing our stem cell therapy for heart failure into pre-clinical development.
- Collaborating with Genomenon to use its AI-driven genomic technology to produce a complete 'Genomic Landscape' for certain rare diseases and enhance its *Mastermind* Genomic Search Engine used by genetic testing laboratories and medical centres worldwide.

Designing the next generation of therapeutics

We are continuing to design new ways to target the drivers of disease to help us create the next generation of therapeutics. At the end of 2021, 30% of our early pipeline consisted of new drug modalities, including oligonucleotide, antibody drug conjugate (ADC), bispecific mini-bodies, and cell therapy approaches. 70% of our small molecule chemistry projects now use AI to help determine the best way to make a molecule in the shortest time. Developments during the year included:

- Adding a new modality – self-amplifying RNA (saRNA) – through a collaboration with VaxEquity. The strategic, long-term research collaboration aims to optimise and validate VaxEquity's saRNA platform, developed at Imperial College London, and apply it to advance novel therapeutic programmes.
- Advancing digital therapeutics. For example, we are currently testing a pulse oximeter in four studies to detect early signs and symptoms of interstitial lung disease (ILD) in patients being treated for metastatic breast cancer. The aim is to enable early intervention where required and reduce the risk of severe-grade ILD.
- Building on our complement technology platform. We are exploring targets in the complement system beyond C5 and new modalities to best target complement dysregulation and offer the optimal therapy for patients. We are also advancing an innovative pipeline of complement inhibitors, including oral small molecules (Factor D inhibitors) and bispecific mini-bodies (C5 and properdin inhibitors) designed for self-administered subcutaneous injection. We are collaborating across therapeutic areas to identify opportunities to expand complement innovation to indications beyond rare diseases.
- Diversifying and expanding our leadership in rare diseases beyond complement. This includes progressing our next-generation alkaline phosphatase enzyme replacement therapy into clinical trials, with the intention of helping more people living with hypophosphatasia.

Pioneering new approaches to drive success in the clinic

We are adopting a range of cutting-edge technologies to improve our ability to predict success of our candidate drugs in the clinic. 2021 developments included:

- Developing 'miniature organs' in collaboration with NovoHeart to recreate the mechanical and electrical properties in a beating mini-heart. We are currently refining and validating this advanced model with the aim of using it to evaluate pipeline compounds next year.
- Changing how clinical trials are designed, run and managed. One of our cardiovascular trials, for example, quickly identifies heart attack patients via patient registries and offers them the opportunity to join the trial via their healthcare professional. Participation is made more accessible by aligning study visits and clinical routine care with data collected through both routine care and remote data collection.
- Using blood-based genetic profiling as a minimally invasive way of identifying the right drug for the right patient at the right time. One of our oncology trials, SERENA-6, is exploring our next-generation oral selective estrogen receptor degrader (SERD) to address endocrine resistance. In this trial, we are measuring genetic alterations in circulating tumour DNA (ctDNA) isolated from blood samples to inform which patients may benefit from switching from standard of care therapy to next-generation SERD therapy. Other studies in non-small cell lung cancer (MERMAID-1 and MERMAID-2) are also using ctDNA to identify patients most at risk of relapse, and intervene with the most appropriate treatment regimen.

- Collaborating with the UK NHS and GRAIL, who this year initiated a world-leading study to screen for cancer in a broad population. We have committed to a Phase III trial using circulating tumour DNA to identify the optimal treatment for early lung cancer patients.
- Improving patient health outcomes by combining our innovative new treatments with evidence-based digital health solutions, including digital biomarkers, digital diagnostics and digital therapeutics. For example, we collaborated with manufacturers to develop a method for performing spirometry (measuring how much air someone can breathe out in one forced breath) remotely, with supervision via video to ensure high-quality data. We are using this method to generate regulatory quality spirometry in clinical trials, reducing the patient burden and allowing us to test more frequently to increase disease and treatment understanding.
- Working with JanaCare to develop an at-home creatinine monitoring test. Home monitoring of serum creatinine will allow for routine and frequent estimations of glomerular filtration rate, a measure of kidney function. With a home device, we can make future trials more patient-centric.
- Launching the Patient Engagement Center of Excellence, a cross-functional process and set of standards for Patient Advocacy and other teams to follow when interacting with rare disease patients, caregivers or patient advocacy groups in the US. The resulting inputs will help ensure we are engaging in a patient-centric way. This will enable us to continue developing innovative medicines that address unmet medical needs, ensure we are designing protocols that include patient-relevant clinical endpoints, and deliver patient-centric clinical trials.

Development pipeline overview (as at 10 February 2022)

2021 was another exceptional year for our science, with our pipeline producing overwhelmingly positive news for patients. This included 49 regulatory events, either submissions or approvals for our medicines in major markets, including five NME first approvals. That performance is backed by a healthy pipeline of high potential medicines, with a total of 32 pipeline progression events, either NME Phase II starts or Phase III investment decisions, indicating our ability to deliver longer-term sustainable growth.

During 2021, we delivered clinical trial data and submissions that resulted in 22 approvals for new medicines in the US, EU, China and Japan. Our pipeline now includes the Alexion Rare Disease portfolio and comprises 177 projects, of which 161 are in the clinical phase of development. We made significant progress in advancing our late-stage programmes through regulatory approval with 27 NME or major life-cycle management (LCM) regulatory submissions in the US, EU, China and Japan during 2021.

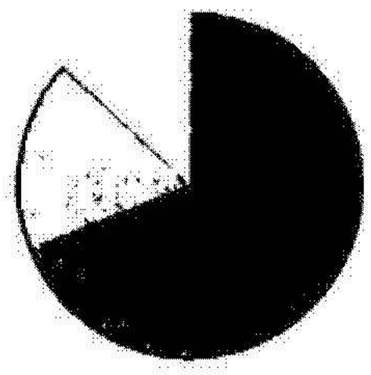
We have 15 NME projects in pivotal trials or under regulatory review, compared with 10 at the end of 2020. Also in 2021, 20 NMEs progressed to their next phase of development and 18 projects were discontinued: nine for poorer than anticipated safety and efficacy results and nine as a result of a strategic shift in the environment or portfolio prioritisation.

Accelerating our pipeline

We are prioritising our investment in specific programmes, focusing on scientific innovation. As a result, we had numerous positive trial readouts in 2021, including the presentation of scientific rationale that resulted in eight Regulatory Designations for Breakthrough Therapy, Priority Review or Fast Track for new medicines which offer the potential to address unmet medical need in certain diseases. We also secured Orphan Drug Designation for the development of three medicines to treat very rare diseases.

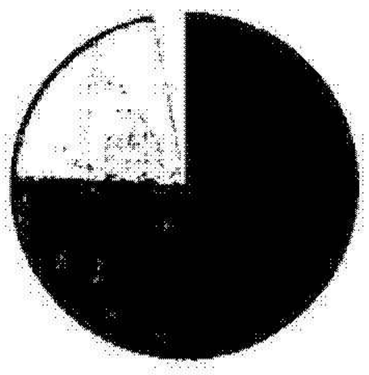
For more information, see Disease Area Review from page 16.

Phase I 32



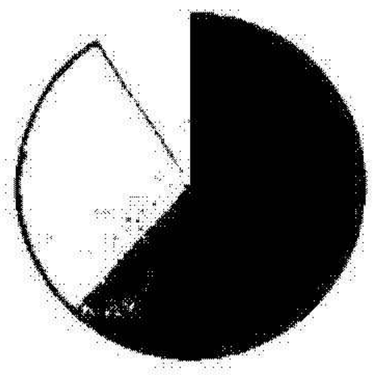
- Oncology 47%
- Cardiovascular, Renal & Metabolism 22%
- Respiratory & Immunology 9%
- Rare Disease 9%
- Other Medicines & COVID-19 13%

Phase II 34



- Oncology 50%
- Cardiovascular, Renal & Metabolism 26%
- Respiratory & Immunology 15%
- Rare Disease 6%
- Other Medicines & COVID-19 3%

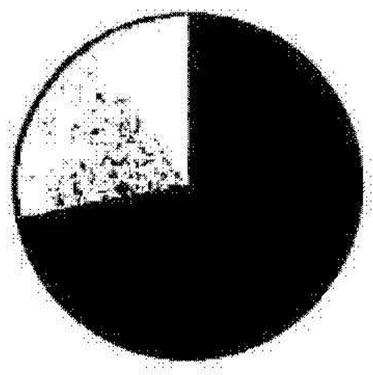
Late-stage development[1] 32



- Oncology 53%
- Cardiovascular, Renal & Metabolism 9%
- Respiratory & Immunology 16%
- Rare Disease 13%
- Other Medicines & COVID-19 9%

[1] NMEs or novel combinations and significant additional indications.

Life-cycle management projects[2] 79



- Oncology 59%
- Cardiovascular, Renal & Metabolism 13%
- Respiratory & Immunology 18%
- Rare Disease 10%
- Other Medicines & COVID-19 0%

[2] Only includes material projects where first indication is already launched.

Bioethics

'Bioethics' refers to the range of ethical issues that arise from the study and practice of biological and medical science. It falls under our ethical business culture sustainability focus. Our Global Standard on Bioethics sets out our principles, which apply to all our scientific activities, whether conducted by us or by third parties acting on our behalf.

Clinical trial transparency

We believe that transparency enhances the understanding of how our medicines work and benefit patients. We publish information about our clinical research, as well as the registration and results of our clinical trials – regardless of whether or not they are favourable – for all products and all phases. This includes marketed medicines, drugs in development and drugs where development has been discontinued. As at 31 December 2021, AstraZeneca has:

- Shared anonymised individual patient-level data from 165 studies with 64 unique research teams and responded to 263 requests from external researchers using our portal, www.vivli.org to request our clinical data and reports to support additional research.
- Published 13 complete Anonymized Clinical Document Packages between Health Canada's PRCI process and EMA's Policy 0070 process.

Since 2015, AstraZeneca has:

- Published 245 Trial Result Summaries in easy-to-understand language on the industry-wide portal www.trialsummaries.com. These have been translated into relevant local languages for all sites where a study is conducted, spanning 59 languages overall.

Research use of human biological samples

The use of human biological samples, such as solid tissue, biofluids and their derivatives, plays a vital role in developing a deeper understanding of human diseases. We are committed to minimising the use of human fetal tissue (hFT) by exploring technological alternatives. Fetal tissue is used to provide invaluable data to advance novel treatments for serious diseases of unmet medical need but only when no other scientifically reasonable alternative is available. There were no new approvals in 2021. As at 31 December 2021, four projects using hFT had progressed and two projects are ongoing.

Animal research

Technology has not yet advanced to the stage where all animal use can be eliminated from research and development. In addition, some animal studies are required by international regulators before medicines progress to human trials. Animal studies therefore remain a small, but necessary, part of developing new medicines. Animal use in research and development varies depending on many interrelated factors, including our amount of pre-clinical research, the nature and complexity of the diseases under investigation and regulatory requirements. We believe that without our active and ongoing commitment to the 3Rs (Replacement, Reduction and Refinement of animals in research), our animal use would be much greater. In 2021, animals were used for in-house studies 93,511 times (2020: 74,684). Animals were also used on our behalf for contract research organisation studies 58,826 times (2020: 51,625). In total, over 95% were rodents or fish.

Our R&D resources

Our R&D organisation comprises more than 14,000 employees working across our global sites. We currently have three global R&D centres: Cambridge, UK; Gaithersburg, MD, US; and Gothenburg, Sweden, as well as several additional R&D sites. The acquisition of Alexion added a Rare Disease R&D Centre of Excellence in New Haven, CT, US.

Cambridge R&D centre

In 2021, we officially unveiled our new R&D centre, the Discovery Centre (DISC), at the heart of the Cambridge Biomedical Campus, one of Europe's leading life sciences clusters, promoting innovation and collaboration. Our new building is designed to encourage interaction between our scientists and the surrounding scientific and medical community. More than 4,000 AstraZeneca employees are now located in the Cambridge area, where our scientists continue to work side-by-side with colleagues from universities, research institutions and biotech companies. The new centre exemplifies how we are making our science and our business sustainable in everything we do – from how we discover and develop new medicines to how we identify and address their environmental impact.

Project costs incurred to the end of 2021 amounted to c. $1.3 billion (£1 billion) and a projected spend of c. $0.1 billion (£0.1 billion) will be incurred during 2022 to complete the installation of primary laboratory equipment, furniture and fixtures, and final commissioning of the building.

Investing in R&D

In 2021, R&D expenditure was $9,736 million (2020: $5,991 million; 2019: $6,059 million), including Core R&D costs of $7,987 million (2020: $5,872 million; 2019: $5,320 million). In addition, we spent $27,042 million on acquiring product rights (such as in-licensing and, in 2021, $26,455 million of product rights as part of the Alexion acquisition) (2020: $1,454 million; 2019: $1,835 million). We also invested $223 million on the implementation of our R&D restructuring strategy (2020: $35 million; 2019: $10 million). The allocations of spend by early- and late-stage development are presented in the R&D spend analysis table below.

Research & Development

	2021	2020	2019
Discovery and early-stage development	**38%**	36%	36%
Late-stage development	**62%**	64%	64%

Deliver Growth and Therapy Area Leadership

We plan to meet our growth and profitability goals through successful innovation, commercial excellence and the creation of sustainable profitability.

Our performance in 2021

- Total Revenue, comprising Product Sales and Collaboration Revenue, increased by 41% (38% at CER) to $37,417 million.
- Growth was well balanced across our disease areas.
- In the US, Total Revenue increased by 38% to $12,228 million and in Europe by 45% (40% at CER) to $8,050 million.
- Total Revenue in Emerging Markets increased by 41% (36% at CER) to $12,281 million, with China growth of 12% (4% at CER) to $6,011 million.
- We continue to collaborate with payers to conclude outcomes- and value-based reimbursement models that improve patient outcomes and had concluded more than 170 such agreements by the end of 2021.
- Committed to high ethical standards: 105 employees and third parties removed from their roles for breaches of sales and marketing regulations or codes.
- Delivered 110 successful market launches and achieved 100% of planned new technology implementation milestones.
- More than 1,000 collaborations around the world.

Performance indicators

Global Product Sales by geography

	2021			2020			2019		
	Product Sales $m	Actual growth %	CER growth %	Product Sales $m	Actual growth %	CER growth %	Product Sales $m	Actual growth %	CER growth %
Emerging Markets	12,161	40	36	8,679	6	10	8,165	18	24
US	12,000	39	39	8,638	12	12	7,747	13	13
Europe	7,604	50	44	5,059	16	15	4,350	(2)	2
Established Rest of World	4,776	36	36	3,514	6	6	3,303	17	18
Total	36,541	41	38	25,890	10	11	23,565	12	15

Sales and marketing

As outlined in Our Strategy and Key Performance Indicators from page 12, we are seeking to transform healthcare delivery with a focus on patients, as well as innovative commercial approaches and pricing strategies.

Our approach to pricing, summarised below, is one that focuses on unlocking the value our medicines bring to patients. Moreover, our focus on patient centricity has seen us move away from a traditional product-centred approach to one based on improving the whole patient experience, from driving earlier diagnosis to improvements in clinical trials. Through the use of data analytics, 'omnichannel' and 'go-to-market' models, we are also working to improve the way in which we engage with HCPs and other customers. This includes accelerating the development of healthcare collaborations to drive changes in practice that improve patient outcomes.

During 2021, growth was well balanced across our disease areas, and we saw double-digit growth in all major regions, including Emerging Markets despite some headwinds in China. Following completion of the Alexion acquisition on 21 July 2021, Rare Disease medicines generated $3,071 million, 8% of Total Revenue, growing 8% (9% at CER) on a pro forma, pro rata basis[1]. Outside the US, sales of *Soliris* and *Ultomiris* were driven by new country launches.

Pricing and value of our medicines

With increasing demand for healthcare, there is increased pressure on health system budgets. This includes downward pressure on pricing and reimbursement in many markets, including the US and China. This pressure is heightened by a shift from primary to specialty care medicines, which comprise a growing share of AstraZeneca's portfolio. Pricing for these products reflects the higher value they bring to patients and payers, as well as the smaller patient numbers as a result of targeted treatment options.

The COVID-19 pandemic has also had an impact. Healthcare resources have been reallocated to meet the greatest need with, for example, payers prioritising treatments that help keep patients out of hospital. The pandemic also demonstrated that healthcare systems can move quickly to grant rapid access to innovative new medicines, such as vaccines, which may enable faster access to promising medicines.

For more information on our broad and equitable supply of our *Vaxzevria* vaccine, see Other Medicines and COVID-19 from page 27.

Against this background, and in our discussions with national, regional and local stakeholders, we continue to base our pricing policy based on four principles:

- Determining the price of our medicines while considering their full value for patients, payers and society, and reflecting factors such as clinical benefit, cost-effectiveness, improvement to life expectancy and quality of life.
- Aiming to ensure the sustainability of both healthcare systems and our research-led business model.
- Working closely with payers and providers to understand their priorities and ensure appropriate patient access to our medicines.
- Pursuing a flexible pricing approach that reflects the wide variation in global health systems. For example, we apply Tiered Pricing Principles, defining price levels based on a country's ability to pay.

For more information, see our Affordability Statement on our website, www.astrazeneca.com/sustainability.

As part of our approach, we collaborate with payers to conclude innovative outcomes- and value-based reimbursement models that improve patient outcomes. We had concluded more than 170 such agreements by the end of 2021. We also offer a number of patient assistance programmes that help increase patients' access to medicines and/or healthcare, and reduce their out-of-pocket costs.

For more information, see Access to healthcare on page 44.

Our commercial regions

US

We have a 3.1% market share of US pharmaceuticals by sales value and we are the fourteenth largest prescription-based pharmaceutical company in the US. Product Sales increased by 39% in 2021 to $12,000 million, driven primarily by the performance of our new medicines across Oncology and BioPharmaceuticals, including *Tagrisso*, *Calquence*, *Farxiga* and *Fasenra*. Product launches and new indications also contributed to this growth. *Breztri* was introduced for patients with COPD; *Farxiga* in a new indication for chronic kidney disease, and *Saphnelo* for systemic lupus erythematosus.

The US healthcare system is complex. Multiple payers and intermediaries exert pressure on patient access to branded medicines through regulatory rebates in government programmes and voluntary rebates paid to managed care organisations and pharmacy benefit managers for commercially insured patients. Significant pricing pressure is driven by payer consolidation, restrictive reimbursement policies and cost control tools, such as exclusionary formularies and price protection clauses. Many formularies employ 'generic first' strategies and/or require physicians to obtain prior approval for the use of a branded medicine where a generic alternative exists.

For prescriptions dispensed in the US in 2021, generics constituted 86.3% of the market by volume (2020: 85.3%) and 17.2% ($101.0 billion) of the market ($587.7 billion) by value (2020: 18.7%, $102.2 billion of $546.2 billion).

Ongoing scrutiny of the US pharmaceutical industry, focused largely on affordability, has been the basis of multiple policy proposals. In addition, lawmakers at both the federal and state levels have sought increased drug transparency and have proposed and implemented such policies. Despite this price scrutiny, we have a diversified product portfolio in the US. We provide a broad spectrum of treatments in many different disease areas, allowing for significant access to patients in need of our innovative medicines.

In Rare Disease, *Soliris* Total Revenue amounted to $1,068 million, representing a pro forma, pro rata* increase of 4%. Sales benefitted from growing use in neurology indications, gMG and NMOSD, offset by the successful conversion to *Ultomiris* in haematological indications, PNH and aHUS. At $381 million, *Ultomiris* sales grew by 20% on a pro forma, pro rata basis.

Europe

The total European pharmaceutical market was worth $228 billion in 2021. We have a 2.6% market share of pharmaceutical sales by value and we are the eleventh largest prescription-based pharmaceutical company in Europe (see Market definitions on page 224). Product Sales increased by 50% at actual rate of exchange (44% at CER) to $7,604 million (2020: $5,059 million). We continued to launch new medicines and saw sustained performance of our existing medicines.

Oncology sales grew by 28% (22% at CER), driven by increased use of *Tagrisso* for the treatment of 1st-line EGFR-mutated (EGFRm) NSCLC patients. *Imfinzi* sales reflect a growing number of reimbursements in SCLC. *Lynparza* saw continued strong performance in the 1st-line ovarian cancer setting and launches in breast and prostate cancer.

BioPharmaceutical sales grew by 14% (9% at CER). *Forxiga* sales growth of 60% (52% at CER) was driven by type-2 diabetes and new indications in heart failure and chronic kidney disease (CKD). *Fasenra* sales increased 41% (34% at CER) while *Trixeo* was launched in major European markets with more to follow in 2022.

Established Rest of World (ROW)

Japan

The pharmaceutical market in Japan was worth $85 billion in 2021, remaining an attractive market for investment in innovation. We have a 3.7% market share of pharmaceutical sales by value and we are the fifth largest prescription-based pharmaceutical company. The government introduced a mid-year price control measurement in April 2021 in order to address continued pressure on healthcare spend.

Total Product Sales grew by 31% (35% at CER) to $3,416 million, despite continued COVID-19 challenges, price cuts and ongoing generic erosion for *Symbicort*. This included sales from Rare Disease medicines after the acquisition of Alexion. The strong performance was driven by new medicines including *Tagrisso*, *Imfinzi*, *Lynparza*, *Fasenra*, *Breztri*, *Lokelma* and *Forxiga*. Additionally, *Calquence* was introduced for patients with chronic lymphocytic leukaemia, *Forxiga* for CKD and *Saphnelo* for systemic lupus erythematosus. We also recovered the distribution rights for *Nexium* and *Synagis*.

Canada

Product Sales in Canada increased by 28% at actual rate of exchange (19% at CER) in 2021. This was primarily driven by strong, sustained growth of our new medicines, particularly *Tagrisso*, *Lynparza*, *Forxiga* and *Fasenra*.

Declines in *Onglyza*, *Crestor* and *Brilinta* sales, linked to loss of exclusivity, combined with pricing pressures, partially offset the growth in innovative medicines.

Australia and New Zealand

Our sales in Australia and New Zealand increased by 89% at actual rate of exchange (73% at CER) in 2021. This was primarily due to growth in key brands such as *Tagrisso*, *Lynparza*, *Fasenra*, *Soliris* and *Forxiga/Xigduo*. *Calquence* achieved a high level of growth in its first full year of reimbursement. However, the overall growth of the business was constrained by the impact of the *Crestor* and *Atacand* divestments in 2020, as well as the flat growth of *Symbicort* despite it maintaining leadership in the LABA/ICS class.

Emerging Markets

With revenues of $12,281 million (2020: $8,711 million), AstraZeneca was the second largest multinational pharmaceutical company, as measured by prescription sales, and the third fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2021. Despite the continued impact of COVID-19 across all geographies, we saw growth across all major areas. This included Latin America at 153% (156% at CER), Russia & Eurasia at 40% (42% at CER), Middle East & Africa at 16% (20% at CER) and Asia Pacific at 96% (93% at CER).

China

In China, AstraZeneca is the largest pharmaceutical company by sales value in the hospital sector. Sales in 2021 increased by 12% at actual rate of exchange (4% at CER) to $5,995 million (2020: $5,345 million). *Forxiga*, roxadustat and *Lokelma* were listed or renewed in the NRDL.

The implementation of Value Based Procurement (VBP), which has opened up more of the hospital volumes to qualifying generics, has impacted several AstraZeneca brands including *Crestor*, *Iressa*, *Brilinta*, *Nexium Oral*, *Losec Oral* and *Arimidex*. In the most recent cycle of VBP implementation, *Pulmicort*, *Nexium IV*, *Onglyza*, *Betaloc Oral* and *Casodex* were included. A number of AstraZeneca brands are expected to be included in the next VBP cycle with an estimated implementation during the first half of 2022.

* Growth rates on Rare Disease medicines have been calculated on a pro forma, pro rata basis by comparing post-acquisition revenues from 2 July 2021 to 31 December 2021 with the corresponding period in the prior year, pre-acquisition as previously published by Alexion. Pro forma, pro rata Total Revenue growth rates have been presented for 2021 Rare Disease area and constituent medicines, and do not impact Group totals.

COVID-19 has continued to impact growth rates in all channels across China and for AstraZeneca's Respiratory & Immunology therapy area. The nebulised brands such as *Pulmicort*, *Fluimucil* and *Bricanyl* were most heavily impacted as demand, while recovering, remained well below pre-pandemic levels.

A healthcare investment fund jointly set up with CICC has progressed with nearly $200 million paid in and over $50 million invested to date. In the last quarter of 2021, Abbisko became the first portfolio company to complete an IPO on the Hong Kong Stock Exchange. An internet hospital venture with Hillhouse Capital, which also includes in-house pharmacy distribution, commenced in early 2021 and has made positive initial progress.

Following the acquisition of Alexion in July 2021, we established a Rare Disease unit in China.

Healthcare in low- and middle-income countries (LMICs) BV
AstraZeneca is committed to equitable access to healthcare for patients globally. Our approach includes adapting our programmes to integrate into local systems and delivering affordable medicines to patients. Our patient access programmes in LMICs are tailored to meet the needs of the healthcare systems, patients and communities they serve. We identify barriers to care and contribute towards health system strengthening by training providers and addressing gaps in awareness, education, prevention and diagnosis.

For more information, see Access to healthcare from page 44.

Responsible sales and marketing BV
We are committed to high ethical standards of sales and marketing, aligned to our Code of Ethics and compliance framework. We maintain a robust compliance programme that aims to ensure compliance with all applicable laws, regulations and adopted industry codes. Our compliance programme is delivered by dedicated compliance professionals who advise on and monitor adherence to our Code and policies.

These compliance professionals support our local managers in ensuring staff meet our ethical standards. A network of nominated signatories reviews product promotional materials and activities to ensure compliance with applicable regulations and codes of practice, and to ensure information is accurate and balanced. Our Internal Audit Services conducts compliance audits on selected marketing companies.

In 2021, we identified 13 confirmed breaches in commercial business units (2020: 14). Within our commercial business units, there were 2,477 instances (instances can involve multiple people) of non-compliance with our policies by employees and third parties (2020: 2,113). We removed a total of 105 employees and third parties from their roles as a result of a breach. Warnings were given to 2,084 others (2020: 861) and we provided further guidance or coaching to another 1,895 (2020: 2,099) regarding our policies. The increase in warnings in 2021 may be attributed to reclassification of discipline in some markets and stronger discipline for equivalent breaches. Every quarter, our Audit Committee is advised of breach statistics, serious breaches and corresponding remediation.

The increase in incidents during the year continues to be driven by low-impact incidents and may be attributed to stronger first-line monitoring, a company environment where employees feel comfortable raising concerns, and evolving external regulations and enforcement priorities (i.e. data privacy globally).

Anti-bribery and anti-corruption BV
We do not tolerate bribery or any other form of corruption. Bribery and corruption remain a business risk and are a focus of our third-party risk management process and our business development due diligence procedures. They are a focus of our monitoring and audit programmes as well. We reinforced our commitment to ethical behaviour through our 2021 annual Code of Ethics training, which was delivered to relevant employees and third parties.

Operations

Our manufacturing and supply function has continued to support our growth by delivering successful launches, and advancing digital and new technology capabilities to support our pipeline.

In 2021, we launched our Operations 2025 plan, which focuses on:

- efficiently scaling our capabilities to support the continued growth of our portfolio
- leveraging the benefits of new manufacturing technology and digital innovation
- taking proactive steps to ensure zero carbon emissions from our global operations.

In 2021, we delivered 110 successful market launches. We achieved 100% of our planned new technology implementation milestones and introduced the first two digital solutions to our eight largest manufacturing sites.

"The COVID-19 pandemic demonstrated that healthcare systems can move quickly to grant access to innovative new medicines."

Ensuring quality and compliance
We are committed to high ethical standards and compliance with laws, regulations and internal policies. We are members of industry associations including IFPMA, EFPIA and PhRMA and adhere to their codes.

Managing our supply chain
We need an uninterrupted supply of high-quality materials along our end-to-end supply chains. This includes our active pharmaceutical ingredients (APIs). As most of our API manufacturing is outsourced, we place great importance on our global external sourcing and procurement organisations and policies, as well as our integrated risk management processes. During 2021, we activated our business continuity plans to ensure continued supply of medicines to patients and mitigate against any risk of disruption caused by COVID-19 and the consequences of the UK leaving the EU. We have continued to focus on increasing the availability of dual and multiple sources of raw materials, maintaining adequate stock levels and mitigating the effect of increasing pricing and service fluctuations across raw materials, services and utilities.

In 2021, Alexion supply chain delivered strongly on objectives despite disruptions to the global supply chain related to COVID-19 and several significant climate events. Working with relevant partners in our supply chain, we ensured sufficient business continuity and risk mitigation plans were activated. These included increasing safety stock levels for products and critical components across our business and distribution centres. We also deployed dual stocking and forward stocking locations to ensure product was located closer to our customers and extended the number of validated shipping routes globally.

In spite of the challenges faced in 2021, our teams were able to maintain supply to patients.

Supply chain finance
AstraZeneca has a supply chain finance programme to support the cash flow of its external supply base. The programme is managed by Taulia Inc. (with funding provided by some of the Group's relationship banks) and provides suppliers with visibility of invoices and payment dates via a dedicated platform. Suppliers can access this platform free of charge and have flexibility to select individual invoices for early payment. On election of an early payment, a charge is incurred by the supplier based on the period of acceleration, central bank interest rate and the rate agreed between Taulia Inc. and each supplier. All early payments are processed by the funders and AstraZeneca settles the original invoice amount with the funders at maturity of the original invoice due date.

The programme operates in the US, UK, Sweden and Germany. As at 31 December 2021, the programme had 389 suppliers enrolled and a potential early payment balance of $44 million.

In addition, a separate programme was established in China in the second half of 2021, delivered through a relationship bank-led platform. As at December 2021, there were a small number of suppliers leveraging that capability.

Responsible supply chain BV
Every employee and contractor who sources goods and services on behalf of AstraZeneca is expected to follow our Global Standard for the Procurement of Goods and Services. We monitor compliance through assessments and improvement programmes and do not work with anyone who is unable to meet our standards. Our Global Standard on Expectations of Third Parties is published on our website. In 2021, we conducted a total of 37 audits (2020: 48) on high-risk commercial suppliers (external manufacturing partners) to ensure appropriate practices and controls. 24% fully met our expectations while 54% had improvement plans for minor instances of non-compliance. We had no examples of high-risk engagements.

Through our Positive Sourcing Programme, we promote ethical behaviour among our suppliers. Our ambition is to achieve 100% ethical spend, ensuring that sustainability is embedded into end-to-end procurement processes. We use our responsible sourcing processes when working with suppliers to support their sustainability journeys, innovate together on challenges and promote supplier diversity.

Our Supplier Diversity Programme aims to ensure that small and diverse businesses are part of our supply base and have appropriate support to be more sustainable. This is in line with our objectives for growth and innovation. Our ambition is to expand the programme to 10 countries outside the US by 2025. In 2021, our programme was launched in Australia, New Zealand and Poland and is now active in six countries outside the US, including Brazil, South Africa and the UK.

Global manufacturing capability
Our principal tablet and capsule formulation sites are in the UK, Sweden, China, Puerto Rico and the US, with local/regional supply sites in Russia, Japan, Indonesia, Egypt, India, Mexico and Brazil. We also have major formulation sites for the global supply of parenteral and/or inhalation products in the US, Sweden, France, Australia and the UK. Most of the manufacture of APIs is delivered through the efficient use of external sourcing, complemented by internal capability in Sweden.

In September 2021, and in line with our Operations 2025 plan to invest in new manufacturing technology, we announced a $360 million investment to establish a next-generation API manufacturing facility for small molecules at our Alexion site in Dublin. Also in 2021, we completed the exit from our manufacturing facility at Wedel, Germany.

For biologics, our principal commercial manufacturing facilities are in the US (Frederick, MD; Greater Philadelphia, PA), the UK (Speke) and the Netherlands (Nijmegen), with capabilities in process development, manufacturing and distribution of biologics, including global supply of mAbs and influenza vaccines. Our new biologics drug product manufacturing facility in Sweden has been approved for Good Manufacturing Practices (GMP) manufacturing, allowing commercial manufacturing to commence.

Alexion uses both internal manufacturing facilities and third-party contract manufacturers to supply clinical and commercial quantities of our products and product candidates. Our internal manufacturing capability is multiproduct and includes a fill/finish facility at our Athlone, Ireland site, bulk drug substance, QC and packaging/labelling facility at our College Park, Dublin, Ireland site. In 2021, we received regulatory approval for our new large-scale drug substance facility located in Dublin and manufacture and release of commercial drug substance has commenced. Following a successful inspection, we expect to receive regulatory approval for our new small-scale drug substance facility at our Athlone site in 2022. We also have a production facility located in Georgia, US.

Third-party contract manufacturers, including Lonza Group AG and its affiliates (Lonza), provide bulk drug substance fill/finish, QC testing, packaging and labelling services. These partnerships have allowed us to successfully manufacture, test and pack our products for worldwide distribution in multiple locations globally. As our internal capability grows via investment and access to the AstraZeneca network, we will optimise our external network to maximise benefit to our customers and patients. This optimisation programme began in 2021.

The Group has 15,800 people in Operations, including 28 manufacturing sites in 16 countries.

Business development

Our business development and partnering activities supplement and strengthen our pipeline and our efforts to achieve scientific leadership.

We work with academia, governments, industry, scientific organisations and patient groups, as well as other pharmaceutical companies, to access the best science, stimulate innovation and accelerate the delivery of new medicines. We currently have more than 1,000 collaborations worldwide.

Alliances, collaborations and acquisitions

We continue to assess opportunities to make strategic, value-enhancing additions to our portfolio and pipeline in our disease areas through in-licensing, collaborations and acquisitions.

Over the past three years, we have completed more than 75 major or strategically important business development transactions, including 19 in 2021. Three of these were completed on behalf of Oncology R&D and four on behalf of BioPharmaceuticals R&D. Seven related to pre-clinical assets or programmes and 10 to precision medicine, genomics or access to genetic data.

In 2021, new deals included:

- Ionis Pharmaceuticals, Inc. (Ionis) collaboration to develop and commercialise eplontersen, a liver-targeted antisense therapy in Phase III development for the treatment of transthyretin amyloidosis, a systemic, progressive and fatal condition. The upfront payment from AstraZeneca to Ionis was $200 million. AstraZeneca will make additional conditional payments of up to $485 million following regulatory approvals. It will also pay up to $2.9 billion of sales-related milestones based on sales thresholds between $500 million and $6 billion, plus low double-digit to mid-twenties percentage royalties.
- Proteros Biostructures GmbH (Proteros) collaboration to jointly discover novel small molecules for the treatment of haematological cancers. AstraZeneca will provide research funding and Proteros will be eligible for success-based research, development and commercial milestone payments up to $75 million plus tiered royalties on annual net sales.
- Regeneron Pharmaceuticals, Inc. collaboration to research, develop and commercialise small molecule compounds directed against the G Protein-Coupled Receptor 75 (GPR75) target with the potential to treat obesity and related co-morbidities. The companies will evenly split research and development costs and share equally in any future potential profits.
- Sierra Oncology, Inc. was granted exclusive global rights to further develop and commercialise AZD5153, a clinical BRD4 inhibitor. AstraZeneca received an upfront payment of $8 million and may also be eligible for future milestone payments of up to $206 million plus single-to-low double-digit royalties on any future AZD5153 product sales.

Divestments

We typically divest medicines that sit outside our disease areas and can be deployed better by other companies. This enables us to redirect resources to our main areas of focus while ensuring continued or expanded patient access. 2021 transactions included:

- *Crestor* (rosuvastatin) and associated medicines in over 30 countries in Europe divested to Grünenthal GmbH. Rights in the UK and Spain were not included in the agreement.
- Global rights to *Eklira* (aclidinium bromide), known as *Tudorza* in the US, and *Duaklir* (aclidinium bromide/formoterol) transferred to Covis Pharma B.V. (completed in January 2022).

The resulting revenue from these activities supports our R&D investments in our disease areas.

"Despite the continued impact of the COVID-19 pandemic, we saw growth across all major Emerging Markets in 2021."

Be a Great Place to Work

Our success depends on recruiting, retaining and developing talented people while operating in a responsible and sustainable way.

Our performance in 2021

- 17,000 external hires. 33% of employees now have less than two years' service.
- 6,700 successful hires through employee referral scheme.
- Gained 4,000 permanent employees through the Alexion acquisition.
- Removal of performance ratings has given managers opportunity to focus on coaching and developing their teams.
- Expanded our Partnership for Health System Sustainability and Resilience with the London School of Economics and World Economic Forum.
- The Science Based Targets initiative verified our net-zero targets.
- HRH The Prince of Wales awarded AstraZeneca his Terra Carta Seal in recognition of our efforts to create a more sustainable future.
- Reached 31 million people through our flagship Access to Healthcare programmes.

Performance indicators

Contribution to the enterprise

This priority is built on three pillars: performing as an enterprise team, commitment to lifelong learning and development, and championing of inclusion and diversity.

For more information, see People from page 41.

Performing as an enterprise team[1]

78%

2021	78%
2020	81%
2019	77%

[1] Source: November Pulse full census survey for each year, based on the percentage of favourable responses to the question about 'effective collaboration between teams'.

Improved my existing/learned new skills, or had a development opportunity[2]

88%

2021	88%
2020	90%
2019	87%

[2] Source: November Pulse full census survey for each year, based on the percentage of favourable responses to the statement 'In the last 12 months, I have improved my existing skills, or learned new skills, or had a development opportunity'.

Inclusion and diversity[3]

48.1%

2021	48.1%
2020	46.9%
2019	45.4%

[3] Female representation at career level F+ (the most senior 13% of the employee population).

Contribution to society

Our sustainability performance indicators measure the progress of our environmental, social and governance practices. They are representative indicators of each of our three sustainability priorities: broaden access to healthcare, protect the environment, and ensure ethical, transparent behaviours.

For more information, see Sustainability from page 44.

Access to healthcare – AstraZeneca is truly patient-oriented[1]

89%

2021	89%
2020	91%
2019	89%

[1] Source: November Pulse full census survey for each year, based on the percentage of favourable responses to the statement 'AstraZeneca is truly patient-oriented'.

Our people

We grow and prosper by recruiting, retaining and developing talented people. We do that by being a great place to work, encouraging and rewarding innovation, entrepreneurship and high performance.

Performing as an enterprise team

Attracting diverse talent and critical capabilities

Our graduate and apprentice programmes are critical to attracting early-career talent and ensuring we build the capabilities we need to deliver our future strategic objectives. We also offer an MBA development programme in our US Commercial Business, which provides our future leaders with broad experience through business rotations.

Our talent scout model continues to successfully support recruitment activity across the business. This is supported by our employee referral scheme, which has become an increasingly important source of hiring. In 2021, we hired 6,700 people as a result of employee referrals.

In 2021, we received over 500,000 job applications and hired 24,000 employees (17,000 external and 7,000 internal), demonstrating our ability to attract key capabilities and talent throughout the COVID-19 pandemic. Hiring increases over recent years have resulted in 33% of our workforce having less than two years' service. A diverse workforce of both new and longer-serving employees can help foster a culture of innovation where fresh ideas are combined with existing business knowledge.

Due to our changing footprint and strategic objectives, most of the hiring activity has been in our Emerging Markets, where we have built new sales teams in recent years. This growth has been particularly strong in China, which accounted for over 7,000 external hires in 2021. Performance data indicates these new recruits are successful in their positions. However, an increased footprint in Emerging Markets also brings challenges such as increased turnover.

In 2021, we also gained an additional 4,000 employees through the acquisition of Alexion. These new employees have become part of our new Rare Disease group or embedded across other functions, such as HR and Finance.

The voluntary employee turnover for AstraZeneca increased in 2021 to 14% (2020: 10%), while the voluntary turnover rate for Alexion also increased to 11%, from 7% in February 2021. The launch of the new exit survey in May 2021 will help us gain a better understanding of the reasons for leaving and enable us to act accordingly to try and reduce turnover. We will continue to monitor the AstraZeneca and Alexion combined resignation rates as mergers and acquisitions can result in increased turnover levels.

Creating a culture of high performance

We no longer give performance ratings to employees and have shifted our focus to coaching, development and contribution to the organisation. Managers are accountable for helping to develop individual and team performance targets. In 2021, we trained 15,000 line managers in our new performance development approach, focusing on building coaching capabilities. In our 2021 performance development survey, 77% of managers who responded felt confident taking a coaching approach with their team members and 70% stated they were regularly practising coaching with their team. Our recognition platform continues to reward behaviours that reflect company Values, drives engagement across teams and ensures we celebrate our achievements. Following the launch in 2020, the recognition platform has continued to be successful with 71% of employees being rewarded through the platform in 2021.

Our salary and bonus budgets are distributed in line with our principles, allowing us to clearly differentiate reward according to performance. Following the removal of performance ratings, we now identify employees who have made exceptional contributions throughout the year. We encourage participation in various employee share plans, some of which are described in the Directors' Remuneration Report from page 98, and in Note 29 to the Financial Statements from page 186.

Listening to our workforce

Employee opinion surveys help us measure employee sentiment and progress in our aim of being a great place to work. In our most recent survey (November 2021), we continued to score highly, achieving an average result of 84% across all questions. Our response rate also reflects the high levels of engagement with 91% of all employees choosing to participate in the survey. We have met or exceeded three of our scorecard goals relating to Patient Centricity, Speaking My Mind and Development.

In 2021, we also continued to track a set of questions relating to the COVID-19 pandemic to understand how well we were supporting our employees through a challenging time. We received a favourable score of 87% for 'I am finding ways to balance managing my family needs while keeping up with my most important work responsibilities' and 91% for 'I am getting the support I need (from my manager, team, etc.) during this time'. These high scores demonstrate our ongoing commitment to the wellbeing of our employees.

Building a culture of lifelong learning and development

Employees are encouraged to take ownership of their own development and leaders are expected to spend time supporting and enabling their employees' development needs. In 2021, we invested $35 million in developing a culture of lifelong learning to support the up-skilling of our people. Learning for Life is part of our ambition to move from performance management to performance development, which focuses on encouraging people to grow their skills and experience so they can maximise their potential.

Our global online learning platform provides employees with access to an extensive amount of educational resources. Over 78% of employees have accessed resources since launching the platform in 2020, with 84% of these employees returning more than once. In addition to providing improved online resources, we offer a range of different learning programmes that have been developed to provide more targeted learning opportunities, as shown in the table below.

Name of programme	Number of attendees	Target group
Women as Leaders	225	Women, Mid-Senior Level roles
Leading Enterprise	113	Top 150 Senior Leaders
Leading Business	818	Senior Managers
Rising Leaders	118	High Potential Mid-Senior Level
Accelerate	52	Mid-Senior Level in Emerging Markets
Empowerment	350	Women, Mid-Junior Level
Leadership Labs	499	Second-Line Leaders in markets
Leading People	947	New First-Line Leaders
Brand Leadership	40	US Women of Color Leaders

Attendees of our development programmes are less likely to resign and have higher rates of promotion. In addition, the programmes have also enabled more accurate succession planning. Of the 2019 Women as Leaders attendees, 32% have since been promoted into more senior positions. Furthermore, the resignation rate of these attendees is lower than the overall target population (5.7% for Women as Leaders attendees compared with 7.6% for women in mid- to senior-level roles).

"In 2021, we made [illegible] up-skilling of our people."

Champions of inclusion and diversity

We believe that building an inclusive culture and making the most of the strength and diversity of our people allows us to unlock the innovation required to deliver life-changing medicines to the patients who need them most.

In 2021, we expanded our inclusion and diversity (I&D) learning programmes to further embed I&D in our day-to-day working practices. This included mandatory digital 'conscious inclusion' training in 10 languages and a set of techniques that foster a psychologically safe environment.

For more information, see our website, www.astrazeneca.com/sustainability.

Our commitments

We include targets on our global scorecard to increase representation of women in leadership positions, as well as to increase the percentage of leaders from Emerging Markets and Japan that report into our Senior Executive Team (SET). We also track employee sentiment on measures of inclusion twice a year. In the November 2021 survey, 90% of employees answered favourably to the statement 'Managers in my function/company support diversity and inclusion in the workplace'. This year we launched a voluntary disclosure campaign to better understand our global workforce demographics, including country of origin, disability status (including visible and invisible disabilities), ethnicity, race, sex, gender identity and sexual orientation where globally permissible.

Women comprise 51.8% (approximately 43,000) of our global workforce. With the appointment of Aradhana Sarin as CFO, there are five women on our Board (38% of the total). Following the appointment of Susan Galbraith as EVP of Oncology R&D, five of 12 SET members are now women (42% of the total). Across the enterprise, the representation of women in senior roles increased to 48.1% in 2021 (2020: 46.9%), above our target of 47.5%.

In the 2020 Hampton-Alexander review, published in 2021, we were named as the highest-ranking pharmaceutical company in the FTSE 100 for representation of women on the combined executive committee and their direct reports, and we moved up from sixth place to third place in the list of the Top 10 Best Performers. We also retained our position as one of 380 companies on the Bloomberg LP Gender-Equality Index 2021, which distinguishes companies committed to transparency in gender reporting and advancing women's equality.

Our employees come from 169 different countries. In 2021, 18.4% of employees who are either members of the SET, or their direct reports, are from Emerging Markets and Japan (18.4% at year end 2020) slightly below our target of 20%.

To support our commitment to racial equity, we work at every stage of our talent pipeline to increase and maintain representation. We are a founding partner of the World Economic Forum's Partnering for Racial Justice in Business initiative, which is focused on eradicating racism in the workplace and setting new global standards for racial equity in business. Within the UK, AstraZeneca is a signatory of the Race at Work Charter.

We are committed to hiring and promoting talent ethically and in compliance with applicable laws. Our Code of Ethics and its supporting Standards are designed to help protect against unlawful discrimination on any grounds (including disability). The Code covers recruitment and selection, performance management, career development and promotion, transfer, training, retraining (including retraining, if needed, for people who have become disabled), and reward. We embrace the unique skills, insights, and experiences held by individuals with both seen and unseen disabilities and are committed to creating a supportive culture by providing reasonable accommodations during the interview/hiring process that continue as needed throughout employees' careers and development within AstraZeneca. Our Global Standard for Inclusion and Diversity sets out how we foster an inclusive and diverse workforce where everyone feels valued and respected because of their individual abilities and perspectives.

For more information on our Standards and Global Policy framework, see our website, www.astrazeneca.com/sustainability.

In 2021, our I&D efforts earned recognition externally. We featured in:

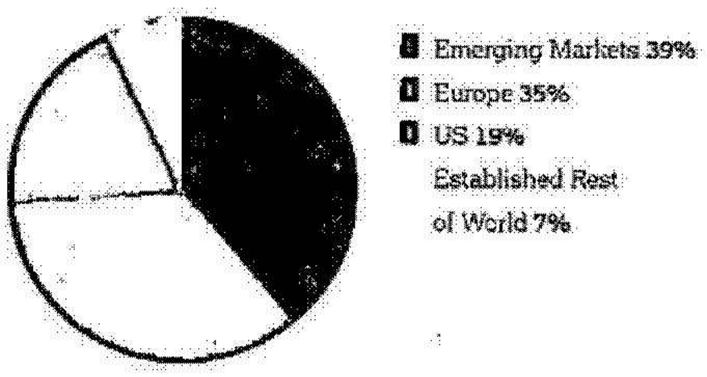
- The Times Top 50 Employers for Women
- Diversity Inc. Top 50 Companies for Diversity
- Forbes Best Employer for Diversity
- Financial Times Diversity Leaders
- 2021 Best Places to Work for LGBTQ Equality.

Human rights BV

Our Code of Ethics and Human Rights Statement commit us to respecting and promoting international human rights – not only in our own operations, but also in our wider spheres of influence, such as our third-party providers. We are committed to ensuring that we identify and eliminate, to the fullest extent practicable, modern slavery or human trafficking in our supply chains or any part of our business. We provide assurance annually to the Audit Committee and our full statement required under section 54 of the UK Modern Slavery Act 2015 and Section II (14) of the Australian Modern Slavery Act 2018 is available on our website, www.astrazeneca.com.

Our global business

Employees by reporting region



83,100
employees

Co-located around three global R&D centres

1. Gaithersburg, MD, US
3,700

2. Cambridge, UK
3,800

3. Gothenburg, Sweden
2,600

By geographical area



1. US
15,900
19%

2. UK
8,800
11%

3. Sweden
6,900
8%

4. Canada
1,100
1%

5. Central and South America
3,500
4%

6. Middle East and Africa
1,800
2%

7. Other Europe
11,400
14%

8. Russia
1,600
2%

9. Other Asia Pacific
7,100
9%

10. China
20,600
25%

11. Japan
3,400
4%

12. Australia and New Zealand
1,000
1%

All numbers as at 31 December 2021.

We support the principles set out in the United Nations Universal Declaration of Human Rights and the International Labour Organization's (ILO) standards on child labour and minimum wages. We have been members of the United Nations Global Compact on Human Rights since 2010.

We continue to engage with Slave Free Alliance (Hope for Justice) and participate in working groups with peer multinationals to benchmark our approach to risk identification and share best practices. We are members of the Pharmaceutical Supply Chain Initiative Human Rights and Labour Group, an industry collaboration supporting responsible supply chain management principles for ethics, labour, health, safety, environment and related management systems.

Employee relations BV

We seek to follow a global approach to employee relations, guided by global employment principles and standards, local laws and good practice. In July 2019, we established a Global Function for Employee Relations.

The purpose of this function is to build and maintain a positive work environment where every employee can feel safe, productive, motivated and able to speak up. The Board of Directors, in collaboration with our Global Compliance and Employee Relations functions, supports our efforts to create a 'Speak Up' culture. Our aim is to encourage employees to express their opinions and to prevent and detect any behaviour not in line with our Values, Code of Ethics and Global Standards. The Audit Committee also checks the sexual harassment, and harassment and bullying process activities and cases periodically.

To achieve this objective, we also work to develop and maintain good relations with local workforces and work closely with our recognised national trade unions. We also regularly consult with employee representatives or, where applicable, trade unions, who share our aim of retaining key skills and mitigating job losses. According to our internal Human Rights survey carried out in 2020, 75% of our employees recognise and have a relationship with trade unions. Where trade unions do not exist in an area of operation, all those areas have established arrangements to engage similarly with their workforce.

Workplace safety and health BV

We work to promote a safe, healthy, and energising work environment for our employees and partners. Our standards apply globally and are stated in our Code of Ethics as described on page 47 and available on www.astrazeneca.com/sustainability. We have established and monitor a set of safety and health targets aimed at supporting our workforce and keeping AstraZeneca among the sector leaders in performance. In 2021, we implemented a new Global Safety, Health and Environment (SHE) Standard that describes our commitment to, management of and accountability for SHE. In 2021, we achieved a 40% reduction in the vehicle collision rate and a 68% reduction in the work-related injury rate from the 2015 baseline. Sadly, there was one employee fatality due to a vehicle accident, and one fatal illness from a potentially work-related COVID-19 exposure during 2021.

"Through our flagship $1 billion Ambition Zero Carbon programme, we are on track to reduce greenhouse gas emissions from our global operations by 98% by 2026 and halve our entire value chain footprint by 2030, on the way to a 90% reduction by 2045."

Sustainability BV

Contributing to society is a fundamental part of our commitment to make a difference to people and our strategic ambition to lead in sustainability, as part of being a great place to work. During 2021, we were recognised for our efforts in sustainability across our strategic priorities. This included:

- inaugural 2021 Terra Carta Seal award
- Dow Jones Sustainability Index constituent
- FTSE4Good Index Series constituent
- Financial Times 2021 European Climate Leader for reduction of greenhouse gas emissions
- CDP Double A List for Climate Change and Water Security for the sixth consecutive year
- Corporate Knights Global 100 Most Sustainable Corporations in the World
- Access to Medicine Index 2021 – seventh out of 20.

Driving the sustainability agenda

During 2021, we increased our engagement on global sustainability issues with external stakeholders and on the global policy agenda.

We actively promoted public-private partnerships to strengthen global health security and health system resilience in light of lessons learned from the COVID-19 pandemic. We did this through our Partnership for Health System Sustainability and Resilience (PHSSR) with the London School of Economics and World Economic Forum (WEF), as well as our long-standing access to healthcare programmes and initiatives to strengthen health systems. We also focused on opportunities to identify innovative solutions to the climate crisis and address its impact on global health.

As a founding member of the Prince of Wales' Sustainable Markets Initiative (SMI) and a supporter of the Terra Carta Sustainability Charter, our CEO attended meetings such as the G7 Leaders' Summit in Cornwall, UK. He also hosted an SMI Roundtable focused on delivering sustainable healthcare. During the COP26 summit in Glasgow, UK, we were one of the first companies to be awarded the inaugural 2021 Terra Carta Seal by HRH The Prince of Wales. The Seal recognises companies from around the world who are driving innovation and leadership in their industry in tackling climate change. The Prince of Wales and our CEO, along with global health leaders, also launched the SMI Health Systems Taskforce, which our CEO will champion.

Our climate change targets were verified by the Science Based Targets initiative (SBTi) as in line with their new Net-Zero Corporate Standard, AstraZeneca being one of only seven companies worldwide at launch and the only pharmaceutical company.

Access to healthcare BV

We are working towards a future where everyone can have access to sustainable health solutions for life-changing treatment and care. This includes collaborating with our partners in support of common goals to strengthen health system resilience, improve equitable access to medicines and promote disease prevention. We innovate and partner to transform solutions across the patient care pathway – from prevention, raising awareness, diagnosis and treatment, to post-treatment and wellness.

Achievements in 2021

- Over 199,000 healthcare workers and others trained since 2010 and over 31 million people reached through Access to Healthcare programmes. Healthy Heart Africa conducted over 23 million screenings for elevated blood pressure and Young Health Programme (YHP) reached more than six million young people through prevention and education programmes in over 30 countries.
- Over 11 million people reached through our patient assistance programmes (cumulatively), which help patients in financial difficulty gain access to AstraZeneca medicines.

Equitable access

We embed practices into the product portfolio to drive equitable access to healthcare – including digital health, clinical trial diversity, patient centricity, investing in rare diseases, open innovation and intellectual property-sharing arrangements.

During 2021, we put broad and equitable access at the heart of our pandemic response. AstraZeneca and our global partners released for supply 2.5 billion vaccine doses to over 180 countries. Approximately two thirds of these went to low- and lower-middle-income countries, and more than 247 million doses have been delivered to 130 countries through the COVAX Facility in 2021. In 2021, the majority of vaccine product sales and doses delivered related to pandemic contracts. AstraZeneca will continue to supply the vaccine around the world in 2022. We have moved to an affordable pricing approach that enables us to maintain broad global access. This includes a tiered pricing approach aligned to Gross National Income per capita, a widely recognised model used by developers of medicines and vaccines. We remain committed to supplying the vaccine at no profit in low-income countries, in line with our agreement with Oxford University.

For more information, see Other Medicines and COVID-19 from page 27.

Diversity in clinical trials

It is important that volunteers testing a potential new medicine appropriately reflect our potential target patient populations. We need to demonstrate a medicine's safety and efficacy for all those who need it, whatever their age, sex, ethnicity, overall health, where they live and their place of origin. Local clinical trials also increase understanding and confidence in medicines. Building on our experience with the COVID-19 vaccine we will work to include more countries to ensure diverse, global representation.

For more information, see Clinical trials transparency on page 34.

Rare diseases

Therapies are only available for 5% of more than 7,000 rare diseases. We believe people with rare diseases deserve the same attention and investment into finding therapies as anyone. We work to help people get medicines through our patient support and expanded access programmes, and we are expanding the geographies where our medicines are available.

For more information, see Rare Disease from page 24.

Affordability and pricing

We want all patients who need medicines to have access to them without financial hardship. We work to expand availability and accessibility of our life-changing medicines to people around the world.

We drive accessibility of medicines for diverse, equitable and inclusive patient groups through company policy and programming, including core pricing principles and access programmes.

For more information, see Pricing and value of our medicines from page 35.

Health system resilience

We strengthen health systems by advocating for health system and policy reform. We build capabilities to address unmet medical need, improve access to quality healthcare and provide solutions along a continuum of care – from prevention, awareness, diagnosis and treatment to post-treatment and wellness; and commit to humanitarian relief, grants and donations.

We also work to advocate for global healthcare policies that support the unique needs of the rare disease community.

The Partnership for Health Systems Sustainability and Resilience (PHSSR)
This partnership is motivated by a shared commitment to improving population health, through and beyond the COVID-19 pandemic. In 2021, we co-led the first PHSSR Summit with over 50 leading experts from eight pilot countries. We discussed the future of health in a post-COVID-19 world and launched the interim report. Phase II of the PHSSR also launched in 2021, with an expansion into 13 new countries and a regional hub in the Central, Eastern Europe and Baltics area, which brought the total number of member countries to more than 30. The PHSSR has acted as the basis for policy improvements in many of the countries where it has been active.

Healthy Heart Africa programme
Our Healthy Heart Africa programme is committed to reducing hypertension and the burden of cardiovascular disease, aiming to reach 10 million people with elevated blood pressure across Africa by 2025. We work with local and global partners to raise awareness and offer training, screening and reduced-cost treatment, as applicable. By the end of 2021, the programme had conducted over 23 million blood pressure screenings and trained over 9,000 healthcare workers since launch in 2014. In 2021, the programme expanded into Côte d'Ivoire, Senegal and Rwanda.

Young Health Programme
Since 2010, the AstraZeneca Young Health Programme has worked to help young people aged 10 to 24 take control of their health, especially to combat long-term conditions such as cancer, diabetes, respiratory and heart disease, and mental health conditions – referred to as non-communicable diseases. In collaboration with UNICEF and Plan International, we support research, advocacy and education to help young people make better choices for healthier lives. In 2021, the programme had reached 1.18 million youths with health information and trained 73,000 peer educators in 30 countries.

Community investment BV
We aim to make a positive impact on people in all the communities where we are present, supporting programmes to advance patient health, increase access to care, drive scientific innovation and build resiliency. Our Global Standard on External Funding covers community investment and provides guidance to ensure a consistent, transparent and ethical approach around the world, based on local need. Our activities are focused on healthcare in the community and supporting science education. They include financial and non-financial contributions. In 2021, we provided $112.9 million to more than 1,220 non-profit organisations across 74 countries. This includes contributions made by Alexion. We also donated more than $2.3 billion (2020: $1.6 billion) of medicines in connection with patient assistance programmes around the world, the largest of which is our AZ&Me programme in the US. This change reflects an increase in requests for assistance and growth across our therapeutic areas, including new indications.

Product donation programmes BV
In 2021, we gave $23 million (2020: $27 million) in product donations for disaster, humanitarian relief and public health need.

We remain committed to working with health system stakeholders and payers towards achieving more systemic solutions.

Environmental protection BV

We aim to demonstrate global leadership by minimising our environmental impact across all our activities and products. Becoming increasingly circular, we are designing out waste and pollution, keeping products and materials in use, and maximising resource efficiency. We are also adopting nature-based solutions to protect, sustainably manage and restore natural and modified ecosystems that address societal challenges, such as the impact of the climate crisis and supporting biodiversity.

Achievements in 2021

- 59% reduction in Scope 1 and 2 greenhouse gas emissions since 2015
- Over three million trees planted by AZ Forest by end of 2021
- 17% reduction in water usage since 2015
- 8% reduction in our waste since 2015
- 75% of development projects met resource efficiency targets at launch in 2021
- 100% safe API discharges for AstraZeneca sites
- 91% for globally managed first-tier supplier sites.

As part of our WEF partnership, in 2021 we contributed to the Alliance of CEO Climate Leaders and as a Corporate Alliance supporter of the Trillion Trees reforestation movement.

Ambition Zero Carbon

We are committed to:

- Achieving net-zero greenhouse gas (GHG) emissions by maximising our energy efficiency, shifting to renewable energy sources, and investing in nature-based removals to compensate for any residual GHG footprint.
- Building resilience by managing the physical (sites, supply chain) and transitional (regulatory, market and product) risks and opportunities from climate change in the value chain through adaptation and business continuity planning.

The climate emergency is a public health emergency. It is changing our planet irreversibly, with warming reaching critical tolerance thresholds for health. Human health and the health of the planet are deeply interconnected. We have an opportunity now to reset how we live and create a more sustainable world – together and without delay.

Through our flagship $1 billion Ambition Zero Carbon programme, we are on track to reduce GHG emissions from our global operations by 98% by 2026 and halve our entire value chain footprint by 2030 on the way to a 90% reduction by 2045. Our emission reduction targets have been verified by the Science Based Targets initiative and we were one of the first seven companies worldwide to have our Scope 1 to 3 and long-term net-zero targets verified under their new Net-Zero Corporate Standard. We were also an early supporter of the UN-backed Race to Zero.

Near-term targets:
- > 98% reduction in Scope 1 and 2 GHG emissions by 2026 from 2015 baseline
- > switching to 100% fully electric vehicle fleet (EV100) by end of 2025
- > using 100% renewable energy (RE100) for power and heat by end of 2025
- > doubling energy productivity (EP100) from 2015 to 2025
- > launching first next-generation respiratory inhalers with near-zero climate impact by 2025
- > aligning supplier spend with companies with approved science-based targets by end of 2025
- > planting and stewarding over 50 million trees by end of 2025 as a nature-based solution to enhance climate, ecological and community resilience through our AZ Forest global initiative.

Long-term targets:
- > 50% reduction in total Scope 3 emissions by 2030 and 90% reduction by 2045, from 2019 baseline
- > carbon negative for all residual emissions from 2030 and science-based net-zero by 2045
- > transitioning to next-generation respiratory inhalers with near-zero climate impact.

Product sustainability
We manage the environmental impact of our products from discovery in the lab through to the end of a product's life. To avoid adverse impacts on the environment and human health, we evaluate all materials and processes used to make our products. We focus on preventing and reducing waste wherever possible, maximising the utility of the natural resources we use.

As part of our continued commitment to transparency in the management of Pharmaceuticals in the Environment (PiE), we launched an EcoPharmacoVigilance dashboard that shows the risks of pharmaceuticals that reach the environment principally through patient use. This helps to monitor any associated risk and ensure the environmental safety of our life-changing medicines. With the dashboard, we can look at real-world environmental risk by comparing measured environmental concentrations with defined 'no effect and safe' concentrations. This is the first time an individual pharmaceutical company has shared this type of data. This initiative highlights our progress on water quality and builds on our established leadership in responsible active pharmaceutical ingredient discharge management from our operations.

For more information on our PiE position paper, see our website: www.astrazeneca.com/sustainability/environmental-protection/pharmaceuticals-in-the-environment.html

In 2021, we launched our internal Product Sustainability Index to ensure we understand the environmental impacts across our product value chains and prioritise improvement opportunities.

A key product-related element of our Ambition Zero Carbon strategy is our commitment to develop the next-generation respiratory inhalers with near zero global warming potential (GWP) propellants. During 2021, we progressed a project spanning all key functions in the business to assess alternative low-GWP propellant options from an environmental, technical, regulatory, medical, non-clinical and commercial viewpoint to enable a Phase III investment decision for the lead propellant in the first half of 2022.

Natural resources
We are committed to:
- > Reducing our impact on the planet through the efficient, circular use of natural resources across the value chain to ensure responsible sourcing, consumption, production and disposal.
- > Protecting and restoring ecosystems to improve health outcomes and tackle environmental drivers of disease, such as water and air quality, through our focus on water stewardship and biodiversity.

To drive our climate action initiatives and meet our environmental targets, we have a dedicated Natural Resource Efficiency Fund, which has invested approximately $130 million in environmental efficiency innovations since 2015. This includes 56 new projects and nearly $30 million spent in 2021.

Water stewardship
Since 2020, we have collaborated in a water stewardship partnership with the World Wide Fund for Nature (WWF) Sweden. Through this collaboration, in 2021, we championed a sector-level water risk assessment of the global pharmaceutical supply chain.

For more information on this assessment, see wwf.panda.org/wwf_news/?4417966/Diagnosing-current-and-future-water-risks-facing-the-pharmaceutical-sector.

This assessment has helped identify sectoral-level water stewardship opportunities, as well as potential shared water challenges that may be strategically relevant in areas of concentrated pharmaceutical manufacturing.

We also introduced a new water stewardship pilot, focused on six key sites in water-scarce areas as these face future water availability and quality risks. In 2022, we will set locally-appropriate water targets for these sites and aim to have long-term contextual water targets in place by 2025.

Green labs
In 2021, our collaboration with the non-profit organisation, My Green Lab, continued to inspire a reduction in the environmental impacts of our labs. A total of 36 laboratory functions across 31 sites are involved in the programme. Of these, 12 received certifications through this initiative across 11 sites: four sites attained the highest Green certification level, one Platinum, six Gold, and one Silver. We aim for all of our R&D labs to be My Green Labs certified by 2026. For the second consecutive year, we won the Biotech/Biopharma organisation category in the International Freezer Challenge, saving approximately 1,858 kWh/day during the challenge across the participating sites.

My Green Lab certification has been recognised by the pharmaceutical sector as part of the UN Race to Zero.

For more information, see www.mygreenlab.org/blog-beaker/green-lab-certification-named-key-player-in-the-un-climate-changes-race-to-zero.

Building a framework for circularity[1]
We are leveraging our experience with LEAN manufacturing, which includes tools to enhance efficiency and eliminate waste, to build a framework for employees to identify and implement initiatives that contribute to our environmental targets. For example, in 2021 a KAIZEN™ pilot event was held to target single-use plastics used in packaging for one of our products. Using LEAN tools, a cross-functional team analysed inventory data to identify options to tackle plastic use and increase recycling, resulting in opportunities to eliminate up to 200 tonnes of plastic annually. This framework will continue to be scaled up and shared across our network.

[1] 'Circularity' means designing out waste and pollution, keeping products and materials in use, for example by designing for durability and recycling, and regenerating natural systems by avoiding non-renewable resources and preserving or enhancing renewable ones.

Ethics and transparency

We seek to create positive societal impact and embed ethical behaviour in all our business activities, markets and value chain. We do this by promoting ethical, transparent and inclusive policies within our company as well as across all our partners and suppliers. It is important that we can create value beyond the impact our medicines have on patients. Building trust by demonstrating integrity, transparency and fair treatment is central to everything we do.

Achievements in 2021

- 48.1% of senior middle management roles and above are held by women
- 72% of all critical manufacturing partners are rated 'bronze' or better by our sustainability framework (2025 target of 75%)
- 83% of employee survey respondents feel that AstraZeneca has a 'Speak Up' culture.

For more information, see:
- Bioethics, see page 34.
- Champions of inclusion and diversity, see page 42.
- Workplace safety and health, see page 43.

Code of Ethics

We are committed to employing high ethical standards when carrying out all aspects of our business globally. Our Code of Ethics (the Code) is based on our Values, expected behaviours and key policy principles. It applies to all Executive and Non-Executive Directors, officers, employees and temporary staff, in all companies within our Group worldwide. The Code empowers employees to make decisions in the best interests of the Group and the people we serve, now and in the long term. It does this by outlining our commitments in simple terms and focusing on why these commitments matter. The Code is at the core of our compliance programme. It has been translated into approximately 40 languages and guides employees on how to make the best day-to-day choices and how to act in a consistent, responsible way, worldwide. There are two mandatory training courses dedicated to the Code: one is for new starters; the second is the annual training for all employees, reminding them of the key commitments. In 2021, 100% of all active employees completed the annual training on the Code.

The Code includes four high-level Global Policies covering Science, Interactions, Workplace and Sustainability. These Global Policies are complemented by underlying Global Standards, which define the global requirements we follow to deliver our business consistent with the Values, behaviours, commitments and principles embodied in our Code and Global Policies. Our Code and Global Policies, together with relevant Global Standards and Position Statements, are published on our website, www.astrazeneca.com. Our policy framework also includes additional requirements at the global, local and business unit level to support employees in their daily work.

The Code recommends that employees report possible violations. It also provides information on how to do so, including via the AZ Ethics helpline or website, which is managed by an independent third party. AZ Ethics is also available to third parties. Reports can be made anonymously where desired and where permitted by local law. Anyone who raises a potential breach in good faith is fully supported by management.

The majority of cases come to our attention through management and employee self-reporting. This can be seen as an indication that employees are comfortable in raising their concerns with line managers or local Human Resources, Legal or Compliance, as recommended in the Code (and reinforced in the 2021 Code training). In 2021, 416 reports of alleged compliance breaches or other ethical concerns were made through AZ Ethics, including reports made by any anonymous route that could be considered whistleblowing (in 2020, there were 385 reports).

A Finance Code complements the Code and applies to the CFO, the Group's principal accounting officers (including key Finance staff in all overseas subsidiaries) and all managers in the Finance function. This reinforces the importance of the integrity of the Group's Financial Statements, the reliability of the accounting records on which they are based and the robustness of the relevant controls and processes.

Non-Financial Information Statement

Under sections 414CA and 414CB of the Companies Act 2006, as introduced by the Companies, Partnerships and Groups (Accounts and Non-Financial Reporting) Regulations 2016, AstraZeneca is required to include, in its Strategic Report, a non-financial statement containing certain information. As required by the Regulations, the Strategic Report contains information on the following matters, which include references to our relevant policies, due diligence processes and information on how we are performing against various measures in these areas:

- **Anti-bribery and anti-corruption, see page 37.**
- **Code of Ethics, see this page.**
- **Access to healthcare, see pages 44 to 45.**
- **Environmental protection, see pages 45 to 46.**
- **Our people, see pages 41 to 43.**
- **Human rights, see pages 42 to 43.**

Information on the Group's Principal Risks is included in Risk Overview (see from page 48) and information on the non-financial key performance indicators relevant to our business is included in Key Performance Indicators (see from page 12). A description of our business model is contained in Business Model and Life-cycle of a Medicine (see from page 10).

Risk Overview

We face a diverse range of risks and uncertainties. Those risks that have the potential to have a material impact on our Strategic Priorities are our Principal Risks.

"We strive to embed sound risk management in our strategy, planning, budgeting and performance management processes."

Managing risk

Our approach to risk management is designed to encourage clear decision making on which risks we take and how we manage these risks. We strive to embed sound risk management in our strategy, planning, budgeting and performance management processes.

The Board defines the Group's risk appetite. This enables the Group, in both quantitative and qualitative terms, to judge the level of risk it is prepared to take in achieving its overall objectives. The Board expresses the acceptable levels of risk for the Group using three key dimensions. These are: (i) earnings and cash flow, (ii) return on investment and (iii) ethics and reputation. Annually, the Group develops a detailed three-year bottom-up business plan and 10-year long-range projection to support the delivery of its strategy. The Board considers these in the context of the Group's risk appetite. Adjustments are made to the plan or risk appetite to ensure they remain aligned.

The SET is required by the Board to oversee and monitor the effectiveness of the risk management processes implemented by management. Within each SET function, leadership teams discuss the risks the business faces. Quarterly, each SET function assesses changes to these risks, new and emerging risks and mitigation plans. These are assimilated into a Group Risk Report for the Board, Audit Committee and SET. Global Compliance, Finance and Internal Audit Services support SET by advising on policy and standard setting, monitoring and auditing, communication and training, as well as reporting on the adequacy of line management processes as they apply to risk management.

The Board believes that existing processes provide it with adequate information on the risks and uncertainties we face. The Board has carried out a robust assessment of the Principal and Emerging risks facing the Group. The table overleaf provides insight into our ongoing Principal Risks. It outlines why effective management of these risks is important and relevant to our business, how we are managing them and which risks have gone up, down or remained static during the past 12 months. Our Principal Risks are those risks that are most likely to have a material impact on our business and are a subset of the total risk landscape facing the Group.

For more information on these Principal Risks and the other risks in our risk landscape, see the Risk supplement at www.astrazeneca.com/annualreport2021.

Emerging risks

Emerging risks are 'new' risks that may challenge us in the future. These risks have the potential to crystallise at some point in the future but are unlikely to impact the business during the next year. The outcome of such risks is often more uncertain. They may begin to evolve rapidly or simply not materialise.

We monitor our business activities and external and internal environments for new, emerging and changing risks to ensure these are managed appropriately. Annually, we combine input from each SET function and external insight to scan the horizon for emerging risks. A summary of emerging risks is presented for assessment to the Audit Committee and the Board. Emerging risks continue to be monitored as part of our ongoing risk management processes outlined above.

Climate risk

The identification and assessment of climate risk form part of our existing risk management processes as described below. 'Failure to meet regulatory and ethical expectations on environmental impact, including climate change' is a component of the Group's risk landscape.

For more information about our Global Compliance function, see page 79 and for our Code of Ethics see page 47.

Task force on Climate-related Financial Disclosures

We support the Task force on Climate-related Financial Disclosures (TCFD) framework and continue to develop our disclosures in line with its recommendations. We first adopted the TCFD framework in our 2020 Annual Report, and continue to apply it to describe activities conducted in the year to 31 December 2021. Our TCFD Statement from page 217 therefore summarises the work undertaken to date to understand the potential impact of climate change on our business and outlines future areas of management focus.

For more information about our TCFD Statement, see page 217.

Viability statement

In accordance with provision 31 of the 2018 UK Corporate Governance Code, the Board has determined that a three-year period to 31 December 2024 constitutes an appropriate period over which to provide its viability statement.

The Board considers annually and on a rolling basis, a three-year bottom-up detailed business plan. The Board also assesses the Company's prospects using a 10-year long-range projection but, given the inherent uncertainty involved, believes that the three-year statement presents readers of this Annual Report with a reasonable degree of assurance while still providing a longer-term perspective.

The three-year detailed business plan captures risks to the sales and cost forecasts at a market and SET function level. The plan is used to perform central net debt and headroom profile analysis. The following scenarios have been applied to this analysis to create a severe but plausible downside combining a number of the Principal Risks detailed on pages 50 to 51:

- **Principal Risks**: Pricing, affordability, access and competitive pressures. Failures or delays in the quality and execution of the Group's commercial strategies.
  - **Scenario 1** – Government action on pricing, higher than anticipated competition and other commercial headwinds result in lower than anticipated growth rates for our medicines.
  - **Scenario 2** – A significant incident leads to reputational damage in a key market resulting in an ongoing 10% revenue reduction in this market.

- **Principal Risk**: Failure or delay in the delivery of our pipeline or launch of new medicines.
  - **Scenario 3** – Assumes no launches of new products.

- **Principal Risk**: Failure to maintain supply of compliant, quality medicines.
  - **Scenario 4** – Major equipment failure or significant regulatory observation at one of our major manufacturing sites results in a 12-month supply interruption for one of our key oncology products.

- **Principal Risks**: Failure in information technology or cybersecurity. Adverse outcome of litigation and/or government investigations.
  - **Scenario 5** – Legal or regulatory non-compliance results in the levy of a $500 million fine payable in 2023.

In addition, the Board has considered more stressed scenarios including restrictions on debt factoring and no access to capital markets to raise new debt. In each scenario (or combination of scenarios), the Group is able to rely on its existing cash, cash equivalents and short-term fixed income investments and committed credit facilities. It may leverage its cost base, reduce capital expenditure and take other cash management measures to mitigate the impacts and still have residual capacity to absorb further shocks.

Based on the results of this analysis, the Directors have a reasonable expectation that the Company will be able to continue in operation and meet its liabilities as they fall due over the three-year period of their assessment.

COVID-19 pandemic

The risk 'failure of critical processes' (which can be found in the Risk Supplement at www.astrazeneca.com/annualreport2021) incorporates the risk of disruption as a result of a pandemic. The Board does not consider this to be a Principal Risk in its own right. However, the impact of the COVID-19 pandemic on the Group's operations remains uncertain and cannot be predicted with confidence. The extent of any adverse impact on Group operations will depend on the global duration, extent and severity of the pandemic. To the extent that the pandemic adversely impacts Group operations and/or performance, the Group expects it to have the effect of heightening certain risks, including Principal Risks. This includes those risks relating to the delivery of the pipeline or launch of new medicines, the execution of the Group's commercial strategy, the manufacturing and supply of new medicines and reliance on third-party goods and services.

"We monitor our business activities and external and internal environments for new, emerging risks to ensure these are managed appropriately."

Risk Overview *continued*

Strategy key

- Accelerate Innovative Science
- Deliver Growth and Therapy Area Leadership
- Be a Great Place to Work
- Achieve Group Financial Targets

Trend key

- Increasing risk
- Decreasing risk
- Unchanged

Principal Risks

Risk category and Principal Risks	Context/potential impact	Management actions	Trend versus prior year
Product pipeline risks			
Failure or delay in the delivery of our pipeline or launch of new medicines	The development of any pharmaceutical product candidate is a complex, risky and lengthy process involving significant resources. A project may fail at any stage of the process due to a number of factors, which could adversely affect our future business and results of operations.	> Prioritise and accelerate our pipeline. Strengthen pipeline through acquisitions, licensing and collaborations. > Focus on innovative science in our main disease areas. > Improve R&D productivity.	
Failure to meet regulatory or ethical requirements for medicine development or approval	We are subject to laws and regulations that control our ability to market our pharmaceutical products. Delays in regulatory reviews and approvals could delay our ability to market our products and may adversely affect our revenue.	> Quality management systems incorporating monitoring, training and assurance activities. > Collaborating with regulatory bodies and advocacy groups to monitor and respond to changes in the regulatory environment, including revised processes, timelines and guidance.	
Commercialisation risks			
Pricing, affordability, access and competitive pressures	Operating in more than 100 countries, we are subject to political, socio-economic and financial factors around the world. The medicines in our Rare Disease unit are significantly more expensive than traditional medicines. Global pressures to reduce healthcare spending may lead to the implementation of various controls, reimbursement mechanisms or cost containment measures, which could adversely affect our business or financial results.	> Focus on key products. > Demonstrate value of medicines/health economics. > Global footprint. > Diversified portfolio.	Global economic and political conditions placing downward pressure on healthcare pricing and spending, and therefore on revenue.
Failure or delays in the quality or execution of the Group's commercial strategies	A failure to execute our commercial strategies or achieve the level of sales anticipated for a medicine could materially impact our business or the result of operations.	> Focus on key products. > Substantial investment in sales and marketing activities. > Accelerate execution of plans and risk share through business development and strategic collaborations and alliances.	Maximising the commercial potential of our new products underpins the success of our strategy and the delivery of our short- and medium-term targets.
Supply chain and business execution risks			
Failure to maintain supply of compliant, quality medicines	Delays or interruptions in supply can lead to product shortages, which may result in lost product sales and adversely affect our reputation and revenues in a material way.	> Establishment of new manufacturing facilities, creating capacity and technical capability to support new product launches. > Contingency plans including dual sourcing, multiple suppliers and close monitoring and maintenance of stock levels. > Business continuity and resilience initiatives, disaster and data recovery and emergency response plans. > Quality management systems.	External factors such as the COVID-19 pandemic, geopolitical tensions and high levels of demand for certain raw materials and components place increased pressure on supply chains and distribution networks.

Risk category and Principal Risks	Context/potential impact	Management actions	Trend versus prior year
Supply chain and business execution risks *continued*			
Failure in information technology or cybersecurity	Significant disruption to our IT systems, including breaches of data security or cybersecurity, or failure to comply with applicable laws or regulations may result in losses or regulatory penalties, which could harm our reputation and materially affect our financial condition or results of operations.	> Cybersecurity framework and dashboard. > Disaster and data recovery plans. > Strategies to secure critical systems and processes. > Regular cybersecurity and privacy training for employees.	Growing multi-faceted cyber threat.
Failure to attract, develop, engage and retain a diverse, talented and capable workforce	The inability to attract and retain highly-skilled personnel may weaken our succession plans for critical positions, may adversely affect the implementation of our strategic objectives and could ultimately impact our business or results of operations.	> Targeted recruitment and retention strategies deployed including in the Rare Disease unit. > Development of our employees. > Evolve our culture.	Strong competition for talent. Complex workforce dynamics as a result of COVID-19 pandemic-related disruption.
Legal, regulatory and compliance risks			
Safety and efficacy of marketed medicines is questioned	Serious safety concerns or adverse events relating to our products may lead to product recalls, seizures, interruption of supply and loss of product approvals, which could adversely affect patient access, our reputation and our revenues. Significant product liability claims could also arise, which may be costly, divert management attention, reduce demand for our products and damage our reputation.	> Robust processes and systems in place to manage patient safety and efficacy trends as well as externally reported risks through regulatory agencies and other parties. This includes a comprehensive pharmacovigilance programme supplemented by close monitoring and review of adverse events.	
Adverse outcome of litigation and/or governmental investigations	Our business operations are subject to a wide range of laws, rules and regulations around the world. Any failure to comply with these may result in AstraZeneca being investigated by relevant government agencies and authorities and/or in legal proceedings being filed against us. Government investigations, litigations, and other legal proceedings, regardless of their outcome, could be costly, divert management attention, or damage our reputation and demand for our products. Unfavourable resolution of current and similar future proceedings against us could subject us to criminal liability, fines, penalties or other monetary or non-monetary remedies and could adversely affect our business or results of operations in a material way.	> Established compliance framework with strong ethical and compliance culture. > Combined internal and external counsel management.	
IP risks related to our products	The pharmaceutical industry is experiencing pressure from governments and other healthcare payors to impose limits on IP protections in an effort to manage healthcare costs. If we are unable to obtain, defend and enforce IP that protects our products, we may experience accelerated and intensified competition from third-parties.	> Active management of IP rights and IP litigation.	
Economic and financial risks			
Failure to achieve strategic plans or meet targets or expectations	Failure to successfully implement our business strategy, including the effective integration of Alexion into our Group, may frustrate the achievement of our targets and materially damage our brand, business, financial position or results of operations.	> Focus on key products and innovative science in our core disease areas. > Direct senior executive-led sponsorship of the integration of the Rare Disease unit. > Strengthen pipeline through acquisitions, licensing and collaborations. > Appropriate capital structure and balance sheet. > Portfolio-driven decision-making process governed by senior executive-led committees.	Global economic and political conditions placing downward pressure on healthcare pricing and spending, and therefore on revenue. Securing the effective integration of the Rare Disease unit.

Exceptional pipeline delivery, the integration of Alexion and the success of *Vaxzevria* made 2021 a momentous year for AstraZeneca.

"AstraZeneca achieved Total Revenue of $37.4 billion in 2021, with growth of 41% (CER: 38%), including $0.9 billion of Collaboration Revenue, $3.9 billion of *Vaxzevria* Product Sales and $3.1 billion of post-acquisition Alexion sales."



I am delighted to present the 2021 Financial Review. My first five months as CFO of AstraZeneca have brought many exciting highlights, including the transformative impact of *Vaxzevria* on combatting the pandemic, the integration of Alexion, 14 positive Phase III readouts in nine medicines and continued growth of our products in spite of multiple challenges. This was only possible through the hard work and dedication of all our colleagues across the globe. In all, 2021 has been a momentous year for this Company and I look forward to enabling our organisation to continue to serve patients, advance science and be a great place to work in 2022.

Strong Total Revenue growth

AstraZeneca achieved Total Revenue of $37.4 billion in 2021, with growth of 41% (CER: 38%), including $0.9 billion of Collaboration Revenue, $3.9 billion of *Vaxzevria* Product Sales and $3.1 billion of post-acquisition Alexion sales.

Product Sales grew by 41% (CER: 38%) to $36.5 billion, with 13* blockbuster medicines, including *Vaxzevria* and the newly acquired *Soliris*. Our continued investment in Oncology and CVRM medicine launches supported strong Product Sales growth of 20% (CER: 18%) and 13% (CER: 10%), respectively, with standout performances from *Tagrisso* ($5.0 billion), *Farxiga* ($3.0 billion) and *Lynparza* ($2.3 billion). In the US, we saw growth of 39%, with Product Sales of $12.0 billion, 45% of which came from Oncology, including $1.1 billion from *Calquence*. In Europe, Product Sales increased by 50% (CER: 44%) to $7.6 billion and in Emerging Markets, Product Sales of $12.2 billion continued to accelerate, with growth of 40% (CER: 36%), including *Vaxzevria* sales of $2.2 billion. Within our new Rare Disease portfolio, we recorded post-acquisition Product Sales of $3.1 billion, contributing 8% to full-year Total Revenue and represented pro rata growth of 8% (CER: 9%). Collaboration Revenue increased by 20% (CER: 20%) to $0.9 billion and included $0.4 billion of milestone income from the ongoing MSD arrangement on *Lynparza* and *Koselugo*.

Investing in future growth

We continue to make investments in the business to support our strategic objectives. Reported R&D expenses increased by 62% (CER: 59%) to $9.7 billion, including $1.5 billion of impairment charges, of which $1.2 billion relates to the discontinuation of verinurad. Core R&D expenses increased by 36% (CER: 33%) to $8.0 billion. Increases to both Core and Reported R&D expenses reflect our continued investment in our COVID-19 medicines, and in several late-stage Oncology trials and Phase II clinical development programmes in BioPharmaceuticals. Reported Selling, general and administrative expenses (SG&A) increased by 35% (CER: 32%) to $15.2 billion. These included the increased amortisation of intangible assets related to the Alexion acquisition and restructuring charges related to supply chain and exit costs for deprioritised R&D projects. Core SG&A expenses increased by 19% (CER: 15%) to $11.1 billion, reflecting our further investment in Oncology and BioPharmaceutical launches.

Strategic divestments

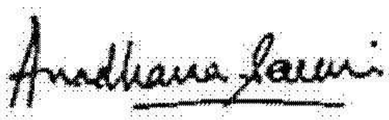
2021 Reported and Core Other operating income was $1.5 billion and included $776 million from the divestment of AstraZeneca's share of Viela Bio and $317 million from the sale of the European rights (excluding the UK, Israel and Spain) for *Crestor*, to Grünenthal.

Profitability

In 2021, Reported Operating profit declined by 80% (CER: 70%) to $1.1 billion and Core Operating profit grew by 35% (CER: 41%) to $9.9 billion. The increased difference between Reported and Core Operating profit in the year is primarily due to items related to the acquisition of Alexion, increased intangible asset impairments and restructuring charges, of which $1.0 billion relates to the Post Alexion Acquisition Group Review (PAAGR), aimed at integrating systems, structure and operations to optimise the global footprint and prioritise resource allocations and investments, following the acquisition of Alexion. Reported Basic earnings per share (EPS) was $0.08 and Core EPS was $5.29.

Our commitment to the fight against COVID-19

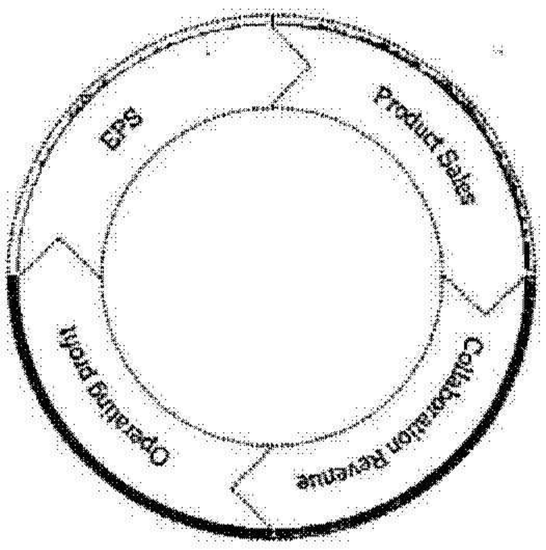
We are very proud of our contribution to fighting the COVID-19 pandemic and remain committed to delivering our vaccine. As at December 2021, AstraZeneca and its sublicensing partner remain the largest contributor to the COVAX programme, having delivered more than 247 million doses to 130 countries. Globally, AstraZeneca and its partners have released more than 2.5 billion vaccine doses, for supply in over 180 countries. Approximately two thirds of the doses have gone to low- and middle-income countries. We were also delighted to see *Evusheld* receive Emergency Use Authorisation in the US and other markets in 2021, for the pre-exposure prevention of COVID-19.



Aradhana Sarin
Chief Financial Officer

* *Calquence*'s designation as a blockbuster medicine includes full year 2021 Product Sales, inclusive of the pre-acquisition period.

Highlights
Financial performance



Product Sales

$36.5bn

Reported and Core
(2020: $25.9bn)

Collaboration Revenue

$0.9bn

Reported and Core
(2020: $0.7bn)

Operating profit

$1.1bn

80% decline – Reported
(CER: 70% decline)

$9.9bn

35% growth – Core
(CER: 41%)

EPS

$0.10

97% decline – Reported
(CER: 84%)

$5.29

32% growth – Core
(CER: 37%)

Sales platforms

Emerging Markets

40%

growth
(CER: 36%)

Japan

31%

growth
(CER: 35%)

Oncology

20%

growth
(CER: 18%)

CVRM

13%

growth
(CER: 10%)

Respiratory & Immunology

13%

growth
(CER: 9%)

Rare Disease

8%

pro rata growth*
(CER: 9%)

* Pro rata growth rates of Rare Disease medicines for the year have been calculated by comparing post-acquisition revenues from July 2021 with the corresponding prior year pre-acquisition revenues published by Alexion.

Summary performance in 2021

	Reported			CER			Core		
	2021 $m	2020 $m	% change	CER growth[1] $m	Growth due to exchange effects $m	% change	2021 $m	2020 $m	% change
Product Sales	**36,541**	25,890	**41**	9,942	709	38	**36,541**	25,890	**41**
Collaboration Revenue	**876**	727	**20**	147	2	20	**876**	727	**20**
Total Revenue	**37,417**	26,617	**41**	10,089	711	38	**37,417**	26,617	**41**
Cost of sales	**(12,437)**	(5,299)	**135**	(6,542)	(596)	123	**(9,444)**	(5,175)	**82**
Gross profit	**24,980**	21,318	**17**	3,547	115	17	**27,973**	21,442	**30**
Operating expenses	**(25,416)**	(17,684)	**44**	(7,124)	(508)	40	**(19,537)**	(15,633)	**25**
Other operating income and expense	**1,492**	1,528	**(2)**	(54)	18	(4)	**1,492**	1,531	**(3)**
Operating profit	**1,056**	5,162	**(80)**	(3,631)	(475)	(70)	**9,928**	7,340	**35**
Net finance expense	**(1,257)**	(1,219)	**3**	(21)	(17)	2	**(862)**	(782)	**10**
Share of after tax losses of joint ventures and associates	**(64)**	(27)	**137**	(36)	(1)	133	**(64)**	(27)	**137**
(Loss)/profit before tax	**(265)**	3,916	**(107)**	(3,688)	(493)	(93)	**9,002**	6,531	**38**
Taxation	**380**	(772)	**(149)**	1,066	86	(137)	**(1,494)**	(1,312)	**14**
Profit after tax	**115**	3,144	**(96)**	(2,622)	(407)	(83)	**7,508**	5,219	**44**
Basic earnings per share ($)	**0.06**	2.44	**(97)**	(2.07)	(0.29)	(84)	**5.29**	4.02	**32**

[1] As detailed on page 55. CER growth is calculated using prior year actual results adjusted for certain exchange rate effects, including hedging.

Business background and results overview

The business background is covered in the Healthcare in a Changing World section from page 7, the Disease Area Review from page 16, and the Our Strategy and Key Performance Indicators section from page 12, which describe in detail the business developments of our products.

As described earlier in this Annual Report, sales of our products are directly influenced by medical need and are generally paid for by health insurance schemes or national healthcare budgets. Our operating results can be affected by a number of factors other than the delivery of operating plans and normal competition.

Further details of the risks faced by the business are given in Risk Overview from page 48 and in the Risk supplement at www.astrazeneca.com/annualreport2021.

Over the longer term, the success of our R&D is crucial and we devote substantial resources to this area. The benefits of this investment are expected to emerge over the long-term and there is considerable inherent uncertainty as to the scale and timing of outcomes and their transition to saleable products.

Measuring performance

Reported and Core performance are referred to in this Financial Review when reporting on our performance in absolute terms, but more often in comparison to earlier years:

- **Reported performance** takes into account all the factors (including those which we cannot influence, such as currency exchange rates) that have affected the results of our business. The Consolidated Financial Statements have been prepared in accordance with UK-adopted IAS and with the requirements of the Companies Act 2006 as applicable to companies reporting under those standards. The Consolidated Financial Statements also comply fully with IFRS as issued by the IASB and IAS as adopted by the EU. On 31 December 2020, EU-adopted IFRS was brought into UK law and became UK-adopted IAS, with future changes to IFRS being subject to endorsement by the UK Endorsement Board.
- **Core performance** measures are adjusted to exclude certain significant items, using a set of established principles.

For a detailed definition of Core measures, please see page 55.

Use of non-GAAP performance measures

Core performance measures, EBITDA, Net debt, CER, Gross profit margin, Operating profit margin and Ongoing Collaboration Revenue are non-GAAP performance measures because they cannot be derived directly from the Financial Statements.

By disclosing non-GAAP performance and growth measures, in addition to our Reported financial information, we are enhancing investors' ability to evaluate and analyse the financial performance and trends of our ongoing business and the related key business drivers. The adjustments are made to our Reported financial information in order to show non-GAAP performance measures that illustrate clearly, on a year-on-year or period-by-period basis, the impact on our performance of factors such as changes in revenues and expenses driven by volume, prices and cost levels relative to such prior years or periods. These non-GAAP performance measures are not a substitute for, or superior to, financial measures prepared in accordance with GAAP.

As shown in the 2021 Reconciliation of Reported results to Core results table on page 56, our reconciliation of Reported financial information to Core performance measures includes a breakdown of the items for which our Reported financial information is adjusted, and a further breakdown by specific line item as such items are reflected in our Reported income statement. This illustrates the significant items that are excluded from Core performance measures and their impact on our Reported financial information, both as a whole and in respect of specific line items.

Management presents these results externally to meet investors' requirements for transparency and clarity. Core financial measures are also used internally in the management of our business performance, in our budgeting process and when determining compensation. As a result, Core performance measures allow investors to differentiate between different kinds of costs but they should not be used in isolation.

Readers should also refer to our Reported financial information in the Summary performance in 2021 table on page 53, our reconciliation of Core performance measures to Reported financial information in the 2021 Reconciliation of Reported results to Core results table and the Excluded from Core results table on page 56 for our discussion of comparative growth measures that reflect all factors that affect our business.

Our determination of non-GAAP measures and our presentation of them within this financial information, may differ from similarly titled non-GAAP measures of other companies.

The SET retains strategic management of the costs excluded from Reported financial information in arriving at Core financial measures, tracking their impact on Reported Operating profit and EPS, with operational management being delegated on a case-by-case basis to ensure clear accountability and consistency for each cost category.

We strongly encourage readers of this Annual Report not to rely on any single financial measure but to review our Financial Statements, including the Notes thereto, and our other publicly filed reports, carefully and in their entirety.

Non-GAAP measures: definitions

Revenue

Constant exchange rate (CER) growth rates

Reconciliation, see page 56.

Definition: Retranslation of the current year's performance at the previous year's average exchange rates, adjusted for other exchange effects, including hedging.

Why we use them: CER measures allow us to focus on the changes in revenues and expenses driven by volume, prices and cost levels relative to the prior period. Revenues and cost growth expressed in CER allow management to understand the true local movement in revenues and costs, in order to compare recent trends and relative return on investment. CER growth rates can be used to analyse revenues in a number of ways but, most often, we consider CER growth by products and groups of products, and by countries and regions.

CER revenue growth can be further analysed by revenue volumes and selling price. Similarly, CER cost growth helps us to focus on the real local change in costs so that we can manage the cost base effectively.

Limitations: CER measures are not always better indicators of performance. Where countries are subject to high inflation and currencies that depreciate persistently, adjusting out the effect of foreign exchange fluctuations could give an overly optimistic view of growth.

Ongoing Collaboration Revenue

Reconciliation, see page 59.

Definition: Collaboration Revenue excluding Initial Collaboration Revenue (which is defined as Collaboration Revenue that is recognised at the point in time control is transferred). Ongoing Collaboration Revenue comprises, among other items, milestone payments, profit sharing and royalties.

For more information, see Group Accounting Policies from page 138.

Why we use it: This measure provides us with an understanding of the ongoing value derived from our collaboration arrangements, removing any distortion driven by the upfront income.

Profitability

Core performance measures

Reconciliation, see page 56.

Core performance measures are adjusted to exclude certain significant items. In determining the adjustments to arrive at the Core result, we use a set of established principles relating to the nature or materiality of individual items or groups of items, excluding, for example, events which are (i) outside the normal course of business, (ii) incurred in a pattern that is unrelated to the trends in the underlying financial performance of our ongoing business, or (iii) related to major acquisitions, to ensure that investors' ability to evaluate and analyse the underlying financial performance of our ongoing business is enhanced.

See the 2021 Reconciliation of Reported results to Core results table on page 56 for a reconciliation of Reported to Core performance, as well as further details of the adjustments.

Our Core adjustments are summarised as:

Restructuring costs, including charges that relate to the impact of our global restructuring programmes on our capitalised manufacturing facilities and IT assets. These can take place over a significant period of time, given the long life-cycle of our business.

Why we use them: We adjust for these charges and provisions because they primarily reflect the financial impact of change to legacy arrangements, rather than the underlying performance of our ongoing business.

Intangible amortisation and impairments, including impairment reversals but excluding any charges relating to IT assets. Intangibles generally arise from business combinations and individual licence acquisitions.

Why we use them: We adjust for these charges because their pattern of recognition is largely uncorrelated with the underlying performance of the business.

Acquisition of Alexion, principally comprising acquisition-related costs related to the acquisition of Alexion.

Why we use them: We adjust for this item to enable a more meaningful comparison of the performance of acquired business and products to that of internally developed products, as well as removing charges whose pattern of recognition is largely uncorrelated to the underlying performance of the business.

Other, principally comprising acquisition-related costs, other than those associated with Alexion, credits arising from fair value adjustments, finance charges and fair value movements relating to contingent consideration on business combinations or asset acquisitions, and costs for legal settlements.

Why we use them: We adjust for these items to enable a more meaningful comparison of the performance of acquired business and products to that of internally developed products, as well as removing charges whose pattern of recognition is largely uncorrelated to the underlying performance of the business.

It should be noted that some costs excluded from our Core results, such as intangibles amortisation and finance charges related to contingent consideration, will recur in future years, and other excluded items such as impairments and legal settlements costs, along with other acquisition-related costs, may recur in the future.

Limitations: Core results exclude significant costs (such as restructuring, intangible amortisation and impairments, and other acquisition-related adjustments), but incorporate associated benefits, including Product Sales arising from business combinations, asset acquisitions and assets which have been amortised, as well as the benefits resulting from restructuring activities and, as such, they should not be regarded as a complete picture of the Group's financial performance, which is presented in its Reported results. The exclusion of the adjusting items may result in Core earnings being materially higher or lower than Reported earnings.

Gross margin percentage

Reconciliation, see page 57.

Definition: Gross Profit margin, as a percentage, by which Product Sales exceeds the Cost of sales, calculated by dividing the difference between the two by the sales figure. 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.

Why we use it: This measure sets out gross profitability of Product Sales when taking account of only direct Cost of sales. It is a key performance measure of the contribution to fund operating costs and overall quality of the business.

Limitations: Gross margin percentage excludes the impact of Collaboration Revenue and related costs and therefore should not be regarded as giving a full picture of revenue performance.

Non-GAAP measures: definitions
continued

Operating margin percentage Reconciliation, see below.	Definition: Operating profit as a percentage of Total Revenue. Why we use it: This measure sets out profitability derived from operating activities before the impact of finance costs and tax. It is a key performance measure of the overall quality of the operations of the business.	Limitations: Operating margin percentage excludes the impact of financing costs and therefore should not be regarded as a full picture of revenue performance.
EBITDA Reconciliation, see page 60.	Definition: Reported Profit before tax plus net finance expense, share of after-tax losses of joint ventures and associates, and charges for depreciation, amortisation and impairment.	Why we use it: EBITDA allows us to understand our baseline profitability, removing any 'non-operational' expenses and non-cash items that are not considered by management to be reflective of the underlying performance of the Group. Limitations: EBITDA does not take account of the cost of investment to generate revenues, hence is not always the best indicator of performance.
Cash flow and liquidity		
Net debt Reconciliation, see page 63.	Definition: Interest-bearing loans and borrowings net of Cash and cash equivalents, Other investments and Net derivative financial instruments.	Why we use it: Net debt is a measure that provides valuable additional information regarding the Group's net financial liabilities and is a measure commonly used by investors and rating agencies. It facilitates the tracking of one of our key financial priorities: deleveraging.

Summary statement of consolidated income
2021 Reconciliation of Reported results to Core results

	2021 Reported $m	Restructuring costs $m	Intangible amortisation and impairments $m	Acquisition[1] of Alexion $m	Other[2] $m	2021 Core[3] $m	Core 2021 compared with Core 2020[3]: Actual growth %	Core 2021 compared with Core 2020[3]: CER growth %
Gross profit	24,980	722	66	2,206	(1)	27,973	30	30
Product Sales gross margin %[4]	*66.0*					*74.2*		
Distribution expenses	(446)	–	–	–	–	(446)	12	7
Research and development expenses	(9,736)	223	1,496	28	2	(7,987)	36	33
Selling, general and administrative expenses	(15,234)	336	3,584	207	1	(11,104)	19	15
Other operating income and expense	1,492	–	–	–	–	1,492	(3)	(4)
Operating profit	1,056	1,283	5,146	2,441	2	9,928	35	41
Operating margin as a % of Total Revenue	*2.8*					*26.5*		
Net finance expense	(1,257)	–	–	–	395	(862)		
Taxation	380	(249)	(1,024)	(531)	(70)	(1,494)		
Basic earnings per share ($)	0.08	0.73	2.91	1.34	0.23	5.29	32	37

2020 Reconciliation of Reported results to Core results

	2020 Reported $m	Restructuring costs $m	Intangible amortisation and impairments $m	Diabetes Alliance[5] $m	Other[2] $m	2020 Core[3] $m	Core 2020 compared with Core 2019[3]: Actual growth %	Core 2020 compared with Core 2019[3]: CER growth %
Gross profit	21,318	53	66	–	5	21,442	9	10
Product Sales gross margin %[4]	*79.5*					*80.0*		
Distribution expenses	(399)	–	–	–	–	(399)	18	19
Research and development expenses	(5,991)	35	84	–	–	(5,872)	10	10
Selling, general and administrative expenses	(11,294)	162	1,657	310	(197)	(9,362)	3	4
Other operating income and expense	1,528	1	2	–	–	1,531	(2)	(2)
Operating profit	5,162	251	1,809	310	(192)	7,340	14	17
Operating margin as a % of Total Revenue	*19.4*					*27.6*		
Net finance expense	(1,219)	–	–	228	209	(782)		
Taxation	(772)	(50)	(376)	(127)	13	(1,312)		
Basic earnings per share ($)	2.44	0.15	1.10	0.31	0.02	4.02	15	18

[1] In 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.
[2] See Excluded from Core results table below for further details of other adjustments.
[3] Each of the measures in the Core columns is a non-GAAP measure.
[4] Gross margin as a percentage of Product Sales reflects Gross profit derived from Product Sales, divided by Product Sales.
[5] In previous years, a separate column had been included for items pertaining to the Diabetes Alliance between AstraZeneca and Bristol-Myers Squibb Company (BMS). From 2021, this column has been removed with amounts now presented in the Intangible asset amortisation and impairments and the Other columns as applicable.

Excluded from Core results

Restructuring costs	> Restructuring costs totalling $1,283 million (2020: $251 million) mainly comprise those incurred on the PAAGR ($1,030 million) and the Global Post Pandemic New Ways of Working Programme ($108 million).
Intangible amortisation and impairments	> Amortisation totalling $3,080 million (2020: $1,511 million) relating to intangible assets, except those related to IT. This includes amortisation on intangible assets recognised at fair value on the acquisition of Alexion. Further information on our intangible assets is contained in Note 10 to the Financial Statements, from page 156. > Intangible impairment charges of $2,067 million (2020: $240 million), excluding those related to IT, include the impact of an impairment charge of $1,172 million recognised on an intangible asset related to the acquisition of Ardea, following the decision to discontinue the development of verinurad and $469 million recognised on *Bydureon*. Further details relating to intangible asset impairments are included in Note 10 to the Financial Statements, from page 156.
Acquisition of Alexion	> Costs associated with our acquisition of Alexion in July 2021 amounting to $2,441 million (2020: $nil), primarily relating to the impact from 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 in line with revenues, resulting in a lower gross margin in the first turn of inventory. The impact of this unwind on Cost of sales in the year was $2,198 million. > 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.
Other	> Other adjustments amounted to $397 million (2020: $17 million). > Other adjustments to Reported SG&A expenses were $1 million, including net legal provisions of $48 million (2020: credit of $9 million) and $14 million (2020: credit of $272 million) net fair value adjustments relating to contingent consideration balances, offset by $61 million (2020: $nil) of fair value adjustments relating to Other Payables. Further details relating to contingent consideration balances are contained in Note 20, from page 166 and further details of legal proceedings, ongoing at year end, are contained within Note 30 to the Financial Statements from page 190. > Other adjustments to Net finance expense of $395 million (2020: $209 million) relate to discount unwind charges on liabilities arising from business combinations.

Sales platforms

	2021 Product Sales $m	2020 Product Sales $m	Actual growth %	CER growth %
Total sales platform Product Sales	**34,215**	24,288	**39**	**37**
Individual sales platform Product Sales (certain Product Sales are included in more than one sales platform)				
Emerging Markets	**12,161**	8,679	**40**	**36**
Japan	**3,416**	2,600	**31**	**35**
Oncology	**13,048**	10,850	**20**	**18**
CVRM[1]	**8,020**	7,096	**13**	**10**
Respiratory & Immunology	**6,034**	5,357	**13**	**9**
Rare Disease	**3,070**	–	–	–
Reconciliation to Note 1 Revenue (page 145) as follows:				
Sum of individual sales platforms	**45,749**	34,582		
Add: Product Sales not included in sales platforms	**2,326**	1,170		
Less: Product Sales double-counted for Emerging Markets				
Oncology	**(3,223)**	(2,906)		
Respiratory & Immunology	**(1,749)**	(1,599)		
CVRM[1]	**(3,780)**	(3,203)		
Rare Disease	**(196)**	–		
Less: Product Sales double-counted for Japan				
Oncology	**(1,665)**	(1,514)		
Respiratory & Immunology	**(284)**	(328)		
CVRM[1]	**(363)**	(141)		
Rare Disease	**(274)**	–		
Total Product Sales	**36,541**	25,890		

[1] CVRM has replaced New CVRM for 2021 and the 2020 comparative has been restated to include all CVRM products.

Revenue

Total Revenue for 2021 was up 41% (CER: 38%) to $37,417 million, comprising Product Sales of $36,541 million, up 41% (CER: 38%), and Collaboration Revenue of $876 million, an increase of 20% (CER: 20%). Total Revenue includes Alexion sales from 21 July 2021, which contributed 8% of Product Sales for the year.

Product Sales

By Geography

Product Sales in Emerging Markets continued to increase, with growth of 40% (CER: 36%) to $12,161 million in 2021. China Product Sales increased by 12% (CER: 4%) to $5,995 million. Product Sales in ex-China Emerging Markets increased by 85% in the year (CER: 86%) to $6,166 million, driven by Oncology medicines and *Farxiga*. US Product Sales were up 39% to $12,000 million, reflecting the success of our Oncology medicines. In Europe, Product Sales grew by 50% (CER: 44%) to $7,604 million, reflecting a strong performance in Oncology, which increased by 28% (CER: 22%) in the year. Established Rest of World Product Sales increased by 36% (CER: 36%) to $4,776 million, with sales in Japan up 31% (CER: 35%) to $3,416 million.

By Product

2021 succeeded in delivering 13[2] blockbuster drugs, including *Vaxzevria* and the newly acquired *Soliris*.

Our largest-selling products in the year were *Tagrisso* ($5,015 million), *Farxiga* ($3,000 million), *Symbicort* ($2,728 million), *Imfinzi* ($2,412 million), and *Lynparza* ($2,346 million). *Tagrisso* sales grew by 16% (CER: 13%) reflecting a strong performance across all markets. *Farxiga* sales increased by 53% (CER: 49%), with growth across all markets including an increase of 74% (CER: 70%) in Emerging Markets. Global sales of *Symbicort* were flat in the year (CER: decline of 2%) with continued growth in the US of 4% offset by declines in Europe and Japan. *Imfinzi* Product Sales grew by 18% (CER: 16%), with recent regulatory approvals and launches in China and continued growth in other markets. *Lynparza* Product Sales delivered a strong performance in all markets, with launches continuing globally, and generated total growth of 32% (CER: 30%) in the year. In addition, *Calquence* achieved blockbuster status for the first time in 2021, with sales of $1,238 million, predominantly in the US.

Following the acquisition of Alexion in 2021, our new Rare Disease portfolio generated 8% of Product Sales, including $1,874 million from *Soliris*.

Our COVID-19 medicines, including *Evusheld*, delivered Total Product Sales of $4,002 million, $2,259 million of which came from Emerging Markets.

Sales platforms

Our sales platforms include products in our four main disease areas (including for 2021 our newly acquired Rare Disease disease area), and a focus on Emerging Markets and Japan. Sales platforms grew by 39% (CER: 37%), representing 91% of Total Revenue after removing the effect of certain Product Sales which are included in more than one sales platform.

Emerging Markets

Product Sales in Emerging Markets grew by 40% (CER: 36%) to $12,161 million, mainly driven by strong performances from Oncology, CVRM and *Vaxzevria*. Product Sales in China increased by 12% in 2021 (CER: 4%), representing 49% of Emerging Markets Product Sales in the year.

Japan

Japan Product Sales grew by 31% (CER: 35%) to $3,416 million, with Oncology making up 49% of Japan sales with growth of 10% (CER: 12%).

Oncology

Product Sales of Oncology medicines grew by 20% (CER: 18%) to $13,048 million in 2021, $5,015 million of which came from *Tagrisso* (2020: $4,328 million), which continues to be our leading medicine for the treatment of lung cancer and had received regulatory approval in more than 69 countries by the end of 2021.

CVRM

CVRM grew by 13% (CER: 10%) with Product Sales of $8,020 million, mainly reflecting the strong performance of *Farxiga* with global sales of $3,000 million, representing growth of 53% (CER: 49%) as it continued to be our largest-selling CVRM medicine.

Respiratory & Immunology

Product Sales of Respiratory & Immunology medicines grew by 13% (CER: 9%) to $6,034 million, with growth from *Fasenra* and a sustained performance by *Symbicort*.

Rare Disease

Our newly acquired Rare Disease medicines achieved post-acquisition sales of $3,070 million and generated 8% of Product Sales, including $1,874 million from *Soliris*.

[2] *Ultomiris*' designation as a blockbuster medicine includes full-year 2021 Product Sales, inclusive of the pre-acquisition period.

Collaboration Revenue

Details of our significant business development transactions which give rise to Collaboration Revenue are given below:

Nexium Authorised Generics

In June 2021, AstraZeneca entered into an agreement with an authorised generic for the outlicense of the rights to *Nexium* Authorised Generics in Japan.

- AstraZeneca has received consideration of $150 million (16.5 billion Japanese Yen) from an authorised generic, of which 50% ($75 million) has been recognised as Collaboration Revenue for 2021, with the remaining 50% being deferred to the balance sheet as a financial liability. The recognition of $75 million as Collaboration Revenue is contingent upon regulatory approval (or potential repayment if the product does not achieve regulatory approval), which is currently expected in 2022.

Zoladex (TerSera)

In March 2017, AstraZeneca entered into an agreement with TerSera for the commercial rights to *Zoladex* in the US and Canada. TerSera paid $250 million upon completion of the transaction. The Group will also receive sales-related income totalling up to $70 million through milestones, as well as recurring quarterly sales-based payments at a mid-teen percentage of Product Sales. AstraZeneca will also manufacture and supply *Zoladex* to TerSera, providing a further source of ongoing income from *Zoladex* in the US and Canada.

Collaboration Revenue in respect of this agreement has been recognised as follows:

- Prior to 2021, AstraZeneca recognised Collaboration Revenue in respect of sales-related milestones totalling $70 million.
- No Collaboration Revenue was recognised in respect of this agreement in 2021.

Daiichi Sankyo

In March 2019, AstraZeneca announced it had entered into an alliance with Daiichi Sankyo to develop and commercialise *Enhertu* for multiple cancer types. In markets where Daiichi Sankyo is selling the product, AstraZeneca is entitled to receive a royalty (in Japan) or a share of costs and income (in other territories). Royalty income and the AstraZeneca share of gross margin from sales made by Daiichi Sankyo are recognised as Collaboration Revenue. *Enhertu* launched in the US on 31 December 2019.

Collaboration Revenue

	2021 $m	2020 $m
Initial Collaboration Revenue		
Nexium Authorised Generics	75	–
Total Initial Collaboration Revenue	**75**	**–**
Ongoing Collaboration Revenue		
Lynparza/selumetinib (MSD) – milestone	400	460
Enhertu (Daiichi Sankyo) – share of gross profits	193	94
Roxadustat (FibroGen) – share of gross profits	6	30
Zoladex (TerSera) – milestone	–	35
Royalty income	138	62
Other	64	46
Total Ongoing Collaboration Revenue	**801**	**727**
Total Collaboration Revenue	**876**	**727**

Collaboration Revenue in respect of this agreement has been recognised as follows:

- Prior to 2021, AstraZeneca recognised Collaboration Revenue of $94 million in relation to AstraZeneca's share of gross profits arising from sales made by Daiichi Sankyo.
- In 2021, AstraZeneca recognised Collaboration Revenue of $193 million in relation to AstraZeneca's share of gross profits arising from sales made by Daiichi Sankyo.

FibroGen

In July 2013, AstraZeneca entered into a strategic collaboration with FibroGen to develop and commercialise roxadustat, a first-in-class oral compound in late-stage development for the treatment of anaemia from chronic kidney disease and end-stage renal disease (ESRD). Under the arrangement, AstraZeneca agreed to pay FibroGen upfront and subsequent non-contingent payments totalling $350 million, as well as potential development-related milestone payments of up to $465 million, and potential future sales-related milestone payments, in addition to tiered royalty payments on future sales of roxadustat in the low 20% range. Additional development milestones will be payable for any subsequent indications which the companies choose to pursue.

Collaboration Revenue in respect of this agreement has been recognised as follows:

- Prior to 2021, Collaboration Revenue of $30 million was recognised in relation to AstraZeneca's share of gross profits arising from sales made by FibroGen.
- In 2021, Collaboration Revenue of $6 million was recognised in relation to AstraZeneca's share of gross profits arising from sales made by FibroGen.

Lynparza/selumetinib (MSD)

In July 2017, the Group announced a global strategic oncology collaboration with MSD to co-develop and co-commercialise AstraZeneca's *Lynparza* for multiple cancer types. As part of the agreement, MSD will pay AstraZeneca up to $8.5 billion in total consideration, including $1.6 billion upfront, $750 million for certain licence options and up to $6.2 billion contingent upon successful achievement of future regulatory and sales milestones. Of the upfront payment of $1.6 billion, $1.0 billion was recognised as Collaboration Revenue on deal completion in 2017, with the remaining $0.6 billion deferred to the balance sheet. AstraZeneca books all Collaboration Revenue of *Lynparza* and selumetinib; gross profits due to MSD under the collaboration will be recorded under Cost of sales.

Collaboration Revenue in respect of this agreement has been recognised as follows:

- Prior to 2021, AstraZeneca recognised Collaboration Revenue totalling $2,110 million, comprising $750 million resulting from the exercise of options, $1.0 billion in respect of sales-related milestones and $360 million in respect of regulatory milestones.
- In 2021, net sales of *Lynparza* reached the $2.0 billion annual sales threshold, triggering a sales-related milestone of $400 million due to AstraZeneca, recognised as Collaboration Revenue for 2021.

Gross profit

Reported Gross profit increased by 17% (CER: 17%) to $24,980 million. Core Gross profit increased by 30% (CER: 30%) to $27,973 million. Reported Gross Profit margin declined 14 (CER: 13) percentage points to 66.0% due to the impact of restructuring charges and the unwind of the fair value adjustment to the Alexion inventory at the date of acquisition. Core Gross Profit margin declined six (CER: five) percentage points, reflecting the equitable supply of *Vaxzevria*, partially offset by Alexion's contribution from July 2021 and growth in Oncology sales.

Operating expenses

Reported Total Operating expenses increased by 44% (CER: 40%) in the year to $25,416 million. Core Total Operating expenses increased by 25% (CER: 22%) to $19,537 million.

Reported R&D expenses increased by 62% (CER: 59%) to $9,736 million and Core R&D expenses increased by 36% (CER: 33%) to $7,987 million. The increase in both Reported and Core R&D expenses reflects the Group's continued investment in *Vaxzevria* and *Evusheld*, as well as investment in several late-stage Oncology trials and the advancement of a number of Phase II clinical development programmes in BioPharmaceuticals. Reported R&D expenses also includes intangible asset impairment charges recognised in the year of $1,464 million, of which $1,172 million related to the impairment of verinurad.

Reported SG&A expenses increased by 35% (CER: 32%) to $15,234 million and Core SG&A expenses increased by 19% (CER: 15%) to $11,104 million. The increase to Reported SG&A expenses includes the increased amortisation of intangible assets related to the Alexion acquisition. Core SG&A expenses growth reflects the investment in Oncology medicine launches, the launch of several new BioPharmaceutical medicines and further expansion into Emerging Markets.

Reconciliation of Reported Profit before tax to EBITDA

	2021 $m	2020 $m	Actual growth %	CER growth %
Reported (Loss)/profit before tax	(265)	3,916	n/m	(93)
Net finance expense	1,257	1,219	3	2
Share of after tax losses of joint ventures and associates	64	27	n/m	n/m
Depreciation, amortisation and impairment	6,530	3,149	n/m	99
EBITDA	7,586	8,311	(9)	(6)

Other operating income and expense

Reported and Core Other operating income and expense in the year was down 2% (CER: 4%) to $1,492 million and includes $776 million from the divestment of AstraZeneca's share in Viela Bio and $317 million from the sale of the European rights, excluding Israel, Spain and UK, for *Crestor* to Grünenthal.

In accordance with our Collaboration Revenue definition in the Group Accounting Policies from page 138 and the requirements of IFRS 15 'Revenue from Contracts with Customers', proceeds from these divestments are recorded as Other operating income and expense and comprise the majority of Other operating income and expense for the year.

Operating profit

Reported Operating profit declined by 80% (CER: 70%) to $1,056 million in the year. The Reported Operating margin decreased by 17 percentage points (CER: 15 percentage points) to 3% of Total Revenue. Core Operating profit grew by 35% (CER: 41%) in the year to $9,928 million. The Core Operating profit margin decreased by one percentage point (CER: increase of one percentage point) to 27% of Total Revenue.

Net finance expense

Reported Net finance expense increased by 3% (CER: 2%) in the year to $1,257 million. Core Net finance expense increased by 10% (CER: 11%) in the year to $862 million. The increase to both Reported and Core Net finance expense was driven by lower interest income on short-term deposits from lower interest rates and increased financing costs related to the facilities to fund the Alexion acquisition.

Profit before tax

Reported (Loss)/profit before tax decreased by 107% (CER: 93%) in 2021 to a loss of $265 million (2020: profit of $3,916 million). Core Profit before tax increased by 38% (CER: 43%) to $9,002 million. Pre-tax adjustments to arrive at Core Profit before tax amounted to $9,267 million in 2021 (2020: $2,615 million), comprising $8,872 million adjustments to Operating profit (2020: $2,178 million) and $395 million to Net finance expense (2020: $437 million).

EBITDA

EBITDA decreased by 9% (CER: 6%) to $7,586 million in the year (2020: $8,311 million) and was negatively impacted by the $2,198 million unwind of inventory fair value uplift recognised on the acquisition of Alexion, as well as increased restructuring charges arising from the PAAGR.

Taxation

The Reported Tax rate for the year was 143% and the Core tax rate in the year was 17%. The income tax paid for the year was $1,743 million. This was $2,123 million higher than the Reported tax charge for the year, which benefited from a net deferred tax credit of $1,575 million (2020: $199 million), relating to the acquisition of Alexion, intangible amortisation and impairments and other deferred tax items, partially offset by a net $51 million deferred tax charge reflecting the change in Dutch and UK income tax rates, updates to estimates of prior period tax liabilities following settlements with tax authorities and on expiry of statute of limitations and other cash tax timing differences. Additional information on these items is contained in Note 4 to the Financial Statements from page 149.

We pay corporate income taxes, customs duties, excise taxes, stamp duties, employment and many other business taxes in all jurisdictions where applicable. In addition, we collect and pay employee taxes and indirect taxes such as value added tax.

Total comprehensive income

Total comprehensive loss/income decreased by $4,782 million to a loss of $30 million in 2021. Other comprehensive loss for the period, net of tax, was $145 million, a decrease of $1,753 million. The decrease was primarily driven by Foreign exchange arising on consolidation losses of $483 million (2020: gains of $443 million). Foreign exchange arising on designated borrowings in net investment hedges losses of $321 million (2020: gains of $573 million). Net losses on equity investments measured at fair value through Other comprehensive income of $187 million (2020: gains of $938 million), offset by Remeasurement of the defined benefit pension liability gains of $626 million (2020: losses of $168 million). A significant proportion of the prior year Net gains/(losses) on equity investments measured at fair value through Other comprehensive income relates to gains recognised during 2020 from the sale of AstraZeneca's full holding in Moderna as detailed in Note 12 of the Financial Statements from page 160.

EPS

Reported EPS of $0.08 in the year was a decrease of 97% (CER: 84%). Core EPS increased by 32% (CER: 37%) to $5.29.

Restructuring

Post Alexion Acquisition Group Review

In conjunction with the acquisition of Alexion, the enlarged Group has initiated a comprehensive PAAGR, aimed at integrating systems, structure and processes, optimising the global footprint and prioritising resource allocations and investments. These activities are expected to be substantially complete by the end of 2025, with a number of planned activities having commenced in late 2021.

The identified activities, including those previously announced regarding the integration of Alexion, are anticipated to incur one-time restructuring costs of approximately $2.1 billion, of which approximately $1.4 billion are cash costs and $0.7 billion are non-cash costs, and capital investments of approximately $0.2 billion. The activities are anticipated to realise run-rate pre-tax benefits, before reinvestment, of approximately $1.2 billion, including previously-announced Alexion synergies, by the end of 2025. In line with established practice, restructuring costs will be excluded from our Core (non-GAAP) financial measures.

During 2021, the Group has recorded restructuring charges of approximately $1.0 billion in relation to the PAAGR. These costs primarily arise from the rationalisation of our manufacturing capacity and footprint, de-prioritisation of various development projects and re-negotiation of manufacturing capacity agreements as well as severance costs.

Other programmes

The Group has also continued to progress the Global Post Pandemic New Ways of Working programme initiated in 2020 in response to the changing business environment, accelerated by the COVID-19 pandemic. This programme is expected to run until the end of 2022 and incorporates the increasing utilisation of digitisation and technology, as well as the new ways of working that reflect the size, nature and footprint of commercial teams, enabling functions, R&D and operations. $108 million of costs were incurred under this programme in 2021.

Legacy programmes include: the 2016 plan to redeploy investment to key disease areas, particularly Oncology; the phase 3/4 plan regarding the centralisation of our global R&D footprint into three strategic centres; transformation of the IT organisation and closure of a number of manufacturing facilities; and the transformation of SG&A functions (principally Finance and HR). $145 million of costs were incurred under legacy programmes in 2021.

The aggregate restructuring charge incurred in 2021 across all our restructuring programmes was $1,283 million (2020: $251 million). Final estimates for programme costs, benefits and headcount impact in all functions are subject to completion of the requisite consultation in the various areas.

Our priority, as we undertake these restructuring initiatives, is to work with our affected employees on the proposed changes, acting in accordance with relevant local consultation requirements and employment law.

Brexit

The UK left the EU on 31 January 2020 with a transition period running to 31 December 2020. In response to the UK referendum outcome, the Group implemented appropriate actions to mitigate the potential risk of disruption to supply chains due to new border processes (including the additional UK documentation requirements introduced on 1 January 2022) and potential port congestion. To date, we have seen no significant disruption to our supply chain.

Summary cash flows

	2021 $m	2020 $m	2019 $m
Net debt brought forward at 1 January	**(12,110)**	(11,904)	(13,003)
(Loss)/profit before tax	**(265)**	3,916	1,548
Sum of changes in interest, depreciation, amortisation, impairment and share of after tax losses on joint ventures and associates	**7,851**	4,395	5,138
Decrease/(increase) in working capital and short-term provisions	**2,021**	361	(346)
Tax paid	**(1,743)**	(1,562)	(1,118)
Interest paid	**(721)**	(733)	(774)
Gains on disposal of intangible assets	**(513)**	(1,030)	(1,243)
Gains on disposal of joint ventures and associates	**(776)**	–	–
Fair value movements on contingent consideration arising from business combinations	**14**	(272)	(614)
Non-cash and other movements	**95**	(276)	378
Net cash available from operating activities	**5,963**	4,799	2,969
Disposal of intangibles (net of purchases)	**(522)**	(694)	595
Acquisition of subsidiaries, net of cash acquired	**(9,263)**	–	–
Net borrowings acquired from subsidiaries	**(2,779)**	–	–
Share-based payments attributable to business combinations	**(211)**	–	–
Payment of contingent consideration from business combinations	**(643)**	(822)	(709)
Other capital (expenditure)/ income (net)	**(569)**	399	(1,016)
Investments	**(13,987)**	(1,117)	(1,130)
Dividends	**(3,856)**	(3,572)	(3,592)
Proceeds from the issue of share capital	**29**	30	3,525
Distributions	**(3,827)**	(3,542)	(67)
Lease liabilities: IFRS 16	**(240)**	(207)	(675)
Other movements	**(121)**	(139)	2
Net debt carried forward at 31 December	**(24,322)**	(12,110)	(11,904)

Bonds issued in 2021 and 2020

	Repayment dates	Face value of bond $m	Net book value of bond at 31 December 2021 $m
Bonds issued in 2021:			
0.3% USD bond	2023	1,400	**1,397**
0.7% USD bond	2024	1,600	**1,598**
1.2% USD bond	2026	1,250	**1,245**
1.75% USD bond	2028	1,250	**1,244**
0.375% EUR bond	2029	975	**898**
2.25% USD bond	2031	750	**746**
3% USD bond	2051	750	**734**
Total 2021		7,975	**7,862**
Bonds issued in 2020:			
0.7% USD bond	2026	1,200	**1,192**
1.375% USD bond	2030	1,300	**1,291**
2.125% USD bond	2050	500	**486**
Total 2020		3,000	**2,969**

Cash flow and liquidity – for the year ended 31 December 2021

Net cash generated from operating activities was $5,963 million (2020: $4,799 million).

Net investment cash outflows were $13,987 million (2020: $1,117 million).

Investment cash outflows for 2021 include:

- an upfront payment of $9,263 million and $2,779 million in net borrowings in respect of the acquisition of Alexion,
- payments of contingent consideration from business combinations of $643 million (2020: $822 million), and
- $1,109 million (2020: $1,645 million) for the purchase of intangible assets, including $340 million of regulatory milestones and a $150 million consideration payment to Daiichi Sankyo for *Enhertu*, the first staged upfront payment of $325 million to Daiichi Sankyo for DS-1062 and an upfront payment of $200 million to Ionis Pharmaceuticals, Inc. for eplontersen.

Investment cash inflows include:

- $587 million from the sale of intangible assets, mainly driven by $317 million from the sale of the European rights, excluding Israel, Spain and UK for *Crestor* to Grünenthal, and
- $776 million from the divestment of AstraZeneca's share of Viela Bio.

Net cash distributions to shareholders were $3,827 million (2020: $3,542 million), including proceeds from the issue of share capital of $29 million (2020: $30 million) less dividends paid of $3,856 million (2020: $3,572 million).

Bonds

In May 2021, AstraZeneca issued $7.0 billion of bonds in the US dollar debt capital markets with maturities from 2023 to 2051. A further 800 EUR million was issued in June 2021 under the Euro Medium Term Note programme with a maturity of 2029. In 2021, AstraZeneca repaid a 500 EUR million 0.250% bond, which matured in May 2021 and a 750 EUR million 0.875% bond, which matured in November 2021.

Net debt

At 31 December 2021, outstanding gross debt (interest-bearing loans and borrowings) was $30,781 million (2020: $20,380 million). Of the gross debt outstanding, $1,893 million is due within one year (2020: $2,386 million). On 1 January 2019, the Group adopted IFRS 16, which eliminates the classification of leases as either operating or finance leases. The adoption of the new standard resulted in the initial recognition of Lease liabilities of $720 million at the start of 2020. Net debt at 31 December 2021 was $24,322 million, compared with $12,110 million at the beginning of the year, primarily due to the financing of the Alexion acquisition.

At 31 December 2021, Cash and cash equivalents and liquid investments totalled $6,398 million (2020: $7,992 million). The Group has committed bank facilities of $4,675 million available to manage liquidity. The commitments mature in April 2025. All facilities contain no financial covenants and were undrawn at 31 December 2021. The Group regularly monitors the credit standing of the banking group and currently does not anticipate any issue with drawing on the committed facilities should this be necessary. Advances under these facilities currently bear an interest rate per annum based on the LIBOR (or other relevant benchmark rate) plus a margin. The facilities contain arrangements to switch to alternative risk free rate benchmarks before June 2023.

In respect of AstraZeneca's announcement on 12 December 2020 to acquire Alexion, the Company entered into $17.5 billion of committed bank facilities. $13.5 billion of these facilities were cancelled in June. July and October 2021 and $4.0 billion were drawn under the term loan facilities during July 2021. $1.0 billion of these term loans was subsequently repaid, using the proceeds of a new bank term loan.

Net debt reconciliation

	2021 $m	2020 $m	2019 $m
Cash and cash equivalents	6,329	7,832	5,369
Other investments[1]	69	160	911
Cash and investments	6,398	7,992	6,280
Overdraft and short-term borrowings	(387)	(658)	(225)
Lease liabilities[2]	(987)	(681)	(675)
Current instalments of loans and borrowings	(1,273)	(1,536)	(1,597)
Loans due after one year	(28,134)	(17,505)	(15,730)
Loans and borrowings	(30,781)	(20,380)	(18,227)
Net derivative financial instruments	61	278	43
Net debt[3]	(24,322)	(12,110)	(11,904)

1 Other investments exclude non-current investments, which are included within the balance of $1,168 million (2020: $1,108 million) in the Consolidated Statement of Financial Position on page 135.
2 Included in the Net debt reconciliation for 2021 are Lease liabilities of $987 million (2020: $681 million), which arose on the adoption of IFRS 16 on 1 January 2019. See Group Accounting Policies from page 136 and Note 8 on page 155 for more information.
3 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 put option of $2,458 million (2020: $2,297 million) shown as $920 million in current Other payables and $1,538 million in non-current Other payables.

Summary statement of financial position – 31 December

All data in this section are on a Reported basis.

	2021 $m	Movement $m	2020 $m	Movement $m	2019 $m
Property, plant and equipment	9,183	932	8,251	563	7,688
Right-of-use assets	988	322	666	19	647
Goodwill and intangible assets	62,489	29,697	32,792	291	32,501
Assets held for sale	368	368	–	(70)	70
Inventories	8,983	4,959	4,024	831	3,193
Trade and other receivables	10,539	2,797	7,742	1,241	6,501
Net deferred tax (liabilities)/assets	(1,876)	(2,396)	520	292	228
Trade and other payables	(23,871)	(2,002)	(21,869)	(1,591)	(20,278)
Provisions	(1,724)	(164)	(1,560)	4	(1,564)
Net income tax payable	(253)	510	(763)	313	(1,076)
Retirement benefit obligations	(2,454)	748	(3,202)	(395)	(2,807)
Non-current other investments	1,168	60	1,108	(231)	1,339
Investments in associates and joint ventures	69	30	39	(19)	58
Net debt	(24,322)	(12,212)	(12,110)	(206)	(11,904)
Net assets	39,287	23,649	15,638	1,042	14,596

Financial position – 31 December 2021

All data in this section are on a Reported basis.

Property, plant and equipment

In 2021, Property, plant and equipment increased by $932 million to $9,183 million, with the increase primarily due to the assets acquired on the Alexion acquisition.

Business combinations

On 21 July 2021, AstraZeneca completed the acquisition of 100% of the issued shares of Alexion, a US-based global biopharmaceutical company focused on serving patients affected by rare diseases for a consideration of $41,058 million.

The acquisition has been accounted for as a business combination using the acquisition method of accounting in accordance with IFRS 3 'Business Combinations'.

For full details of the acquisition, please see Note 27 from page 176.

No business acquisitions were made in 2020 or 2019.

Goodwill and intangible assets

Goodwill increased by $8,152 million in the year to $19,997 million, principally on the acquisition of Alexion. Intangible assets amounted to $42,492 million at 31 December 2021 (2020: $20,947 million), an increase of $21,545 million. The increase was largely due to intangible asset additions with a value of $27 billion assumed as part of the Alexion acquisition, offset by amortisation of $3,143 million (2020: $1,992 million) and net impairment charges of $2,428 million (2020: $253 million) including impairments on verinurad ($1,172 million) and *Bydureon* ($469 million).

Further details of additions to Intangible assets, and impairments recorded, are included in Note 10 to the Financial Statements from page 156.

Payments due by period

	Less than 1 year $m	1-3 years $m	3-5 years $m	Over 5 years $m	Total 2021 $m	Total 2020 $m
Bank loans and other borrowings[1]	2,368	10,889	5,561	19,727	38,545	27,783
Lease liabilities[2]	233	339	205	210	987	738
Contracted capital expenditure	–	–	–	388	388	689
Total	2,601	11,228	5,766	20,325	39,920	29,210

1 Bank loans and other borrowings include interest charges payable in the period, as detailed in Note 28 to the Financial Statements from page 180.
2 Lease liabilities arose on the adoption of IFRS 16 on 1 January 2019. See Note 8 from page 155 for more information

Receivables, payables and provisions

Total current and non-current Trade and other receivables increased by $2,797 million to $10,539 million in the year, driven by balances assumed on the acquisition of Alexion.

Total current and non-current Trade and other payables increased by $2,002 million in 2021 to $23,871 million. The increase was mainly driven by the recognition of the Alexion payables.

Provisions increased by $164 million to $1,724 million in 2021.

Further details of the charges made against provisions are contained in Notes 21 and 30 to the Financial Statements from pages 167 and 189 respectively.

The divestment of the US rights to *Synagis*, which completed in 2019, includes $437 million held as a financial liability (2020: $150 million). AstraZeneca will also receive $175 million following the submission of the Biologics Licence Application for MEDI8897 and potential net payments of $110 million for other MEDI8897 profit-related milestone payments. A non-contingent payment of $20 million for MEDI8897 was received during the year.

Contingent consideration

Some of our past business combinations have included elements of consideration that are contingent on future development milestones, sales milestones and/or royalties. Such future payment liabilities are held at fair value on the Consolidated Statement of Financial Position. The Group's most significant Contingent consideration balance relates to our 2014 acquisition of BMS's interest in our global diabetes alliance and includes sales-related royalties up until 2025.

Further details of the current position, movement in the year and the maximum future milestones in relation to Contingent consideration can be found in Note 20 to the Financial Statements from page 166.

Tax payable and receivable

Net income tax payable has decreased by $510 million (2020: $313 million) to $253 million, principally due to cash tax timing differences and updates to estimates of prior period tax liabilities following settlements with tax authorities and on expiry of statute of limitations. The tax receivable balance of $663 million (2020: $364 million) principally relates to cash tax timing differences.

Net deferred tax assets decreased by $2,396 million (2020: increase of $292 million) in the year, resulting in a Net deferred tax liability of $1,876 million, principally due to the Net deferred tax liability recorded on the acquisition of Alexion, partially offset by movements in deferred tax associated with intangible amortisation and impairments, and the change in Dutch and UK income tax rates.

Additional information on the movement in deferred tax balances is contained in Note 4 to the Financial Statements from page 149.

Defined benefit plan obligations

In terms of the Group's major defined benefit plans, approximately 90% of total defined benefit obligations (or around 71% of net obligations) are concentrated in the UK, the US and Sweden. The UK and US plans are largely legacy arrangements, as they have been closed to new entrants since 2000. In line with local regulations, the collectively bargained Swedish pension plan remains open to employees born before 1979.

Net defined benefit obligations decreased by $748 million in 2021 (2020: increase of $395 million) to $2,454 million. The decrease was driven by actuarial remeasurements of $626 million from higher discount rate assumptions in all major countries, partially offset by higher future inflation expectations, which decreased liability valuations, together with higher than expected investment performance, which increased asset values. A further $110 million remeasurement was due to exchange rate movements, caused by a strengthening USD against GBP, SEK and Euro which reduced deficits in USD terms. Group cash contributions over the year totalled $174 million.

Over the past few years, the Group has undertaken several liability management initiatives to reduce net defined benefit obligations and manage associated long-term financial risks.

Further details of our accounting for post-retirement benefit plans are included in Note 22 to the Financial Statements from page 168.

Commitments and contingencies

We have commitments and contingencies which are accounted for in accordance with the accounting policies described in the Financial Statements in the Group Accounting Policies section from page 138.

We also have taxation contingencies. These are described in the Taxation section in the Critical accounting policies and estimates section from page 66 and in Note 30 to the Financial Statements from page 189.

Off-balance sheet transactions and commitments

We have no off-balance sheet arrangements and our derivative activities are non-speculative. The table on this page sets out our minimum contractual obligations at the year end.

Research and development collaboration payments

Details of future potential R&D collaboration payments are also included in Note 30 to the Financial Statements on page 189. As detailed in Note 30, payments to our partners may not become payable due to the inherent uncertainty in achieving the development and revenue milestones linked to the future payments. We may enter into further collaboration projects in the future that may include milestone payments and as certain milestone payments fail to crystallise due to, for example, development not proceeding, they may be replaced by potential payments under new collaborations.

Investments, divestments and capital expenditure

We have completed more than 75 major or strategically important business development transactions over the past three years.

In addition to the business development transactions detailed under Collaboration Revenue from page 59 of this Financial Review, the following significant collaborations remain in the development phase:

Daiichi Sankyo

> In July 2020, AstraZeneca entered into a new global development and commercialisation agreement with Daiichi Sankyo for DS-1062, their proprietary trophoblast cell-surface antigen 2 (TROP2)-directed ADC and potential new medicine for the treatment of multiple tumour types. AstraZeneca agreed to pay Daiichi Sankyo an upfront payment of $1 billion in staged payments: $350 million was due upon completion, with $325 million after 12 months and $325 million after 24 months from the effective date of the agreement. AstraZeneca also agreed to pay additional conditional amounts of up to $1 billion for the successful achievement of regulatory approvals and up to $4 billion for sales-related milestones. The transaction was accounted for as an intangible asset acquisition, recognised initially at the present value of non-contingent consideration, with any potential future milestone payments capitalised into the intangible asset as they are recognised. The companies will jointly develop and commercialise DS-1062 worldwide, except in Japan where Daiichi Sankyo will retain exclusive rights. AstraZeneca and Daiichi Sankyo will share equally development and commercialisation expenses as well as profits relating to DS-1062 worldwide, except for Japan where Daiichi Sankyo will be responsible for such costs and will pay AstraZeneca mid-single-digit royalties. Daiichi Sankyo will record sales in the US, certain countries in Europe and certain other countries where Daiichi Sankyo has affiliates. Profits shared with AstraZeneca from those countries will be recorded as Collaboration Revenue by AstraZeneca. AstraZeneca will record Product Sales in other countries worldwide, for which profits shared with Daiichi Sankyo will be recorded within Cost of sales. Daiichi Sankyo will manufacture and supply DS-1062.

Innate Pharma

> In April 2015, we entered into two oncology agreements with Innate Pharma: first, a licence which provides us with exclusive global rights to co-develop and commercialise IPH2201 in combination with *Imfinzi*; and, second, an option to license exclusive global rights to co-develop and commercialise IPH2201 in monotherapy and other combinations in certain treatment areas. We jointly fund Phase II studies with Innate Pharma and we lead the execution of these studies. In respect of these agreements, we made an initial payment to Innate Pharma of $250 million. The agreement also includes a Phase III initiation milestone of $100 million, as well as additional regulatory and sales-related milestones. We record all sales and pay Innate Pharma double-digit royalties on net sales. The arrangement includes the right for Innate Pharma to co-promote in Europe for an equal share of costs and income in the territory.

> In October 2018, we exercised our option over IPH2201 and simultaneously entered into a further multi-element transaction with Innate Pharma. Under the agreement, we paid $50 million to collaborate on, and acquire an option to license, IPH5201, a first-in-class anti-CD39 mAb. Additionally, we paid $20 million to acquire options over four future programmes currently being developed by Innate Pharma, and paid 62.6 EUR million to acquire a 9.8% stake in Innate Pharma. The $100 million option fee and $50 million premium paid over market price for the investment in Innate Pharma have been capitalised as intangible assets. The payment for future programmes will be expensed as R&D expenditure over four years. At the same time, we licensed the EU and US rights to *Lumoxiti* to Innate Pharma for $50 million upfront plus future milestone payments of up to $25 million.

> In December 2020, Innate Pharma announced its intention to transfer the rights of *Lumoxiti* back to AstraZeneca. AstraZeneca will not be required to refund the upfront payment but will no longer be entitled to receive milestone payments from Innate Pharma.

> In July 2021, AstraZeneca entered into a Termination Agreement with Innate Pharma to finalise the transfer of rights for *Lumoxiti* back to AstraZeneca, with an agreed final settlement of $6 million. The majority of transition activities back to AstraZeneca were completed in 2021.

We determine these business development transactions to be significant using a range of factors. We look at the specific circumstances of the individual arrangement and apply several quantitative and qualitative criteria. As we consider business development transactions to be an extension of our R&D strategy, the expected total value of development payments under the transaction and its proportion of our annual R&D spend, both of which are proxies for overall R&D effort and cost, are important elements of the determination of the significance. Other quantitative criteria we apply include, without limitation, expected levels of future sales, the possible value of milestone payments and the resources used for commercialisation activities (for example, the number of staff). Qualitative factors we consider include, without limitation, new market developments, new territories, new areas of research and strategic implications.

Capitalisation and shareholder return

Capitalisation

The total number of shares in issue at 31 December 2021 was 1,549 million (2020: 1,313 million).

Shareholders' equity increased by $23,646 million to $39,268 million at the year end. Non-controlling interests were $19 million (2020: $16 million).

Following the approval of *Calquence* in the EU in November 2020, the minority shareholders are now considered to have no further substantive variability in risk and reward related to their shares as it is considered highly likely that one of the options will be exercised, and the price of the options is now fixed. Therefore, no further amounts of the consolidated AstraZeneca results have been attributed to the minority shareholders of Acerta Pharma and the Non-controlling interests reserve relating to the minority shareholders of Acerta Pharma, totalling $1,401 million, were reclassified into Retained earnings in 2020, as detailed in Note 26 to the Financial Statements on page 177. No further adjustments were made for 2021.

Dividend and share repurchases

The Board has recommended a second interim dividend of $1.97 (145.3 pence, 18.00 SEK) to be paid on 28 March 2022. This brings the full-year dividend to $2.87 (210.1 pence, 25.77 SEK). Against Reported EPS, the Group had a dividend cover ratio of 0.03:1 in 2021 (2020: 0.9:1). Against Core Earnings per share, the Group had a dividend cover ratio of 1.84:1 in 2021 (2020: 1.44:1). This dividend is consistent with the progressive dividend policy, by which the Board intends to maintain or grow the dividend each year.

The Board regularly reviews its distribution policy and its overall financial strategy to continue to strike a balance between the interests of the business, our financial creditors and our shareholders. Having regard for business investment, funding the progressive dividend policy and meeting our debt service obligations, the Board currently believes it is appropriate to continue the suspension of the share repurchase programme which was announced in 2012.

The Board reviews the level of distributable reserves of the Parent Company annually and aims to maintain distributable reserves that provide adequate cover for dividend payments. At 31 December 2021, the Profit and loss account reserve of $11,563 million (2020: $10,304 million) was available for distribution, subject to filing these Financial Statements with Companies House. When making a distribution to shareholders, the Directors determine profits available for distribution by reference to guidance on realised and distributable profits under the Companies Act 2006 issued by the Institute of Chartered Accountants in England and Wales and the Institute of Chartered Accountants of Scotland in April 2017.

The profits of the company have been received in the form of receivables due from subsidiaries. The availability of distributable reserves in the Company is dependent on those receivables meeting the definition of qualifying consideration within the guidance, and in particular on the ability of subsidiaries to settle those receivables within a reasonable period of time. The Directors consider that, based on the nature of these receivables and the available cash resources of the Group and other accessible sources of funds, at 31 December 2021 are all (2020: all) of the Company's profit and loss reserves were available for distribution.

For further information regarding Dividends, see Note 25 on page 176.

Future prospects

As outlined earlier in this Annual Report, our strategic priorities support delivery of growth through innovation and our Purpose: to push the boundaries of science to deliver life-changing medicines.

In support of this, we made certain choices around our three strategic priorities:

> Deliver Growth and Disease Area Leadership
> Accelerate Innovative Science
> Be a Great Place to Work.

For more information, see Our Strategy and Key Performance Indicators from page 12.

Full year 2022: additional commentary

Total Revenue is expected to increase by a high-teens percentage, and Core EPS is expected to increase by a mid-to-high twenties percentage.

Total Revenue from COVID-19 medicines is anticipated to decline by a low-to-mid twenties percentage, with an expected decline in sales of *Vaxzevria* being partially offset by growth in *Evusheld* sales. The majority of vaccine revenue in 2022 is expected to come from initial contracts. The Gross Profit Margin from the COVID-19 medicines is expected to be lower than the Company average. Core Operating Expenses are expected to increase by a low-to-mid teens percentage, driven in substantial part by the full year integration of Alexion expenses. Emerging Markets Total Revenue, including China, is expected to grow mid-single digits in 2022. China Total Revenue is expected to decline by a mid-single digit percentage in 2022, primarily due to continued NRDL and VBP programmes impacting various medicines. The Company remains confident in the longer term outlook for Emerging Markets, driven by a large market opportunity, broader patient access and an increased mix of new medicines. A Core Tax Rate between 18% and 22% is expected.

AstraZeneca continues to recognise the heightened risks and uncertainties from the effects of COVID-19.

This commentary represents management's current estimates and is subject to change. See the Cautionary statement regarding forward-looking statements on page 228.

Financial risk management

Financial risk management policies

Insurance

Our risk management processes are described in Risk Overview from page 48. These processes enable us to identify risks that can be partly or entirely mitigated through the use of insurance. We focus our insurance resources on the most critical areas, or where there is a legal requirement, and where we can get the best value for money through structured and traditional insurance. We purchase an external multi-line insurance programme to mitigate against significant financial loss arising from core business risks.

Taxation

Our approach to managing tax risk is integrated with our broader business risk management and compliance framework. Our approach is to manage tax risks and tax costs in a manner consistent with applicable regulatory requirements and with shareholders' best long-term interests, taking into account operational, economic and reputational factors. We manage tax risks in the context of substantive business transactions.

Treasury

The principal financial risks to which we are exposed are those arising from liquidity, interest rates, foreign currency and credit. We have a centralised treasury function to manage these risks in accordance with Board-approved policies. Note 28 to the Financial Statements from page 180 sets out the relevant policies and the way we manage these risks and our capital management objectives, as well as a sensitivity analysis of the Group's exposure to exchange rate and interest rate movements.

For further information on our supply chain financing arrangements, please see the Business Review on page 30.

Critical accounting policies and estimates

The Consolidated Financial Statements have been prepared in accordance with UK-adopted IAS and with the requirements of the Companies Act 2006 as applicable to companies reporting under those standards. The Consolidated Financial Statements also comply fully with IFRS as issued by the IASB and international accounting standards as adopted by the European Union. On 31 December 2020, EU-adopted IFRS was brought into UK law and became UK-adopted international accounting standards, with future changes to IFRS being subject to endorsement by the UK Endorsement Board. The accounting policies employed are set out in the Group Accounting Policies section in the Financial Statements from page 138. In applying these policies, we make estimates and assumptions that affect the Reported amounts of assets and liabilities and disclosure of contingent assets and liabilities. The actual outcome could differ from those estimates. Some of these policies require a high level of judgement because the areas are especially subjective or complex.

We believe that the most critical accounting policies and significant areas of judgement and estimation are in the following areas and align with the accounting policies containing our key accounting judgements and significant accounting estimates as disclosed in the Financial Statements from page 138:

> revenue recognition – see Revenue Accounting Policy from page 139 and Note 1 on page 146
> expensing of internal development expenses – see Research and Development Policy from page 140
> impairment review of Intangible assets – see Note 10 from page 156
> useful economic life of Intangible assets – see Research and Development Policy from page 140 and Note 10 from page 156
> business combinations and Goodwill (and Contingent consideration arising from business combinations) – see Business Combinations and Goodwill Policy on page 142, Note 10 from page 156, Note 20 from page 66 and Note 27 from page 178
> litigation liabilities – see Litigation and Environmental liabilities within Note 30 from page 189
> operating segments – see Note 6 from page 152
> employee benefits – see Note 22 from page 168
> taxation – see Taxation Accounting Policies on page 141 and Note 30 on page 189.

Revenue recognition
Product Sales are recorded at the invoiced amount (excluding inter-company sales and value added taxes), less movements in estimated accruals for rebates and chargebacks given to managed care and other customers, which are a particular feature in the US and are considered to be key estimates. It is the Group's policy to offer a credit note for all returns and to destroy all returned stock in all markets. Cash discounts for prompt payments are also discounted from sales. Sales are recognised when the control of the goods has been transferred to a third party, which is usually when title passes to the customer, either on shipment or on the receipt of goods by the customer, depending on local trading terms.

Rebates, chargebacks and returns in the US
When invoicing Product Sales in the US, we estimate the rebates and chargebacks that we expect to pay, which are considered to be estimates. These rebates typically arise from sales contracts with third-party managed care organisations, hospitals, long-term care facilities, group purchasing organisations and various federal or state programmes (Medicaid contracts, supplemental rebates, etc.). They can be classified as follows:

- Chargebacks, where we enter into arrangements under which certain parties, typically hospitals, long-term care facilities, group purchasing organisations, the Department of Veterans Affairs, Public Health Service Covered Entities and the Department of Defense, are able to buy products from wholesalers at the lower prices we have contracted with them. The chargeback is the difference between the price we invoice to the wholesaler and the contracted price charged by the wholesaler to the other party. Chargebacks are credited directly to the wholesalers.
- Regulatory, including Medicaid and other federal and state programmes, where we pay rebates based on the specific terms of agreements with the US Department of Health and Human Services and with individual states, which include product usage and information on best prices and average market prices benchmarks.
- Contractual, under which entities such as third-party managed care organisations are entitled to rebates depending on specified performance provisions, which vary from contract to contract.

The effects of these deductions on our US pharmaceuticals revenue and the movements on US pharmaceuticals revenue provisions are set out on this page.

Gross to Net Product Sales
US pharmaceuticals

	2021 $m	2020 $m	2019 $m
Gross Product Sales	**23,970**	19,255	18,354
Chargebacks	**(2,095)**	(2,464)	(2,429)
Regulatory – Medicaid and state programmes	**(1,488)**	(1,088)	(1,380)
Contractual – Managed care and Medicare	**(7,121)**	(5,690)	(5,467)
Cash and other discounts	**(312)**	(281)	(303)
Customer returns	**(14)**	(198)	(44)
US Branded Pharmaceutical Fee	**(57)**	(47)	(105)
Other	**(883)**	(849)	(879)
Net Product Sales	**12,000**	8,638	7,747

Movements in accruals
US pharmaceuticals

	Brought forward at 1 January 2021 $m	Additions through business combinations $m	Provision for current year $m	Adjustment in respect of prior years $m	Returns and payments $m	Carried forward at 31 December 2021 $m
Chargebacks	178	2	2,117	(21)	(2,095)	181
Regulatory – Medicaid and state programmes	495	46	1,548	(50)	(1,529)	510
Contractual – Managed care and Medicare	1,937	29	7,204	(83)	(7,056)	2,031
Cash and other discounts	20	–	313	–	(312)	21
Customer returns	253	18	13	–	(88)	196
US Branded Pharmaceutical Fee	115	–	77	(28)	(65)	79
Other	128	4	882	–	(860)	154
Total	3,126	99	12,154	(182)	(12,025)	3,172

	Brought forward at 1 January 2020 $m	Provision for current year $m	Adjustment in respect of prior years $m	Returns and payments $m	Carried forward at 31 December 2020 $m
Chargebacks	245	2,572	(28)	(2,611)	178
Regulatory – Medicaid and state programmes	731	1,268	(93)	(1,412)	495
Contractual – Managed care and Medicare	1,939	5,796	(127)	(5,671)	1,937
Cash and other discounts	19	289	–	(288)	20
Customer returns	180	225	–	(152)	253
US Branded Pharmaceutical Fee	126	92	(51)	(52)	115
Other	145	851	(2)	(866)	128
Total	3,385	11,094	(301)	(11,052)	3,126

	Brought forward at 1 January 2019 $m	Provision for current year $m	Adjustment in respect of prior years $m	Returns and payments $m	Carried forward at 31 December 2019 $m
Chargebacks	271	2,458	(29)	(2,455)	245
Regulatory – Medicaid and state programmes	892	1,477	(97)	(1,541)	731
Contractual – Managed care and Medicare	1,542	5,613	(146)	(5,070)	1,939
Cash and other discounts	4	303	–	(288)	19
Customer returns	361	44	–	(225)	180
US Branded Pharmaceutical Fee	52	111	(6)	(31)	126
Other	144	879	–	(878)	145
Total	3,266	10,885	(278)	(10,488)	3,385

Accrual assumptions are built up on a product-by-product and customer-by-customer basis, taking into account specific contract provisions coupled with expected performance, and are then aggregated into a weighted average rebate accrual rate for each of our products. Accrual rates are reviewed and adjusted on an as needed basis. There may be further adjustments when actual rebates are invoiced based on utilisation information submitted to us (in the case of contractual rebates) and claims/invoices are received (in the case of regulatory rebates and chargebacks). We believe that we have made reasonable estimates for future rebates using a similar methodology to that of previous years. Inevitably, however, these estimates involve assumptions in respect of aggregate future sales levels, segment mix and customers' contractual performance.

Overall adjustments between gross and net US Product Sales amounted to $11,970 million in 2021 (2020: $10,617 million) with the increase driven by an overall increase in our US Product Sales including the addition of the Alexion Rare Disease portfolio in 2021.

Cash discounts are offered to customers to encourage prompt payment. Accruals are calculated based on historical experience and are adjusted to reflect actual experience. Our revenue recognition policy is described within Group Accounting Policies from page 138. Industry practice in the US allows wholesalers and pharmacies to return unused stocks within six months of, and up to 12 months after, shelf-life expiry. The customer is credited for the returned product by the issuance of a credit note. Returned products are not exchanged for products from inventory and once a return claim has been determined to be valid and a credit note has been issued to the customer, the returned products are destroyed. At the point of sale in the US, we estimate the quantity and value of products which may ultimately be returned. Our returns accruals in the US are based on actual experience. Our estimate is based on the historical sales and returns information for established products together with market-related information, such as estimated shelf life, product recall, and estimated stock levels at wholesalers, which we receive via third-party information services. For newly launched products, we use rates based on our experience with similar products or a pre-determined percentage.

Business combinations and goodwill (and contingent consideration arising from business combinations)
Our business model includes investment in targeted business developments to strengthen our portfolio, pipeline and capabilities. These business development transactions include collaborations, asset in-licences and business acquisitions.

Each transaction is considered to establish whether it qualifies as a business combination by applying the criteria assessment detailed in IFRS 3 'Business Combinations', after applying the optional concentration test on an elective basis. The determination of a transaction being a business combination or asset acquisition is considered to be a key judgement as detailed in the accounting policy on page 142.

On the acquisition of a business, fair values are attributed to the identifiable assets and liabilities and contingent liabilities unless the fair value cannot be measured reliably, in which case the value is subsumed into goodwill.

Attributing fair values is a key judgement. Goodwill is the difference between the fair value of the consideration and the fair value of net assets acquired. Fair value is the price that would be received to sell an asset or pay for a liability in an orderly transaction at the date of acquisition. The price may be directly observable but, in most cases, is estimated using valuation techniques which normally involve predicting future cash flows and applying a market participant discount rate.

Future contingent elements of consideration, which may include development and launch milestones, revenue threshold milestones and revenue-based royalties, are fair valued at the date of acquisition using decision-tree analysis with key inputs including probability of success, consideration of potential delays and revenue projections based on the Group's internal forecasts. Unsettled amounts of consideration are held at fair value within payables with changes in fair value recognised immediately in the Consolidated Statement of Comprehensive Income.
Several of our business combinations have included significant amounts of contingent consideration. Details of the movements in the fair value of the contingent consideration in the year and the range of possible contingent consideration amounts that may eventually become payable are contained in Note 10 to the Financial Statements from page 156.

Where not all the equity of a subsidiary is acquired, the non-controlling interest is recognised either at fair value or at the non-controlling interest's proportionate share of the net assets of the subsidiary, on a case-by-case basis. Put options over non-controlling interests are recognised as a financial liability measured at amortised cost, with a corresponding entry in either retained earnings or against non-controlling interest reserves on a case-by-case basis.

As detailed on this page, we have significant investments in goodwill and intangible assets as a result of acquisitions of businesses and purchases of assets, such as product development and marketing rights. Details of the estimates and assumptions we make in our annual impairment testing of goodwill are included in Note 9 to the Financial Statements on page 156. The Group, including acquisitions, is considered a single operating segment for impairment purposes. No impairment of goodwill was identified.
A significant portion of our investments in intangible assets and goodwill arose from the 2021 acquisition of Alexion, restructuring of the joint venture with MSD which commenced in 1998, the acquisition of MedImmune in 2007 and our 2014 acquisition of BMS's interest in the Group's Diabetes Alliance.
We are satisfied that the carrying values of our intangible assets as at 31 December 2021 are fully justified by estimated future cash flows. The accounting for our intangible assets is fully explained in Note 10 to the Financial Statements from page 156, including details of the estimates and assumptions we make in impairment testing of intangible assets.

Litigation and environmental liabilities
In the normal course of business, contingent liabilities may arise from product-specific and general legal proceedings, from guarantees or from environmental liabilities connected with our current or former sites. Where we believe that potential liabilities have a less than 50% probability of crystallising, or where we are unable to make a reasonable estimate of the liability, we treat them as contingent liabilities. These are not provided for, but are disclosed in Note 30 to the Financial Statements from page 189.

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 other similar forms of relief), or where a loss is probable and we are able to make a reasonable estimate of the loss, we generally indicate the loss absorbed or make a provision for our best estimate of the expected loss.

Where it is considered that the Group is more likely than not to prevail, or in the rare circumstances where the amount of the legal liability cannot be estimated reliably, legal costs involved in defending the claim are charged to profit as they are incurred. Where it is considered that we have a valid contract which provides the right to reimbursement (from insurance or otherwise) of legal costs and/or all or part of any loss incurred or for which a provision has been established and we consider recovery to be virtually certain, then the best estimate of the amount expected to be received is recognised as an asset.

Assessments as to whether or not to recognise provisions or assets and of the amounts concerned usually involve a series of complex judgements about future events and can rely heavily on estimates and assumptions. We believe that the provisions recorded are adequate based on currently available information and that any insurance recoveries recorded will be received.

However, given the inherent uncertainties involved in assessing the outcomes of these cases and in estimating the amount of the potential losses and the associated insurance recoveries, we could in future periods incur judgments or insurance settlements that could have a material adverse effect on our results in any particular period.

The position could change over time and 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.

Although there can be no assurance regarding the outcome of legal proceedings, we do not currently expect them to have a material adverse effect on our financial position, but they could significantly affect our financial results in any particular period.

Sarbanes-Oxley Act section 404

As a consequence of our Nasdaq listing, we are required to comply with those provisions of the Sarbanes-Oxley Act applicable to foreign issuers. Section 404 of the Sarbanes-Oxley Act requires companies annually to assess and make public statements about the quality and effectiveness of their internal control over financial reporting. As regards Sarbanes-Oxley Act section 404, our approach is based on the Committee of Sponsoring Organizations (COSO) 2013 framework.

Our approach to the assessment has been to select key transaction and financial reporting processes in our largest operating units and a number of specialist areas (e.g. financial consolidation and reporting, treasury operations and taxation etc.), so that, in aggregate, we have covered a significant proportion of the key lines in our Financial Statements. Each of these operating units and specialist areas has ensured that its relevant processes and controls are documented to appropriate standards, taking into account, in particular, the guidance provided by the SEC. We have also reviewed the structure and operation of our 'entity level' control environment. This refers to the overarching control environment, including structure of reviews, checks and balances that are essential to the management of a well-controlled business. Following the acquisition of Alexion, we have determined to exclude Alexion from the report on Internal Controls Over Financial Reporting (ICOFR) for the first year after acquisition as we understand and integrate Alexion's controls within the AstraZeneca framework.

Financial Review
continued

Section 172(1) statement
When making decisions, the Directors of AstraZeneca PLC must act in the way they consider, in good faith, is most likely to promote the success of the Company for the benefit of its members as a whole, while also considering the broad range of stakeholders who interact with and are impacted by our business. Throughout the year, while discharging their duties, section 172(1) requires a director to have regard, amongst other matters, to the:

- likely consequences of any decisions in the long term
- interests of the company's employees
- need to foster the company's business relationships with suppliers, customers and others
- impact of the company's operations on the community and environment
- desirability of the company maintaining a reputation for high standards of business conduct and
- need to act fairly as between members of the company.

In discharging their section 172(1) duties, the Directors have had regard to the factors set out above, as well as other factors relevant to the decision being made. The Board acknowledges that every decision made will not necessarily result in a positive outcome for all stakeholders. By considering our Purpose and Values, together with our strategic priorities, the Board aims to ensure that the decisions made are consistent and intended to promote the Company's long-term success.

The Group engaged with key stakeholders throughout the year to understand the issues and factors that are significant for these stakeholders, and a number of actions were taken as a result of this engagement. The interaction with stakeholders, and the impact of these interactions, is set out in the Connecting with our stakeholders section on pages 80 to 82 and throughout the Strategic Report.

We are committed to being a great place to work for the global workforce, encouraging and rewarding innovation, entrepreneurship and high performance. Details on engagement with employees can be found on pages 41 to 43 of the Business Review, page 92 of the Audit Committee Report and page 119 to 120 of the Remuneration Committee Report.

We are committed to employing high ethical standards when carrying out all aspects of our business globally. Our Code of Ethics (the Code) is based on our Values, expected behaviours and key policy principles. More information on the Code can be found in the Business Review on page 47.

AstraZeneca recognises patients as people first and puts them at the heart of what we do. Information on the importance of patients to the business can be found on pages 14 and 80, with further information throughout the Business Review.

Information on interactions with suppliers is on pages 38, 39, and 80. The consideration and impact of the Group's operations on the environment can be found on pages 44 to 46 and Ambition Zero Carbon on page 45. Information on how the Group has considered other factors, such as communities, is also set out in Contributing to society from page 45 and Connecting with our stakeholders on page 80.

Details of how the Board operates and matters considered by the Board are set out in the Corporate Governance Report from page 83. Examples of how Directors discharged their section 172(1) duties and considered stakeholders when making Principal Decisions during 2021 are set out on pages 80 and 81. Principal Decisions are decisions and discussions which are material or strategic to the Group, but also those that are significant to any of our stakeholder groups.

Strategic Report
The following sections make up the Strategic Report, which has been prepared in accordance with the requirements of the Companies Act 2006:

- AstraZeneca at a Glance
- Chair's Statement
- Chief Executive Officer's Review
- Healthcare in a Changing World
- Business Model and Life-cycle of a Medicine
- Our Strategy and Key Performance Indicators
- Disease Area Review
- Business Review
- Risk Overview
- Financial Review

and has been approved and signed on behalf of the Board.

A C N Kemp
Company Secretary

10 February 2022

DocuSigned by:
AWKG
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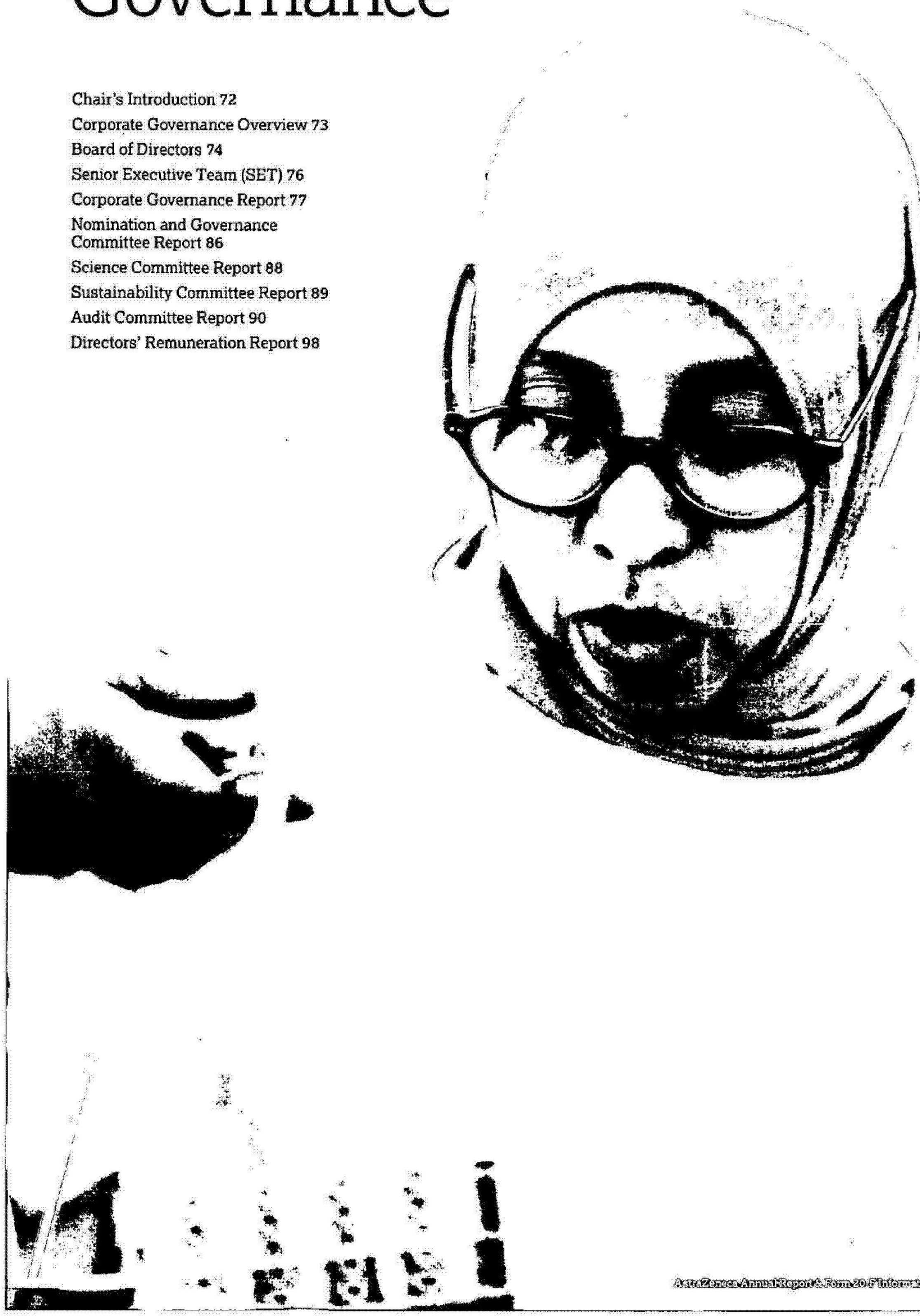
Corporate Governance

Chair's Introduction 72
Corporate Governance Overview 73
Board of Directors 74
Senior Executive Team (SET) 76
Corporate Governance Report 77
Nomination and Governance Committee Report 86
Science Committee Report 88
Sustainability Committee Report 89
Audit Committee Report 90
Directors' Remuneration Report 98



Chair's Introduction

Built on strong foundations of good corporate governance, the Board continued to exercise effective oversight of AstraZeneca activities.

"Oversight of our strategy and its implementation is a key responsibility of the Board."



As in 2020, the pandemic once again tested our solid governance foundations in 2021. Although some Directors were able to meet in person at our offices in London in the second part of the year, all Board meetings during the year were held virtually. However, with good IT support, we continued to collaborate and discharge our responsibilities effectively in what was another busy and successful year for AstraZeneca.

Strategic oversight

Oversight of our strategy and its implementation is, of course, a key responsibility of the Board. In 2021, this included oversight of the completion of the Alexion acquisition and its integration into the rest of the Group. In particular, the Audit Committee held a number of meetings with the Alexion team to better understand the business and its risk environment. The Science Committee undertook an in-depth review of the Alexion portfolio of medicines and development pipeline, scientific capabilities, talent and organisation, while the Remuneration Committee looked at reward-related elements of the organisation.

Effective Committees

Given this additional activity, I am grateful to the Chairs of the Board Committees for the work they have led and responsibilities discharged so ably: Michel Demaré for the Remuneration Committee and Nazneen Rahman for the Science Committee. I am particularly grateful to Philip Broadley for his work with the Audit Committee and as senior independent Non-Executive Director.

I would also like to acknowledge and thank Michel Demaré for his work chairing the Ad Hoc Board Committee on *Vaxzevria*, which operated from March to October of 2021. Michel, ably supported by the Committee's members – Deborah DiSanzo, Diana Layfield and Nazneen Rahman – ensured the rest of the Board and management were fully focused and supported on all matters relating to our COVID-19 vaccine during the year, ranging from safety and efficacy, through manufacturing and supply to reputational matters.

Sustainability Committee

My thanks also go to Nazneen for agreeing to chair our newly established Sustainability Committee, having previously overseen sustainability matters on behalf of the Board since January 2021. The Sustainability Committee was established in October and met for the first time in December, reflecting the increasing significance of sustainability to our business, not least our ambitious Ambition Zero Carbon programme.

I am grateful to all the members of the Board for their continued commitment to AstraZeneca and promoting our success for the benefit of shareholders and stakeholders more generally.



Leif Johansson
Chair

Corporate Governance Overview

The Directors are collectively responsible for the success of the Group. The Board maintains and periodically reviews a list of matters that can only be approved by the Board. Matters that have not been expressly reserved to the Board in this way are delegated to the CEO or one of the Board's five Committees. The diagram below illustrates this governance structure.

The Board's responsibilities include setting our strategy and policies, overseeing risk and corporate governance, and monitoring progress towards meeting our objectives and annual plans. It is accountable to our shareholders for the proper conduct of the business and our long-term success, and seeks to represent the interests of all stakeholders.

The CEO, CFO and Senior Executive Team (SET) take the lead in developing our strategy; proposals are reviewed and constructively challenged by the Board, before the strategy is finally approved.

Governance structure

The Board has delegated some of its powers to the CEO and operates with the assistance of five Committees:

Board
Corporate Governance Report from page 77

- **Audit Committee** – Report from page 90
- **Remuneration Committee** – Report from page 98
- **Nomination and Governance Committee** – Report from page 86
- **Science Committee** – Report from page 88
- **Sustainability Committee** – Report from page 89

Attendance in 2021

Board Committee membership and meeting attendance in 2021

O Board or Committee Chair

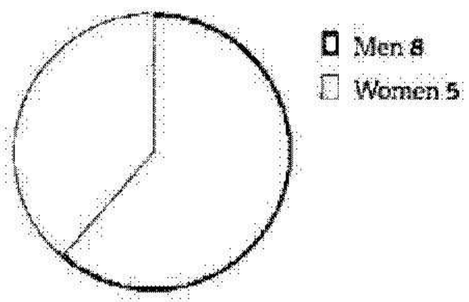
Director	Appointment Date[1]	Board[2]	Audit Committee	Remuneration Committee	Nomination and Governance Committee	Science Committee	Sustainability Committee[3]
Non-Executive Chair and Executive Directors							
Leif Johansson	26/04/2012	O 8/8		5/6	O 5/5		
Pascal Soriot	01/10/2012	8/8					
Aradhana Sarin	01/08/2021	3/3					
Marc Dunoyer – *stepped down on 1 August 2021*	01/11/2013	5/5					
Non-Executive Directors							
Euan Ashley	01/10/2020	8/8				4/5	
Philip Broadley[4]	27/04/2017	8/8	O 6/6	6/6	5/5		
Michel Demaré	01/09/2019	8/8	5/6	O 6/6	5/5		
Deborah DiSanzo	01/12/2017	7/8[5]	6/6				
Diana Layfield	01/11/2020	8/8				2/2[6]	
Sheri McCoy	01/10/2017	8/8	6/6	6/6			1/1
Tony Mok	01/01/2019	8/8				5/5	
Nazneen Rahman	01/06/2017	8/8			5/5	O 5/5	O 1/1
Andreas Rummelt	01/08/2021	3/3					1/1
Marcus Wallenberg	05/04/1999	7/8[7]				4/5	1/1
Geneviève Berger – *retired on 11 May 2021*	26/04/2012	4/4				2/2	
Graham Chipchase – *retired on 11 May 2021*	26/04/2012	4/4			1/1		

1 Date of first appointment or election to the Board.
2 All Board meetings in 2021 were held by videoconference due to COVID-19 restrictions. For certain meetings in the second part of the year, some Directors met in person at the Company's office in London to participate in Board meetings.
3 The Sustainability Committee was constituted on 1 October 2021.
4 Philip Broadley was appointed as senior independent Non-Executive Director on 1 March 2021.
5 Deborah DiSanzo missed one Board meeting due to illness.
6 Diana Layfield became a member of the Science Committee on 1 October 2021.
7 Marcus Wallenberg missed one Board meeting due to the meeting being convened at short notice.

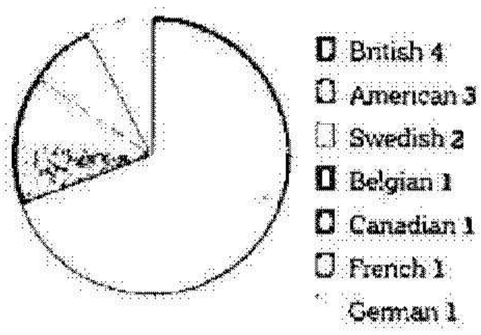
Board of Directors
as at 31 December 2021

Board composition
as at 31 December 2021

Gender split of Directors



Directors' nationalities



Length of tenure of Non-Executive Directors

<3 years

5

Euan Ashley
Michel Demaré
Diana Layfield
Tony Mok
Andreas Rummelt

3-9 years

4

Deborah DiSanzo
Sheri McCoy
Nazneen Rahman
Philip Broadley

>9 years

2

Leif Johansson
Marcus Wallenberg

Committee membership key

- Committee Chair
- NG Nomination and Governance
- A Audit
- Sc Science
- R Remuneration
- Su Sustainability

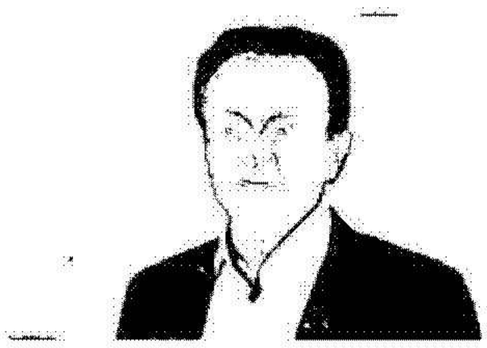


Leif Johansson NG R

Non-Executive Chair of the Board

Skills and experience: From 1997-2011, Leif was CEO of AB Volvo. Leif served at AB Electrolux as CEO from 1994-1997. He was a Non-Executive Director of BMS from 1998-2011, serving on the Audit Committee and Compensation and Management Development Committee. Leif was Chairman of LM Ericsson from 2011-2018. He holds an MSc in Engineering from Chalmers University of Technology, Gothenburg.

Other appointments: Leif holds Board positions at Autoliv, Inc and Ecolean AB. Leif has been a member of the Royal Swedish Academy of Engineering Sciences since 1994 (Chairman 2012-2017), is a member of the European Round Table of Industrialists (Chairman 2009-2014) and also of the Council of Advisors, Boao Forum for Asia.



Pascal Soriot

Executive Director and CEO

Skills and experience: Pascal has a passion for science and medicine, and significant experience in established and emerging markets, together with a strength of strategic thinking and execution, a successful track record of managing change and executing strategy, and the ability to lead a diverse organisation. He served as COO of Roche's pharmaceuticals division from 2010-2012 and previously as CEO of Genentech in San Francisco, where he led its successful merger with Roche. Pascal joined the pharmaceutical industry in 1986 and has worked in senior roles in major companies around the world. He is a Doctor of Veterinary Medicine (École Nationale Vétérinaire d'Alfort, Maisons-Alfort) and holds an MBA from HEC Paris.



Aradhana Sarin

Executive Director and CFO

Skills and experience: Prior to her current role, Aradhana was CFO for Alexion. Aradhana joined Alexion in 2017 and was responsible for driving strategic growth, financial performance and business development at Alexion. She brings operational experience in biopharma plus more than 20 years of professional experience at global financial institutions and has extensive knowledge of global healthcare systems, having closed more than 100 transactions across M&A, equity and debt financing. Before joining Alexion, Aradhana was Managing Director of Healthcare Corporate and Investment Banking at Citi Global Banking, focusing on clients in the life sciences and biopharmaceutical sectors. Previously, she served as Managing Director of Healthcare Investment Banking at UBS, and worked at JP Morgan in the M&A Advisory and Healthcare groups. Aradhana trained as a medical doctor in India and spent two years practising in both India and Africa. She completed her medical training at the University of Delhi and received her MBA from Stanford Business School.



Philip Broadley A R NG

Senior independent Non-Executive Director

Skills and experience: Philip has significant financial and international business experience. He was previously Group Finance Director of Prudential plc for eight years and Old Mutual plc for six years. He has served as Chairman of the 100 Group of Finance Directors in the UK and Board member of Stallergenes Greer plc. He is a Fellow of the Institute of Chartered Accountants in England and Wales. Philip graduated in Philosophy, Politics and Economics from St Edmund Hall, Oxford, where he is now a St Edmund Fellow, and holds an MSc in Behavioural Science from the London School of Economics. Until March 2019, Philip was a member of the Oxford University Audit Committee.

Other appointments: Philip is Senior Independent Director of Legal & General Group plc, where he chairs the Audit Committee. He is Treasurer of the London Library and Chairman of the Board of Governors of Eastbourne College.



Euan Ashley Sc

Non-Executive Director

Skills and experience: Euan studied physiology and medicine at Glasgow University, trained as a junior doctor at Oxford University Hospitals NHS Trust, and gained a DPhil in cardiovascular cellular biology and molecular genetics at the University of Oxford. In 2002 Euan moved to Stanford University, California where his research focuses on genetic mechanisms of cardiovascular health and disease. His laboratory leverages AI and digital health tools, alongside biotechnology and technology partners in Silicon Valley, to advance translational and clinical research. Euan's awards include recognition from the Obama White House for contributions to personalised medicine and the American Heart Association's Medal of Honor for precision medicine.

Other appointments: Associate Dean and Professor of Biomedical Data Science and Professor of Cardiovascular Medicine and Genetics at Stanford University.



Michel Demaré R A NG

Non-Executive Director

Skills and experience: Michel was previously Vice-Chairman of UBS Group AG (2010-2019), Chairman of Syngenta and Syngenta Foundation for Sustainable Agriculture (2013-2017) and Chairman of SwissHoldings (2013-2015). Between 2005 and 2013, Michel was CFO of ABB Ltd and interim CEO during 2008. He joined ABB from Baxter International Inc., where he was CFO Europe from 2002-2005. Prior to that, he spent 18 years at The Dow Chemical Company, serving as CFO of Dow's Global Polyolefins and Elastomers division between 1997-2002.

Other appointments: Michel is a Non-Executive Director of Vodafone Group plc and Louis Dreyfus Int'l Holding BV. Chairman of IMD Business School and Chairman of Nomoko AG.



Deborah DiSanzo (A)

Non-Executive Director

Skills and experience: Deborah is President of Best Buy Health for Best Buy Co. Inc. Best Buy Health provides digital health solutions in active ageing, virtual care, and consumer health. Deborah holds an appointment at the Harvard TH Chan School of Public Health teaching Artificial Intelligence in Health. Until December 2018, she served as General Manager of IBM Watson Health. Prior to IBM, until 2014, Deborah held multiple senior executive positions at Philips Healthcare where she also served as Chief Executive Officer. Deborah has been honoured by multiple organisations as a top health influencer. She holds an MBA from Babson College and is a Harvard University Advanced Leadership Initiative 2019 Fellow.

Other appointments: Deborah is President of Best Buy Health for Best Buy Co. Inc.



Diana Layfield (Sc)

Non-Executive Director

Skills and experience: Diana has broad global business experience which began in the pharmaceutical and biotech sector. She has held senior leadership roles in the technology sector and international banking, including senior positions at Standard Chartered Bank, as the CEO of a start-up technology company, and in Healthcare and Life Sciences at McKinsey & Co. Until December 2020, Diana was a Non-Executive Director of Aggreko plc. She has a BA from Oxford University and an MA in Public Administration and International Economics from Harvard University.

Other appointments: Diana is President, EMEA Partnerships at Google, driving technology transformation and is also Vice-President, 'Next Billion Users' & Product Management, leading the development of products and services for future Google users. She is also a Council Member of the London School of Hygiene & Tropical Medicine and Chair of CDC Group plc.



Sheri McCoy (A) (R) (Su)

Non-Executive Director

Skills and experience: Until February 2018, Sheri was CEO and a Director of Avon Products, Inc. Prior to joining them in 2012, she had a distinguished 30-year career at Johnson & Johnson, latterly serving as Vice Chairman of the Executive Committee, responsible for the Pharmaceuticals and Consumer business segments. Sheri joined Johnson & Johnson as an R&D scientist and subsequently managed businesses in every major product sector, holding positions including Worldwide Chairman, Surgical Care Group and Division President, Consumer. She holds a Bachelor of Science degree in Textile Chemistry from the University of Massachusetts Dartmouth, a Masters degree in Chemical Engineering from Princeton University and an MBA from Rutgers University in New Jersey, US.

Other appointments: Sheri serves on the boards of Stryker, Kimberly-Clark, Novocure and Laronde. She is also an industrial adviser for EQT, in connection with which she chairs Certara, and serves on the boards of Galderma and Parexel.

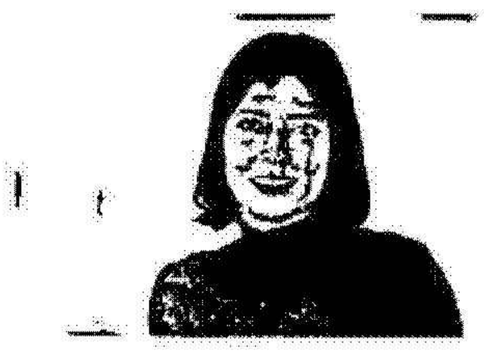


Tony Mok (Sc)

Non-Executive Director

Skills and experience: Tony is the Li Shu Fan Medical Foundation endowed Professor and Chairman of the Department of Clinical Oncology at the Chinese University of Hong Kong. His work includes multiple aspects of lung cancer research, including biomarker and molecular targeted therapy in lung cancer. Tony is a former President of the International Association for the Study of Lung Cancer and is on the Board of Directors of the American Society of Clinical Oncology. His work has achieved numerous awards including the ESMO Lifetime Achievement Award in 2018 and Giant of Cancer Care in 2020.

Other appointments: Tony is a Non-Executive Director of Hutchison China MediTech Limited (Chair of Nomination Committee) and co-founder and Chairman of Sanomics Limited (merged with ACT Genomic Limited since 2021).



Nazneen Rahman (Sc) (Su) (NG)

Non-Executive Director

Skills and experience: Nazneen has significant scientific, medical and data analysis experience in rare disease and cancer genomics. She was Head of the Division of Genetics and Epidemiology at the Institute of Cancer Research, London, and Head of Cancer Genetics at the Royal Marsden NHS Foundation Trust for 10 years to 2018. Nazneen was also founder and Director of the TGLclinical Genetic Testing Laboratory. Nazneen qualified in medicine from Oxford University, and gained a Certificate of Completion of Specialist Training in medical genetics and a PhD in molecular genetics. Nazneen has a strong commitment to open science and has garnered numerous awards, including a CBE in recognition of her contribution to medical sciences.

Other appointments: Nazneen is founder and CEO of YewMaker and Director of the Sustainable Medicines Partnership, delivering science-based solutions to make healthcare more sustainable.



Andreas Rummelt (Su)

Non-Executive Director

Skills and experience: Andreas joined the Board following the acquisition of Alexion, where he had been a director since 2010. Previously he was Group Head of Technical Operations and Quality at Novartis, and from 2006 until 2010 served on the Executive Committee. He was Global CEO of the Generics Division of Sandoz from 2004 to 2008, having originally joined in 1985. Andreas earned his PhD in pharmaceutical sciences from the University of Erlangen-Nuremberg and received his executive training in general management and leadership from IMD in Lausanne; INSEAD in Fontainebleau; and Harvard Business School.

Other appointments: Andreas is Chairman and Managing Partner of InterPharmaLink AG and a director of various privately-held biotech and pharmaceutical companies. He is a member of the Scientific Advisory Committee of the Global Antibiotic Research and Development Partnership.



Marcus Wallenberg (Sc) (Su)

Non-Executive Director

Skills and experience: Marcus has international business experience across various industry sectors, including the pharmaceutical industry from his directorship with Astra prior to 1999.

Other appointments: Marcus is Chairman of Skandinaviska Enskilda Banken AB, Saab AB and FAM AB. He is a member of the boards of Investor AB and the Knut and Alice Wallenberg Foundation.

Senior Executive Team (SET) as at 31 December 2021

In addition to the Board of Directors, the Senior Executive Team, or SET, is the body through which the CEO exercises the authority delegated to him by the Board. The CEO leads the SET and has executive responsibility for the management, development and performance of the business. The CEO, CFO and SET also take the lead in developing the strategy for review, constructive challenge and approval by the Board as part of the annual strategy review process.

Further information about SET members is available on our website, www.astrazeneca.com.



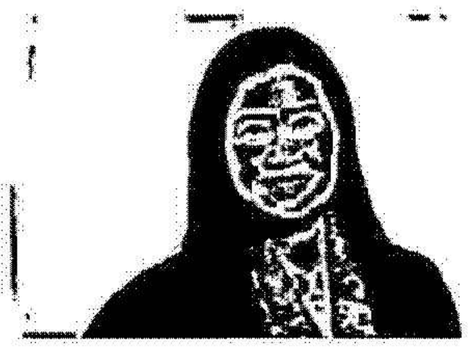
Pascal Soriot
CEO



Aradhana Sarin
CFO



Katarina Ageborg
Executive Vice-President, Sustainability and Chief Compliance Officer



Pam Cheng
Executive Vice-President, Operations & Information Technology



Ruud Dobber
Executive Vice-President, BioPharmaceuticals Business Unit



Marc Dunoyer
Chief Executive Officer, Alexion and Chief Strategy Officer, AstraZeneca



David Fredrickson
Executive Vice-President, Oncology Business Unit



Susan Galbraith
Executive Vice-President, Oncology R&D



Menelas (Mene) Pangalos
Executive Vice-President, BioPharmaceuticals R&D



Jeff Pott
General Counsel and Chief Human Resources Officer



Iskra Reic
Executive Vice-President, Vaccines & Immune Therapies



Leon Wang
Executive Vice-President, International and China President

Corporate Governance Report
Compliance with the UK Corporate Governance Code

Statement of compliance

Our statement of compliance describes how we applied the principles set out in the 2018 UK Corporate Governance Code (the Code) for the year ended 31 December 2021. A copy of the Code can be found on the Financial Reporting Council's website, www.frc.org.uk. Throughout the accounting period we have complied with all the provisions of the Code other than provision 19, which relates to the Chair's tenure. Our approach is described on page 4.

1. Board leadership and company purpose

A. Board's role

The Board's role is to promote the long-term sustainable success of the Company. The Directors' diverse range of skills, experience and industry knowledge, and ability to exercise independent and objective judgement, help the Board to operate effectively in its oversight of delivery of the Group's strategy, generation of shareholder value and contributions to wider society.

The Board's effective operation is underpinned by a sound governance structure, described on page 73. Through a programme of regular Board and Committee meetings, Directors receive information on AstraZeneca's financial performance, the R&D pipeline and critical business issues. The Board is accountable to our shareholders for the proper conduct of the business and our long-term success, and seeks to represent the interests of all stakeholders.

B. Purpose, culture and strategy

The Board believes that our Purpose, to push the boundaries of science to deliver life-changing medicines, positions AstraZeneca for long-term sustainable success.

Our Code of Ethics and our Values underpin the behaviours that support our culture.

For more information on our Purpose, our Values and our Culture, see page 10.

The Board is responsible for setting our strategy and policies, overseeing risk and corporate governance, and monitoring progress towards meeting our objectives and annual plans. The Board conducts an annual review of the Group's overall strategy.

C. Resources and controls

The Board ensures that the necessary resources are in place to help the Company meet its objectives and measure its performance against them.

The Internal Audit Services (IA) and Compliance functions provide quarterly reports to the Audit Committee on their activities and annual reviews of key themes, processes and systems (including arrangements for whistleblowing). The Board has full oversight of these matters by way of the Audit Committee Chair's reports to the Board after each Committee meeting. Board members are also able to access the information provided to the Audit Committee.

For more information, see the Audit Committee Report from page 90.

The Board has a formal system in place for Directors to declare a conflict, or potential conflict, of interest.

For more information, see Conflicts of interest on page 211.

D. Stakeholder engagement

The Board aims to ensure a good dialogue is maintained with shareholders, so that their views are understood and considered. The Board also engages with and considers wider stakeholder groups, including the workforce, in its decision making.

More information is set out on pages 80 to 84 and throughout the Strategic Report. Our section 172(1) statement is set out on page 70.

E. Workforce policies

Based on our Values, expected behaviours and key policy principles, the Code of Ethics empowers our workforce to make decisions that are in the best interests of the Group, society and the Company. It is applicable to all within the Group worldwide, including the Board.

For more information about our Code of Ethics, see page 47.

2. Division of responsibilities

F. Chair

Leif Johansson, our Non-Executive Chair, is responsible for the Board's overall effectiveness in directing the Company. Mr Johansson was first elected to the Board in April 2012 and was considered to be independent on his appointment as Chair in June 2012.

Further information about the Chair's annual evaluation is included on page 85 and information about the Chair's tenure is included on page 79.

G. Board composition, independence and division of responsibilities

The composition of the Board is set out on pages 74 and 75. The majority of the Board consists of independent Non-Executive Directors. Directors' independence is considered annually by the Board, as described on page 79.

The Directors are collectively responsible for the success of the Group. The roles of the Board, Board Committees, Chair and CEO are documented, as are the Board's reserved powers and delegated authorities. The Board's responsibilities and the governance structure by which it delegates authority are outlined on the Corporate Governance Overview on page 73.

The Board maintains a list of matters that are reserved to, and can only be approved by, the Board. These include: the appointment, termination and remuneration of any Director; approval of the annual budget; approval of any item of fixed capital expenditure or any proposal for the acquisition or disposal of an investment or business which exceeds $150 million; the raising of capital or loans by the Company (subject to certain exceptions); the giving of any guarantee in respect of any borrowing of the Company; and allotting shares of the Company. Matters that have not been expressly reserved to the Board are delegated to the Committees of the Board or the CEO.

H. Non-Executive Directors' role and time commitment

The Non-Executive Directors exercise objective judgement in respect of Board decisions, providing scrutiny and challenge so as to hold management to account. Non-Executive Directors offer strategic guidance and specialist advice based on the breadth of experience and knowledge they bring to the Board. Non-Executive Directors regularly meet without the Executive Directors or management present.

The Company's senior independent Non-Executive Director serves as a sounding board for the Chair and as an intermediary for the other Directors when necessary. The senior independent Non-Executive Director is also available to shareholders if they have concerns that contact through the normal channels of Chair or Executive Directors has failed to resolve, or for which such contact is inappropriate. Philip Broadley was appointed senior independent Non-Executive Director on 1 March 2021.

As well as their work in relation to formal Board and Board Committee meetings, Non-Executive Directors commit time throughout the year to meetings and telephone calls with various levels of executive management and other key stakeholders, visits to AstraZeneca's sites throughout the world (whether in person or virtually) and, for new Directors, induction sessions and site visits. Therefore the Board members' actual time commitments exceed the minimum expectation of 15 days a year, particularly for the Chair and Chairs of Board Committees. When contemplating taking up additional appointments, Non-Executive Directors consult the Chair to ensure thought is given to any potential impact on their time commitment to AstraZeneca.

Careful consideration is given to the nature of the potential appointment and the type of company involved (for example, whether the company is a public listed company or privately held), to help assess the likely time requirement.

The performance of the Non-Executive Directors is assessed annually as part of the Board's performance evaluation, as described on page 85.

Subject to specific Board approval, Directors and SET members may accept external appointments as non-executive directors of other companies and retain any related fees paid to them, provided that such appointments are not considered by the Board to prevent or reduce the ability of the executive to perform his or her role within the Group to the required standard.

I. Company Secretary
The Company Secretary is responsible to the Chair for ensuring that all Board and Board Committee meetings are properly conducted, that the Directors receive appropriate information prior to meetings to enable them to make an effective contribution and that governance requirements are considered and implemented. The 2021 Board evaluation set out on page 85 provides details of the effective operation of the Board.

3. Composition, succession and evaluation

J. Appointments and succession planning
The Nomination and Governance Committee and, where appropriate, the full Board, regularly reviews the composition of the Board and the status of succession to both SET and Board-level positions. Directors have regular contact with, and access to, succession candidates for SET positions. The Committee also recognises the importance of diversity when considering potential appointments.

There is a formal, rigorous and transparent procedure for appointments to the Board. The Nomination and Governance Committee Report details changes in Board composition during the year, and the appointment and induction processes, from page 86.

In accordance with Article 66 of the Articles, all Directors retire at each AGM and may offer themselves for re-election by shareholders. The Notice of AGM will give details of those Directors seeking election or re-election.

K. Skills, experience and knowledge
When the Nomination and Governance Committee reviews the composition of the Board and its Committees, it uses a matrix that records the skills and experience of current Board members, and compares this with the skills and experience it believes are appropriate to the Company's overall business and strategic needs, both now and in the future.

The Committee is also mindful of Directors' lengths of tenure and the need to refresh membership over time.

For more information, see the Nomination and Governance Committee Report from page 86.

L. Board evaluation
In 2021, the Board undertook an internal Board performance evaluation. More information on the evaluation process, including the results and actions taken, can be found on page 85.

4. Audit, risk and internal control

M. Internal and external audit
The Audit Committee is responsible for reviewing the relationship and independence of our external auditor, PricewaterhouseCoopers LLP. The Committee maintains a policy for the pre-approval of all audit services and audit-related services undertaken by the external auditor, the principal purpose of which is to ensure that the independence of the external auditor is not impaired.

For more information, see page 97 and Note 31 to the Financial Statements on page 196.

The Audit Committee also reviews the independence and effectiveness of IA.

For more information, see page 92.

N. Fair, balanced and understandable assessment
The Board considers this Annual Report, taken as a whole, to be fair, balanced and understandable, and provides the information necessary for shareholders to assess AstraZeneca's position and performance, business model and strategy. The Board's assessment is described on page 96.

The Board and the Audit Committee review the Company's quarterly financial results announcements to ensure they present a fair, balanced and understandable assessment of the Company's position and prospects to shareholders.

O. Risk management
The Board is responsible for the Company's risk management system and internal controls, and their effectiveness. The Board delegates some responsibilities for risk management oversight to the Audit Committee, such as quarterly reviews of the Company's principal and key active risks. During 2021, the Directors continued to review the effectiveness of our system of controls, risk management (including a robust assessment of the emerging and Principal Risks) and high-level internal control processes. This included an annual Governance and Assurance Report to all Directors, which is considered in detail by the Audit Committee and reviewed by the Board.

Any areas of concern are highlighted in the Audit Committee Chair's update to Directors at the relevant Board meeting and discussed by the Board. The Report is based on a full year end review of the Company's risk and control processes (incorporating financial, operational and compliance controls) and findings from assurance processes.

The Directors believe that the Group maintains an effective, embedded system of internal controls and complies with the FRC's guidance entitled 'Guidance on Risk Management, Internal Control and Related Financial and Business Reporting'.

For more information about the ways in which we manage our business risks, our procedures for identifying our emerging risks, how we describe our Principal Risks and uncertainties, and our Viability statement, see Risk management and controls on the following page, and the Risk Overview from page 48.

5. Remuneration

P. Remuneration policies and practices
The Remuneration Committee is responsible for determining, approving and reviewing the Company's global remuneration principles and frameworks, to ensure that they support the strategy of the Company and are designed to promote long-term sustainable success.

For more information on the Remuneration Committee's work, see page 96.

Q. Developing executive remuneration policy
The Remuneration Committee routinely reviews the Directors' Remuneration Policy and executive remuneration arrangements to ensure they continue to promote the delivery of the long-term strategy and support the Company's ability to recruit and retain executive talent to deliver against that strategy. The Committee also considers remuneration arrangements in the context of corporate governance best practice and arrangements for the wider workforce, and regularly consults with its major investors on remuneration proposals. No Director is involved in determining their own remuneration arrangements or outcomes.

For more information, see the Directors' Remuneration Report, from page 98.

R. Remuneration outcomes and independent judgement
To ensure it maintains independent judgement when determining remuneration outcomes, the Remuneration Committee considers a range of data including detailed business and individual performance information. The Committee also consults with other Board Committees to utilise their expertise when determining performance outcomes.

For more information, see the Directors' Remuneration Report, from page 98.

Corporate Governance Report
Other governance information

Further information on Directors' appointments

Mr Johansson was first elected to the Board in April 2012 and was considered to be independent on his appointment as Chair on 1 June 2012. Provision 19 of the Code recommends a company chair's tenure should not extend beyond nine years from their appointment to the board, although the period can be extended for a limited time to facilitate effective succession planning. Acknowledging that he would have served as a Director for nine years by 31 December 2021, the Board believed it would be in the best interests of shareholders for Mr Johansson to seek re-election at the 2021 AGM and continue to serve as Chair, to lead the Board's oversight of the acquisition and integration of Alexion. Our approach for 2022 is explained on page 4.

In December 2021, the Board considered the independence of the other Non-Executive Directors for the purposes of the UK Corporate Governance Code and the Nasdaq Listing Rules. The Board considers that all the Non-Executive Directors except Marcus Wallenberg are independent. Marcus Wallenberg was appointed as a Director of Astra in May 1989 and subsequently became a Director of the Company in 1999. He is a Non-Executive Director of Investor AB, which has a 3.33% interest in the issued share capital of the Company as at 9 February 2022. For these reasons – his overall length of tenure and relationship with a significant shareholder – the Board does not believe that he can be determined independent under the UK Corporate Governance Code. However, the Board believes that he has brought, and continues to bring, considerable business experience and makes a valuable contribution to the work of the Board.

As well as being a Non-Executive Director of AstraZeneca and Chair of the Board's Sustainability Committee, Nazneen Rahman is the Director of the Sustainable Medicines Partnership (SMP), a multi-stakeholder, not-for-profit collaboration with the aim of advancing the environmental sustainability of medicines. AstraZeneca is a strategic collaborator in the SMP. Dr Rahman has recused herself from acting as the lead contact for the SMP in its relationship with AstraZeneca, and this relationship, including project work and overall programme management, is handled by other members of the SMP team.

2021 AGM voting outcomes

At AstraZeneca's AGM in 2021 some shareholders expressed concerns about the number of Sheri McCoy's other directorships of listed companies and the potential impact on her time commitment to AstraZeneca. The Board believes that Ms McCoy has brought, and continues to bring, considerable business experience and knowledge of the pharmaceutical industry and makes a valuable contribution to the work of the Board and Committees of which she is a member, as set out in the statement on the AGM section of our website at www.astrazeneca.com. The Board is satisfied that all Directors, including Ms McCoy, continue to make effective and valuable contributions to the Board and continue to devote sufficient time to discharging their responsibilities as Directors of AstraZeneca.

At the AGM in 2021, votes to approve a new Directors' Remuneration Policy and amendments to the AstraZeneca Performance Share Plan were passed by shareholders, however a significant portion of shareholders voted against each resolution. The Remuneration Committee Chair and management representatives subsequently held discussions with our major investors, and with proxy voting advisory bodies, to understand the rationale behind those voting outcomes.

Further information is included in the Directors' Remuneration Report, on page 101.

Risk management and controls

Global Compliance and Internal Audit Services (IA)

Global Compliance helps the Group achieve its strategic priorities by doing business the right way, with integrity and high ethical standards. Global Compliance focuses on delivering a globally aligned approach that addresses key risk areas across the business, including those relating to third parties and anti-bribery/anti-corruption. We do this by reinforcing compliant behaviours through our Code of Ethics, our policies, training and advice and guidance. We also conduct risk assessment activities and foster a Speak-Up culture where individuals can raise concerns.

We take all alleged compliance breaches or concerns seriously. We investigate and take appropriate disciplinary and remediation action to address and prevent reoccurrence though our internal Compliance, HR and Legal functions and may also engage external advisers when necessary. Dependent on breach severity, management and Legal may be consulted to determine whether the Group needs to disclose and/or report the findings to a regulatory or government authority.

Global Compliance provides assurance insights to the Audit Committee on compliance matters including compliance breaches, associated disciplinary actions and corresponding remediation. Complementing this, IA carries out a range of audits that include compliance-related audits and periodically reviews the assurance activities of other Group assurance functions.

The results from these activities are reported to the Audit Committee. Global Compliance and IA work with specialist compliance functions throughout our organisation to share outcomes and to coordinate reporting on compliance matters.

IA is established by the Audit Committee on behalf of the Board and acts as an independent and objective assurance function guided by a philosophy of adding value to improve the operations of the Group. The scope of IA's responsibilities encompasses, but is not limited to, the examination and evaluation of the adequacy and effectiveness of the Group's governance, risk management and internal control processes in relation to the Group's defined goals and objectives.

Among others, internal control objectives considered by IA include:

- compliance with significant policies, plans, procedures, laws and regulations
- consistency of operations or programmes with established objectives and goals, and effective performance
- safeguarding of assets.

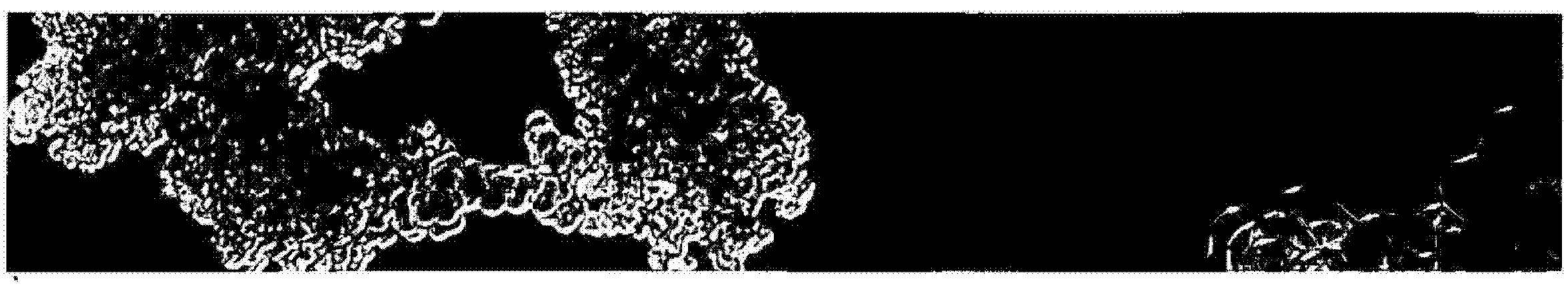
Based on its activity, IA is responsible for reporting significant risk exposures and control issues identified to the Board and to senior management, including fraud risks, governance issues and other matters needed or requested by the Audit Committee. It may also evaluate specific operations at the request of the Audit Committee or management, as appropriate.

Corporate Governance Report
Connecting with our stakeholders

Considering the interests of our stakeholders is fundamental to our Group's strategy. The following table identifies our most strategically significant stakeholders and summarises the engagement that has been undertaken by management during 2021.



	Patients and patient networks	Payers
Overview **Significance of the stakeholder to the business**	Patients are at the heart of what we do. Our stakeholders include individual patients, care-givers and patient advocacy organisations representing the diverse populations that our medicines will serve. We listen to their experiences and embed these insights into every aspect of our work to ensure that the medicines and services we develop have the greatest impact on their lives.	AstraZeneca works closely with payers, which includes governments and medical insurance companies, to understand the impact of pricing medicines on public and private budgets.
Interests **Issues and factors which are most important to the stakeholder group**	> Diverse insights embedded in the drug development process. > Designing clinical trials that reflect real-world clinical practice in a diverse patient population, are minimally burdensome to patients and measure outcomes they care about most. > Ensuring healthcare systems are designed with the patient in mind. > Providing transparent, accessible information in plain, local language. > Ensuring the safety, efficacy and affordable accessibility of our medicines.	> Attracting business investment. > Investment in research and scientific collaborations. > Access to innovative medicines. > Pricing of medicines, including breakthrough therapies and the impact on public budgets. > Containment of reimbursement expenditure. > The safety and efficacy of medicines.
Engagement **Examples of engagement in 2021**	> Engaged people representing diverse patient populations at every stage in our development and clinical trial programmes. > Expanded our Patient Partnership Programmes into new disease areas. > Gathered diverse insights from patients and patient stakeholders to co-create programmes across business units. > Established patient support and affordability programmes.	> Discussions took place with governments and policymakers to increase understanding of the business model and regulation of the pharmaceutical industry, to support investment in life sciences and to improve access to new medicines. > Engaged in discussions on evolving the current reimbursement system for medicines in the US. > Hosted site visits and tours at our manufacturing and R&D facilities for international and local politicians.
Outcomes **Actions which resulted**	> Evolved, enhanced and embedded diverse patient and patient stakeholder insights into our work. > Increased number of patient support programmes. > Collaborated with patient advocacy organisations on key healthcare system transformation projects to bring about tangible healthcare system change at a country level.	> Established working relationships with key government stakeholders. > Regular meetings, roundtables and events organised to increase understanding about how governments can support life-sciences investment and improve patient access to new medicines.



	Investor community	Healthcare professionals	Academic and R&D partners	Commercial collaborators and partners
Overview **Significance of the stakeholder to the business**	The Board and management maintain regular and constructive dialogue with investors to communicate our strategy. We provide objective information about performance to enable investors to put a fair value on the Company and ensure our continued access to capital.	Healthcare professionals (HCPs) are the interface with patients. They support our business by providing insights into clinical trial design and prescribing, advising patients on administering medicines, providing safety reports, collaborating in clinical studies and assisting with the ethical and transparent distribution of medicines.	We collaborate with academic institutions and biotech partners globally to access the best science, to stimulate innovation and to deliver life-changing medicines to patients.	Partnering is an important element of our business, supplementing and strengthening our pipeline. Collaborations help us access disease area expertise through AstraZeneca and non-AstraZeneca medicines. By combining forces, AstraZeneca and our partners can bring scientific innovation to patients around the world more quickly.
Interests **Issues and factors which are most important to the stakeholder group**	> Financial and commercial performance. > R&D strategy, resource allocation and pipeline development. > Culture, values and behaviours. > Exposure to geopolitical and macro-economic risks. > Environmental, social and governance (ESG) matters.	> Development of medicines for unmet clinical needs. > Education and information on advances in medical science. > Accurate and balanced information on licenced medicines, including up-to-date safety data. > Uninterrupted supply of quality medicines. > Ethical and transparent interactions with industry.	AstraZeneca had more than 2,000 active collaborations ongoing in 2021: > To advance innovative technology and science. > To address key scientific challenges. > To access the next generation of science leaders.	> Shared vision/values. > Development and research of medicines that address unmet patient and clinical need. > Trust and transparency in research, disclosures and relationships with stakeholders. > Willingness to collaborate with industry peers to optimise outcomes for common stakeholders, e.g. patients, physicians, policymakers and healthcare systems.
Engagement **Examples of engagement in 2021**	> Ongoing communications including quarterly results calls, in-person and virtual meetings and roadshows. > Regular events at medical conferences and periodic updates on portfolio and pipeline developments.	> Provided and supported HCP educational events > Established HCP advisory boards. > Engaged HCPs as investigators in clinical trials. > Responded to more than 118,000 HCP enquiries and processed over 60,000 adverse event reports from HCPs.	> Sponsored collaborations and more than 500 studentships (PhD, post-doctoral and undergraduate) annually. > Worked side-by-side with academic researchers in more than 10 dedicated university laboratories. > Shared compound assets and data for academic research: more than 35 ongoing or planned clinical trials and more than 425 pre-clinical studies. > Joint seminars, education sessions and consortia with research institutions, e.g. Royal Society, Academy of Medical Sciences and Partner of Choice Network.	> Regular alliance leadership meetings established transparent working relationships with 'one team' mentality and approach across companies. > Joint responsibility for deliverables and outcomes across functions at all levels. > Discussions took place with key stakeholders, e.g. regulators, policy makers, patient groups and the medical community to inform strategy, clinical development and how to best address unmet needs.
Outcomes **Actions which resulted**	> More access to senior and next-level/operational management, including increased virtual engagement. > Following discussion with shareholders, streamlined external-facing materials to provide increased transparency. > Increased focus on ESG matters within results announcements and shareholder engagements.	> HCP advisory boards informed our clinical research and product strategy. > Collaboration in clinical studies has led to new products. > Exchange of information with HCPs which supports clinical decision making.	> Enabled innovative solutions though research collaboration. > New technology, new targets and new biomarkers. > Publications. > Established capability to offer studentship and post-doctoral programmes to facilitate scientific discovery.	> Optimisation of outcomes through combined skillsets and use of technologies/platforms to research new medicines, enabling faster delivery of medicines to patients. > Enhanced speed of recruitment and completion of trials with ability to adapt – multiple trials initiated across multiple disease/patient types. > Greater collaboration and relationships with industry partners and stakeholders.

Corporate Governance Report
Connecting with our stakeholders *continued*

In addition to the principal stakeholders described on pages 80 and 81, the Board considers the following stakeholder groups important for the business operations and strategic direction of the Company.

Community
Wherever we work in the world, we aim to make a positive impact on people and the communities in which they live through our community investment.

Employees
Be a Great Place to Work is a central pillar of AstraZeneca's strategy, as described in our Strategic Report. We need to acquire, retain and develop a talented and diverse workforce in a competitive environment. It is vital our employees are united in pursuit of our Purpose and Values whilst ensuring we maintain a strong AstraZeneca culture. The Board's engagement with the workforce is described on page 84 and more information about Be a Great Place to Work is set out on page 15.

Health authorities
We engage with health authorities globally regarding the manufacturing, development, review and approval, and marketing of our products.

Governments
AstraZeneca partners closely with governments around the world to support healthcare innovation and research, facilitate access to innovative treatments, and build resilient and sustainable healthcare systems.

Multilateral and non-governmental organisations (NGOs)
AstraZeneca partners with multilateral organisations and NGOs to deliver science-based health programming that addresses global health issues and supports the delivery of the UN Sustainable Development Goals. AstraZeneca's commitment to reduce health inequality has also been demonstrated by the supply of *Vaxzevria* where 247 million doses were delivered through the COVAX programme in 2021.

Media
An active and constructive relationship with the media is important to build trust with each one of the Company's key stakeholders by transparently reporting on the Group's activities, including the results of trials and business updates, as well as seeking to enhance and protect the broader reputation of the organisation. The media can influence knowledge of, and sentiment towards, a company.

Suppliers and third-party providers
AstraZeneca relies on integrated supply chains and third-party providers to produce and deliver medicines to patients across the world. During the global pandemic, supply chains across all sectors were compromised. Despite this, AstraZeneca procurement worked closely with our suppliers to understand any risks to supply of goods and services, and agree mitigation strategies that have ensured there has been no disruption to supply. For more information, see page 38.

How the Board engages with stakeholders

The stakeholder table on pages 80 and 81 sets out management's main interactions with certain key stakeholders. Feedback from these interactions is provided to the Board in a variety of ways, which allows the Board to understand the key interests of stakeholders and consider them in its decision making process.

The Board undertakes additional direct engagement with stakeholders to better understand their interests and concerns, so these can be factored into its decision making.

Examples of the Board's engagement are set out in the following columns. Information on how stakeholders and other factors were considered in the Board's principal decisions in 2021 is set out on the following page.

- During 2021, a number of Directors, including the Chair, the CEO and the CFO, met investors at roadshows and one-on-one meetings.
- The Chair of the Remuneration Committee took part in an extensive consultation, which included 16 of our largest shareholders as well three proxy advisers. These engagements provided an insight into how investors viewed the Directors' Remuneration Policy. How these investor views were considered by the Remuneration Committee is set out in the Directors' Remuneration Report from page 98.
- Due to COVID-19 restrictions, the 2021 AGM was a closed meeting. However, all Directors attended the Company's virtual shareholder engagement event in April 2021, which allowed shareholders to interact with, and ask questions of, the Board.
- The Chair of the Board and the Chair of the Remuneration Committee replied to an investor letter to all pharmaceutical companies, which highlighted AstraZeneca's commitment to equitable access to vaccines within the context of the WHO roadmap.
- Investor reports and financial analysts' consensus data are made available to the Board. Feedback is regularly provided to the Board by management on their interactions with investors.
- The Audit Committee reviewed and fed into the Company's response to the UK Government's proposals for restoring trust in audit and corporate governance.
- The CEO and the CFO, along with other members of management, met governmental agencies and regulators to discuss matters including the pricing of medicines and equitable access.
- The CEO attended the G7 and COP26 events, where he met world leaders to discuss and understand concerns regarding various sustainability matters, including the risks arising from climate change and access to healthcare.
- The Board's usual visits to AstraZeneca sites were not possible during 2021 due to COVID-19 travel restrictions. Instead, Directors undertook a number of virtual engagements including deep dives into different business areas, site visits and employee 'roundtable' discussions, which provided insights into the Group's operations and employees' views.
- The integration of Alexion has been a key area of Board focus. To better understand the impact, the Board has received a number of management reports, which identify interests of various stakeholders, including employees, regulators, patients and investors. The Remuneration Committee has also undertaken a thorough review of the existing Alexion remuneration arrangements.

Set out below are examples of how key stakeholders, s.172(1) duties and other matters were considered by the Board when making its Principal Decisions in 2021.

For the s.172(1) statement, see page 70.

Principal Decisions in 2021

Acquisition of Alexion Pharmaceuticals, Inc. and 2021 Group Funding Plan

During 2021, the Board oversaw the acquisition of Alexion (the Acquisition), and approved a number of items connected to completion of the transaction, for example the shareholders' circular and SEC registration statement ahead of the general meetings of shareholders to approve the Acquisition, various financial and accounting reports and representation letters, various legal agreements, including relating to stock exchange listings and debt issuance. Further details of the Acquisition are on page 6.

The Board considered: debt and equity investors; patients; employees' capital allocation priorities; the success of the Company; the consequences of the decision in the long term; and maintaining high standards of business conduct.

How the Board had regard for these matters:

- Reviewed the unmet medical need of rare diseases, the patient benefit and the high-growth, long-term strategic opportunity the Acquisition created.
- Received regular updates from management on progress of the Acquisition.
- Ensured the documentation produced ahead of shareholders' votes on the Acquisition was of a sufficiently high standard, and could be relied upon by shareholders, regulators and other stakeholders.
- Considered the impact of debt issuances on the Group's viability and capital allocation priorities, alongside the financial benefits from the Acquisition, including increased profitability and strengthened cash flow.
- Approved the 2021 Group Funding Plan and issuance of new AstraZeneca shares to be used as consideration.
- Scrutinised integration plans to ensure there was no disruption to the delivery of medicines to patients, to employees or to the operation of the Group.
- Reviewed management's engagement with the workforce to understand employee interests and concerns throughout the transaction.

Establishment of a Sustainability Committee

In October 2021, the Board established a Sustainability Committee to monitor the execution of the Company's sustainability strategy, oversee the communication of the Company's sustainability activities to its stakeholders, and provide input to the Board and Board Committees on sustainability matters, as described on page 85.

The Board considered: investors; communities; employees; governments; regulators; patients; the impact of the Company's operations on the community and environment; the long-term success of the Company; and maintaining high standards of business conduct.

How the Board had regard for these matters:

- Considered feedback received from shareholders to increase the integration of ESG into strategy and performance targets, which had been received during consultations and other engagements.
- Recognised the increasing importance of sustainability matters to our business and all stakeholders, including patients, current and potential employees, governments and regulators, and the expectation that AstraZeneca should be a good corporate citizen.
- Understood the need to have a positive impact in the areas and environments in which AstraZeneca operates.
- Recognised the importance of sustainable operations to ensure long-term value creation for investors.

New executive appointments

In August 2021, Aradhana Sarin was appointed as an Executive Director and CFO of AstraZeneca. Dr Sarin succeeded Marc Dunoyer, who stepped down as CFO and retired from the Board in August 2021. Mr Dunoyer remained part of the SET in his new role as CEO, Alexion and Chief Strategy Officer, AstraZeneca.

The Board considered: investors; employees; the long-term success of the Company; and maintaining high standards of business conduct.

How the Board had regard for these matters:

- Reviewed Dr Sarin's and Mr Dunoyer's experience to ensure that they had the skills required to execute the roles to a high standard and ensure the delivery of our strategy.
- Considered the Board's skills matrix, as well as the needs of the SET and the business, to ensure the appointments would further strengthen management and help the Company to deliver its strategic priorities, in order to deliver value to shareholders, and promote the success of the Company.
- Considered the continuity and reassurance the appointments provided to employees of the enlarged Group and investors. Both candidates were known and trusted by employees and investors, having demonstrated strong leadership and expertise in their previous roles.

Appointment of Philip Broadley as senior independent Non-Executive Director

In March 2021, Philip Broadley succeeded Graham Chipchase as the senior independent Non-Executive Director, ahead of Mr Chipchase's retirement from the Board in May 2021. The senior independent Non-Executive Director is a key role, serving as a sounding board for the Chair and intermediary for the other Directors and shareholders when necessary.

The Board considered, investors; the long-term success of the Company; and maintaining high standards of business conduct.

How the Board had regard for these matters:

- Recognised the importance of ensuring that the senior independent Non-Executive Director had the ability to look after the interests of investors and champion the highest standards of business conduct.
- Reviewed Mr Broadley's experience of the UK listed company regime and understanding of the wider governance and regulatory environment in which AstraZeneca operates to ensure he had the appropriate skills and expertise to fulfil the role.

Ad hoc Board Committee on *Vaxzevria*

- In March 2021, an ad hoc Committee of the Board was formed to have broad oversight of the development and supply of *Vaxzevria*, AstraZeneca's COVID-19 vaccine. The Committee completed its work in October 2021; the Board continues to be regularly updated on development and supply of our COVID-19 treatments.

The Board considered: investors; governments; payers; global partners; suppliers; communities; the Company's reputation; access to healthcare; maintaining high standards of business conduct; the need to foster the Company's business relationships with suppliers, customers and other stakeholders.

How the Board had regard for these matters:

- The Committee supported the Board's oversight of *Vaxzevria* manufacturing, supply chain, efficacy and safety, government relationships and communications strategy by being able to meet frequently with key senior executives over a key period for *Vaxzevria* during 2021.
- When establishing the Committee, the Board considered the best possible short- and long-term outcome for citizens and patients globally, the Company's shareholders and other stakeholders in respect of *Vaxzevria*.

Engaging with our workforce

AstraZeneca is committed to being a great place to work. Engagement with employees is an important element in ensuring an environment in which all employees are respected, where openness is valued, diversity celebrated and every voice heard. We rely on our global workforce to uphold our Values, deliver our strategic priorities and work to sustain and improve short- and long-term performance. For AstraZeneca, 'global workforce' includes our full-time and part-time employees, fixed-term workers and external contractors working full- or part-time, anywhere in the world.

The Directors believe that the Board as a whole is responsible for gathering views of the workforce and consequently chose not to implement any of the three methods of workforce engagement prescribed in the 2018 UK Corporate Governance Code. Instead, the Board continues to utilise and develop the various mechanisms and long-standing channels of engagement in place across the Group that enable and facilitate engagement with the global workforce. These mechanisms include the Board's review of the global workforce Pulse survey and of the Workforce Culture reports. Board Directors also conduct site visits, which facilitate understanding of business operations and provide opportunities for interactions between Directors and the workforce, and engagement with high-potential employees. Due to the global COVID-19 pandemic, these face-to-face engagements took place virtually in 2021.

For more information on how individual Committees interact with the workforce, see the Audit Committee Report from page 90 and the Directors' Remuneration Report from page 98.

Engaging with the wider workforce can present challenges due to the size of the workforce and the global footprint, as well as the variety of roles throughout the organisation. Virtual engagements have helped ensure that individual Directors, as well as Board Committees, have had the opportunity to meet with a range of employees from across the global workforce, and to hear and understand their views.

The channels outlined on this page ensure that the Board has direct access to the views of the global workforce; provide meaningful information and data that the Board can use when considering the impact of its strategic decisions on employees; and provide opportunities for meaningful dialogue. The Board considers these views and the potential impacts on the workforce when it makes key decisions.

For more information, see Be a Great Place to Work, from page 40.

Workforce culture

During 2021, the Board continued to periodically review the Workforce Culture report, which demonstrated how our Values and behaviours are embedded throughout all levels of the workforce. Within the report, there is a summary metrics dashboard, which is divided into categories reflecting key aspects of AstraZeneca's culture (Performance and Development, Integrity, Engagement, Reputation, and Sustainability). Where the Board has concerns that the culture does not reflect our Values, the Board seeks assurances from management that remedial action has been taken and, where necessary, requests senior management's attendance at Board meetings to discuss corrective actions.

Workforce Culture report and Annual Global Remuneration Overview

The Board was provided with information outlining progress against a range of metrics related to workforce culture and engagement. This information is provided biannually to enable Directors to monitor trends and, if required, take action. The Remuneration in the wider context section from page 119 shows how the workforce is rewarded in line with our principles.

91%

of employees took part in the November 2021 Pulse survey.

Employee opinion surveys (Pulse)

Twice a year the workforce is invited to take part in an employee opinion survey, which seeks employees' views of the business. The results are reviewed by management and trends are monitored. The results are shared with the Board, which enables the Directors to understand the views and sentiments of the workforce. In the November 2021 survey, Alexion employees were invited to give their views on working at AstraZeneca across multiple categories such as Talent & Development, Sustainability, Inclusion & Diversity, and Purpose & Values.

87%

of employees stated they believe strongly in AstraZeneca's future direction and key priorities in the November 2021 Pulse survey.

Virtual site visits and engagements with high-potential employees

The Board, its Committees and individual Directors have had numerous virtual interactions to provide exposure to talent and leadership, provide opportunities for dialogue, and enable direct insight and understanding into business operations.

Actions and outcomes

The Board considered the workforce throughout its principal decisions in 2021. Directors ensured that, where required, queries raised during engagements were fed back to management or discussed by the Board. The Board received regular updates on the steps taken by management to create safe working environments and support the mental and physical wellbeing of the workforce.

>10

virtual site visits and engagements with high-potential employees.

Corporate Governance Report
Board performance evaluation

As part of the Board performance evaluation, Directors were asked to consider the following areas:

- Board composition
- Stakeholder oversight
- Board dynamics
- Meeting management and support
- Board Committees
- Pandemic and acquisition of Alexion (case studies)
- Strategic oversight
- Risk management and internal control
- Succession planning and people oversight
- Priorities for change

2021 overview

During the year, the Board conducted the annual evaluation of its own performance and that of its Committees and individual Directors. The 2021 evaluation was carried out internally, although Lintstock Ltd (Lintstock), a London-based corporate advisory firm that provides objective and independent counsel to leading European companies, provided software and services for the evaluation questionnaire. Lintstock has no other commercial relationship with the Company or any individual Directors. Based on Board members' responses to the web-based questionnaire covering a wide range of topics, Lintstock prepared a report which was discussed by the Board at its meeting in December 2021, and was used by the Chair as the basis for individual conversations with each Board member prior to the full Board discussion. The Company's last externally facilitated Board evaluation occurred in 2020.

As part of each Director's individual discussion with the Chair during the Board evaluation, his or her contribution to the work of the Board and personal development needs were considered. Directors' training needs are met by a combination of: internal presentations and updates, and external speaker presentations, as part of Board and Board Committee meetings; specific training sessions on particular topics, where required; and the opportunity for Directors to attend external courses at the Company's expense, should they wish to do so.

The Board intends to continue to comply with the UK Corporate Governance Code guidance that the evaluation should be externally facilitated at least every three years and expects to commission the next externally facilitated review in 2023.

The Nomination and Governance Committee also reviews the composition of the Board to ensure that it has the appropriate expertise, while also recognising the importance of diversity.

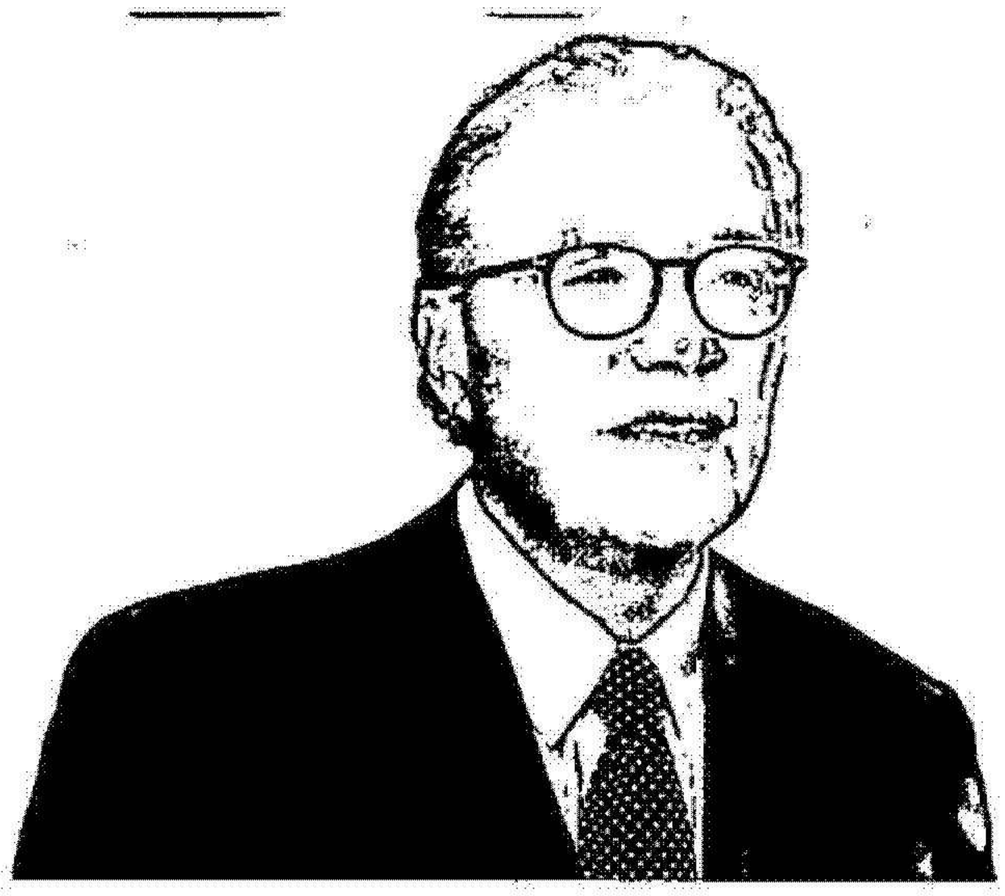
For more information on the Nomination and Governance Committee's work, see the Nomination and Governance Committee Report from page 86.

2021 Outcomes and actions against prior year recommendations

- The Board continues to operate effectively with an atmosphere that enables open and frank discussion, and its relationship with management, including the SET, was highly rated, although the continuing impact of COVID-19 restrictions on Board dynamics and management interactions was noted.
- No significant points were raised regarding the composition or diversity of the Board, although both remain active considerations in annual Board evaluations and the work of the Nomination and Governance Committee.
- The Board's Committees, now supplemented by the Sustainability Committee, which was established in October 2021 and therefore not included in the 2021 evaluation, continue to operate effectively.
- Each Director continues to perform effectively and demonstrate commitment to his or her role, as does the Chair of the Board (whose evaluation by all other Board members, absent the Chair, was led by the senior independent Non-Executive Director).
- The continuing COVID-19 restrictions in 2021 hindered efforts to address two actions arising from the 2020 evaluation – increasing opportunities for Board interaction with stakeholders, and re-assessing the format and cadence of the annual schedule of Board meetings – and these remain objectives as restrictions ease in the future.
- The Board's visibility of how certain key risks are identified and proactively managed – the other theme arising from the 2020 evaluation – was commented on in the 2021 evaluation as an area for further focus, drawing on experience from the pandemic and matters relating to *Vaxzevria* in 2021.
- During 2022, the Board will review the method used for engagement with the Company's workforce to assess whether improvements can be made, and will re-introduce more numerous and structured interactions with employees, as COVID-19 restrictions ease.
- The evaluation identified the need for continued education and briefing sessions to develop further Board members' knowledge and understanding of rare diseases and Alexion, AstraZeneca Rare Disease, acknowledging that the appointment of two new Board members from Alexion during 2021 will also help to underpin the Board's level of expertise in this area.
- The Board's oversight of succession planning for the most senior Board roles, which focused on the roles of CFO and Chair of the Board in 2021, was highly rated, but it was recognised that the Board needs to re-establish a better balance of time between overseeing SET succession plans, as well as Board succession, during 2022.

Nomination and Governance Committee Report

"The Nomination and Governance Committee recommends to the Board new Board appointments and considers, more broadly, succession plans at Board level."



Nomination and Governance Committee members

> Leif Johansson (Chair)
> Philip Broadley
> Michel Demaré
> Nazneen Rahman

The Nomination and Governance Committee's terms of reference are available on our website, www.astrazeneca.com.

Composition of the Board

As part of its role, the Nomination and Governance Committee is responsible for reviewing the composition of the Board, to ensure that it has the appropriate expertise while also recognising the importance of diversity. The Committee reviews the composition of the Board using a matrix that records the skills and experience of current Board members, comparing this with the skills and experience it believes are appropriate to our overall business and strategic needs, both now and in the future. The matrix is set out on page 87. Any decisions relating to the appointment of Directors are made by the entire Board based on the merits of the candidates and the relevance of their background and experience, measured against objective criteria, with care taken to ensure that appointees have enough time to devote to our business.

Inclusion and diversity

Diversity is integrated across our Code of Ethics and associated workforce policy, and we promote a culture of diversity, respect and equal opportunity, where individual success depends only on personal ability and contribution. We strive to treat our employees with fairness, integrity, honesty, courtesy, consideration, respect, and dignity, regardless of gender, race, nationality, age, sexual orientation or other forms of diversity. The Board is provided each year with a comprehensive overview of the AstraZeneca workforce, covering a wide range of metrics and measures (including trends around gender diversity, leadership, ethnic diversity and age profile). The latest Hampton-Alexander Report, published in February 2021, named AstraZeneca PLC as one of the top 10 best performers in the FTSE 100 for representation of women on the combined executive committee and their direct reports. For the year ended 31 December 2021, women represented 41.8% of the SET and its leadership teams.

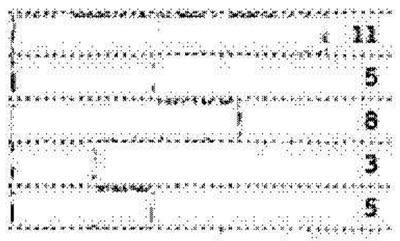
The Board views gender, nationality, cultural and ethnic diversity among Board members as important considerations when reviewing its composition, and has met the recommendations of the Hampton-Alexander and Parker Reviews. Considering diversity in a wider sense, the Board aims to maintain a balance in terms of the range of experience and skills of individual Board members, which includes relevant international business, pharmaceutical industry and financial experience, as well as appropriate scientific and regulatory knowledge. The biographies of Board members set out on pages 74 and 75 give more information about current Directors in this respect.

The Board has adopted an Inclusion and Diversity Policy (the Policy), which is applicable to the Board and its Committees. The Policy reinforces the Board's ongoing commitment to all aspects of diversity and to fostering an inclusive environment in which each Director feels valued and respected. While the Board appoints candidates based on merit and assesses Directors against measurable, objective criteria, the Board recognises that an effective Board, with a broad strategic perspective, requires diversity.

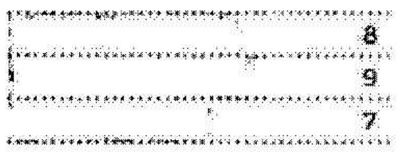
The Policy sets out the Board's aim to maintain a composition of at least 33% female Directors and at least one Director from an ethnic minority background. The Policy provides a commitment to use at least one professional search firm, which has signed up to the 'Voluntary Code of Conduct for Executive Search Firms', to help recruit Directors from a broad, qualified group of candidates, to increase diversity of thinking and perspective.

Non-Executive Directors' experience, as at 31 December 2021

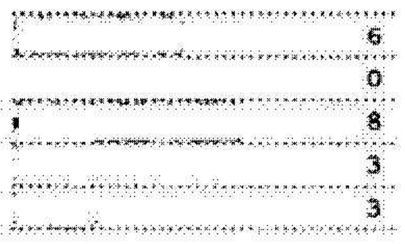
Business



Geographic



Industry-specific



The Board's approach to inclusion and diversity continues to yield successful results. Currently, 36% of the Company's Non-Executive Directors are women, and women make up 38% of the full Board. This meets the Policy's aim of 33% female representation on the Board.

The Board's Inclusion and Diversity Policy can be found on our website, www.astrazeneca.com.

Information about our approach to diversity in the organisation below Board level can be found in the Our People section, from page 41

Appointments during the year

During 2021, and effective 1 August in each case, Aradhana Sarin was appointed as an Executive Director and CFO, succeeding Marc Dunoyer, and Andreas Rummelt was appointed as an independent Non-Executive Director. Dr Sarin was previously EVP, CFO of Alexion, and Dr Rummelt had been a member of Alexion's board since 2010. The appointment processes were led by the Committee and involved meetings with multiple Directors.

Dr Sarin's previous experience as a CFO, extensive knowledge of Alexion, global healthcare systems, capital markets and strategic transactions were important factors in the Committee's decision to recommend her to the Board for appointment as CFO. Knowledge of Alexion was similarly a key factor behind its recommendation to appoint Dr Rummelt, alongside the additional industry-specific experience he brings to the Board, in particular technical R&D, manufacturing and quality assurance expertise. The Board approved the Committee's recommendations in respect of these appointments.

Non-Executive Directors' inductions and training

Newly appointed Non-Executive Directors are provided with comprehensive information about the Group and their role as Non-Executive Directors. They also typically participate in tailored induction programmes that take account of their individual skills and experience. On his appointment as an independent Non-Executive Director, Dr Rummelt commenced an ongoing induction programme intended to provide an understanding of the Group, as well as of his duties as a Director of a listed company. Due to COVID-19 restrictions, this induction programme is mainly taking place virtually, typically by videoconference, until it is possible to recommence face-to-face meetings and site visits. Although elements of his induction will be adjusted for his existing expertise and Committee membership, key areas covered during 2021 and continuing into 2022 include:

- meeting with members of the Board, SET and other senior management
- meeting with external legal advisers
- meeting with the external auditor
- when possible, visits to various sites including R&D centres, commercial sites and operations facilities in the UK, Sweden, the US and elsewhere
- access to a reading room which provides information on the Group, including financial performance, pipeline information, policies including the Global Standard on Dealing in AstraZeneca Securities and rules relating to inside information, investor and analyst reports, and media updates. In addition, the reading room contains guidance on directors' duties and listed company requirements.

Ongoing training and development

AstraZeneca is committed to developing a culture of lifelong learning, including for Directors. At least annually, the Chair discusses with each Director his or her contribution to the work of the Board and personal development needs. Directors' training needs are met by: a combination of internal presentations and updates, and external speaker presentations, as part of Board and Board Committee meetings; specific training sessions on particular topics, where required; and the opportunity for Directors to attend external courses at the Company's expense, should they wish to do so. In addition, Directors are encouraged to attend site visits during the year. During these visits, Directors meet with local management and have tours of AstraZeneca sites and facilities, as well as those of our strategic partners. These site visits further Directors' understanding of the Group's business and operations, as well as providing an insight into the particular challenges faced locally. Additionally, such visits provide Directors with an opportunity to engage with key stakeholders. As mentioned elsewhere in this report, COVID-19 restrictions significantly curtailed Board members' ability to travel for site visits during 2021, but such visits will recommence when possible.

Succession planning

The Nomination and Governance Committee considers both planned and unplanned (unanticipated) succession scenarios, and met five times in 2021. The Committee split the majority of its time between succession planning for Non-Executive Directors, successfully concluding succession plans for the role of CFO, and continued routine succession planning for the roles of Chair of the Board and CEO. The search firm Spencer Stuart was engaged to assist the Committee with its work. Spencer Stuart periodically undertakes executive search assignments for the Company and has no other connection with AstraZeneca or its individual Directors.

Our search for a Chair of the Board as part of routine succession planning is proceeding well, led by Philip Broadley in his capacity as senior independent Non-Executive Director, and he chairs the Committee for this part of its agendas. We have identified a shortlist of strong candidates, and meetings between them and Board members started to take place in the fourth quarter of 2021.

Corporate governance

The Nomination and Governance Committee also advises the Board periodically on significant developments in corporate governance and the Company's compliance with the UK Corporate Governance Code. See from page 77 for the Company's statement of compliance with the UK Corporate Governance Code during 2021.



Leif Johansson
Chair

Science Committee Report

"The Science Committee's core role is to provide assurance to the Board regarding the quality, competitiveness and integrity of the Group's R&D activities."



Science Committee members

> Nazneen Rahman (Chair)
> Euan Ashley
> Geneviève Berger[1]
> Diana Layfield[2]
> Tony Mok
> Marcus Wallenberg
> EVP, Oncology R&D[3]
> EVP, BioPharmaceuticals R&D[3]

[1] Member until retirement from the Board on 11 May 2021.
[2] Appointed to the Committee on 1 October 2021.
[3] Co-opted member of the Committee.

The full role of the Science Committee is set out in its terms of reference, available at www.astrazeneca.com.

Role of the Committee

The Science Committee's core role is to provide assurance to the Board regarding the quality, competitiveness and integrity of the Group's R&D activities. This is done by way of meetings and dialogue with our R&D leaders and other scientist employees, when circumstances allow visits to our R&D sites throughout the world, and review and assessment of:

> the approaches we adopt in respect of our chosen therapy areas
> the scientific technology and R&D capabilities we deploy
> the scientific strategy for maintaining our pipeline and competitiveness
> the decision-making processes for R&D projects and programmes
> the quality of our scientists, their career opportunities and talent development
> benchmarking against industry and scientific best practice, where appropriate.

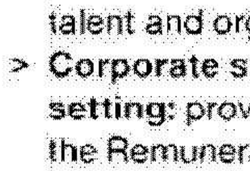
The Science Committee periodically reviews important bioethical issues that we face and assists in the formulation of, and agrees on behalf of the Board, appropriate policies in relation to such issues. It also considers future trends in medical science and technology. The Science Committee does not review individual R&D projects but does review, on behalf of the Board, the R&D aspects of specific business development or acquisition proposals and advises the Board on its conclusions.

Activities during the year

The Science Committee held five meetings in 2021, virtually, as a result of the global COVID-19 pandemic.

Key areas of focus for the Science Committee in 2021 included:

> **AstraZeneca R&D strategic science capabilities:** including digital health, data science and artificial intelligence, knowledge graphs, T-cell circuits and engagers and antibody drug conjugates.
> **Alexion R&D:** providing an in-depth review and introduction for the Science Committee members of the Alexion portfolio, its scientific capabilities, talent and organisation.
> **Corporate scorecard outturn and goal setting:** providing insight and feedback to the Remuneration Committee in support of 2021 achievements and 2022 goal setting.
> **In-licensing agreements:** including a review for the Board of the scientific cases for a global development and commercialisation agreement for eplontersen, a liver-targeted antisense oligonucleotide (ASO), TTR in Phase III development with Ionis Pharmaceuticals and an exclusive global collaboration and licence agreement with Neurimmune AG for NI006, an investigational human monoclonal antibody currently in Phase Ib development for the treatment of transthyretin amyloid cardiomyopathy (ATTR-CM).



Nazneen Rahman
Chair of the Science Committee

Sustainability Committee Report

"At AstraZeneca we are committed to operating in a way that recognises the interconnection between business growth, the needs of society and the limitations of our planet."



Sustainability Committee members

> Nazneen Rahman (Chair)
> Sheri McCoy
> Andreas Rummelt
> Marcus Wallenberg

Standing attendees at Committee meetings include the EVP, Sustainability & Chief Compliance Officer, the EVP Operations & IT and the VP Global SHE & Operations Sustainability.

The full role of the Sustainability Committee is set out in its terms of reference, available at www.astrazeneca.com.

Chair's introduction

I took on responsibility for overseeing sustainability matters on behalf of the Board from January 2021. This position was previously held by Geneviève Berger, Non-Executive Director, who retired from the Board at the 2021 AGM. Since 2015, this role had formed a key part of our sustainability governance framework, providing an additional conduit between the Board and sustainability activities in the business, in addition to the regular direct interactions that take place between the EVP Sustainability & Chief Compliance Officer and the Directors at both Board and Audit Committee meetings.

This year, the existing governance arrangements have evolved naturally to reflect the ever-increasing significance of sustainability to AstraZeneca's business, and the increasing time commitment that oversight of sustainability matters demands – for example, increased reporting requirements and delivery of our Ambition Zero Carbon programme. In October 2021, the Board constituted a new Board Committee – the Sustainability Committee – consisting of myself as Chair, Sheri McCoy, Andreas Rummelt and Marcus Wallenberg who bring a breadth of expertise and experience in sustainability matters.

AstraZeneca's sustainability strategy will continue to be developed by the SET and approved by the full Board. The Sustainability Committee's role is to monitor the execution of that strategy, to oversee the communication of our sustainability activities with our stakeholders and to provide input to the Board and other Board Committees on sustainability matters as required. Committee meetings provide an opportunity for Committee members to interact closely with those charged with executing our sustainability strategy, and thereby bring a deeper understanding to Board members of sustainability initiatives, their progress, who executes them, and how this is done.

Activities during the year

Following a number of introductory meetings and discussions to develop the role and operation of the Committee, the full Committee met formally for the first time in December 2021. Its considerations included:

> **Sustainability strategy:** an overview of the materiality refresh undertaken in 2021. This exercise updated the materiality assessment undertaken in 2018, to identify the areas that are of most importance to AstraZeneca and its stakeholders now, and continues to guide the strategy. More information about the materiality refresh is set out on page 30.
> **Sustainability targets:** consideration of Ambition Zero Carbon targets for Performance Share Plan awards.
> **Finance:** an overview of the investment behind Ambition Zero Carbon and discussion of initiatives to further reduce CO_2 emissions over time.
> **Investor relations update:** an update on investor sentiment and an overview of our engagement with investors on sustainability matters over the year.
> **Disclosures:** a review of draft disclosures relating to sustainability, including the Sustainability Report and TCFD disclosures.

I look forward to continuing to lead this Committee and developing its key role in AstraZeneca's sustainability governance framework in 2022.

Nazneen Rahman
Chair of the Sustainability Committee

Audit Committee Report

"In 2021 the Committee gave particular attention to the presentation of the Alexion acquisition and accounting for the production of *Vaxzevria*, while continuing its regular oversight of the Company's internal controls and financial reporting."



Audit Committee members

> Philip Broadley (Chair)
> Michel Demaré
> Deborah DiSanzo
> Sheri McCoy

Routine attendees at Committee meetings include: the CFO; the General Counsel; the EVP Sustainability and Chief Compliance Officer; the VP Ethics & Transparency and Deputy Chief Compliance Officer; the VP, IA; the SVP Finance, Group Controller; and the Company's external auditor. The Committee, and separately the Committee Chair, also meet privately and on an individual basis with attendees which helps ensure the effective flow of material information between the Committee and management. The CEO and other members of the SET attend when required by the Committee.

The full role of the Audit Committee is set out in its terms of reference, available at www.astrazeneca.com.

Chair's introduction

Welcome to the Report of the Audit Committee (the Committee). This Report describes the work of the Committee and focuses on the significant matters it considered during 2021.

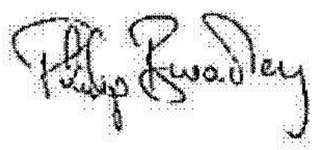
With COVID-19 restrictions continuing to impact Committee members' ability to meet in-person, we have carried on meeting virtually and have worked hard to ensure that our discussions and dialogue are as effective as in person meetings, which we look forward to resuming as soon as practicable. We believe that this has enabled us to continue to provide the level of oversight and challenge to management that is required of the Committee.

Committee meeting agendas through the year include standing items to ensure the Committee is fulfilling its regular responsibilities, as well as ad hoc items that either require the Committee's attention or allow the Committee to gain deeper insight into certain areas of the business or specific matters. We have also arranged numerous virtual interactions with the business outside of formal Committee meetings to enhance the Committee's understanding of the business and provide valuable insights about the key issues and challenges relating to the wider organisation.

Of particular note in 2021, the Committee dedicated significant time to:

> the review of matters related to the acquisition and integration of Alexion, including reviewing the shareholder documents, monitoring the implications on financial reporting of the combined Group, and reviewing the risk management and financial control environments; and
> monitoring the financial reporting implications of *Vaxzevria*, the AstraZeneca COVID-19 vaccine, including supply agreements and inventory. The Committee has focused considerable attention on ensuring a clear understanding of the impact of vaccine arrangements on the Group's financial position and performance, and ensuring disclosures are appropriate.

We hope shareholders find this Report useful and informative, and, as ever, welcome any feedback.



Philip Broadley
Chair of the Audit Committee

Committee overview

Composition of the Committee

In December 2021 the Board determined the Committee met the UK and US composition requirements by virtue of Philip Broadley and Michel Demaré having recent and relevant financial experience for the purpose of the UK Corporate Governance Code (the Code), having competence in accounting and/or auditing for the purpose of the Disclosure and Transparency Rules, and being financial experts for the purposes of the Sarbanes-Oxley Act (SOx). The Board also determined that all members of the Committee are independent for the purposes of the Code and that the Committee members as a whole have competence relevant to the sector in which the Company operates, by virtue of their experience of working in science-driven, healthcare and/or pharmaceutical industries or a result of their tenure with AstraZeneca.

The Committee members' qualifications, skills and experience are detailed in their biographies on pages 74 and 75 and Committee meeting attendance is shown on page 73.

Role of the Committee

The Committee's main respons bilities include monitoring the integrity of financial reporting and formal announcements relating to financial performance, reviewing the effectiveness of internal controls and risk management systems, and overseeing the external and internal audit processes. The Committee reports to the Board the principal matters it considers and any significant concerns it has or that have been reported to it. Further detail about the Committee's role and work during the year is set out below.

Activities during the year

Financial reporting

Effective internal controls, appropriate accounting practices and policies, and the exercise of experienced judgement by the Committee and the Board underpin AstraZeneca's financial reporting integrity.

The Committee reviewed key elements of the Financial Statements and the estimates and judgements contained in the Group's financial disclosures, as well as considering the appropriateness of management's and the external auditor's analysis and conclusions on judgemental accounting matters. The significant financial reporting issues considered are described in detail in the table from page 93. Further information on the significant accounting matters considered is included in the Financial Review under Critical accounting policies, and estimates from page 66 and within our Group Accounting policies from page 138. The Committee also considered the completeness and accuracy of the Group's financial performance against its internal and external key performance indicators.

The Committee discussed and reviewed the preparation of the Directors' Viability statement and considered the adequacy of the analysis supporting the assurance provided by that statement, as well as the going concern assessment and adoption of the going concern basis in preparing this Annual Report and the Financial Statements.

More information on the basis of preparation of Financial Statements on a going concern basis is set out on page 213 and in the Financial Statements on page 136.

The Committee considered the external auditor's reports on its audit of the Group Financial Statements, as well as reports from management, IA, Global Compliance and the external auditor on the effectiveness of our system of internal controls and, in particular, our internal control over financial reporting. This included consideration of compliance with applicable provisions of the Sarbanes-Oxley Act – in particular, the status of compliance with the programme of internal controls over financial reporting implemented pursuant to section 404 of that Act. Following the acquisition of Alexion, management recommended excluding Alexion from the report on Internal Controls Over Financial Reporting for the year of acquisition, as allowed by the SEC. The Committee considered practice in this area, the needs of various stakeholders and the workload required. The Committee concurred with management in taking the exemption, as management works to understand and integrate Alexion's controls with the AstraZeneca framework.

The Committee also spent significant time during the year discussing financial reporting considerations relating to the acquisition of Alexion, including the purchase price accounting valuation and potential impacts on segmental reporting.

The Committee continued to dedicate significant time to considering the effects of COVID-19 on the Company's business, internal controls and financial reporting. The Committee is aware of the significance of vaccine arrangements, and the need to ensure a clear understanding of the impact on the Group's financial position and performance, given the wide public interest in vaccine delivery.

Further information on these significant financial reporting issues considered is set out in the table from page 93.

Risk identification and management

The Committee continued its regular reviews of the Group's approach to risk management, the operation of its risk reporting framework and risk mitigation. This included consideration of how the risk management process was embedded in the Group and the Committee assuring itself that management's accountability for risks was clear and functioning.

When identifying risks, the Committee considers the total landscape of risks. The most significant of these, as measured through potential impact and probability, are our Principal Risks. We then consider those specific risks which are challenging our business presently, our key active risks. Finally, we scan the horizon and identify risks which may challenge us in the future, our emerging risks. This framework provided the context for the Committee's consideration of the Directors' Viability statement. The Directors' Viability statement is underpinned by the assurance provided through a 'stress test' analysis under which key profitability, liquidity and funding metrics are tested against severe downside scenarios.

Each of these scenarios assumes that the associated risks crystallise and that management will take mitigating actions against those risks. The Committee considered in detail the validity of each scenario. This included obtaining additional analysis from management as to the indirect or unintended consequences of its proposed mitigating actions including, for example, assessing the likely response of a broader range of stakeholders. The Committee also assessed whether the proposed mitigations were viable.

The Committee is updated on key active and emerging risks facing the Company through quarterly risk management reports from the CFO. During the year, the Committee considered the particular risks associated with operating during the pandemic, including maintaining manufacture and supply of the Company's products in all markets, and the impact of the acquisition of Alexion on the landscape of risks.

The Committee's consideration of risk management was supported by 'deep dive' reviews of key topics and meetings with teams from within the business, as well as its consideration of cyber risks, as further described on page 92.

Further information about the Principal Risks faced by the Group and the Viability statement is set out in the Risk Overview section from page 46.

Legal and Compliance

The Committee received quarterly reports from the General Counsel to monitor the status of significant litigation matters and governmental investigations. It also received quarterly reports of work carried out by IA and Finance, including the status of follow-up actions with management. Quarterly reports from Global Compliance provided oversight of key compliance incidents (both substantiated and unsubstantiated), trends arising and the dispersion of incidents across our business functions and management hierarchy. The reports included any corrective actions taken so that the Committee could assess the effectiveness of controls, and monitor and ensure the timeliness of remediation.

Audit Committee Report *continued*

The Committee considered the geographic presence, reach and capabilities of the IA and Compliance functions and the appropriateness of the Group's resource allocation for these vital assurance functions.

The Committee's priorities include overseeing compliance with AstraZeneca's Code of Ethics, and ensuring high ethical standards and that we operate within the law in all countries where we operate. During the year, the Committee reviewed data from reports made by employees via the AZethics helpline, online facilities and other routes regarding potential breaches of the Code of Ethics, together with the results of enquiries into those matters.

The Committee continued to monitor and review the effectiveness of our anti-bribery and anti-corruption controls across the Group, prioritising its focus on countries/regions where we have significant operations and countries in which doing business is generally considered to pose higher compliance risks. The Committee also discussed the monitoring, review, education and improvements made to support assurance that the risk of modern slavery and human trafficking is eliminated, to the fullest extent practicable, from AstraZeneca's supply chain.

For more information on our Code of Ethics, see page 47. and on Anti-bribery and anti-corruption, see page 79.

Internal audit (IA)
The Committee carried out the annual effectiveness review of IA by considering its performance against the internal audit plan and key activities. In 2021, IA provided assurance over compliance with significant policies, plans, procedures, laws and regulations, as well as risk-based audits across a broad range of key business activities, and continued its thematic reporting to the business. The 2021 audit plan was aligned to our key active risks and wider risk taxonomy. IA also operates an emerging risk process which was used to dynamically adapt the 2021 audit plan to provide focused, real-time assurance over new and evolving risks impacting the Company. This included a review of the transition planning activities for the integration of Alexion and an audit over the controls around vaccine financing. The Committee noted IA's continued contributions in supporting and delivering value to the business and the Committee during the year. The Committee supports IA's continued efforts to deploy its resources in line with the shape and size of the overall organisation and was satisfied with the quality, experience and expertise of the IA function.

External audit
The Company's external auditor, PwC, provided quarterly reports to the Committee over key audit and accounting matters, and business processes, internal controls and IT systems.

The Committee oversaw the conduct, performance and quality of the external audit, in particular through its review and challenge of the coverage of the external auditor's audit plan and subsequent monitoring of their progress against it. The Committee maintained regular contact with PwC through formal and informal reporting and discussion throughout the year, with a continued focus on maintaining audit efficiency and quality whilst working arrangements continue to involve an element of remote working. The Committee also sought management's feedback on the conduct of the audit and considered the level of and extent to which the auditors challenged management's assumptions.

The Committee engaged with the external auditor in a pilot programme on using Audit Quality Indicators (AQIs). The external auditor and the Committee agreed five initial AQIs to be monitored and reported from 2021. In addition the Audit Committee Chair met with certain PwC audit team members during the year to gain a deeper understanding of the work performed and audit effort required on one of the Group's more significant areas of estimation, being the Group's impairment assessment.

The Committee reviewed audit and non-audit fees of the external auditor during the year, including the objectivity and independence of the external auditor through the application of the Audit and Non-Audit Services Pre-Approval Policy, as described further on page 97.

Further information about the audit and non-audit fees for 2021 is disclosed in Note 31 to the Financial Statements on page 196.

Cybersecurity and information governance
The Committee receives annual presentations from the Chief Digital Officer and Chief Information Officer and her team. In 2021, the Committee reviewed the top cyber risks facing AstraZeneca and the effectiveness of our procedures to defend our IT systems against increased levels and new forms of attack from external agents. The Committee also considered steps being taken to reduce the risk of technology disruption at AstraZeneca sites.

Engagement with employees and other stakeholders
The Committee regularly interacts with members of management below the SET and seeks wider engagement with the Group's employees and other stakeholders. Due to COVID-19 travel restrictions and social distancing measures, the Committee undertook a series of virtual interactions with a wide range of teams from across the organisation. The Committee also arranged 'deep dive' reviews of key topics and interactions to follow up on certain IA findings, to better understand identified areas for improvement and interrogate the business's response to those findings.

In 2021, these interactions and reviews involved Committee members meeting with representatives from the following teams: IT/IS, Operations, Alexion corporate functions (finance, accounting, tax, treasury, internal audit, compliance and legal); the Canadian marketing company; the Italian marketing company; the Malaysian marketing company; the Oncology Business Unit; Procurement; and the Turkish marketing company. The breadth of these interactions is crucial as it enhances the Committee's understanding of the business and provides valuable insights into the key issues and challenges relating to, and current and emerging risks associated with, our activities in these areas. The Committee welcomes the opportunity to engage directly with employees in these meetings which provide an opportunity to gauge employee sentiment and hear their views directly. The Committee also uses these interactions to communicate the importance it attaches to compliance and our 'Speak Up' culture.

Reporting and regulatory environment
The Committee has kept abreast of developments in the reporting and regulatory environment. This has included updates on the Task Force for Climate-related Financial Disclosures framework and AstraZeneca's priorities in preparation for compliance, alongside consideration of reporting implications. The Committee also oversaw AstraZeneca's response to the consultation on the BEIS White Paper on Restoring Trust in Audit and Corporate Governance, and considered the Company's 2020 Annual Report disclosures in light of the Financial Reporting Council's (FRC) review of how issuers had incorporated the new corporate governance disclosures within their 2019 annual reports, as well as considering the observations set out in a number of thematic reviews issued by the FRC during 2021.

Committee performance
The Committee conducted the annual evaluation of its own performance, with each Committee member and other attendees responding to a questionnaire prepared by a third party. The results were reported to and discussed with the Committee and the Board. The Committee was rated very highly overall. Meetings were seen to be well structured, organised and managed. There was a high level of engagement from the Committee members. The Committee was seen to benefit from excellent technical skills, very in-depth discussions and strong leadership from the highly-skilled Chair. The Committee's effective adaptation to virtual meetings was also noted.

Significant financial reporting issues considered by the Committee in 2021

Matter considered		Committee's conclusion and response
Acquisition accounting See Financial Review from page 52 and Note 27 to the Financial Statements from page 178.	AstraZeneca completed the acquisition of Alexion in July 2021 for total consideration of $41.1 billion. At the date of acquisition, AstraZeneca has undertaken a fair valuation of the identifiable assets and liabilities acquired, the consideration paid and the resultant goodwill and recorded the necessary accounting entries in accordance with IFRS 3 Business Combinations. Furthermore, from the date of acquisition onwards, AstraZeneca has consolidated Alexion's results into the Group's financial reporting utilising data transfer processes and financial controls that were thoroughly tested and validated pre-close.	The Committee received regular reports from management during the year providing updates on the transition planning and day one financial readiness for the acquisition. In particular, the Committee focused on securing a stable and controlled financial transition, on ensuring an effective control environment irrespective of the SOx exemption being applied to Alexion controls, and ongoing delivery of external reporting commitments. The Committee considered the approach to the purchase accounting valuation and concurred with management on the areas of estimation or judgement. The Committee reviewed the final acquisition accounting and disclosures and considered management's proposed subsequent treatment of intangible asset amortisation, fair value uplift of inventory and presentation of future acquisition-related costs under our policy for Core financial measures.
Vaccine and other COVID-19 activities' accounting See Group Accounting Policies from page 138.	AstraZeneca continued to enter into arrangements with government bodies, certain vaccine alliances, and external contract manufacturers as part of the Group's determination to develop and supply *Vaxzevria*, the AstraZeneca COVID-19 vaccine. AstraZeneca has supplied a significant proportion of contracted volumes in the year, realising product sales of $3,917 million over the year. Some of these government arrangements included grants or advanced funding to support both research and development costs and the establishment of supply chains. Each government and alliance arrangement required a thorough and considered assessment to determine different performance obligations and ensure appropriate accounting treatment. During the last quarter of the year AstraZeneca commenced supply of *Vaxzevria* on commercial terms as it transitioned the vaccine activities towards business as usual, with moderate profitability. Product Sales of $1,781 million in the last quarter came from a blend of early pandemic (not-for-profit) contracts and recent orders. In the year, the majority of doses delivered related to pandemic (not-for-profit) contracts.	The Committee is aware of the significance of vaccine arrangements, and of the wider public interest in vaccine accounting, and so focused considerable attention on ensuring a clear understanding of the impact on the Group's financial position and performance. The Committee was presented with a detailed assessment of areas of increased risk conducted by management and has been provided with updates throughout the year. The Committee receives quarterly updates on the status (and any financial reporting implications) of vaccine arrangements and transactions. The Committee also discussed and challenged the applicable accounting principles applied, which were assessed to be appropriate. The Committee recognised management's proactive assessment and continual close monitoring of the COVID-19 pandemic on the areas of increased risk, as noted in the Group's Accounting Policies from page 138. The Committee also reviewed the disclosures that have been included in this Annual Report relating to the vaccine supply arrangements and concluded these to be appropriate.

Audit Committee Report *continued*

Significant financial reporting issues considered by the Committee in 2021 *continued*

Matter considered		Committee's conclusion and response
Alternative performance measures (APMs) See Financial Review from page 52.	AstraZeneca reports APMs to provide helpful supplementary information to the IFRS measures to enable a better understanding of the Group's financial performance and position. In 2021, APMs were further set out to report the impact of vaccine activity separate from the rest of the business. The acquisition of Alexion resulted in more significant items being classified as non-core, especially relating to the unwind of fair value uplift of inventory, amortisation of allocated fair value of purchased intangible assets and share-based payment charges. These items, coupled with material impairments booked during the year, resulted in an IFRS quarterly loss and a Core quarterly profit. Management carefully analyses the presentation of various items to ensure it is fair and balanced, and follows guidelines issued by ESMA and the SEC, as well as FRC thematic reviews.	The Committee carefully considered management's presentation of vaccine performance at a revenue level and deemed it appropriate in light of the regulatory and investor focus on vaccine performance. The Committee further considered management's assessment and recommendation to present identified Alexion items as non-core, and concurred with management that the presentation was consistent with previous precedent and enabled a better comparison of performance across periods. The Committee reviewed proposed disclosures for non-GAAP items in line with the various regulatory guidance, and concurred with management that the presentation enabled additional helpful guidance.
Valuation of intangible assets See Financial Review from page 52 and Note 10 to the Financial Statements from page 156.	The Group carries significant intangible assets on its balance sheet arising from the acquisition of businesses and IP rights to medicines in development and on the market. Each quarter, the CFO reports on the carrying value of the Group's intangible assets as well as the specific assets identified as at risk of impairment. In respect of intangible assets that are identified as at risk of impairment, the Committee receives information on the difference between the carrying value and management's current estimate of discounted future cash flows for 'at risk' products (the headroom). Products will be identified as 'at risk' because the headroom is small or, for example, in the case of a medicine in development, there is a significant development milestone such as the publication of clinical trial results which could significantly alter management's forecasts for the product. The reviews also cover the impact on any related contingent consideration arising from previous business combinations.	The Committee considered the impairment reviews of the Group's intangible assets. Impairments of $1,492 million arising from the portfolio prioritisation of strategic projects were considered in the third quarter, with the key product being Ardea's impairment of $1,172 million due to the decision to discontinue development of verinurad. The Committee assured itself of the integrity of the Group's accounting policy and models for its assessment and valuation of its intangible assets, and related headroom, including understanding the key assumptions and sensitivities within those models, along with the internal and external estimates and forecasts for the Group's cost of capital relative to the broader industry. The Committee was satisfied that the Group had appropriately accounted for the identified impairments.
Revenue recognition See Financial Review from page 52 and Note 1 to the Financial Statements from page 145.	The US is our largest single market and sales accounted for 32.8% of our Product Sales in 2021. Revenue recognition, particularly in the US, is affected by rebates, chargebacks, returns, other revenue accruals and cash discounts. Following the Alexion acquisition, these revenue adjustments include items related to Rare Disease products.	The Committee pays attention to management's estimates of these items, its analysis of any unusual movements and their impact on revenue recognition. The Committee receives regular reports from management and the external auditor on this complex area. The US market remains highly competitive with diverse marketing and pricing strategies adopted by the Group and its peers. The Committee recognised the close monitoring and control by management and the continuous drive to improve the accuracy in forecasting for managed market rebates and excise fees, which has supported a stabilisation of the overall gross-to-net deductions.

Significant financial reporting issues considered by the Committee in 2021 *continued*

Matter considered		Committee's conclusion and response
Litigation and contingent liabilities 📖 See Note 30 to the Financial Statements from page 189.	AstraZeneca is involved in various legal proceedings considered typical to its business and the pharmaceutical industry as a whole, including litigation and investigations relating to product liability, commercial disputes, infringement of IP rights, the validity of certain patents, anti-trust law, and sales and marketing practices.	The Committee was regularly informed by the General Counsel of, and considered management and the external auditor's assessments of, IP litigation, actions, governmental investigations, and claims that might result in fines or damages against the Group, to assess whether provisions should be taken and, if so, when and in what amount. Of the matters the Committee considered in 2021, the more significant included: the European Commission Vaccine Litigation; the continued defence of the *Nexium* and *Prilosec* product liability litigation in the US; the Array and Amplimmune commercial litigations; and patent challenges relating to *Symbicort*, *Tagrisso*, *Enhertu*, *Farxiga* and *Ultomiris* in the US. The Committee was satisfied that the Group was effectively managing its litigation risks including seeking appropriate remedies and continuing to defend its IP rights vigorously.
Tax charges and liabilities 📖 See Note 4 to the Financial Statements from page 149. 💻 AstraZeneca's Approach to Taxation, which was published in December 2021 and covers its approach to governance, risk management and compliance, tax planning, dealing with tax authorities and the level of tax risk the Group is prepared to accept, can be found on our website, www.astrazeneca.com.	The Group has business activities around the world and incurs a substantial amount and variety of business taxes. AstraZeneca pays corporate income taxes, customs duties, excise taxes, stamp duties, employment and many other business taxes in all jurisdictions where due. In addition, we collect and pay employee taxes and indirect taxes such as value-added tax. The taxes the Group pays and collects represent a significant contribution to the countries and societies in which we operate. Tax risk can arise from unclear laws and regulations as well as differences in their interpretation.	The Committee reviews the Group's approach to tax, including governance, risk management and compliance, tax planning, dealings with tax authorities and the level of tax risk the Group is prepared to accept. During 2021, the Committee undertook a review of Alexion's tax affairs and the tax implications of integrating it into the Group. In addition at its December meeting, the Committee considered the potential impact of US tax reform on the Group which would arise should substantive enactment occur. The Committee was satisfied with the Group's practices regarding tax liabilities, including, most notably, its response to developments in the corporate income tax environment.
Segmental reporting 📖 See the Key Judgement within Note 6 to the Financial Statements on pages 152.	The nature of the Group's business changed during the year, with material sales of *Vaxzevria* and the acquisition of Alexion. The Group has carried out significant *Vaxzevria* transactions in the period, and externally reported performance excluding the impact of these transactions to align to guidance issued. The acquisition of Alexion resulted in the addition of the Rare Disease Area to AstraZeneca's portfolio, with the Alexion CEO joining the SET and reporting to the CEO. Management has reviewed both changes in the year and determined they do not result in a separate segment based on key decisions on resource allocation and performance monitoring being carried out at a Group level by the SET.	The Committee received reports from management regarding considerations for segmental reporting arising from significant changes in the business. The Committee considered the analysis provided by management related to the reporting of vaccines and acquisition of Alexion, and concurred with management that presenting AstraZeneca's performance under one segment was appropriate.

Audit Committee Report *continued*

Significant financial reporting issues considered by the Committee in 2021 *continued*

Matter considered		Committee's conclusion and response
Retirement benefits See Financial Review from page 52 and Note 22 to the Financial Statements from page 168.	Accounting for defined benefit pension and other retirement benefits is an important area of focus. The Group recognises that the present value of these liabilities is sensitive to changes in long-term interest rates, future inflation and mortality expectations. As a result, the assumptions used to value the liabilities for the Group's main retirement benefit obligations are updated every quarter. Similarly, 'mark-to-market' asset valuations are also procured. This enables an updated funding level to be calculated each quarter. The Group is cognisant of the wider regulatory environment and local requirements around funding levels and contributions. The UK Pension Scheme Act 2021 came into force on 1 October 2021 and a section of the Act focuses on the funding of and security provided to UK defined benefit pension schemes with additional requirements placed on corporate sponsors.	The Committee monitors the funding level of the Group's defined benefit obligations on a quarterly basis and the funding requirements in each case, alongside key developments. The Committee reviews the Group's global funding objective and key activities, engagement with local fiduciary bodies, and comparisons of funding solvency relative to the wider market. The Committee was satisfied that the Group's contribution policy and actuarial assumptions used to value liabilities were appropriate during the year. The Committee was reassured by the Group's engaged and balanced approach to managing the risks associated with the funding of its defined benefit obligations. The Committee is cognisant of the need to adhere to local funding regulations and best practice and to the security provided by the Group, which underwrites obligations to members. In the UK, the Committee is aware that the Group has developed a framework to ensure compliance with the UK Pension Scheme Act 2021 and will monitor implementation in 2022.

Fair, balanced and understandable assessment

As in previous years, at the instruction of the Board, the Committee undertook an assessment of this Annual Report to ensure that, taken as a whole, it is fair, balanced and understandable and provides the information necessary for shareholders to assess the Company's position and performance, business model and strategy. The Committee reviewed the Company's governance structure and assurance mechanisms for the preparation of the Annual Report and, in particular, the contributor and SET member verification process. The Committee received an early draft of the Annual Report to review its proposed content and the structural changes from the prior year and to undertake a review of the reporting for the year, following which the Committee members provided their individual and collective feedback. In addition, in accordance with its terms of reference, the Committee (alongside the Board) took an active part in reviewing the Company's quarterly announcements and considered the Company's other public disclosures which are managed through its Disclosure Committee. To aid its review further, the Committee also received a summary of the final Annual Report's content, including the Company's successes and setbacks during the year and an indication of where they were disclosed within the document.

The processes described above allowed the Committee to provide assurance to the Board to assist it in making the statement required of it under the Code, which is set out from page 78.

Internal controls

Information on the Company's internal controls is included in the Audit, Risk and Internal Control section in the Corporate Governance Report on page 78.

Following the acquisition of Alexion Pharmaceuticals, Inc., the Committee concurred with management's recommendation that the Company exclude this business from its assessment of the effectiveness of internal control over financial reporting as at 31 December 2021, in accordance with SEC Staff Guidance, as described on page 126. The Committee received regular updates to help ensure an effective control environment, irrespective of the Alexion SOx exemption.

During the period covered by this Annual Report there was no change in our internal control over financial reporting that occurred that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

At the February 2022 Committee meeting, the CFO presented the conclusions of the evaluation by the CEO and CFO of the effectiveness of our disclosure controls and procedures that is required by Item 15(a) of Form 20-F at 31 December 2021. Based on their evaluation, the CEO and the CFO concluded that, as at that date, the Company maintained an effective system of disclosure controls and procedures. During the year the Committee was also updated on the matters considered by the Disclosure Committee each quarter.

External auditor

PwC is the Company's external auditor. In May 2021, PwC was reappointed as the Company's auditor for the financial year ended 31 December 2021, its fifth consecutive year as auditor, having first been appointed for the financial year ended 31 December 2017, following a competitive tender carried out in 2015. After five years in the role, Richard Hughes will step down as the lead audit partner at PwC on the conclusion of the 2021 audit, in line with partner rotation requirements. We thank Richard for his conduct of the audit during his tenure. Richard will be replaced by Sarah Quinn. The selection process for the new lead audit partner was designed to identify the best qualified partner for the role, to ensure audit quality. A short list of candidates was identified following discussions between the Committee and PwC. The candidates were then interviewed by the Audit Committee Chair and the CFO. The Committee made the final selection based on feedback from those interviews as well as an assessment of the candidates' experience and expertise. We look forward to working with Ms Quinn, who has extensive knowledge of our industry and of UK and US reporting requirements, and who we believe will continue to ensure the quality of the audit.

Non-audit services and safeguards
The Committee maintains the Audit and Non-Audit Services Pre-Approval Policy (the Policy) for the pre-approval of all audit services, audit-related services and other assurance services undertaken by the external auditor. The principal purpose of the Policy is to ensure that the independence of the external auditor is not impaired.

The pre-approval procedures permit certain audit and audit-related services to be performed by the external auditor, subject to annual fee limits agreed with the Committee in advance. Pre-approved audit and audit-related services below the clearly trivial threshold (within the overall annual fee limit) are subject to case-by-case approval by the SVP Finance, Group Controller.

Pre-approved audit services included services in respect of the annual financial statement audit (including quarterly and half-year reviews), attestation opinions under section 404 of the Sarbanes-Oxley Act, statutory audits for subsidiary entities, and other procedures to be performed by the independent auditor in order to form an opinion on the Group's consolidated Financial Statements. The pre-approved audit-related services, which the Committee believes are services reasonably related to the performance of the audit or review of the Company's Financial Statements, included certain services required by law or regulation, such as financial statements, audits of employee benefit plans and capital market transactions. The Policy prohibits any tax services. Audit-related services included the assurance in relation to tax regulatory certificates required to be issued by the external auditor.

The Committee reviewed and provided approval for PwC to perform non-audit services totalling $6.1 million in relation to supporting the issuance of the Shareholder Circular and US F-4 filings, as well as EMTN debt issuance, in preparation for the Alexion transaction. These services included capital markets technical advice, private opinions on working capital, private diligence reports on working capital, profit forecasts and Financial Position and Prospects procedures, and public opinions on SIR5000 GAAP reconciliation.

The CFO (supported by the SVP Finance, Group Controller), monitors the status of all services being provided by the external auditor. Authority to approve work exceeding the pre-agreed annual fee limits and for any individual service above the clearly trivial threshold is delegated to the Chair of the Committee together with one other Committee member in the first instance. A standing agenda item at Committee meetings covers the operation of the pre-approval procedures and regular reports are provided to the full Committee.

All services other than the pre-approved audit and audit-related services, require approval by the Committee on a case-by-case basis. In 2021, PwC provided audit services including interim reviews of the results of the Group for the periods ended 31 March 2021 and 30 June 2021 and audit-related and other assurance services in relation to the acquisition of Alexion and the associated debt issuance.

Audit/non-audit services

2021	$34.9m
2020	$20.3m

Statutory audit fee[1]
Audit-related and other assurance services[2]

[1] 2021 statutory audit fee excludes $0.3m (2020: $nil), in relation to pre-acquisition Alexion audit fees, recognised in Note 31 to the Financial Statements on page 196.
[2] 2021 audit-related and other assurance services excludes $0.7m (2020: $nil), in relation to pre-acquisition Alexion services, recognised in Note 31 to the Financial Statements on page 196.

The increase to the statutory audit fee for 2021 is largely driven by the inclusion of post-acquisition Alexion audit fees. The increase to audit-related and other assurance services is largely driven by services performed by PwC in the year, in relation to the acquisition of Alexion and the associated debt issuance.

Fees for audit-related and other assurance services amounted to 27% of the fees payable to PwC for audit services in 2021 (2020: 6%). The Committee is mindful of the 70% non-audit services fee cap under EU regulation, together with the overall proportion of fees for audit and audit-related services in determining whether to pre-approve such services. Fees for audit-related and other assurance services payable to PwC in 2021 were 34% of average audit fees over 2018 to 2020. The increase to these percentages is primarily driven by the additional services required in respect of the Alexion acquisition.

PwC were better placed than any alternative provider to provide these services in terms of their familiarity with the Company's business, skills, capability and efficiency. All such services were either within the scope of the pre-approved services set out in the Policy or were presented to Committee members for pre-approval and all such services were permitted by the FRC Ethical Standard.

Further information on the fees paid to PwC for audit, audit-related and other services is provided in Note 31 to the Financial Statements on page 196.

Assessing external audit effectiveness
In accordance with its normal practice, the Committee considered the performance of PwC and its compliance with the independence criteria under the relevant statutory, regulatory and ethical standards applicable to auditors. The Committee assessed PwC's effectiveness principally against four key factors, namely: judgement; mindset and culture; skills, character and knowledge; and quality control. As part of that assessment, it also took account of the views of senior management within the Finance function and regular Committee attendees. The Committee concluded that the PwC audit was effective for the financial year ended 31 December 2021.

In February 2022, the Committee recommended to the Board the reappointment of PwC as the Company's auditor for the financial year ending 31 December 2022. Accordingly, a resolution to reappoint PwC as auditor will be put to shareholders at the Company's AGM in April 2022.

The external audit will be put out to tender in or before the 2027 financial year, in order to comply with UK legal requirements regarding the auditor's tenure and audit tendering. The Committee reviews the effectiveness of PwC as the external auditor on an annual basis and may choose to commence a tender earlier if it deems this to be in the best interests of the Company's shareholders.

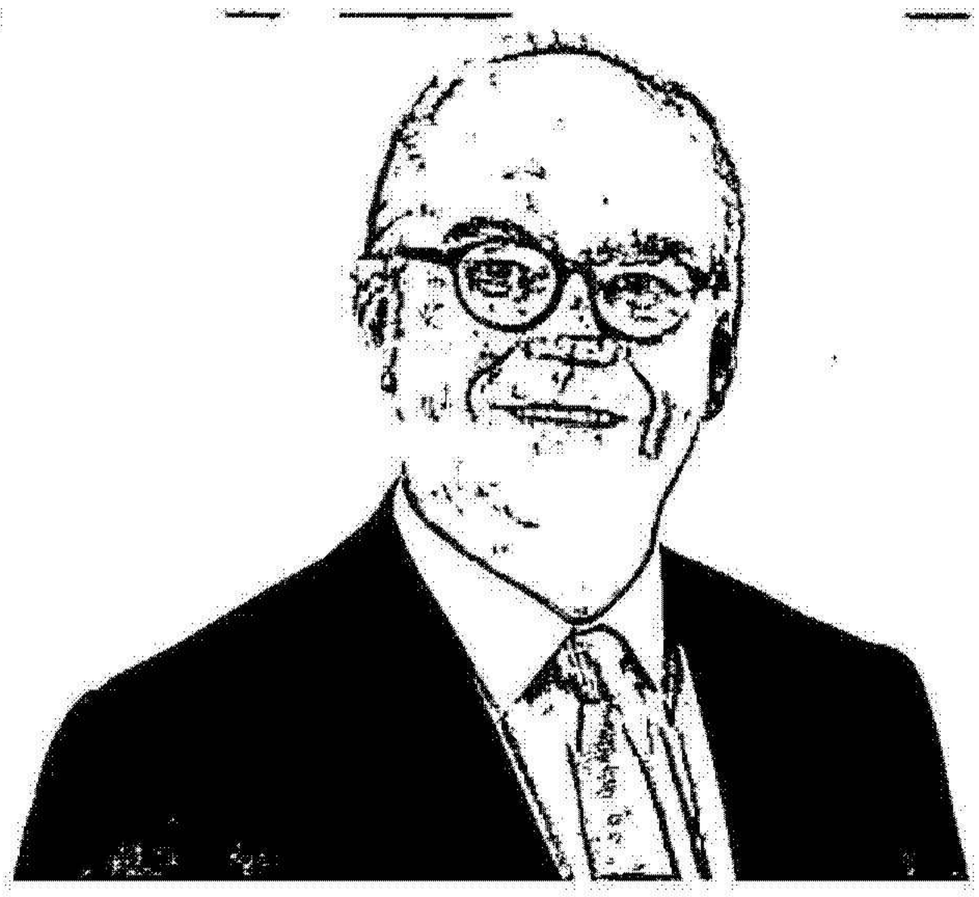
The Committee does not believe that tendering the audit at this time would be in the best interests of shareholders and is cognisant of the scale and complexity of the AstraZeneca Group, particularly following the recent acquisition of Alexion. A sufficiently long transition period would be required to ensure a new auditor built up the necessary knowledge and business familiarity to ensure the delivery of an effective audit and consequently any plans to tender the external audit should allow time for an orderly transition.

Regulation
The Committee considers that the Company has complied with the Competition and Markets Authority's Statutory Audit Services for Large Companies Market Investigation (Mandatory Use of Competitive Tender Processes and Audit Committee Responsibilities) Order 2014 in respect of its financial year commencing 1 January 2021.

Directors' Remuneration Report

We have sought to be clear and transparent in how we link remuneration of our executives to successful delivery of our strategy, our response to the pandemic and shareholder returns.

"Three year TSR of 59% demonstrates another period of excellent performance for shareholders, while successfully delivering the Alexion acquisition and being at the forefront of the response to COVID-19."



The Directors' Remuneration Report contains the following sections:

> Chair's letter page 98
> Remuneration at a glance page 102
> How our performance measures for 2022 support the delivery of our strategy page 103
> How the Remuneration Committee ensures targets are stretching page 104
> Annual Report on Remuneration page 105

Remuneration Committee members

> Michel Demaré (Chair)
> Philip Broadley
> Leif Johansson
> Sheri McCoy

The full role of the Remuneration Committee is set out in its terms of reference, available on our website, www.astrazeneca.com.

On behalf of the Board, I am pleased to present AstraZeneca's Directors' Remuneration Report for the year ended 31 December 2021.

2021 has been a transformational year for AstraZeneca. The Company delivered strong financial performance and completed the acquisition of Alexion, further supporting its strategic ambitions and strengthening its financial position. In addition, AstraZeneca, together with its partners, released for supply 2.5 billion doses of *Vaxzevria* to over 180 countries and launched *Evusheld*, the only long-acting antibody with Phase III data demonstrating benefit in both the prevention and treatment of COVID-19.

Key Committee activities in 2021

At the Company's 2021 AGM, the Board put a new Remuneration Policy forward for approval by shareholders for the second consecutive year. The Committee acknowledges that seeking approval for a revised Policy at two consecutive AGMs was an unusual step, however we are still convinced that doing so was in the best interests of the Company and its shareholders over the long term. The Committee was pleased that the resolutions were approved. However, the Committee also recognised that shareholder support for the 2021 Policy was lower than the previous year's (2021: 60%; 2020: 95%). Following the AGM, I undertook an extensive consultation process to listen to shareholders' and proxies' feedback. Further detail on the 2021 consultations and the steps taken by the Committee to address concerns, can be found later in this letter. I would like to thank those that took part in the extensive consultation for their constructive feedback.

Appointment of the new CFO

On 1 August 2021, Marc Dunoyer stepped down as CFO and Executive Director of AstraZeneca PLC and took on a new role as CEO, Alexion and Chief Strategy Officer, AstraZeneca, while remaining a member of the Senior Executive Team. Following an extensive search, Aradhana Sarin, CFO of Alexion prior to the acquisition, was appointed as CFO and Executive Director of AstraZeneca from 1 August 2021, based in the UK. The Committee carefully considered the terms of our new CFO's remuneration arrangements. In designing a competitive remuneration package, the Committee focused on current market benchmarks, and took into account Dr Sarin's existing reward at Alexion in the US (which included the existence of contractual change of control severance arrangements that Dr Sarin was entitled to choose as an alternative to accepting the CFO role in the UK).

Dr Sarin's 2021 remuneration arrangements, as set out from page 105 of the Annual Report on Remuneration, are aligned to our pay-for-performance philosophy and market-competitive remuneration. It allowed us to act quickly and decisively to secure a strong candidate to succeed Mr Dunoyer as CFO. The short- and long-term incentive opportunities are consistent with the 2021 Policy, and base pay is in line with relevant benchmarks. The on-target pay positioning for the new CFO, as set out on page 101, is around the upper quartile of our European peer group, which appropriately reflects AstraZeneca's relative size within this group.

Review of targets and performance measures following the acquisition of Alexion

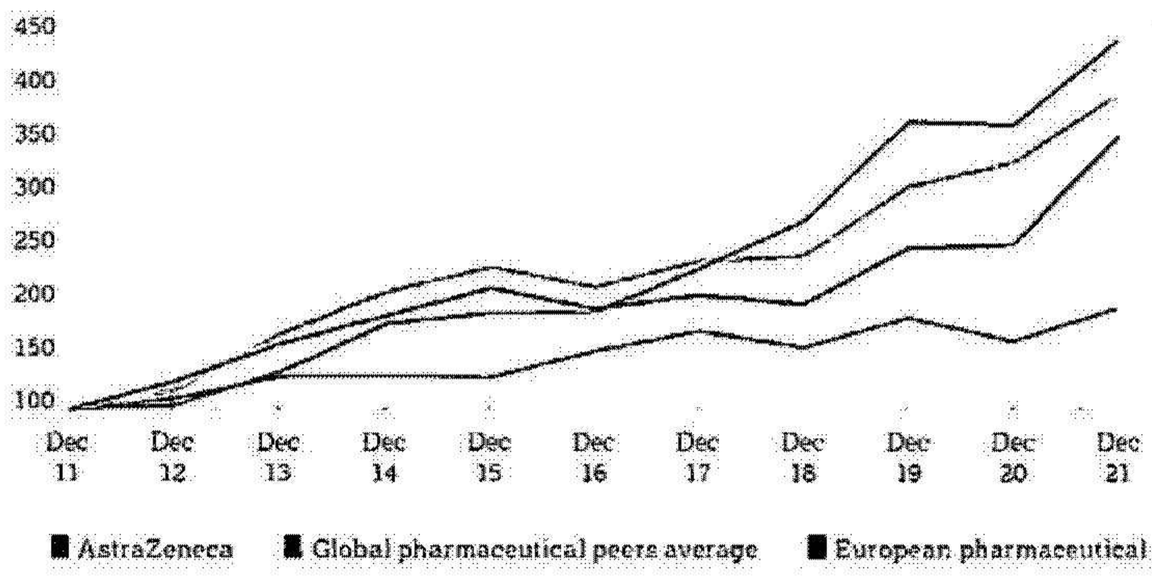
Following the acquisition of Alexion, which completed in July 2021, the Committee reviewed the targets for the 2021 annual bonus scorecard and the 2019 Performance Share Plan (PSP) performance measures. Where required, the existing ambitious targets were increased mid-year to reflect the impact of the Alexion acquisition on the Company's results and the economics of the transaction approved by the Board. Before approving the amendments to the existing targets, the Committee had additional sessions with management to understand and challenge the proposals. We are confident that the revised targets are of equivalent level of stretch, and will continue to incentivise our leaders to deliver exceptional performance.

The process of setting stretching targets is extensive, robust and iterative, involving multiple interactions with management, the Board and the Committee (which includes three members of the Audit Committee). Further details on this process are set out on page 104.

As the Chair of the Committee, I also attended the Science Committee's meeting at which the Science targets were reviewed to ensure I fully understand the assumptions and scenarios which form the foundations of their recommendations. I will work with the recently-established Sustainability Committee next year in a similar manner to ensure that proposed ESG measures and targets are both appropriate and suitably stretching.

How we have performed in 2021

Total shareholder return (TSR)



2019 to 21[1]

+59%

[1] Calculated using a three-month calendar average, from 1 October to 31 December, prior to the start and at the end of the relevant period.

More information on the TSR peer groups for PSP awards can be found on page 122.

Delivery against strategy – 2021 Group scorecard performance[2]

	Target	2021 outcome
Deliver Growth and Therapy Area Leadership		
Total Revenue	$33.1bn	**$34.7bn**
Innovative Science: Annual pipeline progression		
Pipeline progression events	22	**26**
Regulatory events	31	**37**
Achieve Group Financial Targets		
Cash flow	$5.6bn	**$6.3bn**
Core EPS	$5.25	**$5.34**

[2] For details of the Remuneration Committee's consideration of Group scorecard outcomes and a description of performance measures, see from page 102.

Further detail of 2021 commercial and scientific performance can be found in the Strategic Report from page 12.

2021 Performance

Growth and Therapy Area Leadership

Revenue growth has been strong throughout 2021 and well balanced across all disease areas, with double-digit growth in all major regions, including Emerging Markets. We achieved these results despite COVID-19 continuing to impact the diagnosis and treatment of other diseases in some markets and sustained pricing pressures in China. Our strong pipeline progress has underpinned the transition to long-term sustainable growth with five of our medicines crossing new blockbuster thresholds.

In July 2021, the Group completed the acquisition of Alexion, which represents a significant step forward in progressing our strategic and financial development and supports the Company's transition to long-term sustainable growth. Alexion will help to accelerate expansion into immunology and rare disease, further sustain industry-leading double-digit revenue growth and improve our profitability and cash flow. Given Alexion's pipeline, expertise in immunology and strong research platforms, the acquisition will accelerate the combined Group's strategic ambitions – driving innovation and the speed of delivery of the next wave of science and accelerating the development of medicines to help more patients around the world.

For more information on Rare Disease, see page 24.

Accelerate Innovative Science

AstraZeneca delivered unprecedented pipeline results as we continued to realise the full potential of our medicines and advance the next wave of science, with return on investment in our pipeline continuing to outperform our peers. We secured 32 pipeline progression events, either NME Phase II starts or Phase III investment decisions in 2021, of which 26 count towards the annual bonus outcome. Three key highlights from the pipeline delivery include: new NME Approval for *Saphnelo*, the first type I interferon receptor agonist for systemic lupus erythematosus (SLE), which is the only new medicine to be approved in over 10 years; the breakthrough data with *Enhertu* showing enormous promise in breast cancer treatment with data presented in September 2021 demonstrating that DESTINY-Breast03 showed a remarkable 72% reduction in the risk of disease progression or death for *Enhertu* compared to the current standard of care (trastuzumab emtansine or T-DM1); and *Farxiga* approved for chronic kidney disease, significantly reducing risk of death by 31%.

In response to shareholder feedback, the Committee has agreed a new naming convention in relation to the science measures in the annual bonus scorecard and the PSP, to more clearly delineate the difference between the two types of measure, which assess different aspects of the scientific pipeline. You will see throughout this report that the Accelerate Innovative Science measure under the bonus scorecard is now called 'Innovative Science: Annual pipeline progression' and the Accelerate Innovative Science measure under the PSP is now called 'Innovative Science: First approvals and NME volume over three years'. There is no change to the underlying performance metrics, this name change is for clarification only.

Great Place to Work

Ensuring that AstraZeneca is a great place to work continued to be a top priority during 2021. AstraZeneca focused on protecting staff in the face of the continuing global pandemic,

Directors' Remuneration Report *continued*

implementing principles to support the health and safety of employees upon the return to the workplace; and ensuring the safety of our patients, and their continued access to care and medicines. The Company made no staff redundant as a consequence of the pandemic and did not take advantage of furlough arrangements or government support in any country.

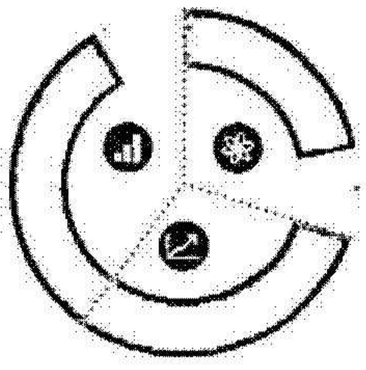
AstraZeneca has continued to contribute to society. We continue to make good progress on our sustainability strategy and have established a Board Committee to monitor the execution of that strategy. The launch of the Sustainability Committee was an important next step in advancing and delivering our sustainability goals and underlines our commitment to change. I look forward to working with the Sustainability Committee in future when reviewing the performance against the existing Ambition Zero Carbon measure within the 2021 PSP and when considering potential further ESG measures.

We also drove change beyond our Company by playing a central role at COP26, to address the climate crisis and promote a green recovery during and post the pandemic. Our efforts were recognised, with HRH The Prince of Wales naming our Company as one of the first holders of his Terra Carta Seal.

Despite these challenging times, employee engagement continued to be high with 85% of employees believing AstraZeneca is a great place to work. Employees also believe AstraZeneca's response to the COVID-19 pandemic has been very positive, reflecting our collective pride in efforts to change the course of the pandemic and provide support and information to employees as we navigate this period.

In particular, employees recognise AstraZeneca's contribution to society with our work on *Vaxzevria* and with the launch of *Evusheld*. During 2021, 2.5 billion doses of the vaccine were released for supply to over 180 countries, approximately two thirds of which went to low- and lower-middle-income countries. More than 300 million doses were delivered to 130 countries through the COVAX Facility. Until October 2021, AstraZeneca supplied *Vaxzevria* on a not-for-profit basis. From the fourth quarter of 2021, we have moved to an affordable pricing model under which AstraZeneca remains committed to providing broad and equitable global access to the vaccine. This includes a tiered pricing approach aligned to Gross National Income per capita, which is a widely recognised and implemented model used by developers of medicines and vaccines. We remain committed to supplying the vaccine at no profit to low-income countries, in line with our agreement with the University of Oxford.

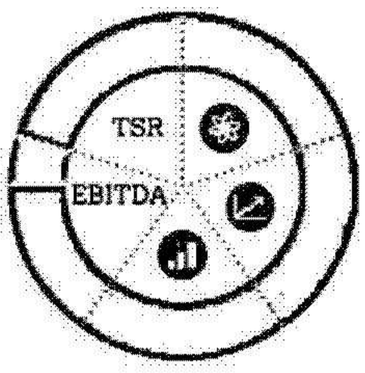
2021 Annual bonus scorecard performance[1]



	Achieved
Innovative Science: Annual pipeline progression	73%
Deliver Growth and Therapy Area Leadership	100%
Achieve Group Financial Targets	79%

■ Achieved

2019 PSP performance



	Achieved
Innovative Science: First approvals and NME volume over three years	100%
Deliver Growth and Therapy Area Leadership	100%
Achieve Group Financial Targets – Cash flow	100%
EBITDA	75%
Relative TSR	100%

■ Achieved

[1] When determining bonus outturns, the Committee considered the formulaic outcome from the Group scorecard along with wider business and individual impact and performance in 2021, including ESG achievements.

Our Executive Directors' roles in leading our response to the pandemic has been considered by the Committee when reviewing their performance against their individual goals, as highlighted from page 109.

For more information on our actions in relation to COVID-19, see page 29.

Improving our diversity and inclusion remains paramount and we have continued to drive change within the organisation by hosting educational events such as the Power of Diversity Week and celebrating the power and potential of girls as showcased in our #GirlsBelongHere campaign. Significant progress towards meeting our ambition of having women represent 50% of our senior roles by 2025 was made over the last year – 48.1% as at year end 2021.

2021 remuneration outcome

The Committee always seeks to ensure that the remuneration of our Executive Directors and our wider workforce reflects the underlying performance of the business. When approving outcomes, we therefore considered the Group scorecard along with wider business and individual performance over 2021, including other achievements across the enterprise, such as the completion of the acquisition of Alexion, advancing our Great Place to Work priorities and ESG goals. In that context, we believe that the payments outlined below fairly reflect performance.

Annual bonus

When determining bonus outturns, the Committee considered the formulaic outcome from the Group scorecard along with wider business and individual impact and performance in 2021, including ESG achievements. The Committee determined to award an annual bonus equivalent to 95% of maximum (237.5% of base pay) to Pascal Soriot. This is in line with the approach to differentiate bonus awards for individuals in the wider workforce that have made an exceptional contribution in 2021. The Committee determined to award annual bonuses equivalent to 84% of maximum (168% of base pay) to Dr Sarin and Mr Dunoyer respectively. Bonuses awarded to Dr Sarin and Mr Dunoyer were pro-rated in relation to their services provided as CFO during the year. Details of the factors considered to determine the bonuses are provided from pages 107 to 111.

One half of each Executive Director's bonus for 2021 will be deferred into AstraZeneca shares for three years to ensure further alignment with shareholder interests.

Long-term incentives (LTI)

2019 PSP – 95% of maximum

Our approach aims to reward sustainable outperformance and hence our 2019 award will vest at the upper end of the possible range. The three-year performance period for Performance Share Plan (PSP) awards granted to Executive Directors in 2019 ended on 31 December 2021. Awards will vest at 95% of maximum, as shown on page 112 and reflect overachievement in each and every three-year target, as well as delivering a three-year TSR of 59%.

Response to voting at the 2021 AGM

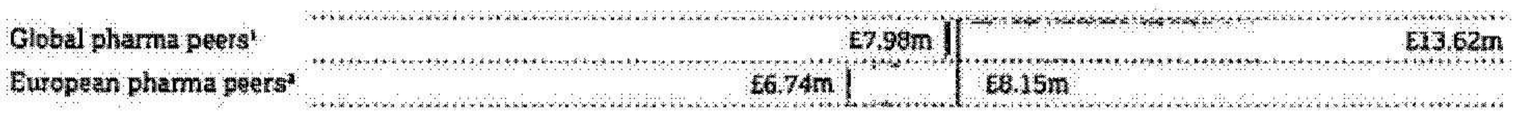
At AstraZeneca's 2021 AGM, the shareholder votes to approve the Directors' Remuneration Policy and to amend the rules of the 2020 PSP were passed with majorities of 60.19% and 61.72% respectively. Since the AGM, on behalf of the Committee, I have met with 16 of the Company's largest shareholders, representing approximately 40% of the share register, as well as three proxy advisors, to understand their concerns in relation to these two resolutions and to discuss future remuneration.

I spoke with the majority of AstraZeneca's largest investors, who remain overwhelmingly supportive of our Executive Directors and the Company's strategic ambition. Shareholders also recognise that our Remuneration Policy appropriately aligns executive pay with performance, and highlighted the importance of the Committee's ongoing commitment to stretching performance targets. They also emphasised the need to remain competitive in the global talent market, and expect the Board to take the necessary measures to position AstraZeneca accordingly. However, a common concern raised by those who voted against the resolutions was that we had sought approval for a new Remuneration Policy at two consecutive AGMs, and in a challenging period because of the pandemic. A minority also expressed concern around the scale of the CEO's total remuneration opportunity in the UK context, albeit recognising the global dimension of the CEO's role. There was also satisfaction that the pension contributions of the Executive Directors have been aligned with the wider UK workforce, thereby resulting in a lower fixed compensation and higher leverage of the pay-for-performance component.

In response to concerns raised by some shareholders, we are committed to a period of stability in our approach to executive remuneration, and confirm our intention that the 2021 Policy will remain in effect until 2024. We have not made any material changes to the structure of executive reward in 2022, with the only adjustment being an increase in the Executive Directors' base pay, in line with base pay increases for wider UK workforce.

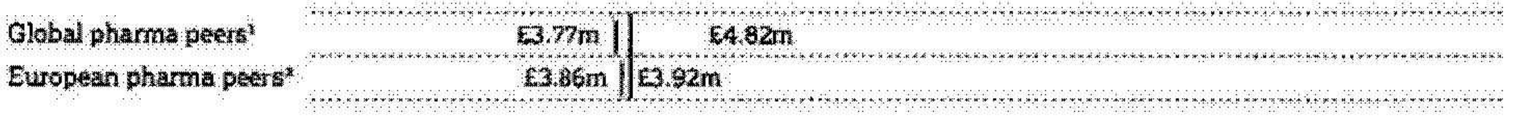
Market positioning of Executive Directors' on-target remuneration for 2021

CEO



□ Lower quartile to median
Median to upper quartile
| Current position

CFO



□ Lower quartile to median
Median to upper quartile
| Current position

¹ Global pharma peer group consists of: AbbVie, Allergan, Amgen, BMS, Eli Lilly, Gilead, GSK, J&J, Merck, Novartis, Novo Nordisk, Pfizer, Roche and Sanofi
² European pharma peer group consists of: Bayer, GSK, Merck KGaA, Novartis, Novo Nordisk, Roche and Sanofi

Remuneration includes base pay, target annual bonus and the expected value of Long Term Incentive (LTI) awards. Benchmarking data has been provided by the Committee's independent adviser.

We remain committed to our pay-for-performance philosophy and market-competitive remuneration, as demonstrated by the arrangements for Aradhana Sarin on her appointment as an Executive Director and CFO. Additionally, we will continue to focus on setting stretching performance targets and have included detail on page 104 around how further stretch has been built into our targets following the acquisition of Alexion. We will continue to improve the transparency and quality of disclosures in our Directors' Remuneration Report.

The Committee will continue to engage regularly with shareholders and other stakeholders.

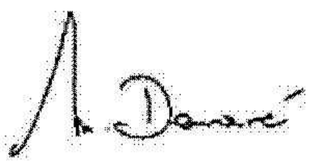
Non-Executive Directors' fees

With effect from January 2022, four elements of the Non-Executive Directors' fee structure have increased. These changes reflect the steady increase in workload and responsibilities of the Non-Executive Directors since the last fee increases at AstraZeneca took effect four years ago in January 2018, as well as the increase in size and complexity of the Group following the acquisition of Alexion. No Board member participated in any decision relating to their own fees. Further detail is provided on page 116.

Next steps

I hope that you find this Remuneration Report clear in explaining the implementation of our Remuneration Policy during 2021, and the meaningful and thorough response we have made to address investor feedback following the 2021 AGM. We trust that we have provided the information you need to be able to support this Remuneration Report at the Company's AGM in April 2022.

Our ongoing dialogue with shareholders and other stakeholders is valued greatly and, as always, we welcome your feedback on this Directors' Remuneration Report.



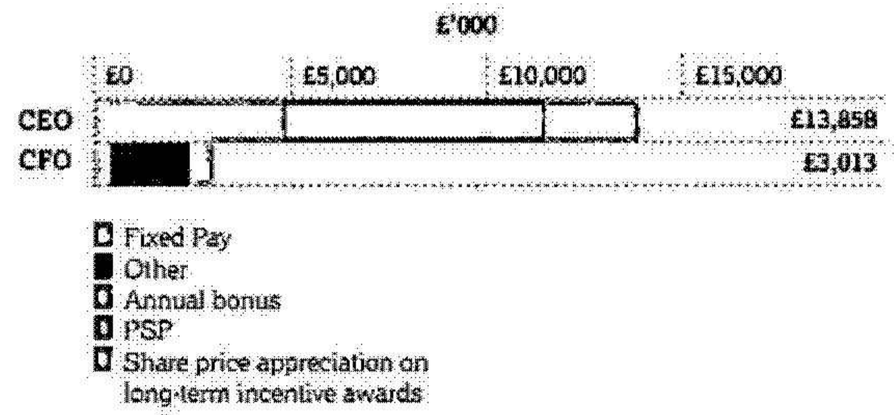
Michel Demaré
Chair of the Remuneration Committee

Remuneration at a glance



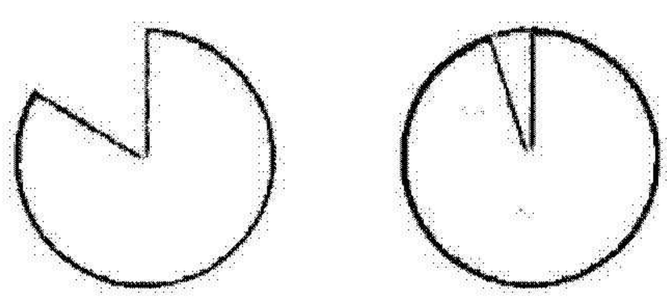
What our Executive Directors earned

Executive Directors' realised pay 2021 outcomes



Fixed pay consists of base pay, benefits fund and pension. Further information on Executive Directors' realised pay for 2021 is on page 105.

Formulaic outcome of 2021 Group scorecard and 2019 PSP



See from page 105 for further information on the annual bonus and PSP outcome

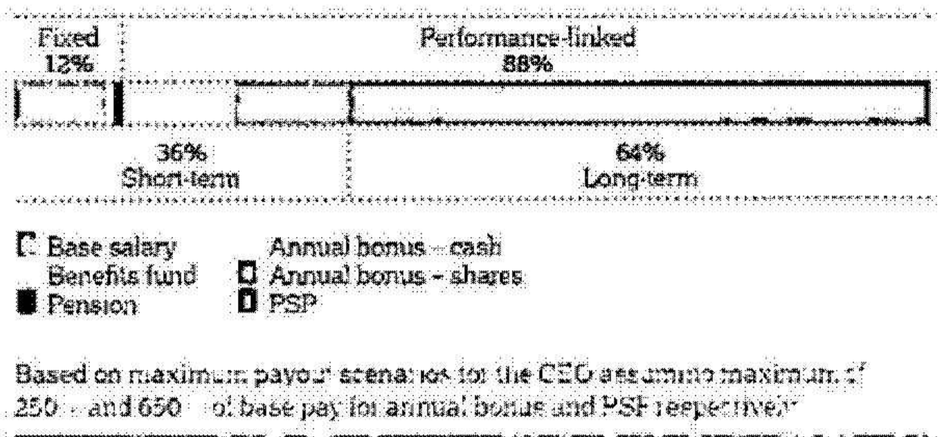
When determining bonus outturns, the Committee considered the formulaic outcome from the Group scorecard along with wider business and individual impact and performance in 2021, including ESG achievements. For the CEO this resulted in a bonus outturn of 95% of maximum.

Looking ahead

Executive Directors' remuneration for 2022

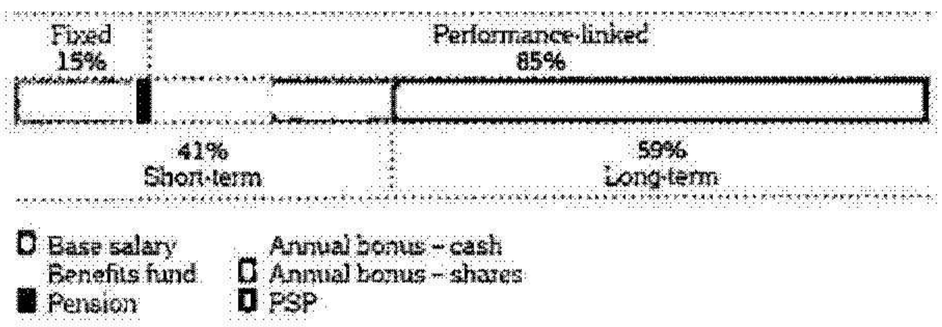
	Fixed remuneration	Annual bonus	Long-term incentives	Shareholding guideline	Post-cessation guideline
Pascal Soriot (CEO)	Base pay: £1,367,002 Benefits fund Pension: £150,370 (equivalent to 11% of base pay)	Max: 250% base pay Target: 125% base pay Deferred: 50% for three years	Max: 650% base pay Performance period: three years Holding period: two years	Holding requirement: 650% base pay	Holding requirement: shares up to 650% base pay for two years post-cessation
Aradhana Sarin (CFO)	Base pay: £875,500 Benefits fund Pension: £96,305 (equivalent to 11% of base pay)	Max: 200% base pay Target: 100% base pay Deferred: 50% for three years	Max: 450% base pay Performance period: three years Holding period: two years	Holding requirement: 450% base pay	Holding requirement: shares up to 450% base pay for two years post-cessation

CEO fixed vs performance-linked (%)



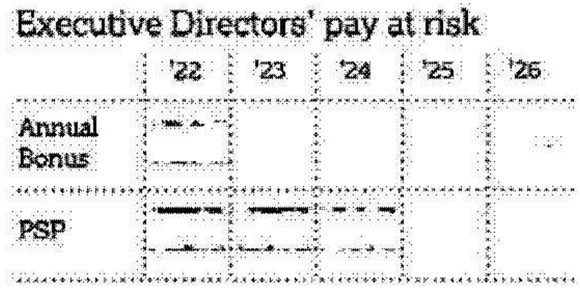
Based on maximum payout scenarios for the CEO assuming maximum of 250% and 650% of base pay for annual bonus and PSP respectively.

CFO fixed vs performance-linked (%)



Based on maximum payout scenarios for the CFO assuming maximum of 200% and 450% for annual bonus and PSP respectively.

Executive Directors' pay at risk



See from page 105 for further details on plan design

How our performance measures for 2022 support the delivery of our strategy

AstraZeneca aims to continue to deliver great medicines to patients while maintaining cost discipline and a flexible cost base, driving operating leverage and increased cash generation. To incentivise and reward delivery of great performance over the short and longer term, the Committee carefully considers the balance of science, financial and ESG measures between the annual bonus and PSP.

Our focus on incentivising innovative science aligns with our patient-centric culture, as we strive to push the boundaries of science to deliver life-changing medicines to patients. The 2022 performance measures are closely aligned with our strategic priorities, as shown below.

For more information about our strategic priorities, see page 12. For more information about the 2022 performance measures, see pages 111 to 115.

Key

- ● Annual bonus
- ● PSP
- ○ KPI

Strategic pillar

Accelerate Innovative Science

Remuneration performance measures

Science indices ● ● ○

Our science measures incentivise the development of new molecular entities (NMEs) and the maximisation of the potential of existing medicines.

Bonus performance is assessed on pipeline progressions through Phase II and Phase III clinical trials. These reflect the outcome of nearer-term strategic investment decisions, whereas in contrast PSP performance is assessed on the volume of NMEs in Phase III and the registration stage, which reflects the outcome of longer-term strategic investment decisions.

Additionally, we measure regulatory submissions and approvals for bonus, and regulatory approvals for PSP to drive the conversion of scientific progress into commercial revenue over the short term (bonus) and the longer term (PSP).

Together, these science measures incentivise innovation and sustainable success along the length and breadth of the pipeline, leading to commercial growth.

Strategic pillar

Deliver Growth and Therapy Area Leadership

Remuneration performance measure

Total Revenue ● ● ○

Our Total Revenue measure is included in the bonus and the PSP, reflecting the importance of incentivising sustainable growth in both the short and longer term.

Financial targets

Achieve Group Financial Targets

Remuneration performance measures

Cash flow ● ● ○

Ensures that we can sustain investment in our pipeline and therapy areas while at the same time meeting our capital allocation priorities. Cash flow is included in both the bonus and the PSP, so as to motivate a focus on the importance of both short and longer term cash flow generation and balance sheet strength..

Core EPS ● ○

Incentivises operational efficiency and cost discipline, remains a key measure of our profitability and is a key focus for our investors.

Total shareholder return (TSR) ●

Assessed relative to our peer group of companies, the measure rewards positive performance that our shareholders also directly benefit from. This measure incentivises outperformance versus our peer group, and promotes the delivery of long-term sustainable returns for our shareholders.

Strategic pillar

Be a Great Place to Work ●

Being a Great Place to Work is critical to delivering our ambition. Assessment of performance against this pillar is captured through a holistic review of each Executive Director's individual performance as part of the final determination of annual bonus, including consideration of our progress against our ESG aspirations through:

- Contribution to the enterprise – their achievement of embedding a culture of life-long learning and development, and performing as an enterprise team, as well as advancement of our inclusion and diversity strategy.
- Contribution to society – their delivery across access to healthcare, environmental protection, ethics and transparency to lead in sustainability.

Ambition Zero Carbon ●

This measure incentivises the elimination of our Scope 1 and Scope 2 greenhouse gas (GHG) emissions by 2025 with targets verified in line with the science of climate change, where we will innovate to avoid, reduce and substitute to become zero carbon.

How the Remuneration Committee ensures targets are stretching

We set stretching targets that incentivise our leaders to deliver exceptional performance, to drive sustainable results for our patients, our employees and our shareholders. Following the acquisition of Alexion, the Committee reviewed the suitability of existing performance targets for our in-flight annual bonus and long-term incentive (LTI) plans in light of the enlarged Group.

The Committee reviewed performance targets in September 2021 and approved increases to targets to ensure they remained stretching and continued to incentivise strong performance. See page 108 for details on the 2021 scorecard targets, and page 112 for the 2019 PSP.

We take the following robust process to setting annual bonus and PSP targets:

Stage 1 – Target setting	Science targets are based on a cohort of scientific opportunities specified at the start of the performance period. Opportunities represent potential achievements through the pipeline, from an early stage where our scientists work to discover new molecules, through to ultimately obtaining approvals and getting new medicines to patients. Rewarding success at each stage recognises the importance of creating and maintaining a long-term sustainable pipeline. Stretch of proposed targets is reviewed by the Science Committee taking into account factors such as the expected Net Present Value of the pipeline and the anticipated financial contribution it will make, past performance, the external regulatory environment, and internal resourcing and efficiencies. Targets for realisation of these opportunities are ambitious. Proposed targets for the Ambition Zero Carbon measure are reviewed by the Sustainability Committee.	Deliver Growth and Therapy Area Leadership and Achieve Group Financial Targets metrics align with the Company's Mid Term Plan (MTP), which sets out the financial framework for delivering our ambitious strategy over the short- and medium-term. The MTP process includes detailed business reviews, during which plans and efficiencies of each unit are challenged, leading to a proposed MTP for the Board to review and challenge. The Committee sets targets based on the Board-approved MTP, considering consensus expectations, independent analytics and anticipated challenges and opportunities. This range of data is used by the Committee to ensure the stretching nature of performance targets is robustly tested. Additionally, the PSP TSR measure is designed to reward strong performance relative to our peers.
Stage 2 – Committee review and approval of targets	The Committee thoroughly reviews and challenges targets proposed by management. The Committee is provided with considerable supporting material for each metric. For science measures, the Committee reviews and approves the full cohort of opportunities and receives briefings from senior science leaders within the business. These targets are set with oversight of the Science Committee, with a focus on ensuring that the targets will result in long-term sustainable value creation underlying the delivery of the LRP. The target in relation to our ESG metric in the PSP is determined with the input of our Sustainability Committee.	Committee members participate in the full Board discussions on the strategy, MTP and budget, which form the basis for the targets. The Committee considers how proposed financial targets align with the MTP and budget; prior years' outcomes (in absolute terms and against target); how the ambition has changed from the prior MTP and budget; external guidance the business has provided or plans to give; consensus from external financial analysts and factors it may be impacted by; and the underlying assumptions. Statistical analysis conducted by the Committee's independent adviser is also used to assess the proposals. This includes an assessment of historical levels of performance volatility.
Stage 3 – Performance assessment	At the end of the period, final performance against each metric is assessed. Outcomes are calculated based on performance against each weighted metric. Each performance measure is assessed on a standalone basis, so that underperformance against one measure cannot be compensated for by overperformance against another.	The Science Committee independently considers and informs the Committee whether science achievements represent a fair and balanced outcome, reflecting genuine achievements and pipeline progression. Apart from Cash flow, which is set at actual rates of exchange, financial metrics are set at budget rates of exchange and evaluated at those rates at year end, which means they are not directly comparable year-on-year. The Committee is, however, provided with data to allow it to conduct year-on-year analyses.
Stage 4 – Determination of Executive Directors' bonuses	For annual bonus, the fairness of the formulaic Group scorecard outcome is considered in the context of overall business performance and the experience of shareholders. Such considerations include TSR performance and each Executive Director's personal impact on the delivery of the strategy, wider ESG performance and other organisational achievements, such as inclusion and diversity targets and the realisation of technology-based milestones. Each year there are important individual deliverables beyond the scorecard metrics which are taken into account when determining individual bonuses.	Having considered the Group scorecard outcome, overall business performance, the experience of shareholders and individual performance, the Committee carefully determines a final bonus outcome for each Executive Director that is considered fair and appropriate for the year's performance and is in the best interests of shareholders.

"We set stretching targets that incentivise our leaders to deliver exceptional performance, to drive sustainable results for our patients, our employees and our shareholders."

2022 targets

- Financial performance goals under the 2022 Group scorecard and PSP would require growth in excess of the average expected of the industry, and above prior year outturns.
- The Committee has reviewed the proposed targets against internal and external forecasts, including market consensus, and is comfortable that the level of stretch promotes exceptional performance.

Annual Report on Remuneration

Key:

Audited information	Planned implementation for 2022
Content contained within the Audited panel indicates that all the information within has been subject to audit.	Content contained within a grey box indicates planned implementation for 2022.

The elements within the Executive Directors' realised pay are colour coded:
> Fixed Remuneration has a light blue border and is found on page 106
> Other items in the nature of remuneration have a purple border and can be found on page 107
> Annual bonus has a yellow border and can be found on pages 107 to 111
> Long-term incentives has a magenta border and can be found on pages 112 to 115

Executive Directors' remuneration

This section of the Remuneration Report sets out the Executive Directors' remuneration for the year ended 31 December 2021, alongside the remuneration that will be paid to Executive Directors during 2022.

Executive Directors' realised pay for 2021 (single total figure of remuneration)

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The table below sets out all elements of take-home pay receivable by the Executive Directors in respect of the year ended 31 December 2021, alongside comparator figures for 2020.

Dr Sarin joined the Board of AstraZeneca PLC as CFO on 1 August 2021. In line with reporting regulations, the realised pay for Dr Sarin reflects the remuneration received in respect of services rendered as an Executive Director during the year ended 31 December 2021 (1 August 2021 – 31 December 2021).

Mr Dunoyer stepped down as CFO and Executive Director of AstraZeneca PLC on 1 August 2021. In line with the reporting regulations, the realised pay for Mr Dunoyer reflects remuneration received in respect of services rendered as an Executive Director during the year ended 31 December 2021 (1 January 2021 – 1 August 2021). Mr Dunoyer did not receive any payments in respect of his stepping down from the Board.

Mr Soriot's and Mr Dunoyer's realised pay for 2021 includes the vesting of PSP awards from 2019 following the three-year performance period. These shares are subject to a further two-year holding period. The significant increase in AstraZeneca's share price over the period of grant to vest has provided a significant increase in value of the equity components of their reward. £2,370,923 of Mr Soriot's and £1,126,512 of Mr Dunoyer's 2021 realised pay is attributable to share price increases. The benefit of the increased share price has also been experienced by shareholders.

The Committee did not exercise any discretion in relation to the Long-term incentive outcomes or the formulaic outcome of the Group scorecard.

£'000		Base pay	Taxable benefits	Pension	Total fixed	Annual bonus	Long-term incentives[1]	Total variable	Other[2]	Single total figure	Share price appreciation as % of single figure total
Pascal Soriot	**2021**	1,327	123	146	1,596	3,152	9,110	12,262	–	13,858	17%
	2020	1,289	121	258	1,668	2,319	11,947	14,266	–	15,934	31%
Aradhana Sarin[3,4]	**2021**	354	6	39	399	595	–	595	2,019	3,013	–
	2020	–	–	–	–	–	–	–	–	–	–
Marc Dunoyer	**2021[5]**	460	53	51	564	772	4,328	5,101	–	5,665	20%
	2020	765	79	184	1,028	1,240	5,676	6,916	–	7,944	29%

[1] Long-term incentive values disclosed in 2020 have been recalculated using the average closing share price for the three months ended 31 December 2021. See page 112.
[2] In accordance with the regulations governing the single figure table, dividend equivalents accrued during deferral or holding periods have not been included within 'Other items of remuneration'. Where share awards have vested and been released to Executive Directors during 2021, the dividend equivalents accrued during the deferral or holding period of these awards, which were reinvested as shares, are shown in the footnotes to the Executive Directors' share plan interests on pages 118–119.
[3] Dr Sarin's 2021 realised pay is for the period following her appointment to the Board of AstraZeneca PLC from 1 August 2021 to 31 December 2021. Dr Sarin was not an Executive Director of AstraZeneca PLC in 2020.
[4] During 2021, Dr Sarin's salary was paid in USD($) via US payroll as she was still located in the US. Dr Sarin's UK totals were converted to USD using the exchange rate of 1.3615USD:1GBP, which was agreed on appointment.
[5] Mr Dunoyer's 2021 realised pay is for the period between 1 January 2021 and 1 August 2021, prior to him stepping down from the Board of AstraZeneca PLC.

The following sections provide further detail on the figures in the above table, including the underlying calculations and assumptions and the Committee's performance assessments for variable remuneration. Mr Dunoyer stepped down from the Board on 1 August 2021 and the information below reflects the period for which he was an Executive Director (1 January 2021 – 1 August 2021). The information below for Dr Sarin reflects the remuneration payable to her in respect of the period for which she has been CFO and Executive Director of AstraZeneca PLC (1 August 2021 – 31 December 2021).

The Annual bonus section is set out from page 107 and the Long-term incentives section from page 112. Information about the Executive Directors' remuneration arrangements for the coming year, ending 31 December 2022, is highlighted in grey boxes.

Fixed remuneration

Base pay

When awarding base pay increases, the Committee considers, among other factors, base pay increases applied across the UK employee population. The current Executive Directors' base pay for 2022 will increase in line with the UK all-employee base pay increase budget at 3%.

Audited

	2021		2022	
£'000	Change from 2020	Base pay	Change from 2021	Base pay
Pascal Soriot	3%	1,327	3%	1,367
Aradhana Sarin – *appointed to the Board on 1 August 2021*	n/a	354	3%	876
Marc Dunoyer – *stepped down from the Board on 1 August 2021*	3%	460	n/a	n/a

Taxable benefits

The Executive Directors may select benefits within AstraZeneca's UK Flexible Benefits Programme and may choose to take their allowance, or any proportion remaining after the selection of benefits, in cash.

Audited

	2021	2022
£'000	Total taxable benefits	Taxable benefits
Pascal Soriot	123	In line with 2021
Aradhana Sarin – *appointed to the Board on 1 August 2021*	6	In line with 2021
Marc Dunoyer – *stepped down from the Board on 1 August 2021*	53	n/a

Pension

The Executive Directors receive a pension allowance of 11% of base pay, in line with the wider UK workforce. During 2021, the Executive Directors took their pension allowance as a cash alternative to participation in a defined contribution pension scheme. None of the Executive Directors who served during 2021 has a prospective entitlement to a defined benefit pension by reason of qualifying service.

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	2021			2022
£'000	Pensionable base pay	Pension allowance	Cash in lieu of pension	Pension allowance
Pascal Soriot	1,327	11% of base pay	146	11% of base pay
Aradhana Sarin – *appointed to the Board on 1 August 2021*	354	11% of base pay	39	11% of base pay
Marc Dunoyer – *stepped down from the Board on 1 August 2021*	460	11% of base pay	51	n/a

Other remuneration

Audited

Other items in the nature of remuneration

	2021		
£'000	Relocation assistance	One-off award	Total Other items in the nature of remuneration
Pascal Soriot	n/a	n/a	–
Aradhana Sarin – *appointed to the Board on 1 August 2021*	3	2,016	2,019
Marc Dunoyer – *stepped down from the Board on 1 August 2021*	n/a	n/a	–

Dr Sarin's previous employment contract with Alexion includes an entitlement to cash severance arrangements, which would have been triggered at the date of closing of the acquisition of Alexion. In order to secure Dr Sarin's services and compensate her for the forfeiture of these contractual entitlements, an award of £2,015,540 was made to Dr Sarin in August 2021 and is included in the Other column. This award was made 50% in cash and 50% in restricted shares. The cash element is subject to repayment in the case of her voluntary cessation of employment within 18 months of appointment. The 50% made by way of restricted shares was granted to Dr Sarin on 13 August 2021, as a one-off restricted share award over 12,276 Ordinary Shares. The face value of the award was £1,007,736, calculated using a grant price of 8,209 pence per share, being the average closing share price over the three dealing days preceding grant. The award will vest 18 months after her appointment and will lapse in the case of her voluntary cessation of employment prior to vesting. For further information on this share award, please see page 123.

Dr Sarin was provided with assistance with her relocation from the US to the UK. The benefits offered were in line with the Group's standard relocation policy which is offered to the wider workforce, comprising six months' temporary accommodation in the UK, removals and storage costs, and reimbursement of expenses associated with home sale and purchase (stamp duty, legal fees and survey costs). The total assistance provided during 2021 was £3,430.

Annual bonus

Audited

2021 Annual bonus

Annual bonuses earned in respect of performance during 2021 are included in the realised pay table.

	Annual bonus in respect of performance during 2021				
	Bonus potential as % of base pay		Bonus payable in cash	Bonus deferred into shares	Total bonus awarded
£'000	Target	Maximum			
Pascal Soriot	125%	250%	1,576	1,576	3,152 95% max
Aradhana Sarin – *appointed to the Board on 1 August 2021*	100%	200%	298[1]	298[1]	595 84% max
Marc Dunoyer – *stepped down from the Board on 1 August 2021*	100%	200%	386	386	772 84% max

[1] Numbers have been rounded.

The annual bonuses shown for Mr Dunoyer and Dr Sarin are in respect of the time during which each served as an Executive Director of AstraZeneca PLC during 2021.

Detailed information on the Committee's approach to target setting and assessment of performance is set out on page 104.

Half of the Executive Director's pre-tax bonus is compulsorily deferred into Ordinary Shares which are released three years from the date of deferral, ordinarily subject to continued employment. Bonuses are not pensionable.

Annual bonus *continued*

Audited

2021 Group scorecard assessment

Performance against the 2021 Group scorecard is set out below.

The Group scorecard is used in the determination of bonus payouts for all AstraZeneca employees. Each metric within the scorecard is assessed on a standalone basis and has a defined payout range. As noted on page 99, the 2021 scorecard targets were reviewed in light of the enlarged Group following the acquisition of Alexion. Accelerate Innovative Science (now renamed Innovative Science: Annual pipeline progression), Total Revenue, Cash flow and Core EPS targets were all adjusted upward in line with the Committee's approach of ensuring performance targets should not be made materially more or less stretching as a result of the transaction and to continue to incentivise strong delivery.

Performance below the specified threshold level for a metric will result in 0% payout for that metric. 100% of target bonus will pay out for on-target performance, and 200% of target bonus will pay out for performance at or above maximum. Maximum bonus payouts for the current CEO and CFO for 2021 were capped at 250% and 200% of base pay respectively. Mr Dunoyer's maximum payout for the period during which he was CFO and an Executive Director was capped at 200% of his base pay for the period for which he served as CFO and an Executive Director of AstraZeneca. The payout range for each metric is capped in line with each Executive Director's maximum bonus opportunity to ensure underperformance against one metric cannot be compensated for by overachievement against another. The table below shows the scorecard formulaic outcomes for the CEO and CFO as a percentage of target bonus.

2021 Group scorecard performance measures and metrics[1]	Weighting	Threshold for payout	Target	Maximum	Outcome	Formulaic outcome (% of target bonus)
Science measures						
Innovative Science: Annual pipeline progression						
Pipeline progression events	15%	11	22	33	26	20%
Regulatory events	15%	22	31	41	37	24%
Subtotal – Science measures	30%					44%
Financial measures						
Deliver Growth and Therapy Area Leadership						
Total Revenue ($bn)	30%	32.1	33.1	34.1	34.7	60%
Achieve Group Financial Targets						
Cash flow ($bn)	20%	4.8	5.6	6.5	6.3	34%
Core EPS ($)	20%	5.04	5.25	5.46	5.34	29%
Subtotal – Financial measures	70%					63%
Total[2]	100%					168%

Key: ☐ Bar charts are indicative of 2021 performance; scales do not start from zero.

1 The Committee reviewed the 2021 Group scorecard targets following the acquisition of Alexion to reflect the impact of the acquisition on the Company's results. The Committee is confident that the increases applied to the targets during that review ensured that they remained ambitious and stretching. The Company does not intend to disclose the original performance targets, set prior to the acquisition, as the adjustment to the targets relates to a single disease area (Rare Disease), which is therefore commercially sensitive.

2 Due to rounding, the total formulaic outcome differs from the arithmetic total of the individual metric outcomes disclosed above.

Pipeline progression events include Phase II starts and progressions, and NME and life-cycle management positive Phase III investment decisions. Regulatory events include NME and major life-cycle management regional submissions and approvals. Further detail on our Accelerate Innovative Science strategic priority and these events is included from page 13 of this Annual Report.

A number of further scientific achievements during 2021 have not been taken into account in the formulaic Group scorecard outcome, as they were additional to the cohort set at the start of the year. These have instead been considered and reflected in the Committee's final bonus determination.

Annual bonus *continued*

In 2021, Deliver Growth and Therapy Area Leadership measured Total Revenue, excluding revenue from *Vaxzevria* until October 2021, when it was supplied on a not-for-profit basis. This target was set and evaluated at budget exchange rates at the beginning of the year and evaluated at those rates at the end of the performance period, so that any beneficial or adverse movements in currency, which are outside the Company's control, do not impact reward outcomes. The Cash flow measure is set and evaluated at the actual exchange rate and is evaluated by reference to net cash flow from operating activities less capital expenditure adding back proceeds from disposal of intangible assets, to be fully transparent with all elements easily derived from the Group IFRS cash flow statement. The Core EPS and Total Revenue measures are evaluated by reference to budget exchange rates, so that any beneficial or adverse movements in currency, which are outside the Company's control, do not impact reward outcomes.

Overall assessment

During 2021, the Executive Directors' individual performance was assessed in the following key areas which align with the Company's objectives.

Pascal Soriot

2021 was another truly exceptional year for AstraZeneca under Mr Soriot's leadership. Along with the delivery of the financial and scientific performance in another unprecedented year, the Committee considered Mr Soriot's strong leadership and response through the continued COVID-19 pandemic in addition to his excellent performance against his personal objectives.

COVID-19 response	In 2021, Mr Soriot continued to work tirelessly with multiple Government policy makers, Ministers of Health and Heads of State around the world in order to secure production and delivery of AstraZeneca's COVID-19 vaccine, *Vaxzevria*. Importantly, Mr Soriot ensured AstraZeneca was the first pharmaceutical company to sign up to COVAX, and within a year of the first dose of the vaccine rolling off the production line, together with our partners we released over 2.5 billion doses of *Vaxzevria* to more than 180 countries across seven continents. Challenges were faced early on due to the complexities involved in manufacturing vaccines which led to delays in the number of doses available for delivery to EU member states against original estimates. However, a settlement was reached, under which AstraZeneca committed to deliver 200 million doses on an agreed schedule over the second half of 2021 and first quarter of 2022. To date, AstraZeneca's vaccine is estimated to have helped prevent 50 million COVID-19 cases, five million hospitalisations, and helped save more than one million lives. Mr Soriot has also reinforced the Group's commitment to continuing the fight against COVID-19 with the launch of a new Vaccines & Immune Therapies Unit. With continued strong demand for AstraZeneca's vaccines, as well as *Evusheld*, the only long-acting antibody with Phase III data demonstrating benefit in both the prevention and treatment of COVID-19, and with a focus on helping the most vulnerable people, Mr Soriot has cemented AstraZeneca's position as an industry leader in the pandemic response.
Demonstrating leadership to support developments in global life sciences	Throughout 2021, Mr Soriot demonstrated his influence and respected position as a world leader on key issues in healthcare through his multiple engagements with senior external stakeholders. Highlights included participation in the World Economic Forum Davos Dialogues, the World Health Assembly and notably also the G7 Leaders' Summit where Mr Soriot was the only business leader and only healthcare executive to be invited to attend.
Leading in Environmental, Social & Governance (ESG) performance	Under Mr Soriot's leadership, AstraZeneca has continued to demonstrate commitment to its ESG practice, and to maintain a leadership position externally across the industry with its sustainability strategy delivery. In 2021, Mr Soriot launched the cross-healthcare sector SMI Health Systems task force with HRH The Prince of Wales and global health leaders to accelerate the delivery of net-zero patient-centric healthcare. Mr Soriot is the Chair for this task force. In recognition of the Company's efforts, AstraZeneca was awarded the Terra Carta seal at COP26 by HRH The Prince of Wales as part of the Sustainable Markets Initiative (SMI). AstraZeneca is also one of only seven companies worldwide (and the only pharmaceutical) to have its climate targets verified by the Science Based Targets initiative (SBTi). AstraZeneca was double A listed on CDP for the sixth year running, and since launching Healthy Heart Africa we have now conducted over 22 million blood pressure screenings.
Making AstraZeneca a Great Place to Work	Mr Soriot continues to oversee and drive accountability for AstraZeneca's I&D strategy throughout the organisation as Chair of AstraZeneca's global I&D council. The Group's progress was recognised externally in 2021, with AstraZeneca's inclusion on the 2021 Bloomberg Gender-Equality Index, Diversity Inc's 2021 Top 50 companies for diversity and Top 50 companies for LGBT employees, the Financial Times 2021 Leaders in Diversity, Forbes 2021 World's Top Female-Friendly Companies and the Time Top 50 employers for women. For the second year running, AstraZeneca earned the maximum score of one hundred on the Human Rights Campaign Index, resulting in a designation as one of the 2021 Best Places to Work for LGBTQIA+ Equality. The Group also launched pilots of the Clinical Trial Diversity Index. This Index will help AstraZeneca to make data driven decisions that improve trial diversity while providing data we need to show the benefit of our medicines in diverse patient populations. We continued to accelerate our Great Place to Work ambition of building a culture of lifelong learning, through development programmes aimed at rising leaders from the Emerging Markets, women leaders, senior leaders and the launch of functional learning academies. Fifteen thousand line managers participated in training to develop their coaching capabilities, underpinning a successful transition to our new performance development approach, with the removal of performance ratings for the first time in 2021. The impact of these development interventions and our continued focus on building a learning culture was reflected in the November Pulse survey, with 90% of employees taking time to complete the survey, 85% of employees believe that AstraZeneca is a Great Place to Work and 88% believe they had an opportunity to improve their existing skills and learn new skills.

Annual bonus *continued*

Aradhana Sarin

Leading in Environmental, Social and Governance (ESG) performance	Since being appointed as CFO, Dr Sarin has become a member of the Ambition Zero Carbon Governance Group. This group holds responsibility for monitoring the progress on Ambition Zero Carbon – AstraZeneca's commitment to become zero carbon by 2025 across operations (sites and fleet) without carbon credits, and carbon negative in the AstraZeneca value chain by 2030. As a leader on this committee and in close partnership with Corporate Affairs and Global Government Affairs and Policy teams, Dr Sarin has helped the Governance Group establish a leadership position for AstraZeneca externally.
Alexion integration	In her short time as CFO, Dr Sarin has demonstrated strong leadership along with the ability to quickly identify efficiencies and improvements. These qualities have been integral to the programme of work to integrate Alexion and secure the anticipated synergies arising from the acquisition.
Creating an enterprise-wide impact through Global Business Services (GBS)	Under Dr Sarin's leadership for the second half of the year, in 2021 a total of over 200,000 hours were freed up, and GBS delivered more than $160 million in benefits with over $20 million saved through process optimisation and innovation. In the second half of the year GBS expanded the scope of its services in procurement, tax, learning and digital solutions, expanding automation, process mining and analytics and AI. Significant changes were made in the operating model to further unlock the potential of the function and reinforce process standardisation.

Marc Dunoyer

Mr Dunoyer held the role of CFO and Executive Director of AstraZeneca in 2021 until he stepped down from the Board with effect from 1 August 2021 to take on his new role as CEO, Alexion and Chief Strategy Officer, AstraZeneca. As CFO, his exceptional global financial leadership enabled AstraZeneca to have another successful year in unprecedented times.

Alexion acquisition	Mr Dunoyer's leadership in the first half of 2021 delivered the successful completion of the Alexion transaction in July 2021. This milestone achievement accelerated AstraZeneca's strategic and financial journey, adding Rare Disease as a third growth engine alongside Oncology and BioPharmaceuticals.
Leading in Environmental, Social and Governance (ESG) performance	In 2021, Mr Dunoyer continued as Executive Sponsor of AstraZeneca's award-winning, global philanthropy initiative: the Young Health Programme (YHP). Led by Mr Dunoyer, YHP expanded into seven new countries in 2021. It reached more than four million young people and trained more than 60,000 healthcare practitioners. Through its partnership with UNICEF, YHP developed five global learning modules and a Youth Advocacy Guide to increase youth involvement.
Japan	In 2021, Mr Dunoyer played a critical role in leading AstraZeneca Japan through another year of strong performance and growth, becoming the largest pharmaceutical company in Japan in 2021, up from 5th in 2020. Significant approvals obtained during the year included *Calquence* for chronic lymphocytic leukemia, *Forxiga* in chronic heart failure and chronic kidney disease and *Saphnelo* for systemic lupus erythematosus. Throughout the year AstraZeneca Japan successfully launched *Breztri* and was the market leader in *Tagrisso* (which in 2021 achieved more than 100 billion YEN in annual sales), *Imfinzi*, *Lynparza*, *Nexium*, *Fasenra*, *Forxiga* and *Lokelma*. Under Mr Dunoyer's leadership, and one year after launch, AstraZeneca has the largest open innovation ecosystem in Japan. Over the year, 15 innovation projects were initiated to develop healthcare solutions that have the potential to transform disease management and patient outcomes.
Creating an enterprise-wide impact through Global Business Services (GBS)	In the first half of 2021, under Mr Dunoyer's leadership, GBS contributed successfully to transforming interactions with healthcare practitioners through support to virtual and hybrid meetings, fostering a culture of lifelong learning by supporting the delivery and the management of digital learning, and standardising and automating adverse events reporting, product quality complaints and medical information requests.

Final determination of Executive Directors' bonuses

In determining the annual bonus outturn for Executive Directors, the Remuneration Committee considers the formulaic Group scorecard outcome, as well as the overall business performance, shareholder experience and the personal contribution of the individual Executive. A description of the Executive Directors' personal achievements is detailed above.

In consideration of his exceptional leadership and personal contribution – particularly in relation to AstraZeneca's COVID-19 response and the successful integration of Alexion – the Committee determined the bonus outturn for Mr Soriot should be 190% of target (or 95% of maximum). This amounted to 237.5% of base pay. This is in line with the approach to differentiate bonus awards for individuals in the wider workforce that have made an exceptional contribution in 2021.

The Committee determined the bonus outturn for Dr Sarin should be 168% of target (or 84% of maximum, 168% of base pay) and, for the period which he served as an Executive Director, the bonus outturn for Mr Dunoyer should be 168% of target (or 84% of maximum, 168% of base pay).

Annual bonus *continued*

Deferred Bonus Plan

A proportion of each Executive Director's pre-tax annual bonus is compulsorily deferred under the Deferred Bonus Plan (DBP). In respect of the bonus deferred, the Executive Director is granted a conditional award over shares. No further performance conditions apply to DBP shares, but release at the end of the three-year deferral period is ordinarily subject to continued employment. One half of the bonus earned in respect of performance during 2020 was deferred and details of the consequent DBP awards granted in 2021 are shown below. One half of the Executive Directors' bonus earned in respect of performance during 2021 has been deferred and the consequent DBP awards are expected to be granted in March 2022.

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			2021 Grant	2022 Grant
	Ordinary Shares granted	Grant date	Grant price (pence per share)[1]	Face value £'000	2021 Bonus deferred £'000
Pascal Soriot	16,944	5 March 2021	6844	1,160	1,576
Aradhana Sarin[2]	n/a	n/a	n/a	n/a	298
Marc Dunoyer	9,057	5 March 2021	6844	620	386

1 The grant price is the average closing share price over the three dealing days preceding grant.

2 Dr Sarin was appointed in August 2021, following the 2021 DBP Grant (which related to performance during the 2020 financial year). 50% of Dr Sarin's pro-rated bonus in respect of the 2021 financial year, will be deferred to shares expected to be granted in March 2022.

2022 Group scorecard performance measures and metrics

	Measure weighting	Underlying metrics (if applicable)	Metric weighting	2022 target	
Innovative Science: Annual pipeline progression	30%	Pipeline progression events	15%	↓	C
		Regulatory events	15%	↑	C
Deliver Growth and Therapy Area Leadership	30%	Total Revenue	30%	↑	C
Achieve Group Financial Targets	40%	Cash flow	20%	↑	C
		Core EPS	20%	↑	C

Key ↑ Target increased vs 2021 target ↓ Target decreased vs 2021 target ↔ Target constant C Commercially sensitive

We intend to disclose the 2022 Group scorecard outcome, and details of the performance hurdles and targets, in the 2022 Directors' Remuneration Report following the end of the performance period. The performance targets are currently considered to be commercially sensitive as prospective disclosure may prejudice the Company's commercial interests. Executive Directors' individual contribution will be assessed by reference to individual goals in line with the Company's objectives for the year.

Long-term incentives

Long-term incentives included in the Executive Directors' realised pay for 2021 figure: 2019 PSP
Mr Soriot's and Mr Dunoyer's realised pay for 2021 includes the value of PSP awards with performance period ended 31 December 2021. These shares and dividend equivalents will not be released to the Directors until the awards vest at the end of their respective holding periods.

The values of the shares due to vest have been calculated using the average closing share price over the three-month period ended 31 December 2021 (8722 pence). The table below provides a breakdown showing the face value of these shares at the time they were granted, the value that is attributable to share price appreciation since grant and the value of dividend equivalents accrued on these shares over the relevant performance period. Further information about the individual awards and performance assessments follows the table.

Dr Sarin was appointed to the Board in August 2021 and therefore does not have a 2019 PSP award.

Audited

Long-term incentive awards with performance periods ended 31 December 2021

				Value of shares due to vest			
		Ordinary Shares granted	Performance outcome	Face value at time of grant[1] £'000	Value due to share price appreciation[2] £'000	Dividend equivalent accrued over performance period £'000	Long-term incentives total £'000
Pascal Soriot	2019 PSP	102,475	95%	6,120	2,371	619	9,110
Marc Dunoyer	2019 PSP	46,690	95%	2,908	1,127	294	4,328

[1] Calculated using the grant price of 6257 pence for 2019 PSP awards.
[2] Calculated using the difference between the grant price and the average closing share price over the three-month period ended 31 December 2021.

The 2019 PSP awards granted on 8 March 2019 are due to vest and be released on 8 March 2024 on completion of a further two-year holding period. Performance over the period from 1 January 2019 to 31 December 2021 will result in 95% of the award vesting, based on the following assessment of performance. As noted on page 99, the 2019 PSP targets were reviewed in light of the enlarged Group following the acquisition of Alexion. The Innovative Science, Deliver Growth and Therapy Area Leadership and EBITDA targets were all increased in line with the Committee's approach of ensuring performance targets are not materially more or less stretching as a result of the transaction and to continue to incentivise strong delivery. No amendments were made to the TSR or Cash flow performance measures.

The Deliver Growth and Therapy Area Leadership target (measuring aggregate Product Sales of the Oncology, New CVRM, Respiratory, Japan and Emerging Markets sales platforms, previously referred to as growth platforms) and EBITDA target are set at budget exchange rates at the beginning of the performance period and evaluated at those rates at the end of the performance period, so that any beneficial or adverse movements in currency, which are outside the Company's control, do not impact reward outcomes.

The EBITDA measure is assessed using cumulative Reported EBITDA, excluding non-cash movements on fair value of contingent consideration on business combinations and gains on disposals of intangible assets.

The Cash flow measure is assessed using cumulative net cash flow from operating activities less capital expenditure adding back proceeds from disposal of intangible assets and movement in profit participation liability.

AstraZeneca ranked fifth within the TSR peer group, in the upper quartile.

For more information about the TSR performance of the Company and the TSR comparator group, see page 122.

2019 PSP performance measures and metrics[1]	Weighting	Threshold (20% vesting)	Maximum (100% vesting)	Outcome	Payout
Innovative Science: First approvals and NME volume over three years					
NME Phase III/registrational volume	8%	7	13	15	100%
Regulatory events	12%	10	19	26	100%
Subtotal – Innovative Science[2]	20%				100%
Deliver Growth and Therapy Area Leadership ($bn)	20%	25.0	30.0	31.0	100%
Cash flow ($bn)	20%	10.0	14.0	15.5	100%
EBITDA ($bn)	20%	19.0	24.0	22.0	75%
Total shareholder return	20%	Median	UQ[3]	UQ	100%
Total[2]	100%				95%

Key: ▯ Bar charts are indicative of 2019 PSP performance; scales do not start from zero.

[1] The Committee reviewed the 2019 PSP targets following the acquisition of Alexion to reflect the impact of the acquisition on the Company's results. The Committee is confident that the increases applied to the targets during that review ensured that they remained ambitious and stretching. The Company does not intend to disclose the original Deliver Growth and Therapy Area Leadership target, set prior to the acquisition, as the adjustment to the target relates to a single disease area (Rare Disease), which is therefore commercially sensitive. The other original targets were disclosed in the Company's Annual Report for the year ended 31 December 2019.
[2] The subtotal and total reflect the weightings of the individual metrics.
[3] UQ = Upper Quartile

Long-term incentives *continued*

Audited

PSP awards granted during 2021

During 2021, conditional awards of shares were granted to the Executive Directors with face values equivalent to 650% of base pay for Pascal Soriot and 450% of base pay for Dr Sarin under the PSP. Dr Sarin's award was pro-rated to reflect that she took up her role as CFO part way through the year. Face value is calculated using the grant price, being the average closing share price over the three dealing days preceding grant. The 14 May 2021 grant, following the approval of the policy at the 2021 AGM, was made at the same share price as the 5 March 2021 grant.

Mr Dunoyer received a conditional award whilst he was CFO and Executive Director with a face value equivalent to 450% of his base pay. Mr Dunoyer stepped down from the Board on 1 August 2021 but remains an employee of AstraZeneca and therefore his in-flight incentive awards will continue to run their course.

Performance will be assessed over the period from 1 January 2021 to 31 December 2023 against the measures outlined below to determine the proportion of the award that vests. A further two-year holding period will then apply before vesting, which is scheduled to occur on the fifth anniversary of grant.

	Ordinary Shares granted	Grant date	Grant price (pence per share)	Face value £'000	End of performance period	End of holding period
Pascal Soriot	106,655	5 March 2021	6844	7,299	31 December 2023	5 March 2026
Pascal Soriot[1]	19,391	14 May 2021	6844	1,327	31 December 2023	14 May 2026
Marc Dunoyer	51,828	5 March 2021	6844	3,547	31 December 2023	5 March 2026
Aradhana Sarin	19,414	13 August 2021	8209	1,594	31 December 2023	13 August 2026

[1] This award forms part of the PSP award granted to Mr Soriot on 5 March 2021 and was made to take account of the revised limits for the PSP approved by shareholders at the Company's 2021 AGM.

The 2021 PSP performance measures focus on scientific, ESG, commercial and financial performance over the three-year performance period. The 2021 PSP performance measure targets were reviewed in light of the enlarged Group following the acquisition of Alexion and adjustments were made in line with the Committee's approach of ensuring performance targets should not be made materially more or less stretching as a result of the transaction and to continue to incentivise strong delivery.

The five performance metrics attached to the 2021 PSP awards are detailed below with targets shown as adjusted by the Committee following its review on completion of the Alexion acquisition, as described on page 99. Twenty percent of the award will vest if the threshold level of performance is achieved; the maximum level of performance must be achieved under each measure for 100% of the award to vest.

Relative total shareholder return (TSR) (20% of award)

TSR performance is assessed against a predetermined peer group of global pharmaceutical companies and consists of AbbVie, Amgen, Astellas, BMS, Daiichi Sankyo, Gilead, GSK, Johnson & Johnson, Lilly, MSD, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi and Takeda. The rank which the Company's TSR achieves over the performance period will determine how many shares will vest under this measure.

TSR ranking of the Company	% of award that vests
Median	20% (threshold for payout)
Between median and upper quartile	Pro rata
Upper quartile	100%

Long-term incentives *continued*

Audited

Net Cash flow (20% of award)

The Cash flow measure is assessed using cumulative net cash flow from operating activities less capital expenditure adding back proceeds from disposal of intangible assets. The level of vesting under this measure is based on a scale between a threshold target and an upper target.

Cash flow	% of award that vests
$19.0bn	20% (threshold for payout)
Between $19.0bn and $23.0bn	Pro rata
$23.0bn	75%
Between $23.0bn and $27.0bn	Pro rata
$27.0bn and above	100%

Deliver Growth and Therapy Area Leadership (20% of award)

For PSP awards granted in 2021, the Deliver Growth and Therapy Area Leadership metric is Total Revenue. Disclosing the threshold and maximum hurdles for this measure could be construed to constitute financial guidance, which is not the Company's intention. The Deliver Growth and Therapy Area Leadership (Total Revenue) measure is thus considered to be commercially sensitive and will be disclosed following the end of the performance period, in the 2023 Directors' Remuneration Report. This measure is evaluated by reference to budget exchange rates.

Innovative Science: First approvals and NME volume over three years (30% of award)

Performance is assessed using dual indices which measure regulatory and pipeline progression events, allowing disclosure of targets at the beginning of the performance period.

NME Phase III/registrational volume (12% of award)	% of award that vests
9	20% (threshold for payout)
Between 9 and 14	Pro rata
14	75%
Between 14 and 18	Pro rata
18	100%

Regulatory events (18% of award)	% of award that vests
13	20% (threshold for payout)
Between 13 and 20	Pro rata
20	75%
Between 20 and 26	Pro rata
26	100%

Ambition Zero Carbon (10% of award)

This measure reflects the importance of eliminating greenhouse gas (GHG) emissions from our Scope 1 and Scope 2 operations by 2025. Reductions are measured against our 2015 baseline, and calculated in line with the World Resources Institute/World Business Council for Sustainable Development GHG Protocol methodology for accounting and reporting of our emissions footprint. As part of the adjustment of 2021 targets to reflect the impact of the Alexion acquisition, described on page 99, the Ambition Zero Carbon target has been expressed in $ktCO_2e$ (kilotonnes of carbon dioxide equivalent) rather than as a percentage change from our 2015 baseline. Expressing the target and our performance in $ktCO_2e$ is intended to be more transparent and understandable, thereby more clearly reflecting the impact we want to have on society.

Emissions ($ktCO_2e$)	% of award that vests
272 $ktCO_2e$	20% (threshold for payout)
Between 272 $ktCO_2e$ and 246$ktCO_2e$	Pro rata
246 $ktCO_2e$	75%
Between 246 $ktCO_2e$ and 220 $ktCO_2e$	Pro rata
220 $ktCO_2e$ and below	100%

PSP performance measures for 2022 grant

The 2022 PSP measures remain unchanged from the 2021 PSP award.

PSP performance measure	Measure weighting	Underlying metrics (if applicable)	Metric weighting	Threshold (20% vesting)	Maximum (100% vesting)
Innovative Science: First approvals and NME volume over three years	30%	NME Phase III/registrational volume	12%	7	14
		Regulatory events	18%	14	28
Deliver Growth and Therapy Area Leadership	20%	Total Revenue		Commercially sensitive until end of performance period	
Cash flow	20%			$20.0bn	$28.5bn
Relative TSR	20%			Median	Upper Quartile
Ambition Zero Carbon	10%			207 $ktCO_2e$	155 $ktCO_2e$

Regulatory events measure NME and major life-cycle management approvals (taking into account the first approval over the performance period). NME Phase III/registrational volume measures the total NME pipeline volume at the end of the performance period. These two items ensure that management are assessed on both R&D late-stage delivery (approvals) and also future pipeline sustainability (volume). The name of the Innovative Science measure has been updated, however the underlying metrics remain unchanged.

Disclosing the threshold and maximum hurdles for the Deliver Growth and Therapy Area Leadership (Total Revenue) measure could be construed to constitute financial guidance, which is not the Company's intention. The Total Revenue measure is thus considered to be commercially sensitive and will be disclosed following the end of the performance period.

The Total Revenue measure is evaluated by reference to budget exchange rates such that beneficial or adverse movements in currency, which are outside the Company's control, do not impact reward outcomes. The Cash flow measure is evaluated using net cumulative cash flow from operating activities less capital expenditure adding back proceeds from disposal of intangible assets. The companies in the TSR comparator group are shown on page 122. As 2021 saw AstraZeneca enter a new chapter in its Growth Through Innovation Strategy, with the acquisition of Alexion and the emergence of the Vaccines & Immune Therapies Unit, the Committee reviewed the composition of the TSR peer group. This review considered size (revenue and market capitalisation), portfolio comparison and geographic presence, with the Committee determining that Merck KGaA and Moderna be added to the peer group for the 2022 PSP award.

Our Ambition Zero Carbon measure is based on our Scope 1 and Scope 2 emissions reductions. Further detail on our commitment can be found from page 45.

As described on page 104, the Committee takes into account a wide range of data to ensure that the stretching nature of PSP hurdles is robustly tested and that financial targets are aligned with the business's Mid Term Plan. The Committee will take consensus into account when determining the appropriate level of stretch.

PSP awards are expected to be granted to the Executive Directors in March 2022. The PSP award to be granted to Dr Sarin will be equivalent to 450% of base pay. The PSP award to be granted to Mr Soriot will be equivalent to 650% of base pay.

Non-Executive Directors' remuneration

Non-Executive Directors' realised pay for 2021 (total single figure of remuneration)

Audited

The table sets out all elements of remuneration receivable by the Non-Executive Directors in respect of the year ended 31 December 2021, alongside comparative figures for the prior year.

	2021 Fees £'000	2020 Fees £'000	**2021 Other £'000**	2020 Other £'000	**2021 Total £'000**	2020 Total £'000
Leif Johansson	**625**	625	**74**	73	**699**	698
Euan Ashley – *appointed 1 October 2020*	**103**	26	**–**	–	**103**	26
Philip Broadley	**173**	148	**–**	–	**173**	148
Michel Demaré	**148**	125	**–**	–	**148**	125
Deborah DiSanzo	**108**	108	**–**	–	**108**	108
Diana Layfield – *appointed 1 November 2020*	**92**	15	**–**	–	**92**	15
Sheri McCoy	**127**	123	**–**	–	**127**	123
Tony Mok	**103**	103	**–**	–	**103**	103
Nazneen Rahman	**131**	118	**–**	–	**131**	118
Andreas Rummelt – *appointed 1 August 2021*	**40**	–	**–**	–	**40**	–
Marcus Wallenberg	**107**	103	**–**	–	**107**	103
Former Non-Executive Directors						
Geneviève Berger – *retired 11 May 2021*	**37**	110	**–**	–	**37**	110
Graham Chipchase – *retired 11 May 2021*	**37**	141	**–**	–	**37**	141
Total	**1,831**	1,745	**74**	73	**1,905**	1,818

The Chair's single total figure includes office costs (invoiced in Swedish krona) of £74,000 for 2021 and £73,000 for 2020.

Payments to former Directors

During 2021, no payments were made to former Directors.

Payments for loss of office

During 2021, no payments were made to Directors for loss of office. Marc Dunoyer stepped down from the Board in August 2021, however has remained an employee of AstraZeneca and therefore his in-flight incentive awards will continue to run their course.

Non-Executive Directors' fee structure

The Non-Executive Directors' fee structure for 2022 is set out in the table below, alongside the structure in place during 2021. Fees for the Non-Executive Directors (other than the Chair of the Board) are determined by the Chair and the Executive Directors. The fee structure is reviewed, but not necessarily increased every two years. Non-Executive Directors' fees were last changed in January 2018, with increases to the Chair's fee, the basic Board fee for other Non-Executive Directors and Science Committee fees.

With effect from January 2022, the basic Board fee for Non-Executive Directors, the senior independent Non-Executive Director's fee, and fees for membership of the Audit Committee and the Remuneration Committee have been increased as shown in the table below. No Board member participated in any decision relating to their own fees.

As part of the latest review, the increased size and complexity of the AstraZeneca Group following the Alexion acquisition was taken into account together with the increase in the Board's and its key Committees' workloads and responsibilities since 2016. Market data on FTSE 10 companies' non-executive directors fees were also considered, in addition to data from FTSE 30 companies, to ensure that the level of fees do not hinder the recruitment of Directors of the right experience and calibre for a Group of our scale in a global market.

Further information on the Non-Executive Directors' fee structure can be found within the Remuneration Policy on the Company's website, www.astrazeneca.com.

Non-Executive Director fees	**2021 £'000**	2022 £'000
Chair of the Board[1]	**625**	625
Basic Non-Executive Director	**88**	95
Senior independent Non-Executive Director	**30**	40
Member of the Audit Committee	**20**	25
Chair of the Audit Committee[2]	**45**	45
Member of the Remuneration Committee	**15**	20
Chair of the Remuneration Committee[2]	**40**	40
Member of the Sustainability Committee[3]	**15**	15
Chair of the Sustainability Committee[2,3]	**30**	30
Member of the Science Committee	**15**	15
Chair of the Science Committee[2]	**30**	30
Non-Executive Director responsible for overseeing sustainability matters on behalf of the Board[2]	**7.5**	N/A

[1] The Chair of the Board does not receive any additional fees for chairing, or being a member of, a committee.
[2] The committee Chairs do not receive additional fees for being a member of the committee.
[3] In October 2021, the Board established the Sustainability Committee, which superseded the previous governance arrangement.

Directors' shareholdings

Minimum shareholding requirements

Audited

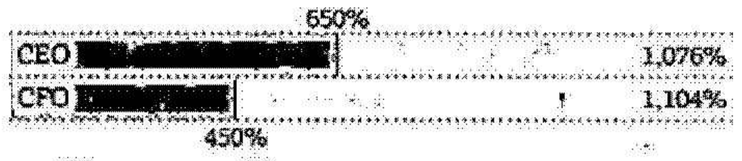
The CEO and CFO are each required to build a shareholding to satisfy their respective minimum shareholding requirements (MSR), each within five years of their dates of appointment. The minimum shareholding requirements for 2021 are set out below. Shares that count towards these minimum shareholding requirements are shares beneficially held by the Executive Director and their connected persons and share awards that are not subject to further performance conditions. Share awards included are DBP shares in deferral periods, and PSP and AstraZeneca Investment Plan (AZIP) shares in holding periods, on a net of tax basis. Dr Sarin's one-off restricted share award and the awards made to replace her in-flight Alexion incentive awards are also included on a net-of-tax basis.

A further post-employment shareholding requirement applies to Executive Directors. For two years following cessation of employment, Executive Directors are required to hold shares to the value of the shareholding guideline that applied at the cessation of their employment; or, in cases where the individual has not had sufficient time to build up shares to meet their guideline, the actual level of shareholding at cessation. The post-cessation requirement will be maintained through self-certification, with the Committee keeping this approach under review.

Position against minimum shareholding requirement (MSR) as a percentage of base pay

	Beneficially owned shares and shares in a holding period[1]	Shares in deferral period[2]	Shares subject to performance conditions	Value of shares counted towards MSR as a % of base pay[3]
Pascal Soriot	293,439	35,527	324,601	1,076%
Aradhana Sarin	27,957	160,385	19,414	1,104%

[1] Holding period shares included are those which are not subject to continued employment.
[2] Shares in deferral periods which are subject to continued employment.
[3] Holding as at 31 December 2021. Shares subject to deferral and holding periods calculated net of a theoretical 50% tax rate. Shares subject to performance conditions are not included in the value of shares counted towards MSR.



Non-Executive Directors are encouraged to build up, over a period of three years, a shareholding in the Company with a value approximately equivalent to the basic annual fee for a Non-Executive Director (£88,000 during 2021) or, in the case of the Chair, approximately equivalent to his basic annual fee (£625,000 during 2021). All Non-Executive Directors who had served for a period of three years or more as at 31 December 2021 substantially met this expectation, based on the three-month average closing share price for the period ended 31 December 2021.

Directors' interests as at 31 December 2021

The following table shows the beneficial interests of the Directors (including the interests of their connected persons) in Ordinary Shares as at 31 December 2021.

	Beneficial interest in Ordinary Shares at 31 December 2021[1]	Beneficial interest in Ordinary Shares at 31 December 2020[1]
Executive Directors		
Pascal Soriot	293,439	358,272
Aradhana Sarin[2]	27,957	–
Marc Dunoyer[3]	363,686	294,875
Non-Executive Directors		
Leif Johansson	39,009	39,009
Euan Ashley[4]	1,150	1,150
Philip Broadley	7,045	7,045
Michel Demaré	2,000	2,000
Deborah DiSanzo	1,000	1,000
Diana Layfield[5]	1,400	1,400
Sheri McCoy	1,736	1,736
Tony Mok	2,000	1,000
Nazneen Rahman	1,017	1,017
Andreas Rummelt[6]	34,790	–
Marcus Wallenberg	60,028	60,028

[1] For the Executive Directors, beneficial interests include shares in holding periods which are not subject to performance measures or continued employment.
[2] Aradhana Sarin was appointed on 1 August 2021.
Marc Dunoyer's 2021 beneficial interests are shown as at 1 August 2021 when he stepped down as CFO and Director of AstraZeneca PLC.
[4] Euan Ashley was appointed on 1 October 2020.
[5] Diana Layfield was appointed on 1 November 2020.
[6] Andreas Rummelt was appointed on 1 August 2021.

Directors' shareholdings *continued*

Executive Directors' share plan interests Audited

The following tables set out the Executive Directors' interests in Ordinary Shares under the Company's share plans.

Pascal Soriot

Share scheme interests	Grant date	Shares outstanding at 1 January 2021	Grant price (pence)	Shares granted in year	Shares released in year	Shares lapsed in year	Shares outstanding at 31 December 2021: Shares subject to performance	Shares outstanding at 31 December 2021: Shares in deferral/ holding period	Performance period end	Vesting and release date
DBP	23/03/2018	13,157	4853	–	13,157	–	n/a	–	n/a	23/03/2021[1,2]
	08/03/2019	9,849	6287	–	–	–	n/a	9,849	n/a	08/03/2022
	06/03/2020	8,734	7376	–	–	–	n/a	8,734	n/a	06/03/2023
	05/03/2021	–	6844	16,944	–	–	n/a	16,944	n/a	05/03/2024[3]
PSP	24/03/2016	102,473	3923	–	102,473	–	–	–	31/12/2018	24/03/2021[4,5]
	24/03/2017	121,258	4880	–	–	–	–	121,258	31/12/2019	24/03/2022
	23/03/2018	128,889	4853	–	–	1,289	–	127,600	31/12/2020	23/03/2023[6]
	08/03/2019	102,475	6287	–	–	–	102,475	–	31/12/2021	08/03/2024
	06/03/2020	87,346	7376	–	–	–	87,346	–	31/12/2022	06/03/2025
	21/05/2020	8,734	7376	–	–	–	8,734	–	31/12/2022	21/05/2025
	05/03/2021	–	6844	106,655	–	–	106,655	–	31/12/2023	05/03/2026[7]
	14/05/2021	–	6844	19,391	–	–	19,391	–	31/12/2023	14/05/2026[7]
AZIP	11/06/2013	89,960	3297	–	89,960	–	–	–	31/12/2016	01/01/2021[8,9]
	28/03/2014	20,677	3904	–	–	–	–	20,677	31/12/2017	01/01/2022
	27/03/2015	13,095	4762	–	–	–	–	13,095	31/12/2018	01/01/2023
	24/03/2016	10,809	3923	–	–	–	–	10,809	31/12/2019	01/01/2024
Total		717,456		142,990	205,590	1,289	324,601	328,966		

1 Market price on 23 March 2021, the actual date of release, was 7344 pence.
2 An additional 1,171 Ordinary Shares were released as a result of the reinvestment of dividend equivalents accrued during the deferral period.
3 Award granted following deferral of one half of the annual bonus earned in respect of performance during 2020, further detail on page 111.
4 Market price on 24 March 2021, the actual date of release, was 7215 pence.
5 An additional 16,782 Ordinary Shares were released as a result of the reinvestment of dividend equivalents accrued during the performance and holding period.
6 99% of the shares entered the holding period, following assessment of performance over the period to 31 December 2020. The remaining shares lapsed.
7 Details of PSP awards granted during 2021 are shown from page 113.
8 An additional 27,945 Ordinary Shares were released as result of the reinvestment of dividend equivalents accrued during the performance and holding period.
9 Market price on 11 February 2021, the actual date of release, was 7247 pence.

Aradhana Sarin

Share scheme interests	Grant/ conversion date	Shares outstanding at 1 August 2021	Grant price (pence)	Shares granted in period	Shares released in period	Shares lapsed in period	Shares outstanding at 31 December 2021: Shares subject to performance	Shares outstanding at 31 December 2021: Shares in deferral/ holding period	Performance period end	Vesting and release date
Alexion incentive shares[1]	21/07/2021	4,589.5	[1]	–	4,589.5	–	n/a	–	n/a	12/11/2021[2]
	21/07/2021	1,331.5	[1]	–	–	–	n/a	1,331.5	n/a	28/02/2022
	21/07/2021	3,252	[1]	–	–	–	n/a	3,252	n/a	21/07/2022
	21/07/2021	3,252	[1]	–	–	–	n/a	3,252	n/a	28/02/2022
	21/07/2021	42,284	[1]	–	–	–	n/a	42,284	n/a	28/02/2022
	21/07/2021	4,289.5	[1]	–	–	–	n/a	4,289.5	n/a	01/02/2023
	21/07/2021	4,289.5	[1]	–	–	–	n/a	4,289.5	n/a	21/07/2022
	21/07/2021	46,525	[1]	–	–	–	n/a	46,525	n/a	21/07/2022
	21/07/2021	4,290	[1]	–	–	–	n/a	4,290	n/a	28/02/2022
	21/07/2021	9,648.5	[1]	–	–	–	n/a	9,648.5	n/a	01/02/2023
	21/07/2021	9,649	[1]	–	–	–	n/a	9,649	n/a	01/02/2023
	21/07/2021	9,649	[1]	–	–	–	n/a	9,649	n/a	21/07/2022
	21/07/2021	9,649	[1]	–	–	–	n/a	9,649	n/a	28/02/2022
RSU award	13/08/2021	–	8209	12,276	–	–	n/a	12,276	n/a	01/02/2023[3]
PSP	13/08/2021	–	8209	19,414	–	–	19,414	–	31/12/2023	13/08/2026
Total		152,669		31,690	4,589.5	0	19,414	160,385		

1 Awards made to replace Dr Sarin's Alexion incentive share awards which were outstanding at the time of the Alexion acquisition, on the same basis as other participants. These outstanding in-flight awards were converted to awards over AstraZeneca ADRs in accordance with the terms of the Merger Agreement, using the average of the volume-weighted averages of the trading price of AstraZeneca ADRs on the Nasdaq from 13 July to 19 July 2021 inclusive ($58.2622). The face value of the converted awards was $17.8m. The number shown is the number of Ordinary Shares underlying the ADRs.
2 Market price of AstraZeneca ADRs on 12 November 2021, the actual date of release, was $62.92.
3 One-off restricted share award granted to Dr Sarin to compensate her for the forfeiture of her previous contractual severance right entitlements, as outlined on page 107.

Directors' shareholdings *continued*

Marc Dunoyer

Share scheme interests	Grant date	Shares outstanding at 1 January 2021	Grant price (pence)	Shares granted in period	Shares released in period	Shares lapsed in period	Shares outstanding at 1 August 2021: Shares subject to performance	Shares outstanding at 1 August 2021: Shares in deferral/ holding period	Performance period end	Vesting and release date
DBP	23/03/2018	7,037	4853	–	7,037	–	**n/a**	–	n/a	23/03/2021[1,2]
	08/03/2019	4,874	6287	–	–	–	**n/a**	**4,874**	n/a	08/03/2022
	06/03/2020	4,323	7376	–	–	–	**n/a**	**4,323**	n/a	06/03/2023
	05/03/2021	–	6844	9,057	–	–	**n/a**	**9,057**	n/a	05/03/2024[3]
PSP	24/03/2016	42,739	3923	–	42,739	–	–	–	31/12/2018	24/03/2021[4,5]
	24/03/2017	57,655	4880	–	–	–	–	**57,655**	31/12/2019	24/03/2022
	23/03/2018	61,240	4853	–	–	613	–	**60,627**	31/12/2020	23/03/2023[6]
	08/03/2019	48,690	6287	–	–	–	**48,690**	–	31/12/2021	08/03/2024
	06/03/2020	41,501	7376	–	–	–	**41,501**	–	31/12/2022	06/03/2025
	05/03/2021	–	6844	51,828	–	–	**51,828**	–	31/12/2023	05/03/2026[7]
AZIP	01/08/2013	8,176	3302	–	8,176	–	–	–	31/12/2016	01/01/2021[8,9]
	28/03/2014	8,709	3904	–	–	–	–	**8,709**	31/12/2017	01/01/2022
	27/03/2015	5,734	4762	–	–	–	–	**5,734**	31/12/2018	01/01/2023
	24/03/2016	4,508	3923	–	–	–	–	**4,508**	31/12/2019	01/01/2024
Total		**295,186**		**60,885**	**57,952**	**613**	**142,019**	**155,487**		

1 Market price on 23 March 2021, the actual date of release, was 7344 pence.
2 An additional 626 Ordinary Shares were released as a result of the reinvestment of dividend equivalents accrued during the deferral period of the 2018 DBP.
3 Award granted following deferral of one half of the annual bonus earned in respect of performance during 2020. further detail on page 111.
4 Market price on 24 March 2021, the actual date of release, was 7215 pence.
5 An additional 6,998 Ordinary Shares were released as a result of the reinvestment of dividend equivalents accrued during the performance and holding period of the 2016 PSP.
6 99% of the shares entered the holding period, following assessment of performance over the period to 31 December 2020. The remaining shares lapsed.
7 Details of PSP awards granted during 2021 are shown from page 113.
8 An additional 2,539 Ordinary Shares were released as a result of the reinvestment of dividend equivalents accrued during the performance and holding period of the 2013 AZIP.
9 Market price on 11 February 2021, the actual date of release, was 7247 pence.

No Director or senior executive beneficially owns, or has options over, 1% or more of the issued share capital of the Company, nor do they have different voting rights from other shareholders. None of the Directors has a beneficial interest in the shares of any of the Company's subsidiaries. Between 31 December 2021 and 10 February 2022, there was no change in the interests in Ordinary Shares for current Directors shown in the tables on pages 117 to 119.

Remuneration in the wider context

In our Corporate Governance Report on page 84, we explain in detail how the Board has chosen to engage with AstraZeneca's workforce, and how important engagement with our employees is if we are to be a great place to work and continue to deliver outstanding performance. The Directors believe that the Board as a whole should continue to take responsibility for gathering the views of the workforce. Consequently, instead of implementing one of the three methods for workforce engagement prescribed in the 2018 UK Corporate Governance Code, the Board chose to enhance and develop the long-standing channels of engagement which already exist in the organisation to ensure that the Board continues to understand the global workforce's views on a wide variety of topics, including matters relating to remuneration.

In light of the challenging conditions in a COVID-19 year, Directors' (including members of the Remuneration Committee) in-person engagement was replaced with virtual interactions. The Committee communicates with, and receives feedback from, employees through a variety of channels, including virtual meetings with high potential employees in the business and attending virtual site visits. This allows the Committee to communicate with employees on remuneration matters where appropriate. Remuneration Committee members review wide-ranging data on reward across our global workforce, as well as broader information on workforce trends and culture, which is also provided to the full Board. The Committee receives in-depth reports throughout the year on colleague pay, benefits, incentives, performance management approach and broader talent policies at AstraZeneca to ensure that the Committee is informed of wider workforce remuneration when making executive pay decisions. Decisions of the Remuneration Committee affecting employees, such as the annual Group scorecard outcomes, are communicated to employees through internal communications as well as through the Remuneration Report. In the event that more significant changes to workforce remuneration are proposed, active engagement with employee representative groups provides feedback to help the Committee understand the impact upon the broader workforce.

When considering executive remuneration, the Committee takes into consideration our global workforce, looking to ensure the global total reward offering is competitive, compelling and aligned to our business performance, while supporting a culture where everyone feels valued and included, as outlined in the table on page 120. Being a great place to work is one of our three strategic priorities. We explain in our Business Review from page 40 the role that reward plays in developing a diverse culture that encourages and rewards innovation, entrepreneurship and high performance.

Remuneration in the wider context *continued*

In carrying out its responsibilities, the Committee has taken into account the principles outlined in the UK Corporate Governance Code. The Committee believes that the remuneration structures in place are aligned to the Company's culture and values and ensure the successful delivery of our strategy, as set out on page 103. The Committee believes the remuneration structures under the Directors' Remuneration Policy, and those for the wider workforce as set out below, are simple, clearly understood and proportionate. The Committee also regularly engages with shareholders, as set from page 98, and considers their feedback when reviewing the Directors' Remuneration Policy and implementation. For example, as outlined on page 99, the Committee amended the names of the Innovative Science measures in response to investor feedback, to provide additional clarity and ensure that the measures are easily understood. Employees are also provided with updates.

Summary of remuneration structure for employees below the Board

Element	Policy features for the wider workforce	Comparison with Executive Director and Senior Executive Team (SET) remuneration
Base pay	Our base pay is the basis for a competitive total reward package for all employees, and we review base pay annually. This review takes account of country budget, relevant market comparators, the skills, capabilities, knowledge and experience of each individual, relative to peers within the Company and individual contribution. In setting the budget each year, we consider affordability as well as assessing how employee base pay is currently positioned relative to market rates, forecasts of any further market increases and turnover.	The base pay of our Executive Directors and SET form the basis of their total remuneration, and we review their base pay annually. The primary purpose of the review is to ensure base pay remains competitive and reflects the value of the individual to the organisation.
Pensions and benefits	We offer market-aligned wellbeing benefit packages reflecting market practice in each country in which we operate. Where appropriate, we offer elements of personal benefit choice to our employees.	The benefit packages of our Executive Directors and SET are broadly aligned with the wider workforce of the country in which they are employed. Pension allowances for current UK Executive Directors are in line with the wider UK workforce.
Annual bonus	With the exception of our sales representatives receiving sales-related incentives, our global workforce participates in the same annual cash bonus plan as the Executive Directors and SET, with the same Group scorecard performance measures outlined on pages 108 and 111. Achievement against the scorecard creates a bonus pool from which all awards are made. For employees within our commercial organisation, the country-level share of the global bonus pool also takes into account country performance against KPIs. Individual outcomes are based on manager assessment of contribution against individual objectives and peers. Awards are based on a 0-200% target range.	The ranges for Executive Directors and the SET align with the wider workforce at 0-200% of target. Half of any award to an Executive Director under the plan is subject to deferral into shares subject to a three-year holding period. One sixth of any award to SET under the plan is deferred into shares subject to a three-year holding period.
Long-term incentives	The PSP is operated with a three-year performance period for employees at Vice-President and Senior Vice-President level, with the same performance measures that apply to Executive Director and SET PSP awards (outlined on pages 112 to 115). A proportion of our workforce below Vice-President level is eligible to be considered for other long-term incentive awards, such as restricted stock awards.	PSP awards to Executive Directors and SET are granted under the same plan as PSP awards granted to Vice-Presidents. PSP awards to Executive Directors and SET are subject to a two-year holding period following the three-year performance period.

Remuneration in the wider context *continued*

Change in Director remuneration compared to other employees

In the table below, as per the requirements of the Companies (Directors' Remuneration Policy and Directors' Remuneration Report) Regulations 2019, changes to the base pay (or fees), taxable benefits and annual bonus of Directors are compared to employees for the previous financial year. The regulations require comparison between the remuneration of each Director and that of all employees of the parent company on a full-time equivalent basis. As AstraZeneca PLC has no direct employees, and in line with our disclosure approach in prior years to changes in employee remuneration, the selected comparator group is comprised of employees in the UK, US and Sweden who represent approximately 30% of our total employee population. We consider that this group is representative of the Group's major science, business and enabling units. These employee populations are also well balanced in terms of seniority and demographics.

	Change in 2021 against 2020 (%)			Change in 2020 against 2019 (%)		
	Base pay/fees	Benefits	Annual bonus	Base pay/fees	Benefits	Annual bonus
Executive Directors						
Pascal Soriot	3.0%	1.1%	35.9%	0.0%	-2.7%	20.0%
Aradhana Sarin[1]	–	–	–	–	–	–
Marc Dunoyer[2]	-39.9%	-32.5%	-37.7%	0.0%	25.0%	29.6%
Non-Executive Directors						
Leif Johansson[3]	0.0%	1.4%	–	0.0%	1.4%	–
Euan Ashley[4]	300.0%	–	–	–	–	–
Geneviève Berger[5]	-66.2%	–	–	0.0%	–	–
Philip Broadley	16.9%	–	–	2.8%	–	–
Graham Chipchase[6]	-73.9%	–	–	-10.8%	–	–
Michel Demaré	18.7%	–	–	247.2%	–	–
Deborah DiSanzo	0.0%	–	–	0.0%	–	–
Diana Layfield[7]	525.6%	–	–	0.0%	–	–
Sheri McCoy	3.0%	–	–	–	–	–
Tony Mok	0.0%	–	–	0.0%	–	–
Nazneen Rahman	11.0%	–	–	0.0%	–	–
Andreas Rummelt[8]	–	–	–	–	–	–
Marcus Wallenberg	3.6%	–	–	0.0%	–	–
Employees	4.9%	4.9%	44.4%	4.1%	4.1%	-11.6%

1 Aradhana Sarin joined the Board of AstraZeneca PLC on 1 August 2021.
2 Marc Dunoyer stepped down from the Board of AstraZeneca PLC on 1 August 2021.
3 Benefits for Leif Johansson are office costs.
4 Euan Ashley was appointed on 1 October 2020.
5 Genevieve Berger retired from the Board on 11 May 2021.
6 Graham Chipchase retired from the Board on 11 May 2021.
7 Diana Layfield was appointed on 1 November 2020.
8 Andreas Rummelt was appointed on 1 August 2021.

CEO and employee pay ratios

The table below sets out the ratios of the CEO's realised pay to the equivalent pay for the lower quartile, median and upper quartile UK employees (calculated on a full-time equivalent basis). The ratios have been calculated in accordance with the Companies (Miscellaneous Reporting) Requirements 2018 (the Regulations).

Year[1]	Method	25th percentile pay ratio	50th percentile pay ratio	75th percentile pay ratio
2021	**Option A**	**240:1**	**162:1**	**106:1**
2020	Option A	284:1	197:1	130:1
2019	Option A	280:1	190:1	123:1
2018	Option A	230:1	160:1	103:1

1 Prior year's figures have not been restated for subsequent share price changes (as shown in the CEO realised pay for 2021 table on page 105)

The comparison with UK employees is specified by the Regulations. This group represents approximately 10% of our total employee population. The Regulations provide flexibility to adopt one of three methods of calculation: we continue to use Option A which is a calculation based on all UK employees on a full-time equivalent basis as we consider this to be the most appropriate method of comparison and in line with the calculation of CEO's realised pay (shown on page 105 for 2021). The ratios are based on total pay, which includes base pay, benefits, bonus and long-term incentives (LTI) with all elements adjusted on a full-time equivalent basis if required. Our calculations are in line with the single figure methodology for UK employees where possible, with quartile data as determined as at 31 December 2021. Calculations for UK employees are based on actual base pay and benefits data for the year, with estimates only used for annual bonus outcomes and LTI dividend equivalent payments. These estimates are based on the 2021 bonus budget and projected payouts, and anticipated dividend equivalent payments on LTI awards, respectively. No elements of pay have been excluded from the calculation, which has been determined following the approach of previous years.

CEO and employee pay ratios *continued*

	CEO		UK employees					
			25th percentile		50th percentile		75th percentile	
Pay data[1] (£'000)	Base pay	Total pay	Base pay	Total pay	Base pay	Total pay	Base pay	Total pay
2021	**1,327**	**13,858**	**43**	**58**	**61**	**86**	**86**	**130**
2020	1,289	15,447	41	54	60	78	82	119
2019	1,289	14,330	38	51	53	75	71	117
2018	1,251	11,356	36	49	50	71	70	110

[1] Prior year's figures have not been restated for subsequent share price changes (as shown in the CEO realised pay for 2021 table on page 105).

The 2021 CEO pay ratios were lower across all quartiles when compared to 2020, primarily due to a lower LTI performance outcomes and share price appreciation. Additionally, 2021 saw a fall in fixed pay as pension contributions for the CEO were reduced to align with the wider UK workforce.

Given the Committee's focus on ensuring CEO pay is performance driven, the majority of the single figure is comprised of variable pay and therefore may vary significantly year-on-year due to annual bonus and PSP outcomes, as well as share price movements. The Committee therefore also considers the CEO pay ratio without the LTI impact. When excluding the LTI, the pay ratio of the CEO compared to the median UK employee is 57:1, an increase on 53:1 in 2020, and 51:1 in both 2018 and 2019. This change is due to a higher annual bonus award in 2021 for the CEO, in line with the approach to differentiate awards for individuals in the wider workforce that have made an exceptional contribution during the year.

The Committee remains mindful of the debate on executive pay and seeks to ensure that when determining the remuneration of the CEO it finds the right balance when rewarding performance in a highly competitive global executive talent market. It believes the median ratio is consistent with the pay and progression policies for UK employees, which ensures our total reward offering is competitive and compelling, and aligned to individual and business performance as set out on page 120.

Relative importance of spend on pay

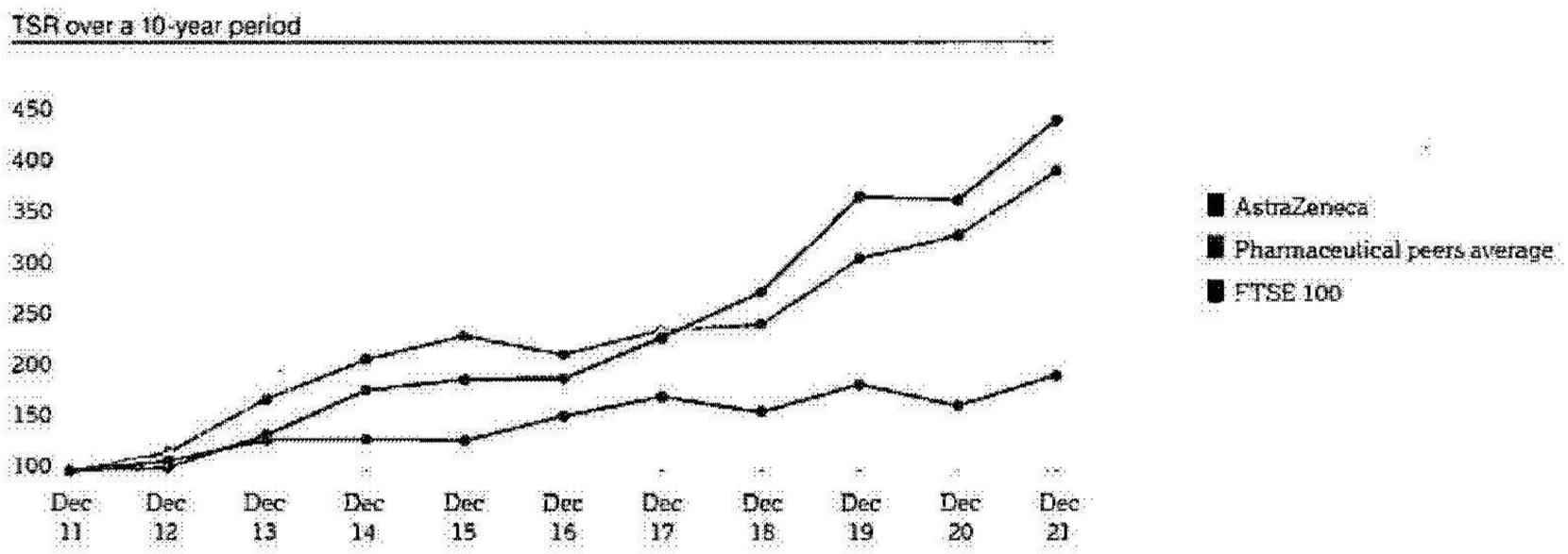
The table below shows the remuneration paid to all employees in the Group, including the Executive Directors, and expenditure on shareholder distributions through dividends. The figures have been calculated in accordance with the Group Accounting Policies and drawn from either the Company's Consolidated Statement of Comprehensive Income on page 134, or its Consolidated Statement of Cash Flows on page 137. Further information on the Group's Accounting Policies can be found from page 138.

	2021 $m	2020 $m	Difference in spend between years $m	Difference in spend between years %
Total employee remuneration	**10,276**	8,247	2,029	24.60
Distributions to shareholders: dividends paid	**3,856**	3,572	284	7.95

Total shareholder return (TSR)

The graph below compares the TSR performance of the Company over the past 10 years with the TSR of the FTSE 100 Index. This graph is re-based to 100 at the start of the relevant period. As a constituent of the FTSE 100, this index represents an appropriate reference point for the Company. To provide shareholders with additional context we have also included a 'Pharmaceutical peers average', reflecting the TSR of our comparator group which is used to assess relative TSR performance for PSP awards granted in 2019. It consisted of AbbVie, Amgen, Astellas, BMS, Celgene, Daiichi Sankyo, Gilead, GSK, Johnson & Johnson, Eli Lilly, MSD, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi, Shire and Takeda. Where a comparator company delisted during the 2019 performance period as a result of an acquisition, TSR performance has been assessed up unto the point of de-listing. The TSR comparator group for PSP awards to be granted in 2022 consists of AbbVie, Amgen, Astellas, BMS, Daiichi Sankyo, Eli Lilly, Gilead, GSK, Johnson & Johnson, Merck KGaA, Moderna, MSD, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi and Takeda. CEO remuneration over the same 10-year period is shown after the TSR graph.

TSR over a 10-year period



Remuneration in the wider context *continued*

CEO total remuneration table

Year	CEO	CEO realised pay £'000	Annual bonus payout against maximum opportunity %	LTI vesting rates against maximum opportunity %
2021	Pascal Soriot	13,858[1]	95	95
2020	Pascal Soriot	15,934[2]	90	99
2019	Pascal Soriot	15,307	83	90
2018	Pascal Soriot	12,868	83	79
2017	Pascal Soriot	10,429	87	81
2016	Pascal Soriot	14,342[3]	54	95
2015	Pascal Soriot	7,963	97	78
2014	Pascal Soriot	3,507	94	–
2013	Pascal Soriot	3,344	94	–
2012	Pascal Soriot – *appointed with effect from 1 October 2012*	3,693[4]	88	–
2012	Simon Lowth – *acted as interim CEO from June to September 2012 inclusive*	3,289	86	38[5]
2012	David Brennan – *ceased to be a Director on 1 June 2012*	4,147[6]	–[7]	38

[1] The 2021 realised pay is shown on page 105.
[2] This figure has been revised using the average closing share price over the three-month period to 31 December 2021, as explained on page 112.
[3] This figure includes shares awarded to Mr Soriot in 2013 under the AZIP to compensate him for LTIs from previous employment forfeited on his recruitment as the Company's CEO.
[4] This figure includes £991,000 paid to compensate Mr Soriot in respect of his forfeited bonus opportunity for 2012 and an award of £2,000,000 to compensate him for his loss of LTI awards, both in respect of his previous employment.
[5] Mr Lowth's LTI awards which vested during 2012 were not awarded or received in respect of his performance as Interim CEO.
[6] This figure includes Mr Brennan's pay in lieu of notice of £914,000.
[7] Mr Brennan informed the Committee that he did not wish to be considered for a bonus in respect of that part of 2012 in which he was CEO. The Committee determined that no such bonus would be awarded and also that there should be no bonus award relating to his contractual notice period.

Grant of Restricted Stock Units under Listing Rule 9.4.2

The Directors' Remuneration Policy (the Policy) specifically permits the Company to introduce a one-off share award under Listing Rule 9.4.2 (LR9.4.2) as part of recruitment arrangements for Executive Directors. The Committee was satisfied that the circumstances of Dr Sarin's recruitment and, in particular, the forfeiture of contractual severance arrangements that she would otherwise have been entitled to with Alexion, were sufficiently unusual such that a one-off share award would meet the requirements of LR9.4.2.

Details of the award (as required by the terms of LR9.4.2) are as follows:

	Ordinary Shares granted	Grant date	Grant price (pence per share)	Vesting date
Aradhana Sarin	12,276	13 August 2021	8209	1 February 2023

The award will normally only vest to the extent that Dr Sarin remains employed by AstraZeneca through to the vesting date. If Dr Sarin leaves employment before that date and is not a good leaver, the award will lapse. If she is a good leaver, her award will vest on the date she ceases employment, pro-rated for the period that she was in employment. The circumstances in which Dr Sarin would be a good leaver include if she leaves by reason of death, ill health, injury or at the discretion of the Remuneration Committee. The award will vest on a change of control of AstraZeneca subject to pro-rating for the period through to the change of control.

The number of shares under the award, the basis for determining Dr Sarin's entitlement to shares, the terms of the award relating to adjustment on any capitalisation issue, rights issue or open offer, subdivision or consolidation or reduction of capital or any other variation of capital cannot be altered to the advantage of Dr Sarin without the prior approval of shareholders in a general meeting (except for minor amendments to benefit the administration of the award, to take account of a change in legislation or to obtain or maintain favourable tax, exchange control or regulatory treatment for Dr Sarin or AstraZeneca).

The award is not pensionable and may only be satisfied by shares purchased on the market. No shares may be issued or transferred from treasury to satisfy the award.

Governance

Committee membership

During 2021, the Committee members were Michel Demaré (Chair of the Committee), Leif Johansson, Sheri McCoy and Philip Broadley. The Deputy Company Secretary acts as secretary to the Committee. The Committee met six times in 2021 and members' attendance records are set out on page 73. During the year, the Committee was materially assisted, except in relation to their own remuneration, by the CEO; the CFO; the VP Finance Group Controller; the SVP, Global Portfolio/Project Management and Strategic Planning; the EVP, Human Resources and General Counsel; the SVP, Reward and Inclusion; the Senior Director Executive Reward; the Company Secretary; the Deputy Company Secretary; EVP, Sustainability and Chief Compliance Officer; the Non-Executive Director responsible for overseeing sustainability matters on behalf of the Board; and the Non-Executive Directors forming the Science and Sustainability Committees. The Committee's independent adviser attended all Committee meetings.

Independent adviser to the Committee

The Committee reappointed Willis Towers Watson (WTW) as its independent adviser. WTW were first appointed in September 2018, following a tender process undertaken in 2018. The tender process involved submission of written proposals, followed by shortlisted candidates being interviewed by both Committee members and members of the Company's management. WTW's service to the Committee during 2021 was provided on a time spent basis at a cost to the Company of £169,950, excluding VAT. During 2021, WTW also provided pensions advice and administration, and advice and support to management including market data to assist in the annual employee pay review and global pay survey data. WTW have no other connection with the Company or individual Directors. The Committee reviewed the potential for conflicts of interest related to WTW and judged that there were no conflicts. WTW is a member of the Remuneration Consultants' Group, which is responsible for the stewardship and development of the voluntary code of conduct in relation to executive remuneration consulting in the UK. The principles on which the code is based are transparency, integrity, objectivity, competence, due care and confidentiality. WTW adheres to the code.

Malus and clawback

The Remuneration Committee regularly reviews the Company's approach to malus and clawback and market practice in this area, and our Directors' Remuneration Policy outlines the trigger events and the time periods these provisions may apply to. As a condition of annual bonus and Performance Share Plan awards, the Committee seeks active acceptance of the malus and clawback terms applicable each year before any payment or grant is made to an individual. Additionally, the Committee's practice is to fully document and evidence any application of malus or clawback to show that it has not acted arbitrarily, capriciously or irrationally in making any determination. This allows the Committee to:

- reduce the amount of bonus or PSP payable, or claw-back some or all of any award in the circumstances and periods as set out within our Policy
- cancel bonus eligibility
- prevent vesting of the PSP and/or DBP awards by holding the shares in AstraZeneca's LTI nominee platform to prevent transactions.

Shareholder voting at the AGM

At the Company's AGM on 11 May 2021, shareholders voted in favour of a resolution to approve the Directors' Remuneration Policy and Annual Report on Remuneration for the year ended 31 December 2020. The Policy can be found on the Company's website, www.astrazeneca.com/annualreport2021.

Resolution	Votes for	% for	Votes against	% against	Total votes cast	% of Issued Share Capital voted	Withheld votes
Ordinary Resolution to approve the Annual Report on Remuneration for the year ended 31 December 2020	915,909,189	95.42	43,957,696	4.58	959,866,885	73.12	1,662,608
Ordinary Resolution to approve the Directors' Remuneration Policy	564,935,789	60.19	373,708,277	39.81	938,644,066	71.50	21,415,088

The response to the shareholder vote to approve the Directors' Remuneration Policy at the 2021 AGM is outlined in the Remuneration Committee Chair's letter on page 101.

Directors' service contracts and letters of appointment

The notice periods and unexpired terms of Executive Directors' service contracts at 31 December 2021 are shown in the table below.

Executive Director	Effective date of service contract	Unexpired term at 31 December 2021	Notice period
Pascal Soriot	15 December 2016	12 months	12 months
Aradhana Sarin	1 August 2021	12 months	12 months

None of the Non-Executive Directors has a service contract but each has a letter of appointment. In accordance with the Company's Articles, following their appointment, all Directors must retire at each AGM and may present themselves for re-election. The Chair of the Board may terminate his appointment at any time, on three months' notice. None of the other Non-Executive Directors has a notice period or any provision in their letters of appointment giving them a right to compensation upon early termination of appointment.

Basis of preparation of this Directors' Remuneration Report

This Directors' Remuneration Report has been prepared in accordance with the Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013 (as amended) (the 2013 Regulations). As required by the 2013 Regulations, a resolution to approve the Annual Report on Remuneration will be proposed at the AGM on 29 April 2022.

On behalf of the Board

A C N Kemp
Company Secretary
10 February 2022

Financial Statements

Preparation of the Financial Statements and Directors' Responsibilities 126

Auditors' Report 127

Consolidated Statements 134

Group Accounting Policies 138

Notes to the Group Financial Statements 145

Group Subsidiaries and Holdings 197

Company Statements 202

Company Accounting Policies 204

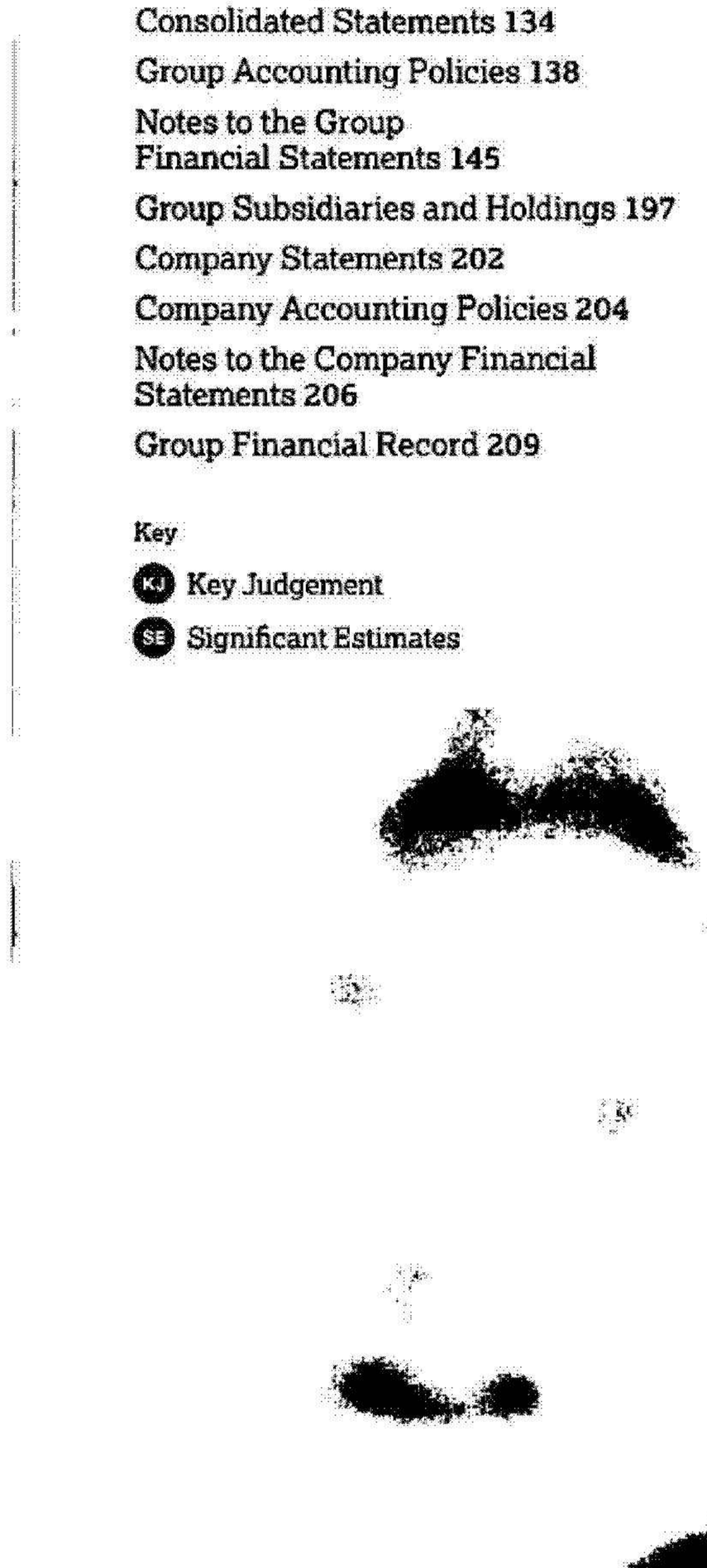
Notes to the Company Financial Statements 206

Group Financial Record 209

Key

KJ Key Judgement

SE Significant Estimates





Preparation of the Financial Statements and Directors' Responsibilities

The Directors are responsible for preparing this Annual Report and Form 20-F Information and the Group and Parent Company Financial Statements in accordance with applicable law and regulations.

Company law requires the Directors to prepare Financial Statements for each financial year. Under that law the Directors have prepared the Group Financial Statements in accordance with UK-adopted International Accounting Standards and with the requirements of the Companies Act 2006 as applicable to companies reporting under those standards and Parent Company Financial Statements in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards, comprising FRS 101 "Reduced Disclosure Framework", and applicable law). In preparing the Group Financial Statements, the Directors have also elected to comply with International Financial Reporting Standards issued by the International Accounting Standards Board (IASB) and International Accounting Standards as adopted by the European Union.

Under company law, the Directors must not approve the Financial Statements unless they are satisfied that they give a true and fair view of the state of affairs of the Group and Parent Company and of their profit or loss for that period. In preparing each of the Group and Parent Company Financial Statements, the Directors are required to:

- select suitable accounting policies and then apply them consistently
- make judgements and estimates that are reasonable and prudent
- for the Group Financial Statements, state whether they have been prepared in accordance with UK-adopted International Accounting Standards
- for the Parent Company Financial Statements, state whether FRS 101 has been followed, subject to any material departures disclosed and explained in the Parent Company Financial Statements
- prepare the Financial Statements on the going concern basis unless it is inappropriate to presume that the Group and the Parent Company will continue in business.

The Directors are responsible for keeping adequate accounting records that are sufficient to show and explain the Parent Company's transactions and disclose with reasonable accuracy at any time the financial position of the Parent Company and enable them to ensure that its Financial Statements comply with the Companies Act 2006. They have general responsibility for taking such steps as are reasonably open to them to safeguard the assets of the Group and to prevent and detect fraud and other irregularities.

Under applicable law and regulations, the Directors are also responsible for preparing a Directors' Report, Strategic Report, Directors' Remuneration Report, Corporate Governance Report and Audit Committee Report that comply with that law and those regulations.

The Directors are responsible for the maintenance and integrity of the corporate and financial information included on our website. Legislation in the UK governing the preparation and dissemination of Financial Statements may differ from legislation in other jurisdictions.

Directors' responsibility statement pursuant to DTR 4

The Directors confirm that to the best of our knowledge:

- the Financial Statements, prepared in accordance with the applicable set of accounting standards, give a true and fair view of the assets, liabilities, financial position and profit or loss of the Company and the undertakings included in the consolidation taken as a whole
- the Directors' Report includes a fair review of the development and performance of the business and the position of the issuer and the undertakings included in the consolidation taken as a whole, together with a description of the principal risks and uncertainties that they face.

On behalf of the Board of Directors on 10 February 2022

Pascal Soriot
Director

DocuSigned by:
Pascal Soriot
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Directors' Annual Report on Internal Controls over Financial Reporting

The Directors are responsible for establishing and maintaining adequate internal control over financial reporting. AstraZeneca's internal control over financial reporting is designed to provide reasonable assurance over the reliability of financial reporting and the preparation of consolidated financial statements in accordance with generally accepted accounting principles.

Due to its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate.

As disclosed in Note 27, the Company completed its acquisition of Alexion Pharmaceuticals, Inc. during 2021. In accordance with SEC Staff Guidance permitting a company to exclude an acquired business from management's assessment of the effectiveness of internal control over financial reporting for the year in which the acquisition is completed, the Company has excluded this business from its assessment of the effectiveness of internal control over financial reporting as at 31 December 2021. This entity is included within our 2021 Consolidated Financial Statements and constituted approximately 9% of Total assets (excluding goodwill and intangible assets resulting from the acquisition) as at 31 December 2021 and approximately 8% of Total Revenue for the year ended 31 December 2021.

The Directors assessed the effectiveness of AstraZeneca's internal control over financial reporting as at 31 December 2021 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013). Based on this assessment, internal control over financial reporting is effective.

PricewaterhouseCoopers LLP, an independent registered public accounting firm, has audited the effectiveness of internal control over financial reporting as at 31 December 2021 and has issued an unqualified report thereon.

Independent auditors' report to the members of AstraZeneca PLC

Report on the audit of the financial statements

Opinion

In our opinion:

- AstraZeneca PLC's Group Financial Statements and Parent Company Financial Statements (the "financial statements") give a true and fair view of the state of the Group's and of the Parent Company's affairs as at 31 December 2021 and of the Group's profit and the Group's cash flows for the year then ended;
- the Group Financial Statements have been properly prepared in accordance with UK-adopted international accounting standards;
- the Parent Company Financial Statements have been properly prepared in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards, comprising FRS 101 "Reduced Disclosure Framework", and applicable law); and
- the financial statements have been prepared in accordance with the requirements of the Companies Act 2006.

We have audited the financial statements, included within the Annual Report and Form 20-F Information 2021 (the "Annual Report"), which comprise: the Consolidated Statement of Financial Position as at 31 December 2021; the Consolidated Statement of Comprehensive Income, the Consolidated Statement of Changes in Equity, and the Consolidated Statement of Cash Flows for the year then ended; the Group Accounting Policies; the Notes to the Group Financial Statements; the Parent Company Balance Sheet as at 31 December 2021; the Parent Company Statement of Changes in Equity for the year then ended; the Parent Company Accounting Policies; and the Notes to the Parent Company Financial Statements.

Our opinion is consistent with our reporting to the Audit Committee.

Separate opinion in relation to international financial reporting standards adopted pursuant to Regulation (EC) No 1606/2002 as it applies in the European Union and in relation to IFRSs as issued by the IASB

As explained in the Group Accounting Policies to the Group Financial Statements, the Group, in addition to applying UK-adopted international accounting standards, has also applied international financial reporting standards adopted pursuant to Regulation (EC) No 1606/2002 as it applies in the European Union and international financial reporting standards (IFRSs) as issued by the International Accounting Standards Board (IASB).

In our opinion, the Group Financial Statements have been properly prepared in accordance with international financial reporting standards adopted pursuant to Regulation (EC) No 1606/2002 as it applies in the European Union and with IFRSs as issued by the IASB.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) ("ISAs (UK)") and applicable law. Our responsibilities under ISAs (UK) are further described in the Auditors' responsibilities for the audit of the financial statements section of our report. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Independence

We remained independent of the Group in accordance with the ethical requirements that are relevant to our audit of the financial statements in the UK, which includes the FRC's Ethical Standard, as applicable to listed public interest entities, and we have fulfilled our other ethical responsibilities in accordance with these requirements.

To the best of our knowledge and belief, we declare that non-audit services prohibited by the FRC's Ethical Standard were not provided.

Other than those disclosed in note 31, we have provided no non-audit services to the Group in the period under audit.

Our audit approach

Overview

Audit scope

- We identified 14 reporting components which required a full scope audit of their complete financial information, either due to their size or risk characteristics. These components are the principal operating units in the US (two components which includes the newly acquired Alexion rare diseases component), UK (two components), Sweden, China (two components), Japan, France, Germany, South Korea, Turkey as well as the Parent Company and AstraZeneca Treasury.
- We also identified a further 12 reporting components which had one or more individual balances that were considered significant to the Group's Financial Statements. For these components our work was solely focussed on the audit of one or more of the following financial statement line items: revenue, accounts receivable, inventory, cash and cash equivalents, non-current interest-bearing loans and borrowings, research and development expense, taxation and/or property, plant and equipment.
- We also identified four shared service centres where audit procedures were performed over certain shared service functions for transaction processing. Audit procedures were performed centrally in relation to various Group functions, including the accounting for the acquisition of Alexion Pharmaceuticals Inc., goodwill, intangible assets (excluding software), pensions, certain cash and borrowings, other investments and litigation matters, as well as the consolidation.
- The above procedures accounted for 87% of the Group's revenue and 74% of the Group's absolute profit before tax.

Key audit matters

- Recognition and measurement of accruals for certain rebates in the US excluding rare diseases (Group)
- Assessment of the recoverability of the carrying value of intangible assets (excluding goodwill and software development costs) (Group)
- Recognition and measurement of legal provisions and contingent liabilities in both the Group and the Parent Company (Group and Parent Company)
- Recognition and measurement of uncertain tax positions (Group)
- Valuation of the Group's defined benefit obligations (Group)
- Accounting for the acquisition of Alexion Pharmaceuticals, Inc – valuation of the acquired intangible assets, inventory and contingent liabilities (Group)
- Accounting for sales, grant income and deferred income relating to Vaxzevria (Group).

Materiality

- Overall Group materiality: US$250m (2020: US$200m) based on 5% of profit before tax after adding back intangible asset impairment charges (Note 10), fair value movements and discount unwind on contingent consideration (Note 20), the discount unwind on the Acerta Pharma put option liability (Note 3), material legal settlements (Note 21), the unwind of the fair value adjustment to Alexion inventories (Note 2) and restructuring charges relating to the Post Alexion Acquisition Group Review (Note 2).
- Overall Parent Company materiality: US$100m (2020: US$100m) based on approximately 0.5% of net assets as constrained by the allocation of overall Group materiality.
- Performance materiality: US$187.5m (Group) and US$75m (Parent Company).

The scope of our audit

As part of designing our audit, we determined materiality and assessed the risks of material misstatement in the financial statements. In particular, we looked at where the directors made subjective judgements, for example in respect of significant accounting estimates that involved making assumptions and considering future events that are inherently uncertain.

Key audit matters

Key audit matters are those matters that, in the auditors' professional judgement, were of most significance in the audit of the financial statements of the current period and include the most significant assessed risks of material misstatement (whether or not due to fraud) identified by the auditors, including those which had the greatest effect on: the overall audit strategy; the allocation of resources in the audit; and directing the efforts of the engagement team. These matters, and any comments we make on the results of our procedures thereon, were addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

This is not a complete list of all risks identified by our audit.

The accounting for the acquisition of Alexion Pharmaceuticals Inc is a new key audit matter this year. The impact of COVID-19 key audit matter has been refined to address the accounting for Vaxzevria, the COVID-19 vaccine. Otherwise, the key audit matters below are consistent with last year.

Independent auditors' report to the members of AstraZeneca PLC *continued*

Key audit matter	How our audit addressed the key audit matter
Recognition and measurement of accruals for certain rebates in the US (excluding rare diseases) (Group) *Refer to Audit Committee Report, Group Accounting Policies and Notes 1 and 20 in the Group Financial Statements* In the US the Group sells to customers under various commercial and government mandated contracts and reimbursement arrangements that include rebates, of which the most significant are Medicare Part D, Managed Care and Medicaid. Rebates provided to customers under these arrangements are accounted for as variable consideration, and recognised as a reduction in revenue, for which unsettled amounts are accrued. Management has determined an accrual of $3,172m to be necessary at 31 December 2021 (2020: $3,126m) related to all US product sales rebates, chargebacks, returns and other revenue accruals for US product sales (which includes an immaterial amount for rare diseases). There is significant measurement uncertainty involved in developing certain of these accruals, as the reserves are based on assumptions developed using contractual and mandated terms with customers, historical experience, and market related information in the US. Changes in these estimates (individually or in combination) can have a significant financial impact.	We evaluated the design and tested the operating effectiveness of controls relating to the assumptions used to estimate the accruals for the Medicare Part D, Managed Care and Medicaid rebate arrangements. We determined that we could rely on these controls for the purposes of our audit. We: > obtained management's calculations for the accruals for the Medicare Part D, Managed Care and Medicaid rebate arrangements; > developed an independent expectation of these accruals using the terms of the specific rebate programmes, third party information on prices and market conditions in the US and the historical trend of actual rebate claims paid; > compared the independent estimate to management's estimates recorded by the Group; > considered the historical accuracy of the Group's estimates in previous years and the effect of any adjustments to prior years' accruals in the current year's results; and > tested rebate claims processed by the Group, including evaluating those claims for consistency with the contractual and mandated terms of the Group's arrangements. Based on the procedures performed, we did not identify any material misstatements in the accruals. We also evaluated the disclosures in Notes 1 and 20, which we considered appropriate.
Assessment of the recoverability of the carrying value of intangible assets (being product, marketing and distribution rights and other intangible assets excluding goodwill and software development costs) (Group) *Refer to Audit Committee Report, Group Accounting Policies and Note 10 in the Group Financial Statements* The Group has product, marketing and distribution rights and other intangible assets excluding goodwill and software development costs (hereafter referred to as the intangible assets) totalling $42,062m at 31 December 2021 (2020: $20,627m). Those intangible assets under development and not available for use are tested annually for impairment and other intangible assets are tested when there is an indication of impairment. The recoverability of the carrying values of cash generating units (to which the intangible assets belong) depends on future cash flows and/or the outcome of research and development activities including decisions by the Company to terminate development. The determination of the recoverable amounts include significant estimates, which are highly sensitive and depend upon key assumptions including the probability of technical and regulatory success, and the amount and timing of projected future cash flows (in particular peak year sales and sales erosion curves). Changes in these assumptions could have an impact on the recoverable amount of intangible assets. For one material asset (Ardea) management determined that there was no recoverable value as the Company has taken the decision to terminate development of verinurad. During 2021, $2,085m (2020: $240m) of impairment charges were recorded (of which $1,464m (2020: $55m) was recorded in Research and development expenses and $621m (2020: $185m) within Selling, general and administrative costs). There is limited headroom in the recoverable amount calculation for those partially impaired assets and they are inherently sensitive to any variations in assumptions, which could give rise to future impairments.	We evaluated the design and tested the operating effectiveness of controls over management's assessment of the impairment of intangible assets. We determined that we could rely on these controls for the purposes of our audit. We selected assets or cash generating units to be in scope based on our risk assessment which considers the materiality of the carrying value, whether the assets had been previously impaired in the last three years and/or whether there have been events in the year which may indicate an impairment trigger. For those assets or cash generating units in the scope of our audit we: > tested management's process for assessing whether there is an indication of impairment and the process for determining the recoverable amount; > evaluated the appropriateness of the methodology used in the impairment models; > tested the completeness and accuracy of the models as well as the underlying data used in the models, including reconciling the cash flows to the Board approved Medium and Long Term Plans; and > evaluated the significant assumptions used by management in determining future cash flows, including the probability of technical and regulatory success, peak year sales and sales erosion curves. In evaluating the reasonableness of management's assumptions we: > compared significant assumptions (including management's probability of technical and regulatory success, peak year sales assumptions and sales erosion curves) to external data and benchmarks; and > performed a retrospective comparison of forecasted revenues and costs to actual past performance. We utilised our in-house valuation experts to assess the valuation techniques used and to assist with the evaluation of certain key assumptions for higher risk assets (primarily the probability of technical and regulatory success). As a result of our work, we determined that the net impairment charge of $2,085m recorded for intangible assets was reasonable. We considered the disclosures in Note 10 of the Group Financial Statements. We are satisfied that these disclosures are appropriate.

Key audit matter	How our audit addressed the key audit matter
Recognition and measurement of provisions and contingent liabilities for legal proceedings in both the Group and the Parent Company (Group and Parent Company) *Refer to Audit Committee Report, Group Accounting Policies, Notes 21 and 30 in the Group Financial Statements* *Refer to Company Accounting Policies and Note 5 in the Parent Company Financial Statements* The Group is engaged in a number of legal proceedings, including patent litigation, product liability, commercial litigation, and government investigations/ proceedings. At 31 December 2021 the Group held provisions of $239m (2020: $348m) in respect of legal claims and settlements (together, legal provisions) and disclosed the more significant legal proceedings as contingent liabilities in Note 30 of the Group Financial Statements. The Parent Company is also named in certain of these legal proceedings, as disclosed in Note 5 in the Parent Company Financial Statements. There is significant judgement by management when assessing the likelihood of a loss being incurred, in determining whether a reasonable estimate can be made for the loss or range of loss for each legal proceeding and whether a legal provision needs to be recorded or a contingent liability disclosed.	We evaluated the design and tested the operating effectiveness of controls in respect of the recognition and measurement of legal proceedings and related disclosures. We determined that we could rely on these controls for the purposes of our audit. We obtained and evaluated letters of audit inquiry with the Group's internal and external legal counsel. We tested the completeness of management's assessment of both the identification of legal proceedings and possible outcomes of each significant legal proceeding. This included assessment of whether the Parent Company was named as a party to these legal proceedings. We evaluated management's judgement that each of the proceedings set out in Note 30 represents a contingent liability and that for one matter management is unable to estimate the possible loss or range of possible losses at this stage. For the provisions recorded and contingent liabilities disclosed, we consider them to be appropriate. We evaluated the disclosures in Notes 21 and 30 of the Group Financial Statements and Note 5 in the Parent Company Financial Statements and considered them to be appropriate.
Recognition and measurement of uncertain tax positions (Group) *Refer to Audit Committee Report, Group Accounting Policies and Note 30 in the Group Financial Statements* The Group operates in a complex multinational tax environment and is subject to a range of tax risks, leading to uncertain tax positions which arise in the normal course of business, including transaction related tax matters, transfer pricing arrangements and a number of audits and reviews with tax authorities, and in some cases is in dispute with tax authorities. At 31 December 2021 the Group recorded accruals of $768m (2020: $1,014m) in respect of these uncertain tax positions. As disclosed in Note 30, accruals can be built up over a long period of time but the ultimate resolution of tax exposures usually occurs at a point in time. Given the inherent uncertainties in management's assessments of the outcomes of these exposures, there could, in future periods, be adjustments to these accruals that have a material positive or negative effect on the results in any particular period.	We evaluated the design and tested the operating effectiveness of controls in respect of the identification, recognition and measurement of uncertain tax positions. We determined that we could rely on these controls for the purposes of our audit. We tested the completeness of management's assessment of both the identification of tax contingencies and the possible outcomes of each significant matter. We also evaluated the status and results of tax audits and enquiries with the relevant tax authorities. With the assistance of our local and international tax specialists, we tested the information used in the determination of the probability of different outcomes for tax contingencies and the estimation of the liability for those tax contingencies by jurisdiction, including management's assessment of the technical merits of tax positions (including where relevant evaluating any advice received from the Group's external advisors) and estimates of the amount of tax benefit expected to be sustained. We noted that the assumptions and judgements that are required to determine the accruals mean that there is a range of possible outcomes. However, from the evidence obtained, we considered the level of provisioning to be acceptable in the context of the Group Financial Statements taken as a whole. We considered the disclosures in Note 30 of the Group Financial Statements. We are satisfied that these disclosures are appropriate.
Valuation of the Group's defined benefit obligations (Group) *Refer to Audit Committee Report, Group Accounting Policies and Note 22 in the Group Financial Statements* The Group has defined benefit obligations of $13,018m at 31 December 2021 (2020: $13,870m), which is significant in the context of the overall balance sheet. The Group's most significant schemes are in the UK and Sweden, which comprise 79% of the Group's defined benefit obligations. The valuation of pension plan obligations requires estimation in determining appropriate assumptions such as mortality, discount rates and inflation levels. Movements in these assumptions can have a material impact on the determination of the defined benefit obligations. Management uses external actuaries to assist in determining these material assumptions.	We evaluated the design and tested the operating effectiveness of controls in respect of the determination of the Group's most significant defined benefit obligations. We determined that we could rely on these controls for the purposes of our audit. We used our actuarial experts to assess whether the assumptions used in calculating the defined benefit obligations for the UK and Sweden were reasonable. Our actuarial experts evaluated whether mortality assumptions, discount rates and inflation rates were: > consistent with the specifics of each plan and where relevant considering national information; > consistent with independently developed ranges; > in line with other companies' recent external reporting; and > in line with the requirements of IAS 19. We evaluated the calculations prepared by management's external actuaries to assess the impact of the assumptions used on the Group Financial Statements. Based on our procedures, we noted no exceptions and considered management's key assumptions to be within reasonable ranges. We assessed the appropriateness of the related disclosures in Note 22 of the Group Financial Statements and considered them to be reasonable.

Key audit matter	How our audit addressed the key audit matter
Accounting for the acquisition of Alexion Pharmaceuticals, Inc. – valuation of the acquired intangible assets, inventory and contingent liabilities *Refer to Audit Committee Report, Group Accounting Policies and Note 27 in the Group Financial Statements* As described in Note 27 to the consolidated financial statements, on 21 July 2021 the Company acquired Alexion Pharmaceuticals, Inc. for consideration of $41,058m. The Company has recorded the assets and liabilities acquired at fair value which included the recognition of $26,855m of intangible assets and $6,769m of inventory. Attributing fair values to assets acquired and liabilities assumed as part of business combinations is considered to be a key judgement. The purchase price allocation was performed with assistance from an independent valuer specialist to advise on the valuation techniques and key assumptions in the valuation, in particular in respect of the valuation of the intangible assets and inventory. The intangible assets were fair valued using the multi-period excess earnings method, which uses a number of estimates regarding the amount and timing of future cash flows. There is significant estimation required in determining the fair value of the intangible assets in relation to the expected future cash flows to be generated, which is highly sensitive to a change in those assumptions. The key assumptions include the probability of technical and regulatory success (PTRS) and the amount and timing of projected future cash flows (in particular peak year sales and sales erosion curves). The fair value of inventory also involves estimation and was calculated as the estimated selling price less estimated costs to complete and sell the inventory, the associated margins on those activities and holding costs. The 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, and involve an assessment of the likelihood of a number of scenarios in relation to those matters. There is judgement by management when assessing the likelihood of a loss being incurred and in determining the fair value of acquired contingent liabilities including a reasonable estimate of the loss or range of loss for each claim.	We evaluated the design and tested the operating effectiveness of controls implemented by the Group relating to the accounting for the acquisition of Alexion Pharmaceuticals, Inc. We determined that we could rely on these controls for the purposes of our audit. For each of intangible assets, inventory and contingent liabilities we: > tested management's process and methodology (including assessing the competency and objectivity of management's specialists) for determining the fair values, > utilised our in-house valuation experts to evaluate the appropriateness of the valuation techniques used by management's specialists; and > tested the completeness and accuracy of the models as well as the underlying data used in the determination of the fair value. For the fair value of the intangible assets acquired we evaluated the reasonableness of the significant assumptions used by management and their specialists in determining PTRS and the amount and timing of projected future cash flows (in particular peak year sales and sales erosion curves). In making this evaluation we: > compared significant assumptions (including management's PTRS, peak year sales assumptions and sales erosion curves) to historical market data, benchmarking and other external data (where appropriate); > used our in-house valuation experts to assist in the evaluation of the methodology and certain significant assumptions (including the PTRS); and > performed a retrospective comparison of forecasted revenues to actual past performance for launched products. In order to assess the reasonableness of the fair value of the inventory, we utilised our in-house valuation experts to evaluate the appropriateness of the valuation techniques and underlying assumptions. We also assessed whether the assumptions relating to the costs to complete and sell the inventory and the associated margins were consistent with evidence obtained from other areas of the acquisition accounting. For the fair value of the contingent liabilities we also tested the completeness of management's assessment of both the identification of legal claims and disputes and whether these meet the definition of a liability to be recorded under IFRS 3. We determined that the fair values ascribed to the acquired intangible assets, inventory and contingent liabilities were reasonable. We assessed the appropriateness of the disclosures in Note 27 of the Group Financial Statements and considered them to be reasonable.
Accounting for sales, grant income and deferred income relating to Vaxzevria (Group) *Refer to Audit Committee Report, Group Accounting Policies and Notes 1, 2 and 20 in the Group Financial Statements* In 2020, the Group entered into an arrangement with the University of Oxford for the global development, production and supply of the COVID-19 vaccine, *Vaxzevria*. The Group has recorded revenue of $3,917m, collaboration revenue of $64m and government grant income of $531m (which relates to both Vaxzevria and Evusheldj in the year ended 31 December 2021. Certain advance sales agreements have been entered into and the Group has recognised vaccine contract liabilities of $1,003m and deferred government grant income of $67m.	We evaluated the design and tested the operating effectiveness of controls in respect of the accounting for *Vaxzevria*. We determined that we could rely on these controls for the purposes of our audit. We read the underlying funding and supply contracts based on our risk assessment which included consideration of the materiality of the individual contract. We assessed management's accounting analysis including where there was both supply and grant income. For revenue recognised we tested transactions, on a sample basis as part of our overall revenue testing to supporting evidence. For vaccine contract liabilities we vouched upfront funding to bank statements for material arrangements. For grant income we satisfied ourselves that income did not exceed related costs. Based on the procedures performed we consider the accounting treatment for sales of Vaxzevria and related grant income and deferred income to be appropriate.

How we tailored the audit scope

We tailored the scope of our audit to ensure that we performed enough work to be able to give an opinion on the financial statements as a whole, taking into account the structure of the Group and the Parent Company, the accounting processes and controls, and the industry in which they operate.

In establishing the overall approach to the Group audit, we determined the type of work that needed to be performed by us, as the Group engagement team, or component auditors within PwC UK and other PwC network firms operating under our instruction. Where the work was performed by component auditors, we determined the level of involvement we needed to have in the audit work in these territories to be able to conclude whether sufficient appropriate audit evidence had been obtained as a basis for our opinion on the Group Financial Statements as a whole.

The Group operates in over 100 countries and the size of operations within each territory varies. We identified 14 reporting components which required a full scope audit of their complete financial information, either due to their size or risk characteristics. These components are the principal operating units in the US (two components which includes the newly acquired Alexion Pharmaceuticals Inc. component), UK (two components), Sweden, China (two components), Japan, France, Germany, South Korea, Turkey as well as the Parent Company and AstraZeneca Treasury.

We also identified a further 12 reporting components which had one or more individual balances that were considered significant to the Group's Financial Statements. For these components our work was solely focussed on the audit of one or more of the following financial statement line items: revenue, accounts receivable, inventory, research and development expense, taxation and/or property, plant and equipment. We also identified four shared service centres where audit procedures were performed over certain shared service functions for transaction processing.

Audit procedures were performed centrally in relation to various Group functions, including the accounting for the acquisition of Alexion Pharmaceuticals Inc., goodwill, intangible assets (excluding software), pensions, certain cash and borrowings, other investments and litigation matters, as well as the consolidation. Our Group engagement team's involvement in the audits of the reporting components was performed primarily by virtual meetings and tools and included regular meetings with component auditors, reviews of the component auditors' planned response to significant risks, the review of auditor working paper reviews for material reporting components and the review of the work performed by the component auditors on the sub-consolidation of Alexion. We attended meetings with local management alongside the component auditors for all full scope and other material components.

In planning and executing our audit, we considered the potential impact of climate change on the Group's business and the financial statements. The Group has set out its intention – as part of the Ambition Zero Carbon programme – to achieve net-zero greenhouse gas emissions by maximising energy efficiency, shifting to renewable energy sources and investing in nature-based removals to compensate for any residual GHG footprint.

As a part of our audit we made enquiries of management to understand the extent of the potential impact of the physical and transitional climate change risk on the Group Financial Statements. We also discussed the climate change initiatives and commitments from Ambition Zero Carbon and other initiatives to reduce CO_2 emissions, and the impact these have on the Group including on future cash flow forecasts. This includes the commitment to develop next-generation respiratory inhalers with near-zero global warming potential propellants for the pMDI inhaled medicines portfolio.

Management considers that the impact of climate change does not give rise to a material financial statement impact. With the assistance of our climate change experts, we evaluated management's risk assessment and understood the Group's governance processes including the newly formed Sustainability Committee. We reviewed relevant Board and Audit Committee papers related to climate change and performed an audit risk assessment of how the impact of the Group's commitments in respect of climate change including Ambition Zero Carbon may affect the financial statements and our audit.

We challenged the extent to which climate change considerations including the expected cash flows from the initiatives and commitments had been reflected, where appropriate, in management's impairment assessment process, going concern assessment and viability assessment. We found that climate change impacts are included within management's forecasts although the initiatives and commitments did not have a material impact including on our key audit matters. We assessed the consistency of other information disclosed in the Annual Report with the Group Financial Statements, and with our knowledge obtained from the audit.

Materiality

The scope of our audit was influenced by our application of materiality. We set certain quantitative thresholds for materiality. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent of our audit procedures on the individual financial statement line items and disclosures and in evaluating the effect of misstatements, both individually and in aggregate on the financial statements as a whole.

Based on our professional judgement, we determined materiality for the financial statements as a whole as follows:

	Financial statements – Group	Financial statements – Parent Company
Overall materiality	US$250m (2020: US$200m).	US$100m (2020: US$100m).
How we determined it	Based on 5% of profit before tax after adding back intangible asset impairment charges (Note 10), fair value movements and discount unwind on contingent consideration (Note 20), the discount unwind on the Acerta Pharma put option liability (Note 3), material legal settlements (Note 21), the unwind of the fair value adjustment to Alexion inventories (Note 2) and restructuring charges relating to the Post Alexion Acquisition Group Review (Note 2).	Approximately 0.5% of net assets as constrained by the allocation of overall Group materiality.
Rationale for benchmark applied	The reported profit of the Group can fluctuate due to intangible asset impairment charges, fair value and discount unwind movements on contingent consideration, the discount unwind on the Acerta Pharma put option liability, material legal settlements and the unwind of the fair value adjustment to Alexion inventories. In 2021, the restructuring costs resulting from the Post Alexion Acquisition Group Review resulted in a significant fluctuation to the Group's reported profit. These amounts are prone to year on year volatility and are not necessarily reflective of the operating performance of the Group and as such they have been excluded from the benchmark amount.	We have considered the nature of the business of AstraZeneca PLC (being holding company investment activities) and have determined that net assets is an appropriate basis for the calculation of the overall materiality level.

For each component in the scope of our group audit we allocated a materiality that is less than our overall Group materiality. The range of materiality allocated across components was between $20m and $150m.

We use performance materiality to reduce to an appropriately low level the probability that the aggregate of uncorrected and undetected misstatements exceeds overall materiality. Specifically, we use performance materiality in determining the scope of our audit and the nature and extent of our testing of account balances, classes of transactions and disclosures, for example in determining sample sizes. Our performance materiality was 75% (2020: 75%) of overall materiality, amounting to US$187.5m (2020: US$150m) for the Group Financial Statements and US$75m (2020: US$75m) for the Parent Company financial statements.

In determining the performance materiality, we considered a number of factors – the history of misstatements, risk assessment and aggregation risk, and the effectiveness of controls – and concluded that an amount at the upper end of our normal range was appropriate.

We agreed with the Audit Committee that we would report to them misstatements identified during our audit above US$12.5m (Group audit) (2020: US$10m) and US$12.5m (Parent Company audit) (2020: US$10m) as well as misstatements below those amounts that, in our view, warranted reporting for qualitative reasons.

Independent auditors' report to the members of AstraZeneca PLC *continued*

Conclusions relating to going concern

Our evaluation of the directors' assessment of the Group's and the Parent Company's ability to continue to adopt the going concern basis of accounting included:

- agreeing the underlying cash flow projections to Board approved Medium and Long Term Plans, assessing how these forecasts are compiled, and assessing the accuracy of management's forecasts;
- evaluating the key assumptions within management's forecasts;
- considering liquidity and available financial resources;
- assessing whether the stress testing performed by management appropriately considered the principal risks facing the business; and
- evaluating the feasibility of management's mitigating actions in the stress testing scenarios.

Based on the work we have performed, we have not identified any material uncertainties relating to events or conditions that, individually or collectively, may cast significant doubt on the Group's and the Parent Company's ability to continue as a going concern for a period of at least twelve months from when the financial statements are authorised for issue.

In auditing the financial statements, we have concluded that the directors' use of the going concern basis of accounting in the preparation of the financial statements is appropriate.

However, because not all future events or conditions can be predicted, this conclusion is not a guarantee as to the Group's and the Parent Company's ability to continue as a going concern.

In relation to the directors' reporting on how they have applied the UK Corporate Governance Code, we have nothing material to add or draw attention to in relation to the directors' statement in the financial statements about whether the directors considered it appropriate to adopt the going concern basis of accounting.

Our responsibilities and the responsibilities of the directors with respect to going concern are described in the relevant sections of this report.

Reporting on other information

The other information comprises all of the information in the Annual Report other than the financial statements and our auditors' report thereon. The directors are responsible for the other information which includes reporting based on the Task Force on Climate-related Financial Disclosures recommendations. Our opinion on the financial statements does not cover the other information and, accordingly, we do not express an audit opinion or, except to the extent otherwise explicitly stated in this report, any form of assurance thereon.

In connection with our audit of the financial statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial statements or our knowledge obtained in the audit, or otherwise appears to be materially misstated. If we identify an apparent material inconsistency or material misstatement, we are required to perform procedures to conclude whether there is a material misstatement of the financial statements or a material misstatement of the other information. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report based on these responsibilities.

With respect to the Strategic Report and Directors' Report, we also considered whether the disclosures required by the UK Companies Act 2006 have been included.

Based on our work undertaken in the course of the audit, the Companies Act 2006 requires us also to report certain opinions and matters as described below.

Strategic Report and Directors' Report

In our opinion, based on the work undertaken in the course of the audit, the information given in the Strategic Report and Directors' Report for the year ended 31 December 2021 is consistent with the financial statements and has been prepared in accordance with applicable legal requirements.

In light of the knowledge and understanding of the Group and Parent Company and their environment obtained in the course of the audit, we did not identify any material misstatements in the Strategic Report and Directors' Report.

Directors' Remuneration

In our opinion, the part of the Directors' Remuneration Report to be audited has been properly prepared in accordance with the Companies Act 2006.

Corporate governance statement

The Listing Rules require us to review the directors' statements in relation to going concern, longer-term viability and that part of the corporate governance statement relating to the Company's compliance with the provisions of the UK Corporate Governance Code specified for our review. Our additional responsibilities with respect to the corporate governance statement as other information are described in the Reporting on other information section of this report.

Based on the work undertaken as part of our audit, we have concluded that each of the following elements of the corporate governance statement, included within the Corporate Governance Report is materially consistent with the financial statements and our knowledge obtained during the audit, and we have nothing material to add or draw attention to in relation to:

- The directors' confirmation that they have carried out a robust assessment of the emerging and principal risks;
- The disclosures in the Annual Report that describe those principal risks, what procedures are in place to identify emerging risks and an explanation of how these are being managed or mitigated;
- The directors' statement in the financial statements about whether they considered it appropriate to adopt the going concern basis of accounting in preparing them, and their identification of any material uncertainties to the Group's and Parent Company's ability to continue to do so over a period of at least twelve months from the date of approval of the financial statements;
- The directors' explanation as to their assessment of the Group's and Parent Company's prospects, the period this assessment covers and why the period is appropriate; and
- The directors' statement as to whether they have a reasonable expectation that the company will be able to continue in operation and meet its liabilities as they fall due over the period of its assessment, including any related disclosures drawing attention to any necessary qualifications or assumptions.

Our review of the directors' statement regarding the longer-term viability of the Group was substantially less in scope than an audit and only consisted of making inquiries and considering the directors' process supporting their statement; checking that the statement is in alignment with the relevant provisions of the UK Corporate Governance Code; and considering whether the statement is consistent with the financial statements and our knowledge and understanding of the Group and Parent Company and their environment obtained in the course of the audit.

In addition, based on the work undertaken as part of our audit, we have concluded that each of the following elements of the corporate governance statement is materially consistent with the financial statements and our knowledge obtained during the audit:

- The directors' statement that they consider the Annual Report, taken as a whole, is fair, balanced and understandable, and provides the information necessary for the members to assess the Group's and Parent Company's position, performance, business model and strategy;
- The section of the Annual Report that describes the review of effectiveness of risk management and internal control systems; and
- The section of the Annual Report describing the work of the Audit Committee.

We have nothing to report in respect of our responsibility to report when the directors' statement relating to the company's compliance with the Code does not properly disclose a departure from a relevant provision of the Code specified under the Listing Rules for review by the auditors.

Responsibilities for the financial statements and the audit

Responsibilities of the directors for the financial statements

As explained more fully in the Preparation of the Financial Statements and Directors' Responsibilities, the directors are responsible for the preparation of the financial statements in accordance with the applicable framework and for being satisfied that they give a true and fair view. The directors are also responsible for such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the directors are responsible for assessing the Group's and the Parent Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the directors either intend to liquidate the Group or the Parent Company or to cease operations, or have no realistic alternative but to do so.

Auditors' responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditors' report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

Irregularities, including fraud, are instances of non-compliance with laws and regulations. We design procedures in line with our responsibilities, outlined above, to detect material misstatements in respect of irregularities, including fraud. The extent to which our procedures are capable of detecting irregularities, including fraud, is detailed below.

Based on our understanding of the Group and industry, we identified that the principal risks of non-compliance with laws and regulations related to patent protection, product safety (including but not limited to the US Food and Drug Administration regulation), anti bribery and competition law (including but not limited to the Foreign Corrupt Practices Act) and tax legislation, and we considered the extent to which non-compliance might have a material effect on the financial statements. We also considered those laws and regulations that have a direct impact on the financial statements such as the Companies Act 2006. We evaluated management's incentives and opportunities for fraudulent manipulation of the financial statements (including the risk of override of controls) and determined that the principal risks were related to journal entries to manipulate financial results and potential management bias in accounting estimates. The Group engagement team shared this risk assessment with the component auditors so that they could include appropriate audit procedures in response to such risks in their work. Audit procedures performed by the Group engagement team and/or component auditors included:

- Evaluation and testing of the design and operating effectiveness of management's controls to prevent and detect irregularities;
- Discussions with VP Group Internal Audit, the Deputy Chief Compliance Officer, the Head of Global Investigations and the Group's General Counsel and Deputy General Counsels, including consideration of known or suspected instances of non-compliance with laws and regulations and fraud;
- Assessment of matters reported on the Group's whistleblowing helpline and the results of management's investigation of such matters;
- Challenging assumptions made by management in its significant accounting estimates, in particular in relation to the accounting for the acquisition of Alexion Pharmaceuticals, Inc., recognition and measurement of certain rebate accruals in the US (excluding rare diseases), the impairment of intangible assets (excluding goodwill and software development costs), the recognition and measurement of legal provisions and contingent liabilities, the recognition and measurement of uncertain tax positions, and the valuation of the defined benefit obligations (see related key audit matters above); and
- Identifying and testing the validity of journal entries, in particular any journal entries posted with unusual account combinations, journals posted by senior management and consolidation journals.

There are inherent limitations in the audit procedures described above. We are less likely to become aware of instances of non-compliance with laws and regulations that are not closely related to events and transactions reflected in the financial statements. Also, the risk of not detecting a material misstatement due to fraud is higher than the risk of not detecting one resulting from error, as fraud may involve deliberate concealment by, for example, forgery or intentional misrepresentations, or through collusion.

Our audit testing might include testing complete populations of certain transactions and balances, possibly using data auditing techniques. However, it typically involves selecting a limited number of items for testing, rather than testing complete populations. We will often seek to target particular items for testing based on their size or risk characteristics. In other cases, we will use audit sampling to enable us to draw a conclusion about the population from which the sample is selected.

A further description of our responsibilities for the audit of the financial statements is located on the FRC's website at: www.frc.org.uk/auditorsresponsibilities. This description forms part of our auditors' report.

Use of this report

This report, including the opinions, has been prepared for and only for the company's members as a body in accordance with Chapter 3 of Part 16 of the Companies Act 2006 and for no other purpose. We do not, in giving these opinions, accept or assume responsibility for any other purpose or to any other person to whom this report is shown or into whose hands it may come save where expressly agreed by our prior consent in writing.

Other required reporting

Companies Act 2006 exception reporting

Under the Companies Act 2006 we are required to report to you if, in our opinion:

- we have not obtained all the information and explanations we require for our audit; or
- adequate accounting records have not been kept by the Parent Company, or returns adequate for our audit have not been received from branches not visited by us; or
- certain disclosures of directors' remuneration specified by law are not made; or
- the Parent Company financial statements and the part of the Directors' Remuneration Report to be audited are not in agreement with the accounting records and returns.

We have no exceptions to report arising from this responsibility.

Appointment

Following the recommendation of the Audit Committee, we were appointed by the members on 27 April 2017 to audit the financial statements for the year ended 31 December 2017 and subsequent financial periods. The period of total uninterrupted engagement is five years, covering the years ended 31 December 2017 to 31 December 2021.

Other required reporting

As required by the Financial Conduct Authority Disclosure Guidance and Transparency Rule 4.1.14R, these Group Financial Statements form part of the ESEF-prepared annual financial report filed on the National Storage Mechanism of the Financial Conduct Authority in accordance with the ESEF Regulatory Technical Standard (ESEF RTS). This auditors' report provides no assurance over whether the annual financial report has been prepared using the single electronic format specified in the ESEF RTS.

Richard Hughes

Richard Hughes (Senior Statutory Auditor)
for and on behalf of
PricewaterhouseCoopers LLP
Chartered Accountants and Statutory Auditors
London
10 February 2022

Consolidated Statement of Comprehensive Income

for the year ended 31 December

	Notes	2021 $m	2020 $m	2019 $m
Product Sales	1	36,541	25,890	23,565
Collaboration Revenue	1	876	727	819
Total Revenue		37,417	26,617	24,384
Cost of sales		(12,437)	(5,299)	(4,921)
Gross profit		24,980	21,318	19,463
Distribution costs		(446)	(399)	(339)
Research and development expense	2	(9,736)	(5,991)	(6,059)
Selling, general and administrative expense	2	(15,234)	(11,294)	(11,682)
Other operating income and expense	2	1,492	1,528	1,541
Operating profit		1,056	5,162	2,924
Finance income	3	43	87	172
Finance expense	3	(1,300)	(1,306)	(1,432)
Share of after tax losses in associates and joint ventures	11	(64)	(27)	(116)
(Loss)/profit before tax		(265)	3,916	1,548
Taxation	4	380	(772)	(321)
Profit for the period		115	3,144	1,227
Other comprehensive income:				
Items that will not be reclassified to profit or loss:				
Remeasurement of the defined benefit pension liability	22	626	(168)	(364)
Net (losses)/gains on equity investments measured at fair value through other comprehensive income		(187)	938	(28)
Fair value movements related to own credit risk on bonds designated as fair value through profit and loss		–	(1)	(5)
Tax on items that will not be reclassified to profit or loss	4	105	(81)	21
		544	688	(376)
Items that may be reclassified subsequently to profit or loss:				
Foreign exchange arising on consolidation	23	(483)	443	40
Foreign exchange arising on designated borrowings in net investment hedges	23	(321)	573	(252)
Fair value movements on cash flow hedges		(167)	180	(101)
Fair value movements on cash flow hedges transferred to profit and loss		208	(254)	52
Fair value movements on derivatives designated in net investment hedges	23	34	8	35
(Costs)/gains of hedging		(6)	9	(47)
Tax on items that may be reclassified subsequently to profit or loss	4	46	(39)	38
		(689)	920	(235)
Other comprehensive (loss)/income for the period, net of tax		(145)	1,608	(611)
Total comprehensive (loss)/income for the period		(30)	4,752	616
Profit attributable to:				
Owners of the Parent		112	3,196	1,335
Non-controlling interests	26	3	(52)	(108)
Total comprehensive (loss)/income attributable to:				
Owners of the Parent		(33)	4,804	723
Non-controlling interests	26	3	(52)	(107)
Basic earnings per $0.25 Ordinary Share	5	$0.08	$2.44	$1.03
Diluted earnings per $0.25 Ordinary Share	5	$0.08	$2.44	$1.03
Weighted average number of Ordinary Shares in issue (millions)	5	1,418	1,312	1,301
Diluted weighted average number of Ordinary Shares in issue (millions)	5	1,427	1,313	1,301
Dividends declared and paid in the period	25	3,882	3,668	3,579

All activities were in respect of continuing operations.

$m means millions of US dollars.

Consolidated Statement of Financial Position
at 31 December

	Notes	2021 $m	2020 $m	2019 $m
Assets				
Non-current assets				
Property, plant and equipment	7	9,183	8,251	7,688
Right-of-use assets	8	988	666	647
Goodwill	9	19,997	11,845	11,668
Intangible assets	10	42,387	20,947	20,833
Investments in associates and joint ventures	11	69	39	58
Other investments	12	1,168	1,108	1,401
Derivative financial instruments	13	102	171	61
Other receivables	14	895	720	740
Deferred tax assets	4	4,330	3,438	2,718
		79,119	47,185	45,814
Current assets				
Inventories	15	8,983	4,024	3,193
Trade and other receivables	16	9,644	7,022	5,761
Other investments	12	69	160	849
Derivative financial instruments	13	83	142	36
Intangible assets	10	105	–	–
Income tax receivable		663	364	285
Cash and cash equivalents	17	6,329	7,832	5,369
Assets held for sale	18	368	–	70
		26,244	19,544	15,563
Total assets		105,363	66,729	61,377
Liabilities				
Current liabilities				
Interest-bearing loans and borrowings	19	(1,660)	(2,194)	(1,822)
Lease liabilities	8	(233)	(192)	(188)
Trade and other payables	20	(18,938)	(15,785)	(13,987)
Derivative financial instruments	13	(79)	(33)	(36)
Provisions	21	(768)	(976)	(723)
Income tax payable		(916)	(1,127)	(1,361)
		(22,594)	(20,307)	(18,117)
Non-current liabilities				
Interest-bearing loans and borrowings	19	(28,134)	(17,505)	(15,730)
Lease liabilities	8	(754)	(489)	(487)
Derivative financial instruments	13	(45)	(2)	(18)
Deferred tax liabilities	4	(6,206)	(2,918)	(2,490)
Retirement benefit obligations	22	(2,454)	(3,202)	(2,807)
Provisions	21	(956)	(584)	(841)
Other payables	20	(4,933)	(6,084)	(6,291)
		(43,482)	(30,784)	(28,664)
Total liabilities		(66,076)	(51,091)	(46,781)
Net assets		39,287	15,638	14,596
Equity				
Capital and reserves attributable to equity holders of the Company				
Share capital	24	387	328	328
Share premium account		35,126	7,971	7,941
Capital redemption reserve		153	153	153
Merger reserve		448	448	448
Other reserves	23	1,444	1,423	1,445
Retained earnings	23	1,710	5,299	2,812
		39,268	15,622	13,127
Non-controlling interests	26	19	16	1,469
Total equity		39,287	15,638	14,596

The Financial Statements from pages 134 to 201 were approved by the Board and were signed on its behalf by

Pascal Soriot
Director
10 February 2022

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Pascal Soriot
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Aradhana Sarin
Director

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Aradhana Sarin
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Consolidated Statement of Changes in Equity

for the year ended 31 December

	Share capital $m	Share premium account $m	Capital redemption reserve $m	Merger reserve $m	Other reserves $m	Retained earnings $m	Total attributable to owners $m	Non-controlling interests $m	Total equity $m
At 1 January 2019	317	4,427	153	448	1,440	5,683	12,468	1,576	14,044
Adoption of new accounting standards[1]	–	–	–	–	–	54	54	–	54
Profit for the period	–	–	–	–	–	1,335	1,335	(108)	1,227
Other comprehensive loss[2]	–	–	–	–	–	(612)	(612)	1	(611)
Transfer to other reserves[3]	–	–	–	–	5	(5)	–	–	–
Transactions with owners									
Dividends	–	–	–	–	–	(3,579)	(3,579)	–	(3,579)
Issue of Ordinary Shares	11	3,514	–	–	–	–	3,525	–	3,525
Share-based payments charge for the period (Note 29)	–	–	–	–	–	259	259	–	259
Settlement of share plan awards	–	–	–	–	–	(323)	(323)	–	(323)
Net movement	11	3,514	–	–	5	(2,871)	659	(107)	552
At 31 December 2019	328	7,941	153	448	1,445	2,812	13,127	1,469	14,596
Profit for the period	–	–	–	–	–	3,196	3,196	(52)	3,144
Other comprehensive income[2]	–	–	–	–	–	1,608	1,608	–	1,608
Transfer to other reserves[3,4]	–	–	–	–	(22)	1,423	1,401	(1,401)	–
Transactions with owners									
Dividends	–	–	–	–	–	(3,668)	(3,668)	–	(3,668)
Issue of Ordinary Shares	–	30	–	–	–	–	30	–	30
Share-based payments charge for the period (Note 29)	–	–	–	–	–	277	277	–	277
Settlement of share plan awards	–	–	–	–	–	(349)	(349)	–	(349)
Net movement	–	30	–	–	(22)	2,487	2,495	(1,453)	1,042
At 31 December 2020	328	7,971	153	448	1,423	5,299	15,622	16	15,638
Profit for the period	–	–	–	–	–	**112**	**112**	**3**	**115**
Other comprehensive loss[2]	–	–	–	–	–	**(145)**	**(145)**	–	**(145)**
Transfer to other reserves[3]	–	–	–	–	**21**	**(21)**	–	–	–
Transactions with owners									
Dividends	–	–	–	–	–	**(3,882)**	**(3,882)**	–	**(3,882)**
Issue of Ordinary Shares	**59**	**27,155**	–	–	–	–	**27,214**	–	**27,214**
Share-based payments charge for the period (Note 29)	–	–	–	–	–	**615**	**615**	–	**615**
Settlement of share plan awards	–	–	–	–	–	**(781)**	**(781)**	–	**(781)**
Issue of replacement Alexion share awards upon acquisition (Note 27)[5]	–	–	–	–	–	**513**	**513**	–	**513**
Net movement[6]	**59**	**27,155**	–	–	**21**	**(3,589)**	**23,646**	**3**	**23,649**
At 31 December 2021	**387**	**35,126**	**153**	**448**	**1,444**	**1,710**	**39,268**	**19**	**39,287**

[1] The Group adopted IFRIC 23 'Uncertainty over Income Tax Treatments' from 1 January 2019. The cumulative effect of initially applying the interpretation was recognised as a decrease to income tax payable of $51m and to trade and other payables of $3m, and a corresponding adjustment to the opening balance of Retained earnings of $54m.

[2] Included within Other comprehensive loss of $145m (2020: income of $1,608m; 2019: loss of $611m) is a charge of $6m (2020: gain of $9m; 2019: charge of $47m), relating to Costs of hedging. Amounts charged or credited to other reserves relate to exchange adjustments arising on goodwill.

[3] The non-controlling interests reserve relating to the minority shareholders of Acerta Pharma, totalling $1,401m, was reclassified into Retained earnings in 2020 (see Note 26).

[4] Replacement share awards were issued as part of the acquisition of Alexion in 2021 (see Note 27).

[5] As part of the acquisition of Alexion in July 2021, a pre-existing non-controlling interest in Caelum Biosciences was recognised (Note 27). This was valued at $150m, the agreed exercise price for the exclusive option to acquire the remaining equity. The option was exercised on 28 September 2021 and the acquisition of Caelum Biosciences closed shortly thereafter on 5 October 2021.

Consolidated Statement of Cash Flows

for the year ended 31 December

	Notes	2021 $m	2020 $m	2019 $m
Cash flows from operating activities				
(Loss)/profit before tax		(265)	3,916	1,548
Finance income and expense	3	1,257	1,219	1,260
Share of after tax losses of associates and joint ventures	11	64	27	116
Depreciation, amortisation and impairment		6,530	3,149	3,762
Increase in trade and other receivables		(961)	(739)	(898)
Decrease/(increase) in inventories		1,577	(621)	(316)
Increase in trade and other payables and provisions		1,405	1,721	868
Gains on disposal of intangible assets	2	(513)	(1,030)	(1,243)
Gains on disposal of investment in associates and joint ventures	2	(776)	–	–
Fair value movements on contingent consideration arising from business combinations	20	14	(272)	(614)
Non-cash and other movements	17	95	(276)	378
Cash generated from operations		8,427	7,094	4,861
Interest paid		(721)	(733)	(774)
Tax paid		(1,743)	(1,562)	(1,118)
Net cash inflow from operating activities		5,963	4,799	2,969
Cash flows from investing activities				
Acquisition of subsidiaries, net of cash acquired	27	(9,263)	–	–
Payments upon vesting of employee share awards attributable to business combinations		(211)	–	–
Payment of contingent consideration from business combinations	20	(643)	(822)	(709)
Purchase of property, plant and equipment		(1,091)	(961)	(979)
Disposal of property, plant and equipment		13	106	37
Purchase of intangible assets		(1,109)	(1,645)	(1,481)
Disposal of intangible assets		587	951	2,076
Movement in profit-participation liability	2	20	40	150
Purchase of non-current asset investments		(184)	(119)	(13)
Disposal of non-current asset investments		9	1,381	18
Movement in short-term investments, fixed deposits and other investing instruments		96	745	194
Payments to associates and joint ventures	11	(92)	(8)	(74)
Disposal of investments in associates and joint ventures		776	–	–
Interest received		34	47	124
Net cash outflow from investing activities		(11,058)	(285)	(657)
Net cash (outflow)/inflow before financing activities		(5,095)	4,514	2,312
Cash flows from financing activities				
Proceeds from issue of share capital		29	30	3,525
Issue of loans and borrowings		12,929	2,968	500
Repayment of loans and borrowings		(4,759)	(1,609)	(1,500)
Dividends paid		(3,856)	(3,572)	(3,592)
Hedge contracts relating to dividend payments		(29)	(101)	4
Repayment of obligations under leases		(240)	(207)	(186)
Movement in short-term borrowings		(276)	286	(516)
Payments to acquire non-controlling interests		(149)	–	–
Net cash inflow/(outflow) from financing activities		3,649	(2,203)	(1,765)
Net (decrease)/increase in Cash and cash equivalents in the period		(1,446)	2,311	547
Cash and cash equivalents at the beginning of the period		7,546	5,223	4,671
Exchange rate effects		(62)	12	5
Cash and cash equivalents at the end of the period	17	6,038	7,546	5,223

Group Accounting Policies

Basis of accounting and preparation of financial information

The Consolidated Financial Statements have been prepared under the historical cost convention, modified to include revaluation to fair value of certain financial instruments as described below, in accordance with UK-adopted International Accounting Standards and with the requirements of the Companies Act 2006 as applicable to companies reporting under those standards. The Consolidated Financial Statements also comply fully with International Financial Reporting Standards (IFRSs) as issued by the International Accounting Standards Board (IASB) and International Accounting Standards as adopted by the European Union.

The Consolidated Financial Statements are presented in US dollars, which is the Company's functional currency.

In preparing their individual financial statements, the accounting policies of some overseas subsidiaries do not conform with IASB issued IFRSs. Therefore, where appropriate, adjustments are made in order to present the Consolidated Financial Statements on a consistent basis.

UK-adopted International Accounting Standards

On 31 December 2020, EU-adopted IFRS was brought into UK law and became UK-adopted International Accounting Standards, with future changes to IFRS being subject to endorsement by the UK Endorsement Board. The Consolidated Financial Statements transitioned to UK-adopted International Accounting Standards for financial periods beginning 1 January 2021. This change constitutes a change in accounting framework. However, there is no impact on recognition, measurement or disclosure in the period reported as a result of the change in framework.

IFRS 9, 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 31 December 2021, the Group held instruments totalling $1,439m that reference USD LIBOR but will either have matured or will have their last LIBOR fixings set before the relevant USD LIBORs cease publication on 30 June 2023. These instruments include floating rate bonds, interest rate swaps and other arrangements. 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.

Basis for preparation of Financial Statements on a going concern basis

The Group has considerable financial resources available. As at 31 December 2021, the Group has $11.2bn in financial resources (cash and cash equivalent balances of $6.3bn and undrawn committed bank facilities of $4.9bn available until April 2025 with only $1.9bn of borrowings due within one year). All facilities contain no financial covenants and were undrawn at 31 December 2021.

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 adversely affect 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, they continue to adopt the going concern basis in preparing the Annual Report and Financial Statements.

Estimates and judgements

The preparation of the Financial Statements in conformity with generally accepted accounting principles requires management to make estimates and judgements that affect the reported amounts of assets and liabilities at the date of the Financial Statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

The accounting policy descriptions set out the areas where judgements and estimates need exercising, the most significant of which include the following Key Judgements (KJ) and Significant Estimates (SE):

- revenue recognition – see Revenue Accounting Policy on page 139 (KJ) and Note 1 on page 145 (SE)
- expensing of internal development expenses – see Research and Development Policy on page 140 (KJ)
- impairment reviews of Intangible assets – see Note 10 on page 156 (SE)
- useful economic life of Intangible assets – see Research and Development Policy on page 140 (KJ) and Note 10 on page 156 (SE)
- business combinations and Goodwill (and Contingent consideration arising from business combinations) – see Business Combinations and Goodwill Policy on page 142 (KJ), Note 10 on page 156 (KJ), Note 20 on page 166 (SE) and Note 27 on page 178 (SE)
- litigation liabilities – see Litigation and Environmental Liabilities within Note 30 on page 189 (KJ)
- operating segments – see Note 6 on page 152 (KJ)
- employee benefits – see Note 22 on page 168 (SE)
- taxation – see Taxation Policy on page 141 (KJ) and Note 30 on page 189 (KJ) (SE).

AstraZeneca has assessed the impact of the uncertainty presented by the COVID-19 pandemic on the Financial Statements, specifically considering the impact on key judgements and significant estimates along with several other areas of increased risk.

A detailed assessment has been performed, focusing 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 and chargebacks 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.

No material accounting impacts relating to the areas assessed above were recognised in the year.

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

The Group has assessed the impact of climate risk on its financial reporting. The impact assessment was primarily focused on the valuation and useful lives of intangible assets and the identification and valuation of provisions and contingent liabilities, as these are judged to be the key areas that could be impacted by climate risks. No material accounting impacts or changes to judgements or other required disclosures were noted.

Financial risk management policies are detailed in Note 28 to the Financial Statements from page 180.

AstraZeneca's management considers the following to be the most important accounting policies in the context of the Group's operations.

Revenue

Revenue comprises Product Sales and Collaboration Revenue.

Product Sales are revenues arising from contracts with customers. Collaboration Revenue arises from other contracts, however, the recognition and measurement principles of IFRS 15 'Revenue from Contracts with Customers' are applied as set out below.

Revenue excludes inter-company revenues and value-added taxes.

Product Sales

Product Sales represent net invoice value less estimated rebates, returns and chargebacks, which are considered to be variable consideration and include significant estimates. Sales are recognised when the control of the goods has been transferred to a third party. This is usually when title passes to the customer, either on shipment or on receipt of goods by the customer, depending on local trading terms. In markets where returns are significant, estimates of returns are accounted for at the point revenue is recognised. Revenue is not recognised in full until it is highly probable that a significant reversal in the amount of cumulative revenue recognised will not occur.

Rebates are amounts payable or credited to a customer, usually based on the quantity or value of Product Sales to the customer for specific products in a certain period. Product sales rebates, which relate to Product Sales that occur over a period of time, are normally issued retrospectively.

At the time Product Sales are invoiced, rebates and deductions that the Group expects to pay, are estimated. These rebates typically arise from sales contracts with government payers, third-party managed care organisations, hospitals, long-term care facilities, group purchasing organisations and various state programmes.

For the markets where returns are significant, we estimate the quantity and value of goods which may ultimately be returned at the point of sale. Our returns accruals are based on actual experience over the preceding 12 months for established products together with market-related information such as estimated stock levels at wholesalers and competitor activity which we receive via third-party information services. For newly launched products, we use rates based on our experience with similar products or a predetermined percentage.

When a product faces generic competition, particular attention is given to the possible levels of returns and, in cases where the circumstances are such that the level of Product Sales are considered highly probable to reverse, revenues are only recognised when the right of return expires, which is generally on ultimate prescription of the product to patients.

The methodology and assumptions used to estimate rebates and returns are monitored and adjusted regularly in the light of contractual and legal obligations, historical trends, past experience and projected market conditions. Once the uncertainty associated with returns is resolved, revenue is adjusted accordingly.

Under certain collaboration agreements which include a profit sharing mechanism, our recognition of Product Sales depends on which party acts as principal in sales to the end customer. In the cases where AstraZeneca acts as principal, we record 100% of sales to the end customer.

Contracts relating to the supply of *Vaxzevria* during the COVID-19 pandemic include conditions whereby payments are receivable from customers in advance of the delivery of product. Such amounts are held on the balance sheet as contract liabilities until the related revenue is recognised, generally upon product delivery. Certain of these contracts contain further provisions that restrict the use of inventory manufactured in specified supply chains to specified customers, resulting in an enforceable right to payment as the activities are performed. Under IFRS 15, such contracts require revenue to be recognised over time using an appropriate and reasonably measurable method to measure progress. Revenue is recognised on these contracts based on the proportion of product delivered compared to the total contracted volumes.

Collaboration Revenue

Collaboration Revenue includes income from collaborative arrangements where either the Group has sold certain rights associated with those products, but retains a significant ongoing economic interest or has acquired a significant interest from a third party. Significant interest can include ongoing supply of finished goods, participation in sharing of profit arrangements or direct interest from sales of medicines.

These arrangements may include development arrangements, commercialisation arrangements and collaborations. Income may take the form of upfront fees, milestones, profit sharing and royalties and includes sharing of profit arising from sales made as principal by a collaboration partner.

KJ Timing of recognition of clinical and regulatory milestones is considered to be a key judgement. There can be significant uncertainty over whether it is highly probable that there would not be a significant reversal of revenue in respect of specific milestones if these are recognised before they are triggered due to them being subject to the actions of third parties. In general, where the triggering of a milestone is subject to the decisions of third parties (e.g. the acceptance or approval of a filing by a regulatory authority), the Group does not consider that the threshold for recognition is met until that decision is made.

Where Collaboration Revenue arises from the licensing of the Group's own intellectual property, the licences we grant are typically rights to use intellectual property which do not change during the period of the licence and therefore related non-conditional revenue is recognised at the point the license is granted and variable consideration as soon as recognition criteria are met. Those licences are generally unique and therefore when there are other performance obligations in the contract, the basis of allocation of the consideration makes use of the residual approach as permitted by IFRS 15.

These arrangements typically involve the receipt of an upfront payment, which the contract attributes to the license of the intangible assets, and ongoing receipts, which the contract attributes to the sale of the product we manufacture. In cases where the transaction has two or more components, we account for the delivered item (for example, the transfer of title to the intangible asset) as a separate unit of accounting and record revenue on delivery of that component, provided that we can make a reasonable estimate of the fair value of the undelivered component.

Where non-contingent amounts are payable over one year from the effective date of a contract, an assessment is made as to whether a significant financing component exists, and if so, the fair value of this component is deferred and recognised over the period to the expected date of receipt.

Where control of a right to use an intangible asset passes at the outset of an arrangement, revenue is recognised at the point in time control is transferred. Where the substance of an arrangement is that of a right to access rights attributable to an intangible asset, revenue is recognised over time, normally on a straight-line basis over the life of the contract.

Where the fair market value of the undelivered component (for example, a manufacturing agreement) exceeds the contracted price for that component, we defer an appropriate element of the upfront consideration and amortise this over the performance period. However, where the fair market value of the

undelivered component is equal to or lower than the contracted price for that component, we treat the whole of the upfront amount as being attributable to the delivered intangible assets and recognise that part of the revenue upon delivery. No element of the contracted revenue related to the undelivered component is ordinarily allocated to the sale of the intangible asset. This is because the contracted revenue relating to the undelivered component is contingent on future events (such as sales) and cannot be recognised until either receipt of the amount is highly probable or where the consideration is received for a licence of intellectual property, on the occurrence of the related sales.

Where the Group provides ongoing services, revenue in respect of this element is recognised over the duration of those services. Where the arrangement meets the definition of a licence agreement, sales milestones and sales royalties are recognised when achieved by applying the royalty exemption under IFRS 15. All other milestones and sales royalties are recognised when considered it is highly probable there will not be a significant reversal of cumulative income. The determination requires estimates to be made in relation to future Product Sales.

Where Collaboration Revenue is recorded and there is a related Intangible asset that is licensed as part of the arrangement, an appropriate amount of that Intangible asset is charged to Cost of sales based on an allocation of cost or value to the rights that have been licenced.

Cost of sales

Cost of sales are recognised as the associated revenue is recognised. Cost of sales include manufacturing costs, royalties payable on revenues recognised, movements in provisions for inventories, inventory write-offs and impairment charges in relation to manufacturing assets. Cost of sales also includes co-collaborator sharing of profit arising from collaborations, and foreign exchange gains and losses arising from business trading activities.

Research and development

Research expenditure is charged to profit and loss in the year in which it is incurred.

KJ Internal development expenditure is capitalised only if it meets the recognition criteria of IAS 38 'Intangible Assets'. This is considered a key judgement. Where regulatory and other uncertainties are such that the criteria are not met, the expenditure is charged to profit and loss and this is almost invariably the case prior to approval of the drug by the relevant regulatory authority. Where, however, recognition criteria are met, Intangible assets are capitalised and amortised on a straight-line basis over their useful economic lives from product launch. At 31 December 2021, no amounts have met the recognition criteria.

Payments to in-license products and compounds from third parties for new research and development projects (in process research and development) generally take the form of upfront payments, milestones and royalty payments. Where payments made to third parties represent consideration for future research and development activities, an evaluation is made as to the nature of the payments. Such payments are expensed if they represent compensation for sub-contracted research and development services not resulting in a transfer of intellectual property. By contrast, payments are capitalised if they represent compensation for the transfer of identifiable intellectual property developed at the risk of the third party. Development milestone payments relating to identifiable intellectual property are capitalised as the milestone is triggered. Any upfront or milestone payments for research activities where there is no associated identifiable intellectual property are expensed. Assets capitalised are amortised, on a straight-line basis, over their useful economic lives from product launch.

KJ The determination of useful economic life is considered to be a key judgement. On product launch, the Group makes a judgement as to the expected useful economic life with reference to the expiry of associated patents for the product, expectation around the competitive environment specific to the product and our detailed long-term risk-adjusted sales projections compiled annually across the Group and approved by the Board.

The useful economic life can extend beyond patent expiry dependent upon the nature of the product and the complexity of the development and manufacturing process. Significant sales can often be achieved post patent expiration.

Intangible assets

Intangible assets are stated at cost less amortisation and impairments. Intangible assets relating to products in development are subject to impairment testing annually. All Intangible assets are tested for impairment when there are indications that the carrying value may not be recoverable. The determination of the recoverable amounts include key estimates which are highly sensitive to, and depend upon, key assumptions as detailed in Note 10 to the Financial Statements from page 156.

Impairment reviews have been carried out on all Intangible assets that are in development (and not being amortised), all major intangible assets acquired during the year and all other intangible assets that have had indications of impairment during the year. Recoverable amount is determined as the higher of value in use or fair value less costs to sell using a discounted cash flow calculation, where the products' expected cash flows are risk-adjusted over their estimated remaining useful economic life. The determination of the recoverable amounts include significant estimates which are highly sensitive and depend upon key assumptions as detailed in Note 10 to the Financial Statements from page 156.
Sales forecasts and specific allocated costs (which have both been subject to appropriate senior management review and approval) are risk-adjusted and discounted using appropriate rates based on our post-tax weighted average cost of capital or for fair value less costs to sell, a required rate of return for a market participant. Our weighted average cost of capital reflects factors such as our capital structure and our costs of debt and equity.

Any impairment losses are recognised immediately in profit. Intangible assets relating to products which fail during development (or for which development ceases for other reasons) are also tested for impairment and are written down to their recoverable amount (which is usually nil).

If, subsequent to an impairment loss being recognised, development restarts or other facts and circumstances change indicating that the impairment is less or no longer exists, the value of the asset is re-estimated and its carrying value is increased to the recoverable amount, but not exceeding the original value, by recognising an impairment reversal in Operating profit.

Government grants

Government grants are recognised in the Consolidated Statement of Comprehensive Income so as to match with the related expenses that they are intended to compensate. Where grants are received in advance of the related expenses, they are initially recognised in the Consolidated Statement of Financial Position under Trade and other payables as deferred income and released to net off against the related expenditure when incurred.

Each contract is assessed to determine whether there are both grant elements and supply of product which need to be separated. In each case, the contracts set out the specified terms for the supply of the product and the provisions for funding for certain costs, primarily research and development associated with the IP. It is considered whether there are any conditions for the funding to be refunded. The consideration in the contract is allocated between the grant and supply elements. The standalone selling price for the supply of products is determined by reference to observed prices with other customers. The amount allocated as a government grant is determined by reference to the specific agreed costs and activities identified in the contract as not directly attributable to the supply of product. Government grants are recorded as an offset to the relevant expense in the Consolidated Statement of Comprehensive Income and are capped to match the relevant costs incurred.

Joint arrangements and associates

The Group has arrangements over which it has joint control and which qualify as joint operations or joint ventures under IFRS 11 'Joint Arrangements'. For joint operations, the Group recognises its share of revenue that it earns from the joint operations and its share of expenses incurred. The Group also recognises the assets associated with the joint operations that it controls and the liabilities it incurs under the joint arrangement. For joint ventures and associates, the Group recognises its interest in the joint venture or associate as an investment and uses the equity method of accounting.

Employee benefits

The Group accounts for pensions and other employee benefits (principally healthcare) under IAS 19 'Employee Benefits' and recognises all actuarial gains and losses immediately through Other comprehensive income. In respect of defined benefit plans, obligations are measured at discounted present value while plan assets are measured at fair value. Given the extent of the assumptions used to determine these values, these are considered to be significant estimates. The operating and financing costs of such plans are recognised separately in profit, current service costs are spread systematically over the lives of employees and financing costs are recognised in full in the periods in which they arise. Remeasurements of the net defined benefit pension liability, including actuarial gains and losses, are recognised immediately in Other comprehensive income.

Where the calculation results in a surplus to the Group, the recognised asset is limited to the present value of any available future refunds from the plan or reductions in future contributions to the plan. Payments to defined contribution plans are recognised in profit as they fall due.

Taxation

The current tax payable is based on taxable profit for the year. Taxable profit differs from reported profit because taxable profit excludes items that are either never taxable or tax deductible or items that are taxable or tax deductible in a different period. The Group's current tax assets and liabilities are calculated using tax rates that have been enacted or substantively enacted by the reporting date.

KJ Deferred tax is provided using the balance sheet liability method, providing for temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. Deferred tax assets are recognised to the extent that it is probable that future taxable profit will be available against which the asset can be utilised. This requires judgements to be made in respect of the availability of future taxable income.

No deferred tax asset or liability is recognised in respect of temporary differences associated with investments in subsidiaries and branches where the Group is able to control the timing of reversal of the temporary differences and it is probable that the temporary differences will not reverse in the foreseeable future.

The Group's Deferred tax assets and liabilities are calculated using tax rates that are expected to apply in the period when the liability is settled or the asset realised based on tax rates that have been enacted or substantively enacted by the reporting date.

Accruals for tax contingencies require management to make judgements of potential exposures in relation to tax audit issues. Tax benefits are not recognised unless the tax positions will probably be accepted by the tax authorities. This is based upon management's interpretation of applicable laws and regulations and the expectation of how the tax authority will resolve the matter. Once considered probable of not being accepted, management reviews each material tax benefit and reflects the effect of the uncertainty in determining the related taxable result.

Accruals for tax contingencies are measured using either the most likely amount or the expected value amount depending on which method the entity expects to better predict the resolution of the uncertainty.

Further details of the estimates and assumptions made in determining our recorded liability for transfer pricing contingencies and other tax contingencies are included in Note 30 to the Financial Statements from page 189.

Share-based payments

All plans have been classified as equity settled after assessment. The grant date fair value of employee share plan awards is calculated using a Monte Carlo model. In accordance with IFRS 2 'Share-based Payment', the resulting cost is recognised in profit over the vesting period of the awards, being the period in which the services are received. The value of the charge is adjusted to reflect expected and actual levels of awards vesting, except where the failure to vest is as a result of not meeting a market condition. Cancellations of equity instruments are treated as an acceleration of the vesting period and any outstanding charge is recognised in profit immediately.

Cash outflows relating to the vesting of share plans for our employees are recognised within operating activities, as they relate to employee remuneration. The cash flows relating to replacement awards issued to employees as part of the Alexion acquisition (see Note 27 from page 178) are classified within investing activities, as they are part of the aggregate cash flows arising from obtaining control of the subsidiary.

Property, plant and equipment

The Group's policy is to write off the difference between the cost of each item of Property, plant and equipment and its residual value over its estimated useful life on a straight-line basis. Assets under construction are not depreciated.

Reviews are made annually of the estimated remaining lives and residual values of individual productive assets, taking account of commercial and technological obsolescence as well as normal wear and tear. It is impractical to calculate average asset lives exactly. However, the total lives range from approximately 10 to 50 years for buildings, and three to 15 years for plant and equipment. All items of Property, plant and equipment are tested for impairment when there are indications that the carrying value may not be recoverable. Any impairment losses are recognised immediately in operating profit.

Borrowing costs

The Group has no borrowing costs with respect to the acquisition or construction of qualifying assets. All other borrowing costs are recognised in profit as incurred and in accordance with the effective interest rate method.

Leases

The Group's lease arrangements are principally for property, most notably a portfolio of office premises and employee accommodation, and for a global car fleet, utilised primarily by our sales and marketing teams.

The lease liability and corresponding right-of-use asset arising from a lease are initially measured on a present value basis. Lease liabilities include the net present value of the following lease payments:

- fixed payments, less any lease incentives receivable
- variable lease payments that depend on an index or a rate, initially measured using the index or rate as at the commencement date
- the exercise price of a purchase option if the Group is reasonably certain to exercise that option
- payments of penalties for terminating the lease, if the lease term reflects the Group exercising that option, and
- amounts expected to be payable by the Group under residual value guarantees.

Right-of-use assets are measured at cost comprising the following:

- the amount of the initial measurement of lease liability
- any lease payments made at or before the commencement date less any lease incentives received
- any initial direct costs, and
- restoration costs.

Group Accounting Policies
continued

Judgements made in calculating the lease liability include assessing whether arrangements contain a lease and determining the lease term. Lease terms are negotiated on an individual basis and contain a wide range of different terms and conditions. Property leases will often include an early termination or extension option to the lease term. Fleet management policies vary by jurisdiction and may include renewal of a lease until a measurement threshold, such as mileage, is reached. Extension and termination options have been considered when determining the lease term, along with all facts and circumstances that may create an economic incentive to exercise an extension option, or not exercise a termination option. Extension periods (or periods after termination options) are only included in the lease term if the lease is reasonably certain to be extended (or not terminated).

The lease payments are discounted using incremental borrowing rates, as in the majority of leases held by the Group the interest rate implicit in the lease is not readily identifiable. Calculating the discount rate is an estimate made in calculating the lease liability. This rate is the rate that the Group would have to pay to borrow the funds necessary to obtain an asset of similar value to the right-of-use asset in a similar economic environment with similar terms, security and conditions. To determine the incremental borrowing rate, the Group uses a risk-free interest rate adjusted for credit risk, adjusting for terms specific to the lease including term, country and currency.

The Group is exposed to potential future increases in variable lease payments that are based on an index or rate, which are initially measured as at the commencement date, with any future changes in the index or rate excluded from the lease liability until they take effect. When adjustments to lease payments based on an index or rate take effect, the lease liability is reassessed and adjusted against the right-of-use asset.

Lease payments are allocated between principal and finance cost. The finance cost is charged to the Consolidated Statement of Comprehensive Income over the lease period so as to produce a constant periodic rate of interest on the remaining balance of the liability for each period.

Payments associated with short-term leases of Property, plant and equipment and all leases of low-value assets are recognised on a straight-line basis as an expense in the Consolidated Statement of Comprehensive Income. Short-term leases are leases with a lease term of 12 months or less. Low-value leases are those where the underlying asset value, when new, is $5,000 or less and includes IT equipment and small items of office furniture.

Contracts may contain both lease and non-lease components. The Group allocates the consideration in the contract to the lease and non-lease components based on their relative standalone prices.

Right-of-use assets are generally depreciated over the shorter of the asset's useful life and the lease term on a straight-line basis. If the Group is reasonably certain to exercise a purchase option, the right-of-use asset is depreciated over the underlying asset's useful life. It is impractical to calculate average asset lives exactly. However, the total lives range from approximately 10 to 50 years for buildings, and three to 15 years for motor vehicles and other assets.

There are no material lease agreements under which the Group is a lessor.

Business combinations and goodwill

In assessing whether an acquired set of assets and activities is a business or an asset, management will first elect whether to apply an optional concentration test to simplify the assessment. Where the concentration test is applied, the acquisition will be treated as the acquisition of an asset if substantially all of the fair value of the gross assets acquired (excluding cash and cash equivalents, deferred tax assets, and related goodwill) is concentrated in a single asset or group of similar identifiable assets.

Where the concentration test is not applied, or is not met, a further assessment of whether the acquired set of assets and activities is a business will be performed.

KJ The determination of whether an acquired set of assets and activities is a business or an asset can be judgemental, particularly if the target is not producing outputs. Management uses a number of factors to make this determination, which are primarily focused on whether the acquired set of assets and activities include substantive processes that mean the set is capable of being managed for the purpose of providing a return. Key determining factors include the stage of development of any assets acquired, the readiness and ability of the acquired set to produce outputs and the presence of key experienced employees capable of conducting activities required to develop or manufacture the assets. Typically, the specialised nature of many pharmaceutical assets and processes is such that until assets are substantively ready for production and promotion, there are not the required processes for a set of assets and activities to meet the definition of a business in IFRS 3.

On the acquisition of a business, fair values are attributed to the identifiable assets and liabilities. Attributing fair values is a key judgement; refer to Note 27 to the Financial Statements on page 178 for additional details of the 2021 acquisition. Contingent liabilities are also recorded at fair value unless the fair value cannot be measured reliably, in which case the value is subsumed into goodwill. Where fair values of acquired contingent liabilities cannot be measured reliably, the assumed contingent liability is not recognised but is disclosed in the same manner as other contingent liabilities. Where the Group fully acquires, through a business combination, assets that were previously held in joint operations, the Group has elected not to uplift the book value of the existing interest in the asset held in the joint operation to fair value at the date full control is taken.

Where not all of the equity of a subsidiary is acquired, the non-controlling interest is recognised either at fair value or at the non-controlling interest's proportionate share of the net assets of the subsidiary, on a case-by-case basis. Put options over non-controlling interests are recognised as a financial liability, with a corresponding entry in either Retained earnings or against non-controlling interest reserves on a case-by-case basis.

The timing and amount of future contingent elements of consideration is considered a significant estimate; see Note 20 from page 166. Contingent consideration, which may include development and launch milestones, revenue threshold milestones and revenue-based royalties, is fair valued at the date of acquisition using decision-tree analysis with key inputs including probability of success, consideration of potential delays and revenue projections based on the Group's internal forecasts. Unsettled amounts of consideration are held at fair value within payables with changes in fair value recognised immediately in profit.

Goodwill is the difference between the fair value of the consideration and the fair value of net assets acquired.

Goodwill arising on acquisitions is capitalised and subject to an impairment review, both annually and when there is an indication that the carrying value may not be recoverable.

The Group's policy up to and including 1997 was to eliminate Goodwill arising upon acquisitions against reserves. Under IFRS 1 'First-time Adoption of International Financial Reporting Standards' and IFRS 3 'Business Combinations', such Goodwill will remain eliminated against reserves.

Subsidiaries
A subsidiary is an entity controlled, directly or indirectly, by AstraZeneca PLC. Control is regarded as the exposure or rights to the variable returns of the entity when combined with the power to affect those returns. Control is normally evidenced by holding more than 50% of the share capital of the company, however other agreements may be in place that result in control where they give AstraZeneca finance decision-making authority over the relevant activities of the company.

The financial results of subsidiaries are consolidated from the date control is obtained until the date that control ceases.

Inventories
Inventories are stated at the lower of cost and net realisable value. The first in, first out or an average method of valuation is used. For finished goods and work in progress, cost includes directly attributable costs and certain overhead expenses (including depreciation). Selling expenses and certain other overhead expenses (principally central administration costs) are excluded. Net realisable value is determined as estimated selling price less all estimated costs of completion and costs to be incurred in selling and distribution.

Write-downs of inventory occur in the general course of business and are recognised in Cost of sales for launched or approved products and in Research and development expense for products in development.

Assets held for sale
Non-current assets are classified as Assets held for sale when their carrying amount is to be recovered principally through a sale transaction and a sale is considered highly probable. A sale is usually considered highly probable only when the appropriate level of management has committed to the sale.

Assets held for sale are stated at the lower of carrying amount and fair value less costs to sell. Where there is a partial transfer of a non-current asset to held for sale, an allocation of value is made between the current and non-current portions of the asset based on the relative value of the two portions, unless there is a methodology that better reflects the asset to be disposed of.

Assets held for sale are not depreciated or amortised.

Trade and other receivables
Financial assets included in Trade and other receivables are recognised initially at fair value. The Group holds the Trade receivables with the objective to collect the contractual cash flows and therefore measures them subsequently at amortised cost using the effective interest rate method, less any impairment losses.

Trade receivables that are subject to debt factoring arrangements are derecognised if they meet the conditions for derecognition detailed in IFRS 9 'Financial Instruments'.

Trade and other payables
Financial liabilities included in Trade and other payables are recognised initially at fair value. Subsequent to initial recognition they are measured at amortised cost using the effective interest rate method. Contingent consideration payables are held at fair value within Level 3 of the fair value hierarchy as defined in Note 12 on page 160 of the Financial Statements.

Financial instruments
The Group's financial instruments include Lease liabilities, Trade and other receivables and payables, liabilities for contingent consideration and put options under business combinations, and rights and obligations under employee benefit plans which are dealt with in specific accounting policies.

The Group's other financial instruments include:

- Cash and cash equivalents
- Fixed deposits
- Other investments
- Bank and other borrowings
- Derivatives.

Cash and cash equivalents
Cash and cash equivalents comprise cash in hand, current balances with banks and similar institutions, and highly liquid investments with maturities of three months or less when acquired. They are readily convertible into known amounts of cash and are held at amortised cost under the hold to collect classification, where they meet the hold to collect 'solely payments of principal and interest' test criteria under IFRS 9. Those not meeting these criteria are held at fair value through profit and loss. Cash and cash equivalents in the Consolidated Statement of Cash Flows include unsecured bank overdrafts at the balance sheet date where balances often fluctuate between a cash and overdraft position.

Fixed deposits
Fixed deposits, principally comprising funds held with banks and other financial institutions, are initially measured at fair value, plus direct transaction costs, and are subsequently measured at amortised cost using the effective interest rate method at each reporting date. Changes in carrying value are recognised in the Consolidated Statement of Comprehensive Income.

Other investments
Investments are classified as fair value through profit or loss (FVPL), unless the Group makes an irrevocable election at initial recognition for certain non-current equity investments to present changes in Other comprehensive income (FVOCI). If this election is made, there is no subsequent reclassification of fair value gains and losses to profit and loss following the derecognition of the investment.

Bank and other borrowings
The Group uses derivatives, principally interest rate swaps, to hedge the interest rate exposure inherent in a portion of its fixed interest rate debt. In such cases the Group will either designate the debt as fair value through profit and loss when certain criteria are met or as the hedged item under a fair value hedge.

If the debt instrument is designated as fair value through profit or loss, the debt is initially measured at fair value (with direct transaction costs being included in profit as an expense) and is remeasured to fair value at each reporting date with changes in carrying value being recognised in profit (along with changes in the fair value of the related derivative), with the exception of changes in the fair value of the debt instrument relating to own credit risk which are recorded in Other comprehensive income in accordance with IFRS 9. Such a designation has been made where this significantly reduces an accounting mismatch which would result from recognising gains and losses on different bases.

If the debt is designated as the hedged item under a fair value hedge, the debt is initially measured at fair value (with direct transaction costs being amortised over the life of the debt) and is remeasured for fair value changes in respect of the hedged risk at each reporting date with changes in carrying value being recognised in profit (along with changes in the fair value of the related derivative).

If the debt is designated in a cash flow hedge, the debt is measured at amortised cost (with gains or losses taken to profit and direct transaction costs being amortised over the life of the debt). The related derivative is remeasured for fair value changes at each reporting date with the portion of the gain or loss on the derivative that is determined to be an effective hedge recognised in Other comprehensive income. The amounts that have been recognised in Other comprehensive income are reclassified to profit in the same period that the hedged forecast cash flows affect profit. The reclassification adjustment is included in Finance expense in the Consolidated Statement of Comprehensive Income.

Other interest-bearing loans are initially measured at fair value (with direct transaction costs being amortised over the life of the loan) and are subsequently measured at amortised cost using the effective interest rate method at each reporting date. Changes in carrying value are recognised in the Consolidated Statement of Comprehensive Income.

Group Accounting Policies
continued

Derivatives
Derivatives are initially measured at fair value (with direct transaction costs being included in profit as an expense) and are subsequently remeasured to fair value at each reporting date. Changes in carrying value are recognised in the Consolidated Statement of Comprehensive Income.

Foreign currencies
Foreign currency transactions, being transactions denominated in a currency other than an individual Group entity's functional currency, are translated into the relevant functional currencies of individual Group entities at average rates for the relevant monthly accounting periods, which approximate to actual rates.

Monetary assets and liabilities arising from foreign currency transactions are retranslated at exchange rates prevailing at the reporting date. Exchange gains and losses on loans and on short-term foreign currency borrowings and deposits are included within Finance expense. Exchange differences on all other foreign currency transactions are recognised in Operating profit in the individual Group entity's accounting records.

Non-monetary items arising from foreign currency transactions are not retranslated in the individual Group entity's accounting records.

In the Consolidated Financial Statements, income and expense items for Group entities with a functional currency other than US dollars are translated into US dollars at average exchange rates, which approximate to actual rates, for the relevant accounting periods. Assets and liabilities are translated at the US dollar exchange rates prevailing at the reporting date. Exchange differences arising on consolidation are recognised in Other comprehensive income.

If certain criteria are met, non-US dollar denominated loans or derivatives are designated as net investment hedges of foreign operations. Exchange differences arising on retranslation of net investments, and of foreign currency loans which are designated in an effective net investment hedge relationship, are recognised in Other comprehensive income in the Consolidated Financial Statements. Foreign exchange derivatives hedging net investments in foreign operations are carried at fair value. Effective fair value movements are recognised in Other comprehensive income, with any ineffectiveness taken to profit. Gains and losses accumulated in the translation reserve will be recycled to profit and loss when the foreign operation is sold.

Litigation and environmental liabilities
AstraZeneca is involved in legal disputes, the settlement of which may involve cost to the Group. Provision is made where an adverse outcome is probable and associated costs, including related legal costs, can be estimated reliably. In other cases, appropriate disclosures are included. Determining the timing of recognition of when an adverse outcome is probable is considered a key judgement, refer to Note 30 to the Financial Statements on page 189.

Where it is considered that the Group is more likely than not to prevail, or in the rare circumstances where the amount of the legal liability cannot be estimated reliably, legal costs involved in defending the claim are charged to the Consolidated Statement of Comprehensive Income as they are incurred.

Where it is considered that the Group has a valid contract which provides the right to reimbursement (from insurance or otherwise) of legal costs and/or all or part of any loss incurred or for which a provision has been established, the best estimate of the amount expected to be received is recognised as an asset only when it is virtually certain.

AstraZeneca is exposed to environmental liabilities relating to its past operations, principally in respect of soil and groundwater remediation costs. Provisions for these costs are made when there is a present obligation and where it is probable that expenditure on remedial work will be required and a reliable estimate can be made of the cost. Provisions are discounted at the relevant risk free rate where the effect is material.

Impairment
The carrying values of non-financial assets, other than Inventories and Deferred tax assets, are reviewed at least annually to determine whether there is any indication of impairment. For Goodwill, Intangible assets under development and for any other assets where such indication exists, the asset's recoverable amount is estimated based on the greater of its value in use and its fair value less cost to sell. In assessing the recoverable amount, the estimated future cash flows, adjusted for the risks specific to each asset, are discounted to their present value using a discount rate that reflects current market assessments of the time value of money, the general risks affecting the pharmaceutical industry and other risks specific to each asset. For the purpose of impairment testing, assets are grouped together into the smallest group of assets that generates cash inflows from continuing use that are largely independent of the cash flows of other assets. Impairment losses are recognised immediately in the Consolidated Statement of Comprehensive Income.

International accounting transition
On transition to using adopted IFRSs in the year ended 31 December 2005, the Group took advantage of several optional exemptions available in IFRS 1 'First-time Adoption of International Financial Reporting Standards'. The major impacts which are of continuing importance are detailed below:

- Business combinations – IFRS 3 'Business Combinations' has been applied from 1 January 2003, the date of transition, rather than being applied fully retrospectively. As a result, the combination of Astra and Zeneca is still accounted for as a merger, rather than through purchase accounting. If purchase accounting had been adopted, Zeneca would have been deemed to have acquired Astra.
- Cumulative exchange differences – the Group chose to set the cumulative exchange difference reserve at 1 January 2003 to nil.

Applicable accounting standards and interpretations issued but not yet adopted
At the date of authorisation of these financial statements, certain amendments were in issue relating to the following standards and interpretations but not yet adopted by the Group:

- amendments to IAS 12 'Income Taxes', IAS 8 'Accounting Policies, Changes in Accounting Estimates and Errors', IAS 1 'Presentation of Financial Statements' and IFRS Practice Statement 2 'Making materiality judgements', effective for periods beginning on or after 1 January 2023 – not endorsed by the UK Endorsement Board (UKEB);
- amendments to IAS 37 'Provisions, Contingent Liabilities and Contingent Assets', IAS 16 'Property, Plant and Equipment' and IFRS 3 'Business Combinations', effective for periods beginning on or after 1 January 2022 – not endorsed by the UKEB;
- amendments to IAS 1 'Presentation of Financial Statements', effective for periods beginning on or after 1 January 2024 – not endorsed by the UKEB; and
- amendments to IFRS 16 'Leases', effective for periods beginning on or after 1 April 2021 – endorsed by the UKEB on 12 May 2021.

These amendments and interpretations are not expected to have a significant impact on the Group's net results.

1 Revenue

Product Sales

	2021					2020					2019				
	Emerging Markets $m	US $m	Europe $m	Rest of World $m	Total $m	Emerging Markets $m	US $m	Europe $m	Rest of World $m	Total $m	Emerging Markets $m	US $m	Europe $m	Rest of World $m	Total $m
Oncology:															
Tagrisso	1,336	1,780	986	913	5,015	1,208	1,566	748	806	4,328	762	1,268	474	685	3,189
Imfinzi	277	1,245	485	405	2,412	158	1,185	370	329	2,042	30	1,041	179	219	1,469
Lynparza	384	1,087	618	259	2,348	264	876	435	201	1,776	133	626	287	152	1,198
Calquence	20	1,089	111	18	1,238	6	511	2	3	522	2	162	–	–	164
Koselugo	1	104	3	–	108	–	38	–	–	38	–	–	–	–	–
Enhertu	12	–	4	1	17	–	–	–	–	–	–	–	–	–	–
Orpathys	16	–	–	–	16	–	–	–	–	–	–	–	–	–	–
Zoladex	619	13	147	169	948	561	5	140	182	888	492	7	135	179	813
Faslodex	167	30	113	121	431	180	55	221	124	580	198	328	229	137	892
Iressa	151	11	5	16	183	221	14	12	21	268	286	17	70	50	423
Casodex	105	–	3	35	143	133	–	3	36	172	127	–	16	57	200
Arimidex	106	–	4	29	139	147	–	3	35	185	152	–	28	45	225
Others	29	–	5	16	50	28	–	4	19	51	29	–	5	60	94
	3,223	5,359	2,484	1,982	13,048	2,906	4,250	1,938	1,756	10,850	2,211	3,449	1,423	1,584	8,667
Cardiovascular, Renal & Metabolism:															
Farxiga	1,195	732	810	263	3,000	686	569	507	197	1,959	471	537	373	162	1,543
Brilinta	328	735	346	63	1,472	461	732	342	58	1,593	462	710	351	58	1,581
Bydureon	3	321	55	6	385	4	382	53	9	448	11	459	66	13	549
Onglyza	179	88	61	32	360	201	166	58	45	470	176	230	70	51	527
Byetta	12	26	11	6	55	8	37	14	9	68	12	68	19	11	110
Other Diabetes	18	22	17	2	59	7	25	13	2	47	1	40	9	2	52
Lokelma	3	115	13	44	175	5	57	4	10	76	–	13	1	–	14
Roxadustat	174	–	–	–	174	–	–	–	–	–	–	–	–	–	–
Crestor	775	80	52	189	1,096	748	92	129	211	1,180	806	104	148	220	1,278
Seloken/Toprol-XL	928	1	11	11	951	782	13	16	10	821	686	37	25	12	760
Atacand	28	4	65	–	97	175	10	35	23	243	160	12	30	19	221
Others	137	–	53	6	196	126	–	57	8	191	193	(1)	59	20	271
	3,780	2,124	1,494	622	8,020	3,203	2,083	1,228	582	7,096	2,978	2,209	1,151	568	6,906
Respiratory & Immunology:															
Symbicort	609	1,065	670	384	2,728	567	1,022	694	438	2,721	547	829	678	441	2,495
Fasenra	20	790	286	162	1,258	12	603	203	131	949	5	482	118	99	704
Pulmicort	770	72	73	47	962	798	71	73	54	996	1,190	110	81	85	1,466
Daliresp/Daxas	4	207	15	1	227	4	190	22	1	217	4	184	26	1	215
Breztri	55	115	7	26	203	14	5	–	9	28	–	–	–	2	2
Bevespi	4	39	11	–	54	1	44	3	–	48	–	42	–	–	42
Saphnelo	–	8	–	–	8	–	–	–	–	–	–	–	–	–	–
Others	287	108	185	14	594	203	6	176	13	398	241	6	204	16	467
	1,749	2,404	1,247	634	6,034	1,599	1,941	1,171	646	5,357	1,987	1,653	1,107	644	5,391
Rare Disease:															
Soliris	170	1,068	439	197	1,874	–	–	–	–	–	–	–	–	–	–
Ultomiris	9	381	169	129	688	–	–	–	–	–	–	–	–	–	–
Strensiq	10	297	36	35	378	–	–	–	–	–	–	–	–	–	–
Andexxa	–	50	18	–	68	–	–	–	–	–	–	–	–	–	–
Kanuma	7	32	20	3	62	–	–	–	–	–	–	–	–	–	–
	196	1,828	682	364	3,070	–	–	–	–	–	–	–	–	–	–
Other:															
Nexium	705	128	62	431	1,326	757	169	71	495	1,492	748	218	63	454	1,483
Synagis	35	23	203	149	410	–	47	325	–	372	–	46	312	–	358
FluMist	2	27	222	2	253	1	70	219	5	295	–	20	93	–	113
Losec/Prilosec	152	1	26	1	180	152	6	20	5	183	179	10	49	25	263
Seroquel XR/IR	46	12	29	5	92	55	17	29	16	117	50	34	86	19	191
Others	14	30	54	8	106	6	55	56	9	126	12	108	64	9	193
	954	221	596	596	2,367	971	364	720	530	2,585	989	436	669	507	2,601
COVID-19:															
Vaxzevria	2,240	64	1,035	578	3,917	–	–	2	–	2	–	–	–	–	–
Evusheld	19	–	66	–	85	–	–	–	–	–	–	–	–	–	–
	2,259	64	1,101	578	4,002	–	–	2	–	2	–	–	–	–	–
Product Sales	12,161	12,000	7,604	4,776	36,541	8,679	8,638	5,059	3,514	25,890	8,165	7,747	4,350	3,303	23,565

1 Revenue *continued*

SE Rebates and chargebacks in the US

The major market where estimates are seen as significant is the US. When invoicing Product Sales in the US, we estimate the rebates and chargebacks we expect to pay. The adjustment in respect of prior year net US Product Sales revenue in 2021 was 1.5% (2020: 3.5%; 2019: 3.6%). The most significant of these relate to the Medicaid and state programmes with an adjustment in respect of prior year net US Product Sales revenue in 2021 of 0.4% (2020: 1.1%; 2019: 1.3%) and Managed Care and Medicare of 0.7% (2020: 1.5%; 2019: 1.9%).

The adjustment in respect of the prior year net US Product sales revenue, excluding the Rare Disease disease area in 2021 was 1.8%, with Medicaid and state programmes of 0.5% and Managed Care and Medicare of 0.8%.

These values demonstrate the level of sensitivity; further meaningful sensitivity is not able to be provided due to the large volume of variables that contribute to the overall rebates, chargebacks, returns and other revenue accruals.

Collaboration Revenue

	2021 $m	2020 $m	2019 $m
Royalty income	138	62	62
Global co-development and commercialisation of *Lynparza* and *Koselugo* with MSD	400	460	610
Transfer of rights to *Zoladex* in the US and Canada to TerSera	–	35	–
Enhertu: share of gross profits	193	94	–
Roxadustat: share of gross profits	6	30	–
Nexium: sale of rights	75	–	–
Licence agreement for *Crestor* in Spain with Almirall	–	–	39
Co-development and commercialisation of MEDI8897 with Sanofi	–	–	34
Grant of authorised generic rights to various medicines in Japan	–	–	19
Other collaboration revenue	64	46	55
	876	727	819

Collaboration Revenue includes some income that does not arise from the satisfaction of performance obligations, in particular profit share entitlements arising from product sales made by collaborators who have licenced intellectual property to AstraZeneca. $200m of Collaboration Revenue in 2021 (2020: $128m; 2019: $nil) relates to such income. Substantially all other Collaboration Revenue relates to performance obligations satisfied in prior periods.

2 Operating profit

Operating profit includes the following significant items:

Cost of sales

In 2021, Cost of sales includes a charge of $2,198m in relation to the release, in line with sales, of fair value uplift to inventory that was recognised under IFRS 3 'Business Combinations' upon the acquisition of Alexion (see Note 27).

During the year $290m (2020: $nil) of government grants were recognised within Cost of sales. Substantially all of the grants recognised relate to funding of manufactured *Vaxzevria* product for the US government, which expired prior to being accepted by the FDA. Historically, AstraZeneca did not receive any substantial government grants prior to the commencement of these programmes in 2020.

Selling, general and administrative expense

In 2021, Selling, general and administrative expense includes a charge of $42m (2020: credit of $51m; 2019: credit of $516m) resulting from changes in the fair value of contingent consideration arising from the acquisition of the diabetes alliance from BMS. These adjustments reflect revised estimates for future sales performance for the products acquired and, as a result, revised estimates for future royalties payable.

In 2021, Selling, general and administrative expense also includes a charge of $5m (2020: credit of $143m; 2019: credit of $58m) resulting from changes in the fair value of contingent consideration arising from the acquisition of Almirall's respiratory business. These adjustments reflect revised estimates for future sales performance for the products acquired and, as a result, revised estimates for future milestones payable.

In 2021, Selling, general and administrative expense also includes a charge of $48m (2020: credit of $9m; 2019: charge of $610m) relating to a number of legal proceedings including settlements in various jurisdictions in relation to several marketed products.

Research and development expense: Government grants

During the year $531m (2020: $222m) of government grants were recognised within Research and development expense. Substantially all of the grants recognised relate to funding for research and development and related expenses for *Vaxzevria* $309m; (2020: $161m) and AZD7442 $222m;(2020: $61m). Historically, AstraZeneca did not receive any substantial government grants prior to the commencement of these programmes in 2020.

Other operating income and expense

	2021 $m	2020 $m	2019 $m
Royalties			
Income	63	149	146
Amortisation	(1)	(2)	(4)
Gains on disposal of intangible assets	513	1,030	1,243
Gains on disposal of investments in associates and joint ventures	776	–	–
Net (losses)/gains on disposal of other non-current assets	(4)	25	(21)
Impairment of property, plant and equipment	–	(12)	–
Other income[1]	453	406	285
Other expense	(308)	(68)	(108)
Other operating income and expense	**1,492**	1,528	1,541

[1] Other income in 2021 includes $99m of payments from Allergan in respect of the development of brazikumab (2020: $107m; 2019: $nil).

Royalty amortisation relates to intangible assets recorded in respect of income streams acquired with MedImmune.

Gains on disposal of intangible assets in 2021 includes $317m on disposal of rights to *Crestor* in over 30 countries in Europe, except in the UK and Spain.

Gains on disposal of intangible assets in 2020 includes $350m on disposal of global rights excluding US, India and Japan to established hypertension medicines to Atnahs Pharma, $400m on disposal of rights in over 70 countries to *Atacand* to Cheplapharm and $120m on the sale of an FDA Priority Review Voucher.

Gains on disposal of intangible assets in 2019 includes $515m on disposal of US rights to *Synagis* to Sobi, $243m on disposal of rights to *Losec* globally excluding China, Japan, the US and Mexico to Cheplapharm, $181m on disposal of rights to *Arimidex* and *Casodex* in Europe and certain additional countries to Juvisé Pharmaceuticals and $213m on disposal of commercialisation rights to *Seroquel* and *Seroquel XR* in Europe, Russia, US and Canada to Cheplapharm.

Gains on disposal of investments in associates and joint ventures in 2021 relates to the disposal of the 26.7% ownership in Viela Bio, as part of the acquisition of Viela by Horizon Therapeutics plc. AstraZeneca received cash proceeds and profit of $776m upon closing, with the profit recorded as Other operating income.

As part of the total consideration received in respect of the agreement to sell US rights to *Synagis* in 2019, $150m related to the rights to participate in the future cash flows from the US profits or losses for nirsevimab. A further $40m was received in 2020 and $20m in 2021. The total amount has been recognised as a financial liability as the Group has not fully transferred the risks and rewards of the underlying cash flows arising from nirsevimab to Sobi. This liability is presented in Other payables within Non-current liabilities. The associated cash flow is presented within investing activities as the Group has received the cash in exchange for agreeing to transfer future cash flows relating to an intangible asset. In 2021, as a result of the Probability of Technical/Regulatory Success unwind, an increase of $114m to the Profit Participation Liability has been recorded in Other operating expense.

Restructuring costs

In conjunction with the acquisition of Alexion, the enlarged Group has initiated a comprehensive Post Alexion Acquisition Group Review, aimed at integrating systems, structure and processes, optimising the global footprint and prioritising resource allocations and investments. These activities are expected to be substantially complete by the end of 2025, with a number of planned activities having commenced in late 2021. The Group has also continued to progress other legacy restructuring programmes, including the Global Post-Pandemic New Ways of Working programme that was initiated in 2020 in response to the changing business environment, accelerated by the COVID-19 pandemic.

During 2021, the Group has incurred $1,283m of restructuring costs, of which $1,030m resulted from activities that are part of the Post Alexion Acquisition Group Review. These included $449m within Cost of sales due to the rationalisation of our manufacturing capacity and footprint across certain production sites, $161m within Research and development expense and $81m in Cost of sales due to the de-prioritisation of various development projects within the enlarged Group's pipeline, $144m within Cost of sales in relation to the renegotiation of manufacturing capacity agreements with third parties and $98m, recognised principally in Selling, general and administrative expense, of severance payments and the associated costs of compensating those Alexion employees whose roles were eliminated due to duplication with existing AstraZeneca roles.

Total restructuring costs in 2021 included impairments of property, plant and equipment ($343m) and impairments of software intangibles ($16m).

The tables below show the costs that have been charged in respect of restructuring programmes by cost category and type. Severance provisions are detailed in Note 21.

	2021 $m	2020 $m	2019 $m
Cost of sales	722	53	73
Research and development expense	223	35	101
Selling, general and administrative expense	338	162	173
Other operating income and expense	–	1	–
Total charge	1,283	251	347

2 Operating profit *continued*

	2021 $m	2020 $m	2019 $m
Severance costs	**217**	26	137
Accelerated depreciation and impairment charges[1]	**371**	17	(67)
Other[2]	**695**	208	277
Total charge	**1,283**	251	347

[1] Included within accelerated depreciation and impairment in 2019 is a credit relating to the impairment reversal of two manufacturing sites in Colorado, US. Refer to Note 7 for further details.
[2] Other costs are those incurred in designing and implementing the Group's various restructuring initiatives, including costs of integrating systems, structure and processes as part of our Post Alexion Acquisition Group Review, costs relating to the Alexion acquisition, internal project costs and external consultancy fees.

Financial instruments

Included within Operating profit are the following net gains and losses on financial instruments:

	2021 $m	2020 $m	2019 $m
Losses on forward foreign exchange contracts	**(21)**	(86)	(112)
(Losses)/gains on receivables and payables	**(42)**	89	66
Total	**(63)**	3	(46)

Impairment charges

Details of impairment charges for 2021, 2020 and 2019 are included in Notes 7 and 10.

3 Finance income and expense

	2021 $m	2020 $m	2019 $m
Finance income			
Returns on fixed deposits and equity securities	**1**	1	1
Returns on short-term deposits	**11**	40	122
Fair value gains on debt and interest rate swaps	**–**	4	7
Discount unwind on other long-term assets	**–**	6	20
Interest income on income tax balances	**31**	36	22
Total	**43**	87	172
Finance expense			
Interest on debt and commercial paper	**(700)**	(669)	(698)
Interest on overdrafts, lease liabilities and other financing costs	**(74)**	(67)	(74)
Net interest on post-employment defined benefit plan net liabilities (Note 22)	**(26)**	(37)	(53)
Net exchange losses	**(20)**	(34)	(30)
Discount unwind on contingent consideration arising from business combinations (Note 20)	**(226)**	(278)	(356)
Discount unwind on other long-term liabilities[*]	**(248)**	(219)	(213)
Fair value losses on debt and interest rate swaps	**(4)**	–	–
Interest expense on income tax balances	**(2)**	(2)	(8)
Total	**(1,300)**	(1,306)	(1,432)
Net finance expense	**(1,257)**	(1,219)	(1,260)

[*] Included within Discount unwind on other long-term liabilities is $161m relating to the Acerta Pharma share purchase liability (2020: $151m; 2019: $136m), see Note 20 for further details.

Financial instruments

Included within finance income and expense are the following net gains and losses on financial instruments:

	2021 $m	2020 $m	2019 $m
Interest and fair value adjustments in respect of debt designated at fair value through profit or loss, net of derivatives	**(5)**	(8)	(12)
Interest and changes in carrying values of debt designated as hedged items in fair value hedges, net of derivatives	**(9)**	(6)	(10)
Interest and fair value changes on fixed and short-term deposits, equity securities, other derivatives and tax balances	**16**	42	110
Interest on debt, commercial paper, overdrafts and lease liabilities held at amortised cost	**(738)**	(660)	(662)

Fair value loss of $33m (2020: gain of $33m; 2019: loss of $5m) on interest rate fair value hedging instruments and $29m fair value gain (2020: loss of $32m; 2019: gain of $8m) on the related hedged items have been included within Interest and changes in carrying values of debt designated as hedged items, net of derivatives. All fair value hedge relationships were effective during the year.

Fair value loss of $19m (2020: gain of $2m; 2019: gain of $4m) on derivatives related to debt instruments designated at fair value through profit or loss and $19m fair value gain (2020: loss of $3m; 2019: loss of $4m) on debt instruments designated at fair value through profit or loss have been included within Interest and fair value adjustments in respect of debt designated at fair value through profit or loss, net of derivatives.

4 Taxation

Taxation recognised in the Consolidated Statement of Comprehensive Income is as follows:

	2021 $m	2020 $m	2019 $m
Current tax expense			
Current year	1,200	981	1,243
Adjustment to prior years	(5)	(10)	66
Total	1,195	971	1,309
Deferred tax expense			
Origination and reversal of temporary differences	(1,417)	(178)	(875)
Adjustment to prior years	(158)	(21)	(113)
Total	(1,575)	(199)	(988)
Taxation recognised in the profit for the period	(380)	772	321

Taxation relating to components of Other comprehensive income is as follows:

	2021 $m	2020 $m	2019 $m
Current and deferred tax			
Items that will not be reclassified to profit or loss:			
Remeasurement of the defined benefit liability	(117)	36	81
Net losses/(gains) on equity investments measured at fair value through other comprehensive income	27	(180)	(60)
Deferred tax (credit)/charge relating to change of tax rates	195	63	–
Total	105	(81)	21
Items that may be reclassified subsequently to profit or loss:			
Foreign exchange arising on consolidation	57	(61)	34
Foreign exchange arising on designated borrowings in net investment hedges	(19)	22	4
Deferred tax charge relating to change of tax rates	8	–	–
Total	46	(39)	38
Taxation relating to components of other comprehensive income	151	(120)	59

The reported tax rate in the year was 143% and reflected the favourable one-off impacts of the non-taxable divestment of the investment in Viela Bio and a reduction of tax liabilities arising from updates to estimates of prior period tax liabilities following settlements with tax authorities and on expiry of statute of limitations partially offset by a tax charge on recalculation of deferred tax balances following substantive enactment of Dutch and UK Corporation Tax rate increases.

The income tax paid for the year was $1,743m.

Taxation has been provided at current rates on the profits earned for the periods covered by the Group Financial Statements. The 2021 prior period current tax adjustment relates mainly to tax accrual to tax return adjustments. The 2020 prior period current tax adjustment relates mainly to net reductions in provisions for tax contingencies and tax accrual to tax return adjustments. The 2019 prior period current tax adjustments relate mainly to net increases in provisions for tax contingencies and tax accrual to tax return adjustments.

The 2021 prior period deferred tax adjustments relate mainly to tax accrual to tax return adjustments and updates to estimates of prior period tax liabilities following settlements with tax authorities. The 2020 prior period deferred tax adjustments relate mainly to tax accrual to tax return adjustments offset by net increases in provisions for tax contingencies. The 2019 prior period deferred tax adjustments relate mainly to tax accrual to return adjustments.

To the extent that dividends remitted from overseas subsidiaries, joint ventures and associates are expected to result in additional taxes, appropriate amounts have been provided for. Unremitted earnings or differences in the carrying value and tax basis of investments may be liable to additional taxes if distributed as dividends or on a liquidation event. Deferred tax is provided for such differences in relation to Group entities where management is intending to remit earnings in the foreseeable future. The aggregate amount of gross temporary differences associated with investments in subsidiaries, partnerships and branches for which deferred tax liabilities have not been recognised totalled approximately $5,597m at 31 December 2021 (2020: $2,270m; 2019: $1,779m). $3,095m of which has a corresponding deductible temporary difference of the same gross value which is not recognised as it is not probable of reversing in the foreseeable future but on which different tax rates apply. Prior years' amounts have been adjusted to reflect only those unremitted earnings that would be subject to additional taxes.

Factors affecting future tax charges

As a Group with worldwide operations, AstraZeneca is subject to several factors that may affect future tax charges, principally the levels and mix of profitability in different jurisdictions, transfer pricing regulations, tax rates imposed and tax regime reforms. In 2021, the UK Government enacted legislation to increase the main rate of UK statutory Corporation Tax to 25% effective 1 April 2023. In December 2021, the OECD issued model rules for a new global minimum tax framework and the UK has announced the intention to bring these into effect from 2023. Whilst the overarching framework has been published, we are awaiting the legislation and detailed guidance to assess the full implications upon AstraZeneca.

4 Taxation *continued*

Tax reconciliation to UK statutory rate

The table below reconciles the UK statutory tax charge to the Group's total tax (credit)/charge:

	2021 $m	2020 $m	2019 $m
(Loss)/profit before tax	(265)	3,916	1,548
Notional taxation charge at UK corporation tax rate of 19%	(50)	744	294
Differences in effective overseas tax rates	1	(49)	(49)
Deferred tax charge relating to change in tax rates[1]	54	138	39
Unrecognised deferred tax asset[2]	32	3	(16)
Items not deductible for tax purposes	208	36	92
Items not chargeable for tax purposes	(163)	(4)	(13)
Other items[3]	(299)	(65)	21
Adjustments in respect of prior periods[4]	(163)	(31)	(47)
Total tax (credit)/charge for the year	(380)	772	321

1 The 2021 item relates to substantive enactment of the increase in UK Corporation Tax rate from 19% to 25% effective 1 April 2023 (debit of $12m), the increase in the Dutch Corporate Income Tax rate from 25% to 25.8% effective 1 January 2022 (debit of $39m) and other (debit of $3m). The 2020 item relates to the increase in the 2020 substantively enacted Dutch Corporate Income Tax rate (debit of $151m) and other (debit of $5m). In 2020, it was substantively enacted that the planned reduction in the Dutch Corporate Income Tax rate to 21.7% from 25% effective 1 January 2021 would not take place. In addition, the planned reduction in the UK corporation tax rate to 17% was not enacted with the corporation tax rate remaining at 19% (credit of $18m). The 2019 item relates to the increase in the 2019 substantively enacted Dutch Corporate Income Tax rate (debit of $66m) and other (credit of $27m). In 2019, it was substantively enacted that the Dutch Corporate Income Tax rate for the year ended 31 December 2020 would increase from 22.55% to 25% and effective 1 January 2021 would increase from 20.5% to 21.7%.

2 The 2021 item includes a $15m debit arising on de-recognition of previously recognised deferred tax assets. The 2020 item includes a $22m credit arising on recognition of previously unrecognised deferred tax assets. The 2019 item includes a $27m credit arising on recognition of previously unrecognised deferred tax assets.

3 Other items in 2021 relate to a net credit of $299m relating to the reduction of tax liabilities arising from updates to estimates of prior period tax liabilities following settlements with tax authorities and on expiry of the relevant statute of limitations partially offset by a provision for transfer pricing and other contingencies. Other items in 2020 relate to a net credit of $65m relating to the release of tax contingencies following the expiry of the relevant statute of limitations partially offset by a provision for transfer pricing and other contingencies. Other items in 2019 relate to a charge of $309m relating to collaboration and divestment activity, a credit of $70m relating to internal transfers of intellectual property and a net credit of $218m relating to the release of tax contingencies following the expiry of the relevant statute of limitations and on the conclusion of tax authority review partially offset by a provision for transfer pricing and other contingencies.

4 Further details explaining the adjustments in respect of prior periods is set out on page 149.

AstraZeneca is domiciled in the UK but operates in other countries where the tax rates and laws are different to those in the UK. The impact on differences in effective overseas tax rates on the Group's overall tax charge is noted above. Profits arising from our manufacturing operation in Puerto Rico are granted special status and are taxed at a reduced rate compared with the normal rate of tax in that territory under a tax incentive grant continuing until 2031.

Deferred tax

The total movement in the net deferred tax balance in the year was $2,396m. The movements are as follows:

	Intangibles, property, plant & equipment[1] $m	Pension and post-retirement benefits $m	Elimination of unrealised profit on inventory $m	Untaxed reserves[2] $m	Losses and tax credits carried forward $m	Accrued expenses and other $m	Total $m
Net deferred tax balance at 1 January 2019	(3,368)	495	980	(557)	1,008	535	(907)
Income statement	1,055	(9)	312	(63)	(480)	173	988
Other comprehensive income	34	79	–	–	–	(30)	83
Equity	–	–	–	–	–	12	12
Exchange	14	(4)	1	22	18	1	52
Net deferred tax balance at 31 December 2019	(2,265)	561	1,293	(598)	546	691	228
Income statement	(226)	(64)	444	(92)	136	1	199
Other comprehensive income	(78)	101	–	(1)	–	72	94
Equity	–	–	–	–	–	(16)	(16)
Exchange	(58)	58	70	(110)	32	23	15
Net deferred tax balance at 31 December 2020	(2,627)	656	1,807	(801)	714	771	520
Income statement	**782**	**(166)**	**(59)**	**(139)**	**307**	**850**	**1,575**
Other comprehensive income	52	83	–	–	–	40	175
Equity	–	–	–	–	–	14	14
Additions through business combinations[3]	(3,744)	13	166	–	507	(1,116)	(4,174)
Exchange	57	(33)	(53)	78	(10)	(25)	14
Net deferred tax balance at 31 December 2021[4]	(5,480)	553	1,861	(862)	1,518	534	(1,876)

1 Includes deferred tax of $367m on contingent consideration liabilities in respect of intangibles.

2 Untaxed reserves relate to taxable profits where the tax liability is deferred to later periods.

3 The deferred tax liability of $4,174m relates to the acquisition of Alexion (Note 27 from page 178).

4 The Group recognises deferred tax assets to the extent that it is probable that sufficient future taxable profits will arise, against which these deductible temporary differences can be utilised. The US includes a net deferred tax asset of $245m and the UK includes a net deferred tax asset of $1,070m as at 31 December 2021 which include tax losses and other deductible temporary differences. The Group has performed an assessment of recovery of deferred tax assets and for these entities, the Group has forecasted future taxable profits and considers that it is probable that sufficient future taxable profits will arise against which these deductible temporary differences can be utilised. In arriving at these forecasts, the Group has reviewed the Group level budgets and forecasts and the ability of those entities to generate future income from developing and commercialising products, including local tax laws and the scheduling of reversal of deductible temporary differences and losses are forecast to be utilised within ten years. It is considered that these sources of income are sufficiently predictable or diversified to support a recognition period in excess of five years. A sensitivity assessment has been performed which shows that there is minimal impact on timing of reversal. Assessing the availability of future taxable income to support recognition of deferred tax assets is considered a key judgement and changes in Group forecasts will impact the recoverability of deferred tax assets. To the extent that this is not the case, no deferred tax asset is recognised and details of unrecognised deferred tax assets are included in the table below.

The net deferred tax balance, before the offset of balances within countries, consists of:

	Intangibles, property, plant & equipment $m	Pension and post-retirement benefits $m	Elimination of unrealised profit on inventory $m	Untaxed reserves $m	Losses and tax credits carried forward $m	Accrued expenses and other $m	Total $m
Deferred tax assets at 31 December 2019	1,091	591	1,543	–	608	959	4,792
Deferred tax liabilities at 31 December 2019	(3,356)	(30)	(250)	(598)	(62)	(268)	(4,564)
Net deferred tax balance at 31 December 2019	(2,265)	561	1,293	(598)	546	691	228
Deferred tax assets at 31 December 2020	1,061	690	2,286	–	852	1,130	6,019
Deferred tax liabilities at 31 December 2020	(3,688)	(34)	(479)	(801)	(138)	(359)	(5,499)
Net deferred tax balance at 31 December 2020	(2,627)	656	1,807	(801)	714	771	520
Deferred tax assets at 31 December 2021	1,476	574	1,910	–	1,571	1,735	7,266
Deferred tax liabilities at 31 December 2021	(6,956)	(21)	(49)	(862)	(53)	(1,201)	(9,142)
Net deferred tax balance at 31 December 2021	(5,480)	553	1,861	(862)	1,518	534	(1,876)

Analysed in the Consolidated Statement of Financial Position, after offset of balances within countries, as follows:

	2021 $m	2020 $m	2019 $m
Deferred tax assets	4,330	3,438	2,718
Deferred tax liabilities	(6,206)	(2,918)	(2,490)
Net deferred tax balance	(1,876)	520	228

Unrecognised deferred tax assets

Deferred tax assets (DTA) of $719m (2020: $428m; 2019: $441m) have not been recognised in respect of deductible temporary differences because it is not probable that future taxable profit will be available against which the Group can utilise the benefits there from.

	2021 Temporary differences $m	2021 Unrecognised DTA $m	2020 Temporary differences $m	2020 Unrecognised DTA $m	2019 Temporary differences $m	2019 Unrecognised DTA $m
Trading and capital losses expiring:						
Within 10 years	4	1	2	–	33	9
More than 10 years	53	11	–	–	1	–
Indefinite	300	79	234	63	218	62
	357	91	236	63	252	71
Tax credits and State tax losses expiring:						
Within 10 years		101		36		44
More than 10 years		441		255		259
Indefinite		86		74		67
		628		365		370
Total		719		428		441

5 Earnings per $0.25 Ordinary Share

	2021	2020	2019
Profit for the year attributable to equity holders ($m)	112	3,196	1,335
Basic earnings per Ordinary Share	$0.08	$2.44	$1.03
Diluted earnings per Ordinary Share	$0.08	$2.44	$1.03
Weighted average number of Ordinary Shares in issue for basic earnings (millions)	1,418	1,312	1,301
Dilutive impact of share options outstanding (millions)	9	1	–
Diluted weighted average number of Ordinary Shares in issue (millions)	1,427	1,313	1,301

The earnings figures used in the calculations above are post-tax.

6 Segment information

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.

KJ This determination is considered to be a Key Judgement and this judgement has been taken with reference to the following factors:

1 The level of integration across the different functions of the Group's pharmaceutical business:
AstraZeneca is engaged in a single business activity of pharmaceuticals and the Group does not have multiple operating segments. AstraZeneca's pharmaceuticals business consists of the discovery and development of new products, which are then manufactured, marketed and sold. All of these functional activities take place (and are managed) globally on a highly integrated basis. These individual functional areas are not managed separately.

2 The identification of the Chief Operating Decision Maker (CODM) and the nature and extent of the financial information reviewed by the CODM:
The SET, established and chaired by the CEO, is the vehicle through which the CEO exercises the authority delegated to him from the Board for the management, development and performance of AstraZeneca as a whole. It is considered that the SET is AstraZeneca's Chief Operating Decision Making body (as defined by IFRS 8). The operation of the SET is principally driven by the management of the Commercial operations, R&D, manufacturing and supply and enabling functions. All significant operating decisions are undertaken by the SET. While members of the SET have responsibility for implementation of decisions in their respective areas, operating decision making is at SET level as a whole. Where necessary, these are implemented through cross-functional sub-committees that consider the Group-wide impact of a new decision. For example, product launch decisions would be initially considered by the SET and, on approval, passed to an appropriate sub team for implementation. The ability of the enterprise to develop, produce, deliver and commercialise a wide range of pharmaceutical products are central to the SET decision-making process.

In assessing performance, the SET reviews financial information on an integrated basis for the Group as a whole, substantially in the form of, and on the same basis as, the Group's IFRS Financial Statements. The high upfront cost of discovering and developing new products, coupled with the relatively insignificant and stable unit cost of production, means that there is not the clear link that exists in many manufacturing businesses between the revenue generated on an individual product sale and the associated cost and hence margin generated on a product. Consequently, the profitability of individual drugs or classes of drugs is not considered a key measure of performance for the business and is not monitored by the SET. The focus of additional financial information reviewed is at brand sales and gross margin level within specific geographies. Expenditure analysis is completed for the science units, operations and enabling functions; there is no allocation of these centrally managed group costs to the individual product or brands. The bonus of SET members' continues to be derived from the Group scorecard outcome as discussed in our Directors' Remuneration Report.

3 How resources are allocated:
Resources are allocated on a Group-wide basis according to need. In particular, capital expenditure, in-licensing, and R&D resources are allocated between activities on merit, based on overall therapeutic considerations and strategy under the aegis of the Group's Early Stage Product Committees and Late Stage Product Committees.

Geographic areas

The following table shows information for Total Revenue by geographic area and material countries. The additional tables show the Operating profit and Profit before tax made by companies located in that area, together with Non-current assets, Total assets, assets acquired, net operating assets, and Property, plant and equipment owned by the same companies. Product Sales by geographic market are included in the area/country where the legal entity resides and from which those sales were made.

	Total Revenue		
	2021 $m	2020 $m	2019 $m
UK	3,245	1,741	1,822
Rest of Europe			
France	915	653	578
Germany	1,486	937	704
Italy	577	431	396
Spain	578	398	359
Sweden	2,322	1,026	834
Others	1,949	1,391	1,291
	7,827	4,836	4,162
The Americas			
Canada	772	596	466
US	12,047	8,955	8,047
Others	1,203	761	814
	14,022	10,312	9,327
Asia, Africa & Australasia			
Australia	547	282	266
China	6,002	5,345	4,867
Japan	3,395	2,567	2,522
Others	2,379	1,534	1,418
	12,323	9,728	9,073
Total Revenue	37,417	26,617	24,384

Total Revenue outside of the UK totalled $34,172m for the year ended 31 December 2021 (2020: $24,876m, 2019: $22,562m).

	Operating profit/(loss)			(Loss)/profit before tax		
	2021 $m	2020 $m	2019 $m	2021 $m	2020 $m	2019 $m
UK	(950)	824	466	(1,477)	518	93
Rest of Europe	2,999	2,838	1,502	2,682	2,356	1,006
The Americas	(1,936)	758	(8)	(2,401)	297	(474)
Asia, Africa & Australasia	943	742	964	931	745	923
Continuing operations	1,056	5,162	2,924	(265)	3,916	1,548

	Non-current assets[1]			Total assets		
	2021 $m	2020 $m	2019 $m	2021 $m	2020 $m	2019 $m
UK	7,692	7,900	6,874	16,615	17,851	15,302
Rest of Europe	39,171	15,821	15,245	48,383	19,738	18,182
The Americas	26,570	18,501	19,663	34,301	23,640	23,380
Asia, Africa & Australasia	1,254	1,354	1,253	6,064	5,500	4,513
Continuing operations	74,687	43,576	43,035	105,363	66,729	61,377

	Assets acquired[2]			Net operating assets[3]		
	2021 $m	2020 $m	2019 $m	2021 $m	2020 $m	2019 $m
UK	810	1,611	2,255	3,239	5,244	4,206
Rest of Europe	26,527	505	386	40,161	10,242	9,201
The Americas	10,810	286	236	24,786	15,697	15,929
Asia, Africa & Australasia	94	116	120	736	607	1,432
Continuing operations	38,241	2,518	2,997	68,922	31,790	30,768

[1] Non-current assets exclude Deferred tax assets and Derivative financial instruments.

[2] Included in Assets acquired are those assets that are expected to be used during more than one period (Property, plant and equipment, Goodwill and Intangible assets) and include those acquired through business combinations (Note 27).

[3] Net operating assets exclude short-term investments, cash, short-term borrowings, loans, Derivative financial instruments, retirement benefit obligations and non-operating receivables and payables.

	Property, plant and equipment		
	2021 $m	2020 $m	2019 $m
UK	2,542	2,227	1,920
Ireland	969	–	–
Sweden	1,593	1,755	1,488
US	2,660	2,662	2,758
Rest of the world	1,419	1,607	1,522
Continuing operations	9,183	8,251	7,688

Geographic markets

The table below shows Product Sales in each geographic market in which customers are located.

	2021 $m	2020 $m	2019 $m
UK	1,206	611	458
Rest of Europe	6,792	4,446	3,891
The Americas	14,893	10,004	9,032
Asia, Africa & Australasia	13,650	10,829	10,184
Continuing operations	36,541	25,890	23,565

Product Sales are recognised when control of the goods has been transferred to a third party. A significant proportion of this is upon delivery of the products to wholesalers. One wholesaler (2020: one; 2019: one) individually represented greater than 10% of Product Sales. The value of Product Sales to this wholesaler was $4,862m (2020: $3,321m; 2019: $3,078m).

7 Property, plant and equipment

	Land and buildings $m	Plant and equipment $m	Assets in course of construction $m	Total property, plant and equipment $m
Cost				
At 1 January 2019	5,366	7,096	2,177	14,639
Capital expenditure	8	48	940	996
Transfer of assets into use	403	620	(1,023)	–
Disposals and other movements	(236)	(324)	(11)	(571)
Exchange adjustments	(9)	(57)	3	(63)
At 31 December 2019	5,532	7,383	2,086	15,001
Capital expenditure	10	42	874	926
Transfer of assets into use	137	462	(599)	–
Disposals and other movements	(48)	(615)	(18)	(681)
Exchange adjustments	220	466	135	821
At 31 December 2020	5,851	7,738	2,478	16,067
Additions through business combinations (Note 27)	**542**	**339**	**254**	**1,135**
Capital expenditure	**9**	**31**	**1,112**	**1,152**
Transfer of assets into use	**236**	**611**	**(847)**	**–**
Disposals and other movements	**(92)**	**(469)**	**(200)**	**(761)**
Exchange adjustments	**(169)**	**(347)**	**(69)**	**(585)**
At 31 December 2021	**6,377**	**7,903**	**2,728**	**17,008**
Depreciation and impairment				
At 1 January 2019	2,504	4,714	–	7,218
Depreciation charge for the year	209	438	–	647
Impairment (reversal)/charge	(67)	14	–	(53)
Disposals and other movements	(120)	(313)	–	(433)
Exchange adjustments	(21)	(45)	–	(66)
At 31 December 2019	2,505	4,808	–	7,313
Depreciation charge for the year	227	462	–	689
Impairment (reversal)/charge	(1)	2	12	13
Disposals and other movements	(42)	(606)	(12)	(660)
Exchange adjustments	137	324	–	461
At 31 December 2020	2,826	4,990	–	7,816
Depreciation charge for the year	**231**	**493**	**–**	**724**
Impairment (reversal)/charge	**(1)**	**121**	**223**	**343**
Disposals and other movements	**(74)**	**(428)**	**(223)**	**(725)**
Exchange adjustments	**(105)**	**(228)**	**–**	**(333)**
At 31 December 2021	**2,877**	**4,948**	**–**	**7,825**
Net book value				
At 31 December 2019	3,027	2,575	2,086	7,688
At 31 December 2020	3,025	2,748	2,478	8,251
At 31 December 2021	**3,500**	**2,955**	**2,728**	**9,183**

Impairment charges in 2021 totalling $343m were recognised for Plant and equipment and Assets in course of construction due to the rationalisation of our manufacturing capacity and footprint across certain production sites as a result of restructuring programmes, including the Post Alexion Acquisition Group Review (see Note 2). These charges have been recognised in Cost of sales. The revised carrying value of the impacted assets is nil, under fair value less costs to sell.

Impairment charges in 2019 were recognised for Land and buildings and Plant and equipment as a result of the announcement of the closure of the Wedel manufacturing site and the cessation of specific operations in Algeria. These charges were recognised in Cost of sales in 2019. Impairment reversals were recognised in 2019 of $23m in relation to the Longmont, Colorado manufacturing site (sold in March 2019) and the Boulder, Colorado manufacturing site of $70m (sold in May 2020). These assets had been fully impaired during 2018.

Included within other movements in 2019 is a transfer of $70m from Land and buildings to Assets held for sale in relation to the Boulder manufacturing site.

	2021 $m	2020 $m	2019 $m
The net book value of land and buildings comprised:			
Freeholds	**2,985**	2,583	2,657
Leaseholds	**515**	442	370

8 Leases

Right-of-use assets

	Land and buildings $m	Motor vehicles $m	Other $m	Total right-of-use assets $m
Cost				
At 1 January 2019	–	–	–	–
Opening balance	580	124	18	722
Additions – separately acquired	85	85	3	173
Disposals and other movements	(44)	(7)	1	(50)
Exchange adjustments	6	–	–	6
At 31 December 2019	627	202	22	851
Additions – separately acquired	87	89	15	191
Disposals and other movements	–	(27)	(2)	(29)
Exchange adjustments	21	8	1	30
At 31 December 2020	735	272	36	1,043
Additions through business combinations (Note 27)	255	8	–	263
Additions – separately acquired	145	98	2	245
Disposals and other movements	25	(44)	(4)	(23)
Exchange adjustments	(27)	(13)	(1)	(41)
At 31 December 2021	1,133	321	33	1,487
Depreciation and impairment				
At 1 January 2019	–	–	–	–
Depreciation charge for the year	130	70	7	207
Impairment charge	4	–	–	4
Disposals and other movements	(3)	(6)	1	(8)
Exchange adjustments	1	–	–	1
At 31 December 2019	132	64	8	204
Depreciation charge for the year	131	75	9	215
Disposals and other movements	(24)	(26)	(4)	(54)
Exchange adjustments	8	4	–	12
At 31 December 2020	247	117	13	377
Depreciation charge for the year	144	85	6	235
Disposals and other movements	(54)	(42)	–	(96)
Exchange adjustments	(11)	(6)	–	(17)
At 31 December 2021	326	154	19	499
Net book value				
At 31 December 2019	495	138	14	647
At 31 December 2020	488	155	23	666
At 31 December 2021	807	167	14	988

Lease Liability

	2021 $m	2020 $m	2019 $m
The present value of lease liabilities is as follows:			
Within one year	(233)	(192)	(188)
Later than one year and not later than five years	(544)	(389)	(368)
Later than five years	(210)	(100)	(119)
Total lease liabilities	(987)	(681)	(675)

The interest expense on lease liabilities included within finance costs was $22m (2020: $21m; 2019: $22m). The expense relating to short-term leases was $4m (2020: $2m; 2019: $1m). The expense relating to leases of Low-value assets that are not shown above as short-term leases was $1m (2020: $1m; 2019: $1m). The expense relating to variable lease payments not included in lease liabilities was $4m (2020: income of $1m; 2019: $nil). Income recognised from subleasing was $3m (2020: $7m; 2019: $4m).

The total cash outflow for leases in 2021 was $262m (2020: $228m; 2019: $208m).

9 Goodwill

	2021 $m	2020 $m	2019 $m
Cost			
At 1 January	**12,164**	11,982	12,022
Additions through business combinations (Note 27)	**8,287**	–	–
Exchange and other adjustments	**(140)**	182	(40)
At 31 December	**20,311**	12,164	11,982
Amortisation and impairment losses			
At 1 January	**319**	314	315
Exchange and other adjustments	**(5)**	5	(1)
At 31 December	**314**	319	314
Net book value			
At 31 December	**19,997**	11,845	11,668

Goodwill is tested for impairment at the operating segment level, this being the level at which goodwill is monitored for internal management purposes. As detailed in Note 6, the Group does not have multiple operating segments and is engaged in a single business activity of pharmaceuticals.

Recoverable amount is determined on a fair value less costs to sell basis using the market value of the Company's outstanding Ordinary Shares. Our market capitalisation is compared to the book value of the Group's net assets and this indicates a significant surplus at 31 December 2021 (and 31 December 2020 and 31 December 2019). No goodwill impairment was identified.

10 Intangible assets

	Product, marketing and distribution rights $m	Other intangibles $m	Software development costs $m	Total $m
Cost				
At 1 January 2019	39,136	2,526	1,839	43,501
Additions – separately acquired	1,835	99	67	2,001
Disposals	(35)	–	(151)	(186)
Exchange and other adjustments	(282)	24	26	(232)
At 31 December 2019	40,654	2,649	1,781	45,084
Additions – separately acquired	1,454	2	136	1,592
Disposals	(970)	(66)	(636)	(1,672)
Exchange and other adjustments	1,539	57	7	1,603
At 31 December 2020	42,677	2,642	1,288	46,607
Additions through business combinations (Note 27)	**26,455**	**430**	**70**	**26,955**
Additions – separately acquired	**587**	**6**	**119**	**712**
Transferred to Assets held for sale (Note 18)	**(1,266)**	**(47)**	–	**(1,313)**
Disposals	**(801)**	**(402)**	**(23)**	**(1,226)**
Exchange and other adjustments	**(1,062)**	**(18)**	**(22)**	**(1,102)**
At 31 December 2021	**66,590**	**2,611**	**1,432**	**70,633**
Amortisation and impairment losses				
At 1 January 2019	17,907	2,035	1,600	21,542
Amortisation for year	1,808	52	68	1,928
Impairment charges	1,034	–	2	1,036
Impairment reversals	(3)	–	–	(3)
Disposals	(29)	–	(147)	(176)
Exchange and other adjustments	(112)	10	26	(76)
At 31 December 2019	20,605	2,097	1,549	24,251
Amortisation for year	1,872	59	61	1,992
Impairment charges	405	–	–	405
Impairment reversals	(165)	–	–	(165)
Disposals	(899)	(66)	(636)	(1,601)
Exchange and other adjustments	746	38	(6)	778
At 31 December 2020	22,564	2,128	968	25,660
Amortisation for year	**2,908**	**172**	**63**	**3,143**
Impairment charges	**2,067**	–	**18**	**2,085**
Transferred to Assets held for sale (Note 18)	**(931)**	**(14)**	–	**(945)**
Disposals	**(797)**	**(402)**	**(21)**	**(1,220)**
Exchange and other adjustments	**(535)**	**(21)**	**(26)**	**(582)**
At 31 December 2021	**25,276**	**1,863**	**1,002**	**28,141**
Net book value				
At 31 December 2019	20,049	552	232	20,833
At 31 December 2020	20,113	514	320	20,947
At 31 December 2021	**41,314**	**748**	**430**	**42,492**

	2021 $m	2020 $m	2019 $m
Net book value			
Current intangible assets	105	–	–
Non-current intangible assets	42,387	20,947	20,833
At 31 December	42,492	20,947	20,833

Other intangibles consist mainly of research and device technologies and the Alexion brand name.

Included within Additions – separately acquired are amounts of $124m (2020: $835m; 2019: $1,093m), relating to deferred payments and other non-cash consideration for the acquisition of Product, marketing and distribution rights, which are not reflected in the current year Consolidated Statement of Cash Flows. Disposals include amounts related to fully depreciated assets that are no longer in use by the Group.

Amortisation charges are recognised in profit as follows:

	Product, marketing and distribution rights $m	Other intangibles $m	Software development costs $m	Total $m
Year ended 31 December 2019				
Cost of sales	87	–	–	87
Research and development expense	–	29	–	29
Selling, general and administrative expense	1,721	19	68	1,808
Other operating income and expense	–	4	–	4
Total	1,808	52	68	1,928
Year ended 31 December 2020				
Cost of sales	66	–	–	66
Research and development expense	–	29	–	29
Selling, general and administrative expense	1,806	28	61	1,895
Other operating income and expense	–	2	–	2
Total	1,872	59	61	1,992
Year ended 31 December 2021				
Cost of sales	66	–	–	66
Research and development expense	–	33	–	33
Selling, general and administrative expense	2,842	138	63	3,043
Other operating income and expense	–	1	–	1
Total	2,908	172	63	3,143

Net impairment charges/(reversals) are recognised in profit as follows:

	Product, marketing and distribution rights $m	Other intangibles $m	Software development costs $m	Total $m
Year ended 31 December 2019				
Research and development expense	609	–	–	609
Selling, general and administrative expense	425	–	2	427
Other operating income and expense	(3)	–	–	(3)
Total	1,031	–	2	1,033
Year ended 31 December 2020				
Research and development expense	55	–	–	55
Selling, general and administrative expense	185	–	–	185
Total	240	–	–	240
Year ended 31 December 2021				
Research and development expense	1,464	–	–	1,464
Selling, general and administrative expense	603	–	18	621
Total	2,067	–	18	2,085

10 Intangible assets *continued*

Impairment charges and reversals

Intangible assets under development and not available for use are tested annually for impairment and other intangible assets are tested when there is an indication of impairment loss or reversal. Where testing is required, the recoverable amount of the assets is estimated in order to determine the extent of the impairment loss or reversal. Where it is not possible to estimate the recoverable amount of an individual asset, the Group estimates the recoverable amount of the Cash Generating Unit (CGU) to which it belongs. The Group considers that as the intangible assets are linked to individual products and that product cash flows are considered to be largely independent of other product cash flows, the CGU for intangibles is at the product level. Group level budgets and forecasts include forecast capital investment and operational impacts related to sustainability projects, and form the basis for the value in use models used for impairment testing.

An asset's recoverable amount is determined as the higher of an asset's or CGU's fair value less costs to sell or value in use, in both cases using discounted cash flow calculations where the asset's expected post-tax cash flows are risk-adjusted over their estimated remaining period of expected economic benefit. Where the value in use approach is used, the risk-adjusted cash flows are discounted using AstraZeneca's post-tax weighted average cost of capital (7% for 2021, 2020 and 2019). There is no material difference in the approach taken to using pre-tax cash flows and a pre-tax rate compared to post-tax cash flows and a post-tax rate, as required by IAS 36. Where fair value less costs to sell is used to determine recoverable value, the discount rate is assessed with reference to a market participant; this is not usually materially different to the AstraZeneca post-tax weighted average cost of capital rate of 7%.

SE The estimates used in calculating the recoverable amount are considered significant estimates, highly sensitive and depend on assumptions specific to the nature of the Group's activities including:

- outcome of R&D activities
- probability of technical and regulatory success
- market volume, share and pricing (to derive peak year sales)
- amount and timing of projected future cash flows
- sales erosion curves following patent expiry.

For assets held at fair value less costs to sell, we make appropriate adjustments to reflect market participant assessments.

In 2021, the Group recorded impairment charges of $603m in respect of launched products, including *Bydureon* ($469m, revised carrying amount of $50m) under value in use model, roxadustat ($121m, revised carrying amount of $215m) under value in use model and other launched products totalling $13m. As these assets have been impaired in the current year, there is limited headroom in the recoverable amount calculation and they are inherently sensitive to any changes in assumptions, which could give rise to future impairments.

Impairment charges recorded against products in development, based on fair value less costs to sell, totalled $1,464m, principally Ardea ($1,172m) which was fully impaired following the decision to discontinue development of verinurad. The remaining impairments relate to full impairments of various products in development, due to either management's decision to discontinue development as part of a Group-wide portfolio prioritisation review, or due to the outcome of research activities.

In 2020, the Group recorded impairment charges of $350m in respect of launched products, including *Duaklir* ($200m, revised carrying amount of $210m) under fair value less costs to sell, *Bydureon* ($102m, revised carrying amount of $581m) under value in use model, and other launched products totalling $48m. The fair value less costs to sell valuation model for *Duaklir* was based on discounted cash flows, and was categorised at Level 3 in the fair value hierarchy. Key assumptions in this model were forecast future revenue and costs of production. Impairment charges recorded against products in development totalled $55m.

In 2019, the Group recorded impairment charges of $425m in respect of launched products *Bydureon* ($154m, revised carrying amount of $747m) under value in use model, *Otern* ($89m, revised carrying amount of $233m) under value in use model, *Eklira/Tudorza* ($84m, revised carrying amount of $192m) under value in use model, *FluMist* ($52m, revised carrying amount of $172m) under fair value less costs to sell and $46m relating to other launched products. Impairment charges recorded against products in development related to *Epanova* ($533m) and other intangible assets ($76m).

The Group has performed an assessment on assets which have had impairments recorded in previous periods to determine if any reversals of impairments were required. Impairment reversals of $165m were recorded in 2020 in respect of launched products, including *FluMist* ($147m, revised carrying amount of $300m, driven by expanded vaccination efforts increasing global demand), and other launched products of $18m. No impairment reversals were recorded against launched products in 2021 or 2019.

No impairment reversals were recorded against products in development in 2021 (2020: $nil; 2019: $3m).

Sensitivities

When launched products, such as the ones detailed above, are partially impaired, the carrying values of these assets in future periods are particularly sensitive to changes in forecast assumptions, including those assumptions set out above, as the asset is impaired down to its recoverable amount.

SE Were the useful economic lives to be adjusted to reduce them all by one year, the net book value would be reduced by $868m. If the useful economic lives were to be extended by one year, the net book value would increase by $481m.

Significant assets

	Carrying value $m	Remaining amortisation period
C5 franchise (*Soliris/Ultomiris*) intangible assets arising from the acquisition of Alexion	17,724	6 to 15 years
Intangible assets arising from the acquisition of Acerta Pharma	5,299	11 years
Strensiq, *Kanuma* and *Andexxa* intangible assets arising from the acquisition of Alexion	5,019	11 to 17 years
Intangible asset products in development arising from the acquisition of Alexion[1]	2,760	Not amortised
Intangible assets arising from the acquisition of ZS Pharma	2,381	10 years
Enhertu intangible assets acquired from Daiichi Sankyo	1,684	12 years
Other intangible assets (DS-1062) acquired from Daiichi Sankyo[1]	1,050	Not amortised
Farxiga/Forxiga intangible assets acquired from BMS	739	5 years
Intangible assets arising from the restructuring of a historical joint venture with MSD	666	5 to 8 years
Intangible assets arising from the acquisition of Pearl Therapeutics	611	7 to 8 years
RSV franchise assets arising from the acquisition of MedImmune	611	4 years
Monalizumab intangible assets acquired from Innate Pharma[1]	340	Not amortised

[1] Assets in development are not amortised but are tested annually for impairment.

The acquisition of intangible assets relating to DS-1062 in 2020 was assessed under the optional concentration test in IFRS 3 and was determined to be an asset acquisition, as substantially all of the value of the gross assets acquired was concentrated in a single asset.

KJ In assessing whether the intangible assets and associated processes acquired from Daiichi Sankyo in 2019 were a business, we determined that they were not at a stage of readiness to be able to obtain regulatory approval and manufacture and commercialise at scale. The transaction was treated as an asset acquisition.

11 Investments in associates and joint ventures

	2021 $m	2020 $m	2019 $m
At 1 January	39	58	89
Additions	92	8	74
Share of after tax losses	(64)	(27)	(116)
Exchange and other adjustments	2	–	11
At 31 December	69	39	58

On 29 January 2021, AstraZeneca entered into an agreement with IHP Holdings Limited to create and run an online platform (iHospital) offering consultations with physicians, repeat prescriptions and e-pharmacy in China. The agreement resulted in the formation of a new entity, IHP HK Holdings Limited. AstraZeneca contributed $30m in initial funds and holds a 50% interest in the associate entity.

On 1 December 2020, AstraZeneca and China International Capital Corporation (CICC) entered into an agreement to set up a Global Healthcare Industrial Fund to drive healthcare system innovation by leveraging local capital and accelerating China-related innovation incubation. The agreement resulted in the formation of a new entity, Wuxi AstraZeneca-CICC Venture Capital Partnership (Limited Partnership). AstraZeneca holds a 22% interest in the associate entity and contributed $1m in initial funds in 2020, with a further contribution of $45m made in 2021.

On 23 September 2021, AstraZeneca entered into an agreement with VaxEquity Limited to collaborate and develop self-amplifying RNA technology with the aim of generating treatments for target diseases. AstraZeneca has contributed $14m in initial funds and holds a 40% interest in the associate entity.

On 23 February 2018, AstraZeneca entered into an agreement with a consortium of investors to form a new, US-domiciled standalone company called Viela Bio. This agreement was to divest a number of assets in MedImmune's non-core inflammation and autoimmunity portfolio to Viela Bio, including MEDI-551, which is an advanced Phase IIb/III asset, and a number of other clinical and pre-clinical assets. AstraZeneca contributed $142m in initial funds and held an initial 45% interest in the joint venture. Viela Bio completed an IPO on 7 October 2019 with AstraZeneca investing $8m. After the IPO, AstraZeneca's holding was reduced to 29%. In May 2020, Viela Bio completed a follow-on financing reducing AstraZeneca's holding to 26.7% with one member on a board size of seven. Given the shareholding and board representation, the investment was treated as an associate. In February 2021, AstraZeneca agreed to divest its 26.7% ownership in Viela Bio, as part of the acquisition of Viela Bio by Horizon Therapeutics plc. AstraZeneca received cash proceeds and profit of $776m upon closing with the profit recorded as Other operating income. Prior to divestment, the Group provided transitional research and development services to Viela Bio, comprising $nil (2020: $3m; 2019: $13m) of services provided directly by the Group and $1m (2020: $15m; 2019: $24m) of passed-through third-party costs incurred by the Group on behalf of Viela Bio.

On 27 November 2017, AstraZeneca entered into a joint venture agreement with Chinese Future Industry Investment Fund (FIIF), to discover, develop and commercialise potential new medicines to help address unmet medical needs globally, and to bring innovative new medicines to patients in China more quickly. The agreement resulted in the formation of a joint venture entity based in China, Dizal (Jiangsu) Pharmaceutical Co., Limited (Dizal). AstraZeneca contributed $55m in initial funds and held an initial 46% interest in the joint venture. An additional contribution of $25m was made in 2019. In July 2020, Dizal completed a follow-on financing reducing AstraZeneca's holding to 30%. Dizal completed an IPO in December 2021, reducing AstraZeneca's holding to 27% with two members on a board size of eleven. Given the shareholding and board representation, the investment continues to be treated as an associate.

10 Intangible assets *continued*

On 1 December 2015, AstraZeneca entered into a joint venture agreement with Fujifilm Kyowa Kirin Biologics Co., Ltd. to develop a biosimilar using the combined capabilities of the two parties. The agreement resulted in the formation of a joint venture entity based in the UK, Centus Biotherapeutics Limited (Centus). Since its establishment, AstraZeneca has contributed $130m in cash to the joint venture entity and has a 50% interest in the joint venture. At the end of the year Centus had net assets of $4m, of which AstraZeneca's share is $2m, and the investment is held at $nil value.

On 30 April 2014, AstraZeneca entered into a joint venture agreement with Samsung Biologics Co., Ltd. to develop a biosimilar using the combined capabilities of the two parties. The agreement resulted in the formation of a joint venture entity based in the UK, Archigen Biotech Limited (Archigen). Since its establishment, AstraZeneca has contributed $131m in cash to the joint venture entity and has a 50% interest in the joint venture. At the end of the year Archigen had net assets of $3m, of which AstraZeneca's share is $2m, and the investment is held at $nil value.

All investments are accounted for using the equity method. At 31 December 2021, unrecognised losses in associates and joint ventures totalled $73m (2020: $56m; 2019: $3m) which have not been recognised due to the investment carrying value reaching $nil value.

Aggregated summarised financial information for the associate and joint venture entities is set out below:

	2021 $m	2020 $m	2019 $m
Non-current assets	215	324	298
Current assets	506	552	447
Total liabilities	(99)	(105)	(89)
Net assets	622	771	656
Amount attributable to AstraZeneca	65	38	64
Exchange adjustments	4	1	(6)
Carrying value of investments in associates and joint ventures	69	39	58

12 Other investments

	2021 $m	2020 $m	2019 $m
Non-current investments			
Equity securities at fair value through Other comprehensive income	1,168	1,108	1,339
Fixed income securities at fair value through profit and loss	–	–	62
Total	1,168	1,108	1,401
Current investments			
Fixed income securities at fair value through profit and loss	16	118	811
Fixed deposits	53	42	38
Total	69	160	849

Other investments held at fair value through Other comprehensive income include equity securities which are not held for trading and which the Group has irrevocably elected at initial recognition to recognise in this category. Other investments held at fair value through profit and loss comprise fixed income securities that the Group holds to sell.

The fair value of listed investments is based on year end quoted market prices. Fixed deposits are held at amortised cost with carrying value being a reasonable approximation of fair value given their short-term nature.

Fair value hierarchy

The table below analyses equity securities and bonds, contained within Other investments and carried at fair value, by valuation method. The different levels have been defined as follows:

- Level 1: quoted prices (unadjusted) in active markets for identical assets or liabilities
- Level 2: inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly (i.e. as prices) or indirectly (i.e. derived from prices)
- Level 3: inputs for the asset or liability that are not based on observable market data (unobservable inputs).

	2021 FVPL $m	2021 FVOCI $m	2020 FVPL $m	2020 FVOCI $m	2019 FVPL $m	2019 FVOCI $m
Level 1	16	1,064	118	891	873	1,112
Level 2	–	–	–	–	–	–
Level 3	–	104	–	217	–	227
Total	16	1,168	118	1,108	873	1,339

During 2020, AstraZeneca sold a proportion of its equity portfolio receiving consideration of $1,381m, a large proportion of which related to the disposal of its full holding in Moderna Therapeutics, Inc. All related gains were accounted through Other comprehensive income.

Equity securities that are analysed at Level 3 include investments in private biotech companies. In the absence of specific market data, these unlisted investments are held at fair value based on the cost of investment and adjusting as necessary for impairments and revaluations on new funding rounds, which approximates to fair value. Movements in Level 3 investments are detailed below:

	2021 FVOCI $m	2020 FVOCI $m	2019 FVOCI $m
At 1 January	217	227	166
Additions	1	96	5
Revaluations	–	63	56
Net transfers (out)/in	(113)	(103)	2
Disposals	–	(86)	(5)
Impairments and exchange adjustments	(1)	20	3
At 31 December	104	217	227

Assets are transferred in or out of Level 3 on the date of the event or change in circumstances that caused the transfer.

13 Derivative financial instruments

	Non-current assets $m	Current assets $m	Current liabilities $m	Non-current liabilities $m	Total $m
Interest rate swaps related to instruments designated at fair value through profit and loss	43	–	–	–	43
Cross currency swaps designated in a net investment hedge	4	–	–	(1)	3
Cross currency swaps designated in a cash flow hedge	4	–	–	(17)	(13)
Cross currency swaps designated in a fair value hedge[1]	10	–	–	–	10
Other derivatives	–	36	(36)	–	–
31 December 2019	61	36	(36)	(18)	43

	Non-current assets $m	Current assets $m	Current liabilities $m	Non-current liabilities $m	Total $m
Interest rate swaps related to instruments designated at fair value through profit and loss	45	–	–	–	45
Cross currency swaps designated in a net investment hedge	19	–	–	(2)	17
Cross currency swaps designated in a cash flow hedge	107	43	–	–	150
Cross currency swaps designated in a fair value hedge[1]	–	43	–	–	43
Forward FX designated in a cash flow hedge[2]	–	8	(3)	–	5
Other derivatives	–	48	(30)	–	18
31 December 2020	171	142	(33)	(2)	278

	Non-current assets $m	Current assets $m	Current liabilities $m	Non-current liabilities $m	Total $m
Interest rate swaps related to instruments designated at fair value through profit and loss	25	–	–	–	25
Cross currency swaps designated in a net investment hedge	62	–	–	(2)	60
Cross currency swaps designated in a cash flow hedge	–	–	–	(43)	(43)
Forward FX designated in a cash flow hedge[2]	–	13	–	–	13
Other derivatives	15	70	(79)	–	6
31 December 2021	102	83	(79)	(45)	61

[1] Cross currency swaps designated in a fair value hedge refers to a cross currency interest rate swap that hedges a designated euro 300m portion of our euro 750m 0.875% 2021 non-callable bond against exposure to movements in the euro:US dollar exchange rate. The swap matured in November 2021 when the related bond matured.

[2] Forward FX designated in a cash flow hedge relates to contracts hedging anticipated CNY, EUR, GBP, JPY and SEK transactions occurring in the quarter immediately after the balance sheet date.

All derivatives are held at fair value and fall within Level 2 of the fair value hierarchy as defined in Note 12, except for an equity warrant which falls within Level 3 (valued at $15m, held within Non-current assets). None of the derivatives have been reclassified in the year.

The fair value of interest rate swaps and cross currency swaps is estimated using appropriate zero coupon curve valuation techniques to discount future contractual cash flows based on rates at the current year end.

The fair value of forward foreign exchange contracts and currency options are estimated by cash flow accounting models using appropriate yield curves based on market forward foreign exchange rates at the year end. The majority of forward foreign exchange contracts for existing transactions had maturities of less than one month from year end.

The interest rates used to discount future cash flows for fair value adjustments, where applicable, are based on market swap curves at the reporting date, and were as follows:

	2021	2020	2019
Derivatives	(0.5)% to 3.6%	(0.5)% to 2.4%	(0.5)% to 2.7%

14 Non-current other receivables

	2021 $m	2020 $m	2019 $m
Prepayments	**391**	395	392
Accrued income	**61**	56	10
Other receivables	**443**	269	338
Non-current other receivables	**895**	720	740

Prepayments include $92m (2020: $121m; 2019: $125m) in relation to our research collaboration with Moderna. Other receivables include $nil (2020: $nil; 2019: $118m) of outstanding payments relating to the out-licence of *Duaklir* and *Tudorza* to Circassia in 2017 and $44m (2020: $56m; 2019: $53m) owed by FibroGen for promotional activity in China pursuant to the roxadustat collaboration.

15 Inventories

	2021 $m	2020 $m	2019 $m
Raw materials and consumables	**1,755**	1,262	830
Inventories in process	**5,216**	1,331	1,272
Finished goods and goods for resale	**2,012**	1,431	1,091
Inventories	**8,983**	4,024	3,193

The Group recognised $9,640m (2020: $3,110m; 2019: $2,708m) of inventories as an expense within Cost of sales during the year.

Inventory write-offs in the year amounted to $552m (2020: $149m; 2019: $231m).

16 Current trade and other receivables

	2021 $m	2020 $m	2019 $m
Amounts due within one year			
Trade receivables	**6,054**	3,829	3,606
Less: Amounts provided for doubtful debts (Note 28)	**(23)**	(23)	(21)
	6,031	3,806	3,585
Other receivables	**1,808**	1,278	1,083
Prepayments	**1,512**	1,735	865
Government grants receivable	**–**	53	–
Accrued income	**293**	150	228
Trade and other receivables	**9,644**	7,022	5,761

Trade receivables includes $1,865m (2020: $1,250m; 2019: $892m) measured at FVOCI classified 'hold to collect and sell' as they are due from customers that the Group has the option to factor.

All other financial assets included within current Trade and other receivables are held at amortised cost with carrying value being a reasonable approximation of fair value.

17 Cash and cash equivalents

	2021 $m	2020 $m	2019 $m
Cash at bank and in hand	1,461	1,182	755
Short-term deposits	4,868	6,650	4,614
Cash and cash equivalents	6,329	7,832	5,369
Unsecured bank overdrafts	(291)	(286)	(146)
Cash and cash equivalents in the cash flow statement	6,038	7,546	5,223

The Group holds $nil (2020: $nil; 2019: $1m) of Cash and cash equivalents which is required to meet insurance solvency, capital and security requirements.

AstraZeneca invests in constant net asset value funds and low volatility net asset value funds with same day access for subscription and redemption. These investments fail the 'solely payments of principal and interest' test criteria under IFRS 9. They are therefore measured at fair value through profit and loss, although the fair value will be materially the same as amortised cost.

Non-cash and other movements, within operating activities in the Consolidated Statement of Cash Flows, includes:

	2021 $m	2020 $m	2019 $m
Changes in fair value of put option (Acerta Pharma)	–	–	172
Share-based payments charge for the period	615	277	259
Settlement of share plan awards	(570)	(349)	(323)
Pension contributions	(174)	(172)	(175)
Pension charges recorded in operating profit	136	84	59
Long-term provision charges recorded in operating profit	270	66	506
Non-cash intangible additions	–	(120)	–
Foreign exchange and other	(182)	(62)	(120)
Total operating activities non-cash and other movements	95	(276)	378

18 Assets held for sale

Assets held for sale of $368m (2020: $nil; 2019: $70m) comprise intangible assets relating to the rights to certain respiratory assets acquired from Almirall and Actavis (including *Tudorza* and *Duaklir*). AstraZeneca agreed to dispose of the global rights to *Tudorza* and *Duaklir* to Covis Pharma GmbH on 1 November 2021 with completion of the transaction subject to certain closing conditions and regulatory clearances. The associated contingent consideration liability of $126m is held within current Other payables at 31 December 2021 (see Note 20). The transaction closed and control of the assets transferred on 4 January 2022.

In 2019, Assets held for sale comprised tangible assets relating to the Boulder Manufacturing Centre, which was subsequently sold in May 2020.

19 Interest-bearing loans and borrowings

		Repayment dates	2021 $m	2020 $m	2019 $m
Current liabilities					
Bank overdrafts		On demand	**291**	286	146
Other short-term borrowings excluding overdrafts			**3**	84	8
Bank collateral			**93**	288	71
Lease liabilities			**233**	192	188
2.375% Callable bond	US dollars	2020	–	–	1,597
0.25% Callable bond	euros	2021	–	614	–
0.875% Non-callable bond	euros	2021	–	919	–
Floating rate notes	US dollars	2022	**250**	–	–
2.375% Callable bond	US dollars	2022	**999**	–	–
Other loans (including commercial paper)		Within one year	**24**	3	–
Total			**1,893**	2,386	2,010
Non-current liabilities					
Lease liabilities			**754**	489	487
0.25% Callable bond	euros	2021	–	–	559
0.875% Non-callable bond	euros	2021	–	–	837
Floating rate notes	US dollars	2022	–	250	250
2.375% Callable bond	US dollars	2022	–	996	996
0.3% Callable bond	US dollars	2023	**1,397**	–	–
2023 Floating bank loan	US dollars	2023	**1,998**	–	–
Floating rate notes	US dollars	2023	**400**	400	400
3.5% Callable bond	US dollars	2023	**848**	847	846
7% Guaranteed debentures	US dollars	2023	**320**	339	335
0.75% Callable bond	euros	2024	**1,014**	1,102	1,003
0.7% Callable bond	US dollars	2024	**1,598**	–	–
2024 Floating bank loan	US dollars	2024	**1,997**	–	–
3.375% Callable bond	US dollars	2025	**1,988**	1,985	1,983
0.7% Callable bond	US dollars	2026	**1,193**	1,192	–
1.2% Callable bond	US dollars	2026	**1,245**	–	–
3.125% Callable bond	US dollars	2027	**745**	744	743
1.25% Callable bond	euros	2028	**896**	973	885
1.75% Callable bond	US dollars	2028	**1,244**	–	–
4% Callable bond	US dollars	2028	**994**	993	992
0.375% Callable bond	euros	2029	**898**	–	–
1.375% Callable bond	US dollars	2030	**1,292**	1,291	–
2.25% Callable bond	US dollars	2031	**746**	–	–
5.75% Non-callable bond	pounds sterling	2031	**470**	475	457
6.45% Callable bond	US dollars	2037	**2,724**	2,722	2,721
4% Callable bond	US dollars	2042	**988**	988	987
4.375% Callable bond	US dollars	2045	**980**	980	980
4.375% Callable bond	US dollars	2048	**737**	737	737
2.125% Callable bond	US dollars	2050	**486**	486	–
3% Callable bond	US dollars	2051	**734**	–	–
Other loans	US dollars		**202**	5	19
Total			**28,888**	17,994	16,217
Total interest-bearing loans and borrowings[1,2]			**30,781**	20,380	18,227

1 All loans and borrowings above are unsecured apart from $24m of current and $198m of non-current in 2021, both included within Other loans.

2 The $2bn USD 2023 floating rate loan and $2bn USD 2024 floating rate loan pay interest linked to 3 month LIBOR. The Group has the right to switch these loans to compounded daily USD Secured Overnight Funding Rate (SOFR) with five days notice. The loans will automatically switch to compounded SOFR on 30 June 2023 if the Group has not already switched before this date. All other floating rate debt is not impacted by LIBOR reference as it either uses non-LIBOR fixings or will mature before the relevant LIBOR rate is withdrawn.

	Total loans and borrowings 2021 $m	Total loans and borrowings 2020 $m	Total loans and borrowings 2019 $m
At 1 January	**20,380**	18,227	19,113
Adoption of new accounting standards – Lease liabilities	–	–	720
Changes from financing cash flows			
Issue of loans and borrowings	**12,929**	2,968	500
Repayment of loans and borrowings	**(4,759)**	(1,609)	(1,500)
Movement in short-term borrowings	**(276)**	288	(516)
Repayment of obligations under leases	**(240)**	(207)	(186)
Total changes in cash flows arising on financing activities from borrowings	**7,654**	1,440	(1,702)
Movement in overdrafts	**31**	138	(13)
New lease liabilities	**503**	174	173
Additions through business combinations	**2,523**	–	–
Exchange	**(378)**	363	(62)
Other movements	**68**	38	(2)
At 31 December	**30,781**	20,380	18,227

Set out below is a comparison by category of carrying values and fair values of all the Group's interest-bearing loans and borrowings:

	Instruments in a fair value hedge relationship[1] $m	Instruments designated at fair value[2] $m	Instruments designated in cash flow hedge $m	Amortised cost $m	Total carrying value $m	Fair value $m
2019						
Overdrafts	–	–	–	146	146	146
Lease liabilities due within one year	–	–	–	188	188	188
Lease liabilities due after more than one year	–	–	–	487	487	487
Loans due within one year	–	–	–	1,676	1,676	1,684
Loans due after more than one year	339	335	2,447	12,609	15,730	18,044
Total at 31 December 2019	339	335	2,447	15,106	18,227	20,549
2020						
Overdrafts	–	–	–	286	286	286
Lease liabilities due within one year	–	–	–	192	192	192
Lease liabilities due after more than one year	–	–	–	489	489	489
Loans due within one year	371	–	614	923	1,908	1,922
Loans due after more than one year	–	339	2,075	15,091	17,505	20,936
Total at 31 December 2020	371	339	2,689	16,981	20,380	23,825
2021						
Overdrafts	–	–	–	**291**	**291**	**291**
Lease liabilities due within one year	–	–	–	**233**	**233**	**233**
Lease liabilities due after more than one year	–	–	–	**754**	**754**	**754**
Loans due within one year	–	–	–	**1,369**	**1,369**	**1,378**
Loans due after more than one year	–	**320**	**1,910**	**25,904**	**28,134**	**30,596**
Total at 31 December 2021	–	**320**	**1,910**	**28,551**	**30,781**	**33,252**

[1] Instruments designated as hedged items in a fair value hedge relationship relate to a designated euro 300m portion of our euro 750m 0.875% 2021 non-callable bond which matured on 24 November 2021. The accumulated amount of fair value hedge adjustments to the bond was a loss of $10m.
[2] Instruments designated at fair value through profit or loss include the US dollar 7¼% guaranteed debentures repayable in 2023

The fair value of fixed-rate publicly traded debt is based on year end quoted market prices: the fair value of floating rate debt is nominal value, as mark-to-market differences would be minimal given the frequency of resets. The carrying value of loans designated at fair value through profit or loss is the fair value; this falls within the Level 1 valuation method as defined in Note 12. For loans designated in a fair value hedge relationship, carrying value is initially measured at fair value and remeasured for fair value changes in respect of the hedged risk at each reporting date. All other loans are held at amortised cost. Fair values, as disclosed in the table above, are all determined using the Level 1 valuation method as defined in Note 12, with the exception of overdrafts and lease liabilities, where fair value approximates to carrying values.

During the year, changes to credit risk caused minimal changes to the fair value of bonds designated at fair value through profit or loss. A gain of $29m has been made on these bonds since designation due to increased credit risk. Under IFRS 9, the Group records the component of fair value changes relating to the component of own credit risk through Other comprehensive income. Changes in credit risk had no material effect on any other financial assets and liabilities recognised at fair value in the Group Financial Statements. The change in fair value attributable to changes in credit risk is calculated as the change in fair value not attributable to market risk. The amount payable at maturity on bonds designated at fair value through profit or loss is $287m.

The interest rates used to discount future cash flows for fair value adjustments, where applicable, are based on market swap curves at the reporting date, and were as follows:

	2021	2020	2019
Loans and borrowings	**0.1% to 0.6%**	(0.5)% to 0.1%	(0.5)% to 1.6%

20 Trade and other payables

	2021 $m	2020 $m	2019 $m
Current liabilities			
Trade payables	**2,824**	2,350	1,774
Value-added and payroll taxes and social security	**463**	390	323
Rebates, chargebacks, returns and other revenue accruals	**5,298**	4,772	4,410
Clinical trial accruals	**1,047**	699	736
Other accruals	**5,649**	3,905	4,026
Collaboration Revenue contract liabilities	**12**	12	28
Vaccine contract liabilities	**1,003**	1,616	–
Deferred government grant income	**67**	253	–
Contingent consideration	**849**	647	897
Acerta Pharma share purchase liability (Note 26)	**920**	–	–
Other payables	**806**	1,141	1,793
Total	**18,938**	15,785	13,987
Non-current liabilities			
Accruals	**25**	56	34
Collaboration Revenue contract liabilities	**26**	38	50
Contingent consideration	**2,016**	2,676	3,242
Acerta Pharma share purchase/put option liability (Note 26)	**1,538**	2,297	2,146
Other payables	**1,328**	1,017	819
Total	**4,933**	6,084	6,291

Included within Rebates, chargebacks, returns and other revenue accruals are contract liabilities of $99m (2020: $77m; 2019: $97m). The revenue recognised in the year for contract liabilities is $70m, comprising $58m relating to other revenue accruals and $12m Collaboration Revenue contract liabilities. Significant markets where Rebates, chargebacks, returns and other revenue accruals are seen relate to the US where the liability at 31 December 2021 amounted to $3,172m (2020: $3,126m; 2019: $3,385m) and China where the liability at 31 December 2021 amounted to $814m (2020: $740m; 2019: $452m).

Trade payables includes $44m (2020: $248m; 2019: $492m) due to suppliers that have signed up to a supply chain financing programme, under which the suppliers can elect on an invoice-by-invoice basis to receive a discounted early payment from the relationship bank rather than being paid in line with the agreed payment terms. If the option is taken, the Group's liability is assigned by the supplier to be due to the relationship bank rather than the supplier. The value of the liability payable by the Group remains unchanged. The Group assesses the arrangement against indicators to assess if debts, which vendors have sold to the funder under the supplier financing scheme, continue to meet the definition of trade payables or should be classified as borrowings. At 31 December 2021, the payables met the criteria of Trade payables.

Vaccine contract liabilities relate to amounts received from customers, primarily government bodies, in advance of supply of product. Substantially all of the Vaccine contract liabilities are expected to be recognised as revenue during the next financial year. The revenue recognised in the year related to Vaccine contract liabilities held at the beginning of the year was $1,389m.

Deferred government grant income relates to government grants received or receivable but for which the related expenses have not been incurred.

Included within current Other payables are liabilities to Daiichi Sankyo totalling $nil (2020: $146m; 2019: $795m) resulting from the collaboration agreement in relation to *Enhertu* entered into in March 2019 and $324m (2020: $324m; 2019: $nil) in relation to DS-1062 entered into in July 2020. Additionally, included within non-current Other payables are liabilities totalling $100m (2020: $100m; 2019: $241m) as a result of the *Enhertu* collaboration agreement and $nil (2020: $323m; 2019: $nil) as a result of the DS-1062 collaboration agreement.

In November 2020, *Calquence* received marketing approval in the EU, which removed all remaining conditionality in respect of the Acerta Pharma put and call options regarding the non-controlling interest; the option was exercised in April 2021 (see Note 26). Based on the latest assessment of the expected timing and amount of the Acerta Pharma put option redemption, no remeasurement was required in 2021 or in 2020. In 2019, remeasurement of the liability resulted in an increase in the liability for the year before the effect of interest costs, with the remeasurement taken to Selling, general and administrative expense (see Note 2). In October 2019, an amendment to the share purchase and option agreement (SPOA) with the sellers of Acerta Pharma (originally entered into in December 2015) came into effect, changing certain terms of the SPOA on both the timing and also reducing the maximum consideration that would be required to be made to acquire the remaining outstanding shares of Acerta Pharma if the options were exercised. The payments will be made in similar annual instalments commencing at the earliest from 2022 through to 2024. The changes to the terms have been reflected in the assumptions used to calculate the amortised cost of the liability as at 31 December 2021 of $2,458m (2020: $2,297m; 2019: $2,146m). Interest arising from amortising the liability is included within Finance expense (see Note 3). The associated cash flows will be disclosed as financing activities within the Consolidated Statement of Cash Flows.

With the exception of Contingent consideration payables of $2,865m (2020: $3,323m; 2019: $4,139m) which are held at fair value within Level 3 of the fair value hierarchy as defined in Note 12, all other financial liabilities are held at amortised cost with carrying value being a reasonable approximation of fair value.

Contingent consideration

	2021 $m	2020 $m	2019 $m
At 1 January	3,323	4,139	5,106
Settlements	(643)	(822)	(709)
Revaluations	14	(272)	(614)
Reclassification to Other payables	(55)	–	–
Discount unwind (Note 3)	226	278	356
At 31 December	**2,865**	3,323	4,139

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.

Revaluations of Contingent consideration are recognised in Selling, general and administrative expense and include an increase of $42m in 2021 (2020: a decrease of $51m; 2019: a decrease of $516m) based on revised milestone probabilities, and revenue and royalty forecasts, relating to the acquisition of BMS's share of the Global Diabetes Alliance. Discount unwind on the liability is included within Finance expense (see Note 3).

The discount rate used for the Contingent consideration balances range from 3% to 9%. The most significant Contingent consideration balance is the Global Diabetes Alliance and this is discounted at 8%.

Management has identified that reasonably possible changes in certain key assumptions, including the likelihood of achieving successful trial results, obtaining regulatory approval, the projected market share of the therapy area and expected pricing for launched products, may cause the calculated fair value of the above contingent consideration to vary materially in future years.

SE The contingent consideration balance relating to BMS's share of Global Diabetes Alliance of $2,544m (2020: $2,932m; 2019: $3,300m) would increase/decrease by $254m with an increase/decrease in sales of 10% as compared with the current estimates.

The maximum development and sales milestones payable under outstanding Contingent consideration arrangements arising on business combinations are as follows:

Acquisitions	Year	Nature of contingent consideration	Maximum future milestones $m
Spirogen	2013	Milestones	180
Amplimmune	2013	Milestones	150
Almirall[1]	2014	Milestones and royalties	420

[1] These contingent consideration liabilities have been designated as the hedge instrument in a net investment hedge of foreign currency risk arising on the Group's underlying US dollar net investments held in non-US dollar denominated subsidiaries. Exchange differences on the retranslation of the contingent consideration liability are recognised in Other comprehensive income to the extent that the hedge is effective. Any ineffectiveness is taken to profit.

The amount of royalties payable under the arrangements is inherently uncertain and difficult to predict, given the direct link to future sales and the range of outcomes. The maximum amount of royalties payable in each year is with reference to net sales.

21 Provisions

	Severance $m	Environmental $m	Employee benefits $m	Legal $m	Other provisions $m	Total $m
At 1 January 2019	226	97	119	198	251	891
Charge for year	158	31	18	618	236	1,061
Cash paid	(115)	(39)	(13)	(147)	(24)	(338)
Reversals	(30)	(1)	–	(28)	(17)	(76)
Exchange and other movements	2	8	6	1	9	26
At 31 December 2019	241	96	130	642	455	1,564
Transfers in	–	–	–	–	258	258
Charge for year	116	34	15	16	95	276
Cash paid	(62)	(30)	(48)	(295)	(56)	(491)
Reversals	(69)	–	(2)	(14)	(27)	(132)
Exchange and other movements	8	–	33	(1)	45	85
At 31 December 2020	214	100	128	348	770	1,560
Additions through business combinations (Note 27)	–	–	41	73	27	141
Charge for year	238	23	46	109	456	872
Cash paid	(172)	(32)	(49)	(285)	(84)	(622)
Reversals	(62)	–	–	(5)	(175)	(242)
Exchange and other movements	(6)	(1)	29	(1)	(6)	15
At 31 December 2021	212	90	195	239	988	1,724

	2021 $m	2020 $m	2019 $m
Due within one year	768	976	723
Due after more than one year	956	584	841
Total	1,724	1,560	1,564

21 Provisions *continued*

Severance provisions arise predominantly in connection with global restructuring initiatives which involve rationalisation of the global supply chain, the sales and marketing organisation, IT and business support infrastructure, and R&D.

During 2021, in conjunction with the acquisition of Alexion, the enlarged Group has initiated a comprehensive Post Alexion Acquisition Group Review, aimed at integrating systems, structure and processes, optimising the global footprint and prioritising resource allocations and investments. The Group has also continued to progress other legacy restructuring programmes, including the Global Post-Pandemic New Ways of Working programme that was initiated in 2020 in response to the changing business environment, accelerated by the COVID-19 pandemic.

Employee costs in connection with the initiatives are recognised in severance provisions when a detailed formal plan has been communicated to those employees affected. Final severance costs are often subject to the completion of the requisite consultations on the areas impacted, with the majority of the cost expected to be paid within one year. AstraZeneca endeavours to support employees affected by restructuring initiatives to seek alternative roles within the organisation. Where the employee is successful, any severance provisions will be released.

Details of the Environmental and Legal provisions totalling $90m (2020: $100m; 2019: $96m) and $239m (2020: $348m; 2019: $642m), respectively, and ongoing matters are provided in Note 30. The legal issues are often subject to substantial uncertainties with regard to the timing and final amounts of any payments. As such, once established these provisions remain in Provisions until settlement is reached and uncertainty resolved, with no transfer to Trade and other payables prior to payment. A significant proportion of the total legal provision relates to matters settled, but not paid, in previous periods. These uncertainties can also cause reversal in previously established provisions once final settlement is reached.

The majority of Employee benefit provisions relate to Executive Deferred Compensation Plans.

Other provisions comprise amounts relating to specific contractual or constructive obligations and disputes. Included within Other provisions are amounts associated with long-standing product liability settlements that arose prior to the merger of Astra and Zeneca, which given the nature of the provision, the amounts are expected to be settled over many years. Also included in Other provisions is an amount of $185m (2020: $258m; 2019: $nil), in relation to third-party liability and other risks (including incurred but not yet reported claims) arising on the Group's captive insurance arrangements. The Group revised its presentation of these provisions in 2020; prior to this, the balance had been presented within current Other payables. The claims are considered to be uncertain as to timing and amount and therefore treatment as a provision was deemed more appropriate. Charges to Other provisions in 2021 include $243m in relation to the Post Alexion Acquisition Group Review restructuring programme.

No provision has been released or applied for any purpose other than that for which it was established.

22 Post-retirement and other defined benefit schemes

Background

This section predominantly covers defined benefit arrangements like post-retirement pension and medical plans which make up the vast bulk of the Group's liabilities. However, it also incorporates other benefits which fall under IAS 19 rules and which require an actuarial valuation, including but not limited to: Lump Sum plans, Long Service Awards and defined contribution pension plans which have some defined benefit characteristics (e.g. a minimum guaranteed level of benefit).

The Group and most of its subsidiaries offer retirement plans which cover the majority of employees. The Group's policy is to provide defined contribution (DC) orientated pension provision to its employees unless otherwise compelled by local regulation. As a result, many of these retirement plans are DC, where the Group contribution and resulting charge is fixed at a set level or is a set percentage of employees' pay. However, several plans, mainly in the UK, the US and Sweden, are defined benefit (DB), where benefits are based on employees' length of service and linked to their salary. The major DB plans are largely legacy arrangements as they have been closed to new entrants since 2000, apart from the collectively bargained Swedish plan (which is still open to employees born before 1979). During 2010, following consultation with its UK employees' representatives, the Group introduced a freeze on pensionable pay at 30 June 2010 levels for DB members of the UK Pension Fund. The number of active members in the Fund continues to decline and is now 497 employees. In November 2017, the Group closed the qualified and non-qualified US DB pension plans to future accrual (and removed any salary link) from 31 December 2017.

The major DB plans are funded through separate, fiduciary-administered assets. The cash funding of the plans, which may from time to time involve special Group payments, is designed, in consultation with independent qualified actuaries, to ensure that the assets are sufficient to meet future obligations as and when they fall due. The funding level is monitored by the Group and local fiduciaries, who take into account the strength of the Group's covenant, local regulation, cash flows, and the solvency and maturity of the pension scheme.

Financing Principles and Funding Framework

Ninety per cent of the Group's total DB obligations (or 71% of net obligations) at 31 December 2021 are in schemes within the UK, the US and Sweden. In these countries, the pension obligations are funded in line with the Group's financing principles, as disclosed in prior years. There were no fundamental changes to these principles during 2021.

The Group has developed a long-term funding framework to implement these principles. This framework targets either full funding on a low-risk funding measure or buy-out with an external insurer as the pension funds mature, with affordable long-term de-risking of investment strategy along the way. Unless local regulation dictates otherwise, this framework determines the cash contributions payable.

UK

The UK Pension Fund represents approximately 61% of the Group's DB obligations at 31 December 2021. The financing principles are modified in light of the UK regulatory requirements (summarised below) and resulting discussions with the Trustee.

Role of Trustee and Regulation
The UK Pension Fund is governed and administered by a corporate Trustee which is legally separate from the Group. The Trustee Directors are comprised of representatives appointed by both the employer and employees and include an independent professional Trustee Director. The Trustee Directors are required by law to act in the interest of all relevant beneficiaries and are responsible in particular for investment strategy and the day-to-day administration of the benefits. They are also responsible for jointly agreeing with the employer the level of contributions due to the UK Pension Fund.

The UK pensions market is regulated by The Pensions Regulator whose statutory objectives and regulatory powers are described on its website, www.thepensionsregulator.gov.uk.

The Pension Scheme Act 2021 became effective in the UK from 1 October 2021. A section of this Act places additional legal requirements on companies who sponsor UK defined benefit pension schemes, with a focus on the ongoing security of these benefits. The Group has considered the implications of the Act and developed a framework to ensure it meets its responsibilities on an ongoing basis.

There have been two UK High Court Rulings relating to Guaranteed Minimum Pensions (GMP) equalisation in 2018 and 2020. Following the publication of guidance around implementation in 2021, the Trustee, with input from the Group, has begun the process of equalising benefits, with implementation likely to be in 2023. An estimate of the impact of these changes has already been recognised in 2018 and 2020.

Funding requirements
UK legislation requires that DB pension schemes are funded prudently. On a triennial basis, the Trustee and the Group must agree on a set of assumptions used to value the liabilities as a part of an actuarial valuation. Together with the asset valuation, this facilitates the calculation of a funding level and of the contributions required (if any) to ensure the UK Pension Fund is fully funded over an appropriate time period and on a suitably prudent measure. The technical provisions assumptions used to value the liabilities for the triennial actuarial valuation are usually set more prudently than the assumptions used to prepare an accounting valuation of the liabilities, which are set under IAS 19 rules to be a 'best estimate'.

The last full actuarial valuation of the UK Pension Fund was carried out by a qualified actuary as at 31 March 2019. It was finalised in June 2020 and in early 2021, the Pensions Regulator acknowledged the outcome and no issues were raised. The funding assumptions used in this actuarial valuation were set out in the Group's prior year report. The next actuarial valuation is due to take place as at 31 March 2022, with a likely timescale for completion in early to mid-2023.

Aspects of the triennial actuarial valuation are governed by a long-term funding agreement, effective since October 2016 and which sets out a path to full funding on a low-risk measure. Under this agreement, if a deficit exists, the Group will grant a charge in favour of the Trustee over land and buildings on the Cambridge Biomedical Campus, effective upon practical completion of the site, or from 30 September 2022 (whichever is earlier). This charge is not currently in force. When effective, the charge would only crystallise in the event of the Group's insolvency. This charge will provide long-term security in respect of future UK Pension Fund contributions and will be worth up to £350m.

In relation to deficit recovery contributions, a lump sum contribution of £39m was made in March 2021, with a further £39m contribution due before 31 March 2022. In addition, a contribution of £29m was also made in March 2021, with a final contribution of £30m due before 31 March 2022, in relation to part payment of the deferred contribution explained below.

During 2017, the Group provided a letter of credit to the Trustee, to underwrite the deferral of an additional deficit recovery contribution of approximately £126m which was due in 2017. This contribution will be paid in five instalments (with interest) from March 2018 to March 2022 and to date, four instalments have been paid. The letter of credit underwriting these payments will reduce in value as each annual payment is made.

Under the governing documentation of the UK Pension Fund, any future surplus in the Fund would be returnable to the Group by refund assuming gradual settlement of the liabilities over the lifetime of the Fund. In particular, the Trustee has no unilateral right to wind up the Fund without Company consent nor does it have the power to unilaterally use surplus to augment benefits prior to wind-up. As such, there are no adjustments required in respect of IFRIC14 'IAS 19 – The Limit on a Defined Benefit Asset, Minimum Funding Requirements and their Interaction'.

On current bases, it is expected that ongoing contributions (excluding those in respect of past service deficit contributions) during the year ending 31 December 2022 for the UK scheme will be approximately $19m.

United States and Sweden
The US and Sweden plans account for 11% and 18%, respectively, of the Group's defined benefit obligations. The US and Sweden pension plans are governed by Fiduciary Bodies with responsibility for the investment policies of the assets. These plans are funded in line with the Group's financing principles and local regulations.

The US defined benefit pension plans were actuarially revalued at 31 December 2021, when plan obligations were $1,257m and plan assets were $1,198m. This includes obligations in respect of the non-qualified plan which is unfunded. The qualified US pension plan is fully funded on an IAS 19 basis and has a positive funding balance on the local statutory measure. As such, no contributions are required, and the investment strategy is largely de-risked.

The Swedish defined benefit pension plans were actuarially valued at 31 December 2021, when plan obligations were estimated to amount to $2,373m and plan assets were $1,234m. It should be noted that the Swedish plans have a funding surplus on the local GAAP accounting basis and this influences contribution policy. A deficit recovery contribution of $39m is expected to be paid in 2022.

On current bases, it is expected that ongoing contributions (excluding those in respect of past service deficit contributions) during the year ending 31 December 2022 for the United States and Sweden will be approximately $10m.

22 Post-retirement and other defined benefit schemes *continued*

Other defined benefit plans

The Group provides benefit plans other than pensions which have to be reported under IAS 19. These include Lump Sum plans, Long Service Awards and defined contribution pension plans which have a guaranteed minimum benefit. However, the largest category of these 'other' non-pension plans are healthcare benefits.

In the US, and to a lesser extent in certain other countries, the Group's employment practices include the provision of healthcare and life assurance benefits for eligible retired employees. As at 31 December 2021, some 2,831 retired employees and covered dependants currently benefit from these provisions and some 1,691 current employees will be eligible on their retirement. The Group accrues for the present value of such retiree obligations over the working life of the employee. In practice, these benefits will be funded with reference to the financing principles.

In the US, there was a change to the level of benefit provision for members aged 65 and over within the Group's healthcare plans, effective from 1 January 2021. The changes were communicated to the membership in September 2020 and resulted in an estimated liability reduction of $64m which was recognised as a past service credit for the year ending 31 December 2020. Following these changes, the plans became fully funded on an IAS 19 basis and are projected to have a small surplus. As a result, the investment strategy has been fully de-risked.

The cost of post-retirement benefits other than pensions for the Group in 2021 was $1m (2020: $1m; 2019: $3m). Plan assets were $215m and plan obligations were $170m at 31 December 2021. These benefit plans have been included in the disclosure of post-retirement benefits under IAS 19.

Financial assumptions

Qualified independent actuaries have updated the actuarial valuations under IAS 19 for the major defined benefit schemes operated by the Group to 31 December 2021. The assumptions used may not necessarily be borne out in practice, due to the inherent financial and demographic uncertainty associated with making long-term projections. These assumptions reflect the changes which have the most material impact on the results of the Group and were as follows:

2020	UK	US	Sweden	Rest of Group[4]
Inflation assumption	2.9%	–	1.5%	1.6%
Rate of increase in salaries	–[1]	–	3.0%	3.1%
Rate of increase in pensions in payment	2.8%	–	1.5%	1.6%
Discount rate – defined benefit obligation	1.4%	2.5%	1.2%	0.7%
Discount rate – interest cost	1.1%	1.8%	1.0%	0.5%
Discount rate – service cost	1.4%	1.7%	1.2%	0.8%

2021	UK	US	Sweden	Rest of Group[4]
Inflation assumption	3.3%	–	2.3%	2.2%
Rate of increase in salaries	–[1]	–	3.8%	3.7%
Rate of increase in pensions in payment	3.1%	–	2.3%	2.2%
Discount rate – defined benefit obligation[2]	1.9%	2.8%	1.8%	1.2%
Discount rate – interest cost[3]	1.9%	2.2%	1.6%	1.0%
Discount rate – service cost[3]	1.9%	n/a	1.9%	1.4%

[1] Pensionable pay frozen at 30 June 2010 levels following UK fund changes.
[2] Group defined benefit obligation as at 31 December 2021 calculated using discount rates based on market conditions as at 31 December 2021.
[3] 2021 interest costs and service costs calculated using discount rates based on market conditions as at 31 December 2020.
[4] Rest of Group reflects the assumptions in Germany as these have the most material impact on the Group.

The weighted average duration of the post-retirement scheme obligations is approximately 16 years in the UK, 11 years in the US, 19 years in Sweden and 17 years for the Rest of the Group (including Germany).

Demographic assumptions

The mortality assumptions are based on country-specific mortality tables. These are compared to actual experience and adjusted where sufficient data are available. Additional allowance for future improvements in life expectancy is included for all major schemes where there is credible data to support a continuing trend.

The table below illustrates life expectancy assumptions at age 65 for male and female members retiring in 2021 and male and female members expected to retire in 2041 (2020: 2020 and 2040 respectively).

	Life expectancy assumption for a male member retiring at age 65				Life expectancy assumption for a female member retiring at age 65			
Country	**2021**	**2041**	2020	2040	**2021**	**2041**	2020	2040
UK	**22.5**	**23.7**	22.4	23.7	**23.9**	**25.2**	23.9	25.1
US	**21.9**	**23.2**	21.8	24.5	**23.3**	**24.9**	23.2	26.1
Sweden	**21.9**	**23.6**	21.9	23.6	**24.5**	**25.6**	24.5	25.6

In the UK, the Group adopted the CMI 2020 Mortality Projections Model with a 1% long-term improvement rate. No other demographic assumptions have changed since they were updated in 2019 following the actuarial valuation. The Group has continued to assume that 30% of members (2020: 30%) will transfer out of the defined benefit section of the AstraZeneca Pension Fund at the point of retirement.

The assumption used for the US plans was updated in 2021 to use the mortality tables (MP-2021) that were published during the year.

Risks associated with the Group's defined benefit pension schemes

The UK defined benefit plan accounts for 61% of the Group's defined benefit obligations and exposes the Group to a number of risks, the most significant of which are:

Risk	Description	Mitigation
Volatile asset returns	The Defined Benefit Obligation (DBO) is calculated using a discount rate set with reference to AA-rated corporate bond yields; asset returns that differ from the discount rate will create an element of volatility in the solvency ratio. The UK Pension Fund holds a significant proportion of assets (around 72.5%) in a growth portfolio. Although these growth assets are expected to outperform AA-rated corporate bonds in the long term, they can lead to volatility and mismatching risk in the short term. The allocation to growth assets is monitored to ensure it remains appropriate given the UK Pension Fund's long-term objectives.	In order to mitigate investment risk, the Trustee invests in a suitably diversified range of asset classes, return drivers and investment managers. The investment strategy will evolve to further improve the expected risk/return profile as opportunities arise. The Trustee has hedged approximately 75% of unintended non-sterling, overseas currency risk within the UK Pension Fund assets.
Changes in bond yields	A decrease in corporate bond yields will increase the present value placed on the DBO for accounting purposes.	The interest rate hedge of the UK Pension Fund is implemented via holding gilts and swaps of appropriate duration and set at approximately 96% of total assets and protects to some degree against falls in long-term interest rates (approximately 91% hedged at the end of 2020). There are some differences in the bonds and instruments held by the UK Pension Fund to hedge interest rate risk on the statutory and long-term funding basis (gilts and swaps) and the bonds analysed to set the DBO discount rate on an accounting basis (AA corporate bonds). As such, there remains some mismatching risk on an accounting basis should yields on gilts and swaps diverge compared to AA corporate bonds.
Inflation risk	The majority of the DBO is indexed in line with price inflation (mainly inflation as measured by the UK Retail Price Index (RPI) but also for some members a component of pensions is indexed by the UK Consumer Price Index (CPI)) and higher inflation will lead to higher liabilities (although, in most cases, this is capped at an annual increase of 5%). It was confirmed in November 2020, the intention to align RPI with Consumer Price Index including Housing (CPIH) from 2030. Other things being equal, this will lead to lower liability valuations.	The UK Pension Fund holds RPI index-linked gilts and derivative instruments such as swaps. The inflation hedge of the UK Pension Fund is set at approximately 76% of total assets and protects to some degree against higher-than-expected inflation increases on the DBO (approximately 83% hedged at the end of 2020). There is a framework in place to gradually increase the level of inflation hedging to 100% of assets over time, via a combination of liability management exercises and additional market-based hedging.
Life expectancy	The majority of the UK Pension Fund's obligations are to provide benefits for the life of the member, so increases in life expectancy will result in an increase in the liabilities.	The UK Pension Fund entered into a longevity swap during 2013 which provides hedging against the longevity risk of increasing life expectancy over the next 75 years for around 10,000 of the UK Pension Fund's current pensioners and covers $2.4bn of the UK Pension Fund's liabilities. A one-year increase in life expectancy would result in a $390m increase in pension fund obligations, which would be partially offset by a $203m increase in the value of the longevity swap and hence the pension fund assets. The impact of the COVID-19 pandemic on long-term mortality assumptions is not yet known. The Group will conduct a mortality review once robust data is available.

Other risks

There are a number of other risks of administering the UK Pension Fund including counterparty risks from using derivatives (mitigated by using a specialist investment manager to oversee a diversified range of counterparties of high standing and ensuring positions are collateralised daily). Furthermore, there are operational risks (such as paying out the wrong benefits) and legislative risks (such as the government increasing the burden on companies through new legislation). These are mitigated so far as possible via the governance structure in place which oversees and administers the pension funds.

The Group's pension plans in the US and Sweden also manage these key risks, where they are relevant, in a similar way, with the local fiduciary bodies investing in a diversified manner and employing a framework to hedge interest rate risk.

Local fiduciary boards are aware of Environmental, Social and Governance (ESG) risks as they pertain to investment policy, and where local regulation allows, have policies in place to monitor and manage such risks and comply with local legislation and disclosure requirements.

Assets and obligations of defined benefit schemes

The assets and obligations of the defined benefit schemes operated by the Group at 31 December 2021, as calculated in accordance with IAS 19, are shown below. The fair values of the schemes' assets are not intended to be realised in the short term and may be subject to significant change before they are realised. The present value of the schemes' obligations is derived from cash flow projections over long periods and is therefore inherently uncertain.

22 Post-retirement and other defined benefit schemes *continued*

Scheme assets

2020

	UK		US		Sweden		Rest of Group		Total		
	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Total $m
Government bonds[1]	1,929	–	321	–	–	–	52	–	2,302	–	2,302
Corporate bonds[2]	–	–	878	–	–	–	30	–	908	–	908
Derivatives[3]	–	(170)	–	–	–	333	1	–	1	163	164
Investment funds: Listed Equities[4]	–	1,771	93	90	–	119	72	5	165	1,985	2,150
Investment funds:											
Absolute Return/Multi Strategy[4]	–	2,463	–	72	–	668	12	–	12	3,203	3,215
Investment funds: Corporate Bonds/Credit[4]	–	969	–	80	–	211	39	12	39	1,272	1,311
Cash and cash equivalents	64	153	31	–	–	7	–	4	95	164	259
Other	–	–	–	5	–	–	(1)	355	(1)	360	359
Total fair value of scheme assets[5]	1,993	5,186	1,323	247	–	1,338	205	376	3,521	7,147	10,668

2021

	UK		US		Sweden		Rest of Group		Total		
	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Total $m
Government bonds[1]	2,500	–	303	–	–	–	75	–	2,878	–	2,878
Corporate bonds[2]	–	–	877	–	–	–	16	–	893	–	893
Derivatives[3]	–	(237)	2	(1)	–	259	(1)	–	1	21	22
Investment funds: Listed Equities[4]	–	1,427	–	–	–	134	55	6	55	1,567	1,622
Investment funds:											
Absolute Return/Multi Strategy[4]	–	2,342	–	–	–	647	8	–	8	2,989	2,997
Investment funds: Corporate Bonds/Credit[4]	–	1,006	–	–	–	192	53	11	53	1,209	1,262
Cash and cash equivalents	34	261	227	–	–	2	–	2	261	265	526
Other	–	–	–	5	–	–	1	358	1	363	364
Total fair value of scheme assets[5]	2,534	4,799	1,409	4	–	1,234	207	377	4,150	6,414	10,564

[1] Predominantly developed markets in nature and investment grade (AAA-BBB).

[2] Includes interest rate swaps, inflation swaps, longevity swap, equity total return swaps and other contracts. More detail is given in the section Risks associated with the Group's defined benefit pensions on page 171. Valuations are determined by independent third parties.

[3] Investment Funds are pooled, commingled vehicles, whereby the pension scheme owns units in the fund, alongside other investors. The pension schemes invest in a number of Investment Funds, including Listed Equities (primarily developed markets with some emerging markets), Corporate Bonds/Credit (a range of investment grade and non-investment grade credit) and Absolute Return/Multi Strategy (multi-asset exposure both across and within traditional and alternative asset classes). The price of the funds is set by independent administrators/custodians employed by the investment managers and based on the value of the underlying assets held in the fund. Details of pricing methodology is set out within internal control reports provided for each fund. Prices are updated daily, weekly or monthly depending upon the frequency of the fund's dealing.

[4] Included in scheme assets is $nil (2020: $nil) of the Group's own assets.

Scheme obligations

2020

	UK $m	US $m	Sweden $m	Rest of Group $m	Total $m
Present value of scheme obligations in respect of:					
Active membership	(598)	(99)	(953)	(468)	(2,118)
Deferred membership	(1,887)	(787)	(783)	(504)	(3,961)
Pensioners	(5,940)	(715)	(789)	(347)	(7,791)
Total value of scheme obligations	(8,425)	(1,601)	(2,525)	(1,319)	(13,870)

2021

	UK $m	US $m	Sweden $m	Rest of Group $m	Total $m
Present value of scheme obligations in respect of:					
Active membership	(532)	(81)	(926)	(523)	(2,062)
Deferred membership	(1,709)	(693)	(718)	(465)	(3,585)
Pensioners	(5,700)	(630)	(729)	(312)	(7,371)
Total value of scheme obligations	(7,941)	(1,404)	(2,373)	(1,300)	(13,018)

Net deficit in the scheme

	UK $m	US $m	Sweden $m	Rest of Group $m	2020 Total $m
Total fair value of scheme assets	7,179	1,570	1,338	581	10,668
Total value of scheme obligations	(8,425)	(1,601)	(2,525)	(1,319)	(13,870)
Deficit in the scheme as recognised in the Consolidated Statement of Financial Position	(1,246)	(31)	(1,187)	(738)	(3,202)

	UK $m	US $m	Sweden $m	Rest of Group $m	2021 Total $m
Total fair value of scheme assets	7,333	1,413	1,234	584	10,564
Total value of scheme obligations	(7,941)	(1,404)	(2,373)	(1,300)	(13,018)
Deficit in the scheme as recognised in the Consolidated Statement of Financial Position	(608)	9	(1,139)	(716)	(2,454)

Fair value of scheme assets

	UK $m	US $m	Sweden $m	Rest of Group $m	2021 Total $m	UK $m	US $m	Sweden $m	Rest of Group $m	2020 Total $m
At beginning of year	7,179	1,570	1,338	581	10,668	6,464	1,506	1,123	512	9,605
Interest income on scheme assets	75	27	12	4	118	111	39	14	5	169
Expenses	(7)	–	–	–	(7)	(6)	(2)	–	(1)	(9)
Actuarial gains/(losses)	372	(22)	62	3	415	501	148	84	27	760
Exchange and other adjustments	(77)	(5)	(132)	1	(213)	299	–	162	38	499
Employer contributions	122	19	5	28	174	131	14	2	25	172
Participant contributions	2	–	–	2	4	2	–	–	2	4
Benefits paid	(333)	(176)	(51)	(35)	(595)	(323)	(135)	(47)	(27)	(532)
Scheme assets' fair value at end of year	7,333	1,413	1,234	584	10,564	7,179	1,570	1,338	581	10,668

The actual return on the plan assets was a gain of $533m (2020: gain of $929m).

Movement in post-retirement scheme obligations

	UK $m	US $m	Sweden $m	Rest of Group $m	2021 Total $m	UK $m	US $m	Sweden $m	Rest of Group $m	2020 Total $m
Present value of obligations in scheme at beginning of year	(8,425)	(1,601)	(2,525)	(1,319)	(13,870)	(7,580)	(1,592)	(2,160)	(1,080)	(12,412)
Current service cost	(18)	(2)	(69)	(34)	(123)	(18)	(1)	(59)	(26)	(104)
Past service (cost)/credit	(4)	–	(1)	–	(5)	(9)	64	(2)	(24)	29
Participant contributions	(2)	–	–	(2)	(4)	(2)	–	–	(2)	(4)
Benefits paid	333	176	51	35	595	323	135	47	27	532
Interest expense on post-retirement scheme obligations	(87)	(28)	(22)	(8)	(145)	(130)	(40)	(26)	(10)	(206)
Actuarial gains/(losses)	199	46	(43)	9	211	(637)	(167)	(28)	(96)	(928)
Exchange and other adjustments	63	5	236	19	323	(372)	–	(297)	(108)	(777)
Present value of obligations in scheme at end of year	(7,941)	(1,404)	(2,373)	(1,300)	(13,018)	(8,425)	(1,601)	(2,525)	(1,319)	(13,870)

The obligations arise from the following plans:

	UK $m	US $m	Sweden $m	Rest of Group $m	2021 Total $m	UK $m	US $m	Sweden $m	Rest of Group $m	2020 Total $m
Funded – pension schemes	(7,927)	(1,178)	(2,371)	(1,160)	(12,636)	(8,405)	(1,335)	(2,525)	(603)	(12,868)
Funded – post-retirement healthcare	–	(143)	–	–	(143)	–	(169)	–	–	(169)
Unfunded – pension schemes	–	(83)	(2)	(127)	(212)	–	(97)	–	(696)	(793)
Unfunded – post-retirement healthcare	(14)	–	–	(13)	(27)	(20)	–	–	(20)	(40)
Total	(7,941)	(1,404)	(2,373)	(1,300)	(13,018)	(8,425)	(1,601)	(2,525)	(1,319)	(13,870)

22 Post-retirement and other defined benefit schemes *continued*

Consolidated Statement of Comprehensive Income disclosures

The amounts that have been charged to the Consolidated Statement of Comprehensive Income, in respect of defined benefit schemes for the year ended 31 December 2021, are set out below.

	2021					2020				
	UK $m	US $m	Sweden $m	Rest of Group $m	Total $m	UK $m	US $m	Sweden $m	Rest of Group $m	Total $m
Operating profit										
Current service cost	(18)	(2)	(69)	(35)	(124)	(18)	(1)	(59)	(26)	(104)
Past service (cost)/credit	(4)	–	(1)	–	(5)	(9)	64	(2)	(24)	29
Expenses	(7)	–	–	–	(7)	(6)	(2)	–	(1)	(9)
Total (charge)/credit to Operating profit	(29)	(2)	(70)	(35)	(136)	(33)	61	(61)	(51)	(84)
Finance expense										
Interest income on scheme assets	75	27	12	5	119	111	39	14	5	169
Interest expense on post-retirement scheme obligations	(87)	(28)	(22)	(8)	(145)	(130)	(40)	(26)	(10)	(206)
Net interest on post-employment defined benefit plan liabilities	(12)	(1)	(10)	(3)	(26)	(19)	(1)	(12)	(5)	(37)
(Charge)/credit before taxation	(41)	(3)	(80)	(38)	(162)	(52)	60	(73)	(56)	(121)
Other comprehensive income										
Difference between the actual return and the expected return on the post-retirement scheme assets	372	(22)	62	3	415	501	148	84	27	760
Experience (losses)/gains arising on the post-retirement scheme obligations	(43)	(9)	–	74	22	43	(19)	(24)	(17)	(17)
Changes in financial assumptions underlying the present value of the post-retirement scheme obligations	239	59	(43)	(61)	194	(649)	(160)	(4)	(79)	(892)
Changes in demographic assumptions	3	(4)	–	(4)	(5)	(31)	12	–	–	(19)
Remeasurement of the defined benefit liability	571	24	19	12	626	(136)	(19)	56	(69)	(168)

Past service costs include granting early retirement in the UK and Sweden. Past service cost in 2020 includes a credit of $64m relating to the change in coverage of the US healthcare plans. In addition, the freeze of the Netherlands pension plan effective from 1 January 2021 yielded a past service credit, taken in 2020, of $7m. The past service cost in 2020 also includes costs predominantly related to enhanced pensions in early retirement in the UK and Sweden.

Total Group pension costs in respect of defined contribution and defined benefit schemes during the year are set out below (see Note 29).

	2021 $m	2020 $m
Defined contribution schemes	428	351
Defined benefit schemes – current service costs and expenses	131	113
Defined benefit schemes – past service credit	5	(29)
Pension costs	564	435

SE Rate sensitivities

The following table shows the US dollar effect of a change in the significant actuarial assumptions used to determine the retirement benefits obligations in our three main defined benefit pension obligation countries.

	2021		2020	
Discount rate	+0.5%	-0.5%	+0.5%	-0.5%
UK ($m)	565	(634)	610	(687)
US ($m)	79	(84)	93	(99)
Sweden ($m)	197	(226)	214	(246)
Total ($m)	841	(944)	917	(1,032)

	2021		2020	
Inflation rate[1]	+0.5%	-0.5%	+0.5%	-0.5%
UK ($m)	(386)	375	(396)	378
US ($m)	n/a	n/a	n/a	n/a
Sweden ($m)	(207)	196	(245)	216
Total ($m)	(593)	571	(641)	594

	2021		2020	
Rate of increase in salaries	+0.5%	-0.5%	+0.5%	-0.5%
UK ($m)	n/a	n/a	n/a	n/a
US ($m)	n/a	n/a	n/a	n/a
Sweden ($m)	(90)	82	(62)	70
Total ($m)	(90)	82	(62)	70

	2021		2020	
Mortality rate	**+1 year**	**–1 year**	**+1 year**	**–1 year**
UK ($m)	(390)[2]	388[3]	(396)	395
US ($m)	(29)	29	(32)	32
Sweden ($m)	(94)	93	(106)	96
Total ($m)	**(513)**	**510**	(534)	523

[1] Rate of increase in pensions in payment follows inflation.
[2] Of the $390m increase, $203m is covered by the longevity swap.
[3] Of the $388m decrease, $203m is covered by the longevity swap.

The sensitivity to the financial assumptions shown above has been estimated taking into account the approximate duration of the liabilities and the overall profile of the plan membership.

The inflation sensitivity allows for the impact of a change in inflation on salary increases and pension increases (where these assumptions are inflation-linked).

The salary increase sensitivity reflects the impact of an increase of only salary relative to inflation.

The sensitivity to the life expectancy assumption is estimated based on a revised mortality assumption that extends/reduces the current life expectancy by one year for a particular age.

23 Reserves

Retained earnings

The cumulative amount of goodwill written off directly to reserves resulting from acquisitions, net of disposals, amounted to $615m (2020: $636m; 2019: $614m) using year-end rates of exchange.

At 31 December 2021, 3,922,122 shares, at a cost of $239m, have been deducted from Retained earnings (2020: 556,106 shares, at a cost of $51m; 2019: 907,239 shares, at a cost of $37m) to satisfy future vesting of employee share plans.

There are no significant statutory or contractual restrictions on the distribution of current profits of subsidiaries; undistributed profits of prior years are, in the main, permanently employed in the businesses of these companies. The undistributed income of AstraZeneca companies overseas might be liable to overseas taxes and/or UK taxation (after allowing for double taxation relief) if they were to be distributed as dividends (see Note 4).

	2021 $m	2020 $m	2019 $m
Cumulative translation differences included within Retained earnings			
At 1 January	(1,143)	(2,189)	(2,007)
Foreign exchange arising on consolidation	(483)	443	40
Exchange adjustments on goodwill (recorded against other reserves)	(21)	22	(5)
Foreign exchange arising on designated borrowings in net investment hedges[1]	(321)	573	(252)
Fair value movements on derivatives designated in net investment hedges	34	8	35
Net exchange movement in Retained earnings	(791)	1,046	(182)
At 31 December	(1,934)	(1,143)	(2,189)

Foreign exchange arising on designated borrowings in net investment hedges includes $100m in respect of designated bonds and $(421)m in respect of designated contingent consideration and other liabilities. The change in value of designated contingent consideration liabilities relates to $(266)m in respect of BMS' share of Global Diabetes Alliance, $(5)m in respect of Almirall and $(150)m in relation to the Acerta Pharma share purchase liability.

The cumulative gain with respect to costs of hedging is $4m (2020: $9m; 2019: $nil) and the loss during the year was $6m (2020: gain of $9m; 2019: loss of $47m).

The balance remaining in the foreign currency translation reserve from net investment hedging relationships for which hedge accounting no longer applied is a gain of $527m.

Other reserves

The Other reserves arose from the cancellation of £1,255m of share premium account by the Company in 1993 and the redenomination of share capital of $157m in 1999. The reserves are available for writing off goodwill arising on consolidation and, subject to guarantees given to preserve creditors at the date of the court order, are available for distribution.

24 Share capital

	Allotted, called-up and fully paid		
	2021 $m	2020 $m	2019 $m
Issued Ordinary Shares ($0.25 each)	387	328	328
Redeemable Preference Shares (£1 each – £50,000)	–	–	–
At 31 December	**387**	328	328

The Redeemable Preference Shares carry limited class voting rights and no dividend rights. This class of shares is capable of redemption at par at the option of the Company on the giving of seven days' written notice to the registered holder of the shares.

The Company does not have a limited amount of authorised share capital.

The movements in the number of Ordinary Shares during the year can be summarised as follows:

	No. of shares		
	2021	2020	2019
At 1 January	1,312,668,724	1,312,137,976	1,267,039,436
Issue of shares (share placing)	–	–	44,386,214
Issue of share capital (business combinations)	236,321,411	–	–
Issue of shares (share schemes)	410,530	530,748	712,326
At 31 December	1,549,400,665	1,312,668,724	1,312,137,976

Share issues
Issue of share capital (business combinations) represents share capital issued as part of the acquisition of Alexion (see Note 27).

Share repurchases
No Ordinary Shares were repurchased by the Company in 2021 (2020:nil; 2019:nil).

Shares held by subsidiaries
No shares in the Company were held by subsidiaries in any year.

25 Dividends to shareholders

	2021 Per share	2020 Per share	2019 Per share	2021 $m	2020 $m	2019 $m
Second interim (March 2021)	$1.90	$1.90	$1.90	2,490	2,489	2,403
First interim (September 2021)	$0.90	$0.90	$0.90	1,392	1,180	1,180
Total	$2.80	$2.80	$2.80	3,882	3,669	3,583

The Company has exercised its authority in accordance with the provisions set out in the Company's Articles of Association, that the balance of unclaimed dividends outstanding past 12 years be forfeited. $nil (2020: $1m; 2019: $4m) of unclaimed dividends have been adjusted for in Retained earnings in 2021.

The 2020 second interim dividend of $1.90 per share was paid on 29 March 2021. The 2021 first interim dividend of $0.90 per share was paid on 13 September 2021.

Reconciliation of dividends charged to equity to cash flow statement:

	2021 $m	2020 $m	2019 $m
Dividends charged to equity	3,882	3,669	3,583
Exchange losses on payment of dividend	3	4	5
Hedge contracts relating to payment of dividends (cash flow statement)	(29)	(101)	4
Dividends paid (cash flow statement)	3,856	3,572	3,592

26 Non-controlling interests

The Group Financial Statements at 31 December 2021 reflect equity of $19m (2020: $16m; 2019: $13m) and total comprehensive income of $3m (2020: $3m; 2019: $4m) attributable to the non-controlling interests in AstraZeneca Pharma India Limited, P.T. AstraZeneca Indonesia and Beijing Falikang Pharmaceutical (China) Co. Limited.

In addition to the non-controlling interests in AstraZeneca Pharma India Limited, P.T. AstraZeneca Indonesia and Beijing Falikang Pharmaceutical (China) Co. Limited, the Group Financial Statements at 31 December 2021 also reflect equity of $nil (2020: $nil; 2019: $1,456m) and total comprehensive losses of $nil (2020: $55m; 2019: $111m) attributable to the non-controlling interest in Acerta Pharma, resulting in reported total comprehensive income of $3m (2020: losses of $52m; 2019: losses of $107m).

In February 2016, AstraZeneca acquired a 55% controlling stake in Acerta Pharma where the non-controlling interest was subject to put and call options. The put option gave rise to a liability (see Note 20). The ability of the parties to exercise their respective put and call options, as well as the timing and amount of exercise, was dependent on certain conditions, the last of which was based on regulatory outcomes of *Calquence* (acalabrutinib) in the EU. In November 2020, *Calquence* received marketing approval in the EU, which removed all remaining conditionality in respect of the options. From November 2020, the minority shareholders were considered to have no further substantive variability in risk and reward related to their shares as it was considered highly likely that one of the options would be exercised, and the price of the options was fixed. Therefore, from November 2020, no further amounts of the consolidated AstraZeneca result were attributed to the minority shareholders of Acerta Pharma. The Non-controlling interests reserve relating to the minority shareholders of Acerta Pharma, totalling $1,401m, was reclassified into Retained earnings (see Consolidated Statement of Changes in Equity) in 2020. AstraZeneca exercised its option to acquire the remaining 45% of shares in Acerta Pharma in April 2021.

The following summarised financial information, for Acerta Pharma and its subsidiaries, prior to full consolidation in 2020, is presented on a standalone basis since the acquisition date, and before the impact of Group-related adjustments, some of which are incorporated into the calculation of the loss attributable to the non-controlling interests:

	2019 $m
Total Revenue	–
Loss after tax	(422)
Other comprehensive income	–
Total comprehensive loss	(422)

	2019 $m
Non-current assets	157
Current assets	475
Total assets	632
Current liabilities	(310)
Non-current liabilities	(267)
Total liabilities	(577)
Net assets	55

	2019 $m
Net cash outflow from operating activities	(13)
Net cash inflow from investing activities	7
Net cash inflow from financing activities	7
Increase in cash and cash equivalents in the year	1

As part of the acquisition of Alexion in July 2021, a pre-existing non-controlling interest in Caelum Biosciences was recognised (Note 27). This was valued at $150m, the agreed upon exercise price for the exclusive option to acquire the remaining equity. The option was exercised on 28 September 2021 and the acquisition of Caelum Biosciences closed shortly thereafter on 5 October 2021.

27 Acquisition of business operations

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.

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.

As part of the Alexion acquisition in 2021, we identified the assets (comprising principally launched products and post pre-clinical stage) and liabilities acquired. Attributing fair values to assets acquired and liabilities assumed as part of business combinations is considered to be a key judgement. The purchase price allocation was performed with assistance from an independent valuer to advise on the valuation techniques and key assumptions in the valuation, in particular in respect of the valuation of the intangible assets and inventory.

The fair values assigned to the Alexion business combination in 2021 were:

	Fair value $m
Non-current assets	
Property, plant and equipment	1,135
Right-of-use assets	263
Intangible assets	26,855
Other non-current assets	301
	28,554
Current assets	
Inventories	6,769
Trade and other receivables	2,096
Intangible assets	100
Cash and cash equivalents	4,086
	13,051
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	32,921
Less: non-controlling interests	(150)
Goodwill	8,287
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

The estimated fair value and useful lives of intangible assets were as follows:

	Fair value $m	Useful lives Years
Launched products – C5 franchise (*Soliris/Ultomiris*)	18,480	6 to 15
Launched products – *Strensiq, Kanuma, Andexxa*	5,215	11 to 17
Products in development	2,760	Not amortised
Other intangibles	500	5 to 10
	26,955	

The fair value attributed to intangible assets was $26,955m and primarily represents intellectual property rights over launched products $23,695m and products under development $2,760m. These were fair valued using the multi-period excess earnings method, which uses a number of estimates regarding the amount and timing of future cash flows. The key assumptions in the cash flows are PTRS, peak year sales and revenue erosion curves. In accordance with the Group's policy on impairment assessments as set out on page 144, the assets were assessed for impairment in Q4 2021. Future milestones have been included in the valuation of the intangible assets (as a deduction of cash flows).

The fair value of inventory, which includes raw materials, work in progress and finished goods related to the launched products was estimated at $6,769m, an uplift of $5,635m 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 costs to complete and sell the inventory, 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 $1,135m represents an uplift of $111m 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, and involve an assessment of the likelihood of a number of scenarios in relation to those matters. 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 deferred 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 $8,287m 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 upon exercise price for the exclusive option to acquire the remaining equity. The option was exercised on 28 September 2021 and the acquisition of Caelum Biosciences closed shortly thereafter on 5 October 2021 (Note 26).

Alexion's results have been consolidated into the Group's results from 21 July 2021. For the period from acquisition to 31 December 2021, before reflecting the fair value adjustments arising on the acquisition, Alexion's Total Revenues were $3,071m and Profit after tax was $889m. 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 the acquisition, the Total Revenue of the combined Group for the year ended 31 December 2021 would have been $41,132m and the Loss after tax would have been $1,152m. 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 $171m 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 expense.

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 six months after the acquisition, or earlier. In the period since acquisition, a cost of $24m has been recorded in the Statement of Comprehensive Income ($2m in Cost of sales, $9m in Research and development expense and $13m in Selling, general and administrative expense).

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 $257m has been recorded in the Statement of Comprehensive Income ($9m in Cost of sales, $73m in Research and development expense and $175m in Selling, general and administrative expense). Payments made to the Employee Benefit Trust 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 Consolidated Statement of Cash Flows.

28 Financial risk management objectives and policies

The Group's principal financial instruments, other than derivatives, comprise bank overdrafts, loans and other borrowings, lease liabilities, current and non-current investments, cash and short-term deposits. The main purpose of these financial instruments is to manage the Group's funding and liquidity requirements. The Group has other financial assets and liabilities such as trade receivables and trade payables, which arise directly from its operations.

The principal financial risks to which the Group is exposed are those of liquidity, interest rate, foreign currency and credit. Each of these is managed in accordance with Board-approved policies. These policies, together with the Group's approach to capital management, are set out below.

Hedge accounting

The Group uses foreign currency borrowings, foreign currency forwards and swaps, currency options, interest rate swaps and cross-currency interest rate swaps for the purpose of hedging its foreign currency and interest rate risks. The Group may designate certain financial instruments as fair value hedges, cash flow hedges or net investment hedges in accordance with IFRS 9. Hedge effectiveness is determined at the inception of the hedge relationship, and through periodic prospective effectiveness assessments to ensure that an economic relationship exists between the hedged item and hedging instrument. Sources of hedge effectiveness will depend on the hedge relationship designation but may include:

- a significant change in the credit risk of either party to the hedging relationship
- a timing mismatch between the hedging instrument and the hedged item
- movements in foreign currency basis spread for derivatives in a fair value hedge
- a significant change in the value of the foreign currency denominated net assets of the Group in a net investment hedge.

The hedge ratio for each designation will be established by comparing the quantity of the hedging instrument and the quantity of the hedged item to determine their relative weighting; for all of the Group's existing hedge relationships the hedge ratio has been determined as 1:1. Designated hedges are expected to be effective and therefore the impact of ineffectiveness on profit is not expected to be material. The accounting treatment for fair value hedges and debt designated as fair value through profit or loss is disclosed in the Group Accounting Policies section from page 138.

The following table represents the Group's continuing designated hedge relationships under IFRS 9:

2019

			Other comprehensive income						
	Nominal amounts in local currency	Carrying value $m	Opening balance 1 January 2019 $m	Fair value (gain)/loss deferred to OCI $m	Fair value loss recycled to the income statement $m	Closing balance 31 December 2019 $m	Average maturity year	Average USD FX rate	Average pay interest rate
Fair value hedge – foreign currency and interest rate risk[1]									
Cross currency interest rate swap – Euro bond	EUR 300m	10	–	–	–	–	2021	1.09	USD LIBOR + 1.27%
Cash flow hedges – foreign currency and interest rate risk[2,4]									
Cross currency interest rate swaps – Euro bonds	EUR 2,200m	(13)	(92)	114	(52)	(30)	2025	1.14	USD 2.69%
Net investment hedge – foreign exchange risk[3,4]									
Transactions matured pre 2019		–	(356)	–	–	(356)	–	–	–
Cross currency interest rate swap – JPY investment[5]	JPY 58.5bn	–	(213)	4	–	(209)	2019	78.01	JPY 0.35%
Cross currency interest rate swap – JPY investment	JPY 58.3bn	4	–	(4)	–	(4)	2029	106.03	JPY 1.53%
Cross currency interest rate swap – CNY investment	CNY 456m	(1)	4	(3)	–	1	2026	6.68	CNY 4.80%
Foreign currency borrowing – GBP investment	GBP 350m	(457)	(265)	14	–	(251)	2031	n/a	GBP 5.75%
Foreign currency borrowing – EUR investment	EUR 450m	(498)	44	(10)	–	34	2021	n/a	EUR 0.88%
Contingent consideration liabilities and Acerta Pharma put option liability – AZUK and AZAB USD investments	USD 5,583m	(5,583)	1,805	248	–	2,053	–	–	–

2020

	Nominal amounts in local currency	Carrying value $m	Other comprehensive income: Opening balance 1 January 2020 $m	Other comprehensive income: Fair value (gain)/loss deferred to OCI $m	Other comprehensive income: Fair value loss recycled to the income statement $m	Other comprehensive income: Closing balance 31 December 2020 $m	Average maturity year	Average USD FX rate	Average pay interest rate
Fair value hedge – foreign currency and interest rate risk[1]									
Cross currency interest rate swap – Euro bond	EUR 300m	43	–	–	–	–	2021	1.09	USD LIBOR + 1.27%
Cash flow hedges – foreign currency and interest rate risk[2,4,6]									
Cross currency interest rate swaps – Euro bonds	EUR 2,200m	150	(30)	(163)	239	46	2025	1.14	USD 2.69%
FX Forwards – short term FX risk	USD 618m	5	–	(20)	15	(5)	2021	–	–
Net investment hedge – foreign exchange risk[3,4]									
Transactions matured pre 2020		–	(565)	–	–	(565)	–	–	–
Cross currency interest rate swap – JPY investment	JPY 58.5bn	19	(4)	(15)	–	(19)	2029	108.03	JPY 1.53%
Cross currency interest rate swap – CNY investment	CNY 458m	(2)	1	1	–	2	2026	6.68	CNY 4.80%
Foreign currency borrowing – GBP investment	GBP 350m	(475)	(251)	18	–	(233)	2031	n/a	GBP 5.75%
Foreign currency borrowing – EUR investment	EUR 450m	(548)	34	51	–	85	2021	n/a	EUR 0.88%
Contingent consideration liabilities and Acerta Pharma put option liability – AZUK and AZAB USD investments	USD 5,252m	(5,252)	2,053	(642)	–	1,411	–	–	–

2021

	Nominal amounts in local currency	Carrying value $m	Other comprehensive income: Opening balance 1 January 2021 $m	Other comprehensive income: Fair value (gain)/loss deferred to OCI $m	Other comprehensive income: Fair value gain recycled to the income statement $m	Other comprehensive income: Closing balance 31 December 2021 $m	Average maturity year	Average USD FX rate	Average pay interest rate
Fair value hedge – foreign currency and interest rate risk[1]									
Cross currency interest rate swap – Euro bond	–	–	–	–	–	–	–	–	–
Cash flow hedges – foreign currency and interest rate risk[2,4,6]									
Cross currency interest rate swaps – Euro bonds	**EUR 1,700m**	(43)	46	182	(201)	27	2026	1.14	**USD 2.85%**
FX Forwards – short term FX risk	**USD 1,220m**	12	(5)	–	(7)	(12)	2022	–	–
Net investment hedge – foreign exchange risk[3,4]									
Transactions matured pre 2021		–	(565)	–	–	(565)	–	–	–
Cross currency interest rate swap – JPY investment	**JPY 58.3bn**	62	(19)	(43)	–	(62)	2029	108.03	**JPY 1.53%**
Cross currency interest rate swap – CNY investment	**CNY 458m**	(2)	2	–	–	2	2026	6.68	**CNY 4.80%**
Foreign currency borrowing – GBP investment	**GBP 350m**	470	(233)	(5)	–	(238)	2031	n/a	**GBP 5.75%**
Foreign currency borrowing – EUR investment[7]	**EUR 450m**	–	85	(47)	–	38	2021	n/a	**EUR 0.88%**
Foreign currency borrowing – EUR investment[8]	**EUR 800m**	898	–	(50)	–	(50)	2029	n/a	**EUR 0.38%**
Contingent consideration liabilities and Acerta Pharma share purchase liability – AZUK and AZAB USD investments	**USD 2,658m**	(2,658)	1,411	421	–	1,832	–	–	–

[1] Swaps designated in a fair value hedge matured on 24 November 2021 and hedge ineffectiveness during the period was $nil (2020: gain of $1m).
[2] Hedge ineffectiveness recognised on swaps designated in a cash flow hedge during the period was $nil (2020: $nil).
[3] Hedge ineffectiveness recognised on swaps designated in a net investment hedge during the period was $nil (2020: $nil).
[4] Fair value movements on cross currency interest rate swaps in cash flow hedge and net investment hedge relationships are shown inclusive of the impact of costs of hedging.
[5] In September 2019, the maturity of our JPY 58.5bn cross currency interest rate swap resulted in a net cash inflow of $209m. The cash flow associated with the settlement has been reflected in cash flows from investing activities within the Consolidated Statement of Cash Flows on page 137, as its primary purpose was to hedge the translation foreign exchange risk arising on the consolidation of the Group's net investment in Japan.
[6] Nominal amount of FX forwards in a cash flow hedge of $1,220m represents the USD equivalent notional of the FX forwards. By currency, the nominal amounts were RMB 666m at FX rate 6.373, SEK 3,929m at 9.0742, JPY 29,289m at 115.1550, GBP 278m at 1.3506 and EUR 123m at 1.1306. All FX forwards in a cash flow hedge mature on 25 January 2022.
The EUR 450m net investment hedge matured in November 2021, when the hedging instrument, a EUR bond, matured.
[7] On 3 June 2021, upon issuance of the EUR 800m 0.375% 2029 non-callable bond, EUR 550m was designated in a net investment hedge of the foreign currency exposure in relation of an equivalent amount of EUR-denominated net assets. The remaining EUR 250m was subsequently designated in a net investment hedge upon maturity of the EUR 450m bond on 24 November 2021.

Key controls applied to transactions in derivative financial instruments are to use only instruments where good market liquidity exists, to revalue all financial instruments regularly using current market rates and to sell options only to offset previously purchased options or as part of a risk management strategy. The Group is not a net seller of options, and does not use derivative financial instruments for speculative purposes. The Group held no options during the reporting period.

Capital management

The capital structure of the Group consists of Shareholders' equity (Note 24), Debt (Note 19), Other current investments (Note 12) and Cash (Note 17). For the foreseeable future, the Board will maintain a capital structure that supports the Group's strategic objectives through:

- managing funding and liquidity risk
- optimising shareholder return
- maintaining a strong, investment-grade credit rating.

28 Financial risk management objectives and policies *continued*

The Group utilises factoring arrangements for selected trade receivables. These factoring arrangements qualify for full derecognition of the associated trade receivables under IFRS 9. Amounts due on invoices that have not been factored at year end, from customers that are subject to factoring arrangements, are disclosed in Note 16.

Funding and liquidity risk are reviewed regularly by the Board and managed in accordance with policies described below.

The Board's distribution policy comprises a regular cash dividend and, subject to business needs, a share repurchase component. The Board regularly reviews its shareholders' return strategy, and, in 2012, decided to suspend share repurchases in order to retain strategic flexibility.

The Group's net debt position (loans and borrowings net of Cash and cash equivalents, Other investments and Derivative financial instruments) has increased from a net debt position of $12,110m at the beginning of the year to a net debt position of $24,322m at 31 December 2021. The increase in net debt was principally due to the acquisition of Alexion.

Liquidity risk

The Board reviews the Group's ongoing liquidity risks annually as part of the planning process and on an ad hoc basis. The Board considers short-term requirements against available sources of funding, taking into account forecast cash flows. The Group manages liquidity risk by maintaining access to a number of sources of funding which are sufficient to meet anticipated funding requirements. Specifically, the Group uses US and European commercial paper, bank loans, committed bank facilities and cash resources to manage short-term liquidity and manages long-term liquidity by raising funds through the capital markets. At 31 December 2021, the Group was assigned short-term credit ratings of P-2 by Moody's and A-2 by Standard and Poor's. The Group's long-term credit rating was A3 Negative outlook by Moody's and A- Stable outlook by Standard and Poor's.

In addition to Cash and cash equivalents of $6,329m, short-term fixed income investments of $16m, fixed deposits of $53m, less overdrafts of $291m at 31 December 2021, the Group has committed bank facilities of $4,875m available to manage liquidity. The commitments mature in April 2025. None of the above facilities contain any financial covenants. The Group regularly monitors the credit standing of the banking group and currently does not anticipate any issue with drawing on the committed facilities should this be necessary. Advances under these facilities currently bear an interest rate per annum based on US dollar LIBOR (or other relevant benchmark rate) plus a margin. The facilities contain arrangements to switch to alternative risk free rate benchmarks before June 2023.

At 31 December 2021, the Group has $3,278m outstanding from debt issued under a Euro Medium Term Note programme and $21,908m under a SEC-registered programme. The funds made available under these facility agreements may be used for the general corporate purposes of the Group.

The maturity profile of the anticipated future contractual cash flows including interest in relation to the Group's financial liabilities, on an undiscounted basis and which, therefore, differs from both the carrying value and fair value, is as follows:

	Bank overdrafts and other loans $m	Bonds $m	Lease liability $m	Trade and other payables $m	Total non-derivative financial instruments $m	Derivative financial instruments receivable $m	Derivative financial instruments payable $m	Total derivative financial instruments $m	Total $m
Within one year	234	2,207	205	14,054	16,700	(11,956)	11,985	29	16,729
In one to two years	14	1,970	158	1,769	3,911	(955)	976	21	3,932
In two to three years	–	1,810	117	1,811	3,738	(54)	67	13	3,751
In three to four years	–	2,068	79	1,592	3,739	(54)	67	13	3,752
In four to five years	–	1,479	50	1,652	3,181	(1,051)	1,079	28	3,209
In more than five years	–	15,906	128	1,052	17,086	(1,648)	1,654	6	17,092
	248	25,440	737	21,930	48,355	(15,718)	15,828	110	48,465
Effect of interest	(1)	(8,038)	–	–	(8,039)	409	(488)	(79)	(8,118)
Effect of discounting, fair values and issue costs	(3)	(94)	(62)	(1,619)	(1,778)	(20)	(54)	(74)	(1,852)
31 December 2019	244	17,308	675	20,311	38,538	(15,329)	15,286	(43)	38,495

	Bank overdrafts and other loans $m	Bonds $m	Lease liability $m	Trade and other payables $m	Total non-derivative financial instruments $m	Derivative financial instruments receivable $m	Derivative financial instruments payable $m	Total derivative financial instruments $m	Total $m
Within one year	667	2,136	207	15,812	18,822	(9,719)	9,620	(99)	18,723
In one to two years	–	1,839	168	2,584	4,591	(60)	67	7	4,598
In two to three years	–	2,101	120	1,656	3,879	(59)	67	8	3,887
In three to four years	–	1,617	82	1,728	3,427	(1,151)	1,080	(71)	3,356
In four to five years	–	2,502	53	722	3,277	(36)	40	4	3,281
In more than five years	–	16,921	108	1,435	18,464	(1,707)	1,652	(55)	18,409
	667	27,116	738	23,939	52,460	(12,732)	12,526	(206)	52,254
Effect of interest	–	(7,974)	–	–	(7,974)	379	(405)	(26)	(8,000)
Effect of discounting, fair values and issue costs	(1)	(109)	(57)	(2,070)	(2,237)	(70)	24	(46)	(2,283)
31 December 2020	666	19,033	681	21,869	42,249	(12,423)	12,145	(278)	41,971

	Bank overdrafts and other loans $m	Bonds $m	Lease liability $m	Trade and other payables $m	Total non-derivative financial instruments $m	Derivative financial instruments receivable $m	Derivative financial instruments payable $m	Total derivative financial instruments $m	Total $m
Within one year	387	1,981	256	19,007	21,631	(11,766)	11,774	8	21,639
In one to two years	–	5,647	210	2,521	8,378	(55)	66	11	8,389
In two to three years	–	5,242	163	1,669	7,074	(1,060)	1,079	19	7,093
In three to four years	–	2,591	130	862	3,583	(35)	39	4	3,587
In four to five years	–	2,970	96	233	3,299	(118)	111	(7)	3,292
In more than five years	–	19,727	221	2,212	22,160	(1,521)	1,480	(41)	22,119
	387	38,158	1,076	26,504	66,125	(14,555)	14,549	(6)	66,119
Effect of interest	–	(8,609)	–	–	(8,609)	299	(325)	(26)	(8,635)
Effect of discounting, fair values and issue costs	–	(142)	(89)	(2,633)	(2,864)	(36)	7	(29)	(2,893)
31 December 2021	387	29,407	987	23,871	54,652	(14,292)	14,231	(61)	54,591

* The maturity profile table has been amended in 2019 to show gross derivative flows and to include all derivatives shown in Note 13 on page 161. In previous periods the table separately disclosed the net cash flows on interest rate swaps and cross currency swaps.

Where interest payments are on a floating rate basis, it is assumed that rates will remain unchanged from the last business day of each year ended 31 December.

The Group has $2bn of bank loans that mature in July 2023 and $2bn of bank loans that mature in July 2024, which the Group can repay before maturity at face value. Other than that, it is not expected that the cash flows in the maturity profile could occur significantly earlier or at significantly different amounts, with the exception of $2.865m of contingent consideration held within Trade and other payables (see Note 20).

Market risk

Interest rate risk

The Group maintains a Board approved mix of fixed and floating rate debt and uses underlying debt, interest rate swaps and forward rate agreements to manage this mix.

At 31 December 2021, interest rate swaps with a notional value of $288m are fair valued through profit or loss and this has effectively converted the 7% guaranteed debentures payable in 2023 to floating rates. No new interest rate swaps were entered into during 2021.

The majority of surplus cash is currently invested in US dollar liquidity funds and investment-grade fixed income securities.

The interest rate profile of the Group's interest-bearing financial instruments are set out below. In the case of current and non-current financial liabilities, the classification includes the impact of interest rate swaps which convert the debt to floating rate.

	2021			2020			2019		
	Fixed rate $m	Floating rate $m	Total $m	Fixed rate $m	Floating rate $m	Total $m	Fixed rate $m	Floating rate $m	Total $m
Financial liabilities									
Interest-bearing loans and borrowings									
Current	1,232	661	1,893	1,357	1,029	2,386	1,785	225	2,010
Non-current	23,985	4,903	28,888	17,005	989	17,994	14,893	1,324	16,217
Total	25,217	5,564	30,781	18,362	2,018	20,380	16,678	1,549	18,227
Financial assets									
Fixed deposits	53	–	53	42	–	42	38	–	38
Cash and cash equivalents	–	6,329	6,329	–	7,832	7,832	–	5,369	5,369
Total	53	6,329	6,382	42	7,832	7,874	38	5,369	5,407

In addition to the financial assets above, there are $8,765m (2020: $6,328m; 2019: $6,765m) of other current and non-current asset investments and other financial assets. Of these, $nil receive floating rate interest (2020: $nil; 2019: $111m).

The Group is also exposed to market risk on equity securities, which represent non-controlling interests in third-party biotech companies.

	2021 $m	2020 $m	2019 $m
Equity securities at fair value through Other comprehensive income (Note 12)	1,168	1,108	1,339
Total	1,168	1,108	1,339

28 Financial risk management objectives and policies *continued*

Foreign currency risk

The US dollar is the Group's most significant currency. As a consequence, the Group results are presented in US dollars and exposures are managed against US dollars accordingly.

Translational

Approximately 68% of Group external sales in 2021 were denominated in currencies other than the US dollar, while a significant proportion of manufacturing, and research and development costs were denominated in pounds sterling and Swedish krona. Surplus cash generated by business units is substantially converted to, and held centrally in, US dollars. As a result, operating profit and total cash flow in US dollars will be affected by movements in exchange rates.

This currency exposure is managed centrally, based on forecast cash flows. The impact of movements in exchange rates is mitigated significantly by the correlations which exist between the major currencies to which the Group is exposed and the US dollar. Monitoring of currency exposures and correlations is undertaken on a regular basis and hedging is subject to pre-execution approval.

As at 31 December 2021, before the impact of derivatives, 2% of interest-bearing loans and borrowings were denominated in pounds sterling and 9% were denominated in euros. Where there is non-US dollar debt and an underlying net investment of that amount in the same currency, the Group applies net investment hedging. Exchange differences on the retranslation of debt designated as net investment hedges are recognised in Other comprehensive income to the extent that the hedge is effective. Any ineffectiveness is taken to profit.

The Group holds cross-currency swaps to hedge against the impact of fluctuations in foreign exchange rates. Fair value movements on the revaluation of the cross-currency swaps are recognised in Other comprehensive income to the extent that the hedge is effective, with any ineffectiveness taken to profit.

Foreign currency risk arises when the Group has inter-company funding and investments in certain subsidiaries operating in countries with exchange controls or where there is risk of significant future currency devaluation. One indicator of potential foreign currency risk is where a country is officially designated as hyperinflationary. As at 31 December 2021, the Group operates in two countries designated as hyperinflationary, being Argentina and Venezuela.

The foreign exchange risk to the Group from Argentina and Venezuela has been assessed and deemed to be immaterial.

Transactional

The Group aims to hedge all its forecast major transactional currency exposures on working capital balances, which typically extend for up to three months. Where practicable, these are hedged using forward foreign exchange. In addition, the Group's external dividend, which is paid principally in pounds sterling and Swedish krona, is fully hedged from announcement to payment date. Foreign exchange gains and losses on forward contracts transacted for transactional hedging are taken to profit. Foreign exchange gains and losses on forward contracts transacted for transactional hedging are taken to profit or to Other comprehensive income if the contract is in a designated cash flow hedge.

Sensitivity analysis

The sensitivity analysis set out below summarises the sensitivity of the market value of our financial instruments to hypothetical changes in market rates and prices. The range of variables chosen for the sensitivity analysis reflects our view of changes which are reasonably possible over a one-year period. Market values are the present value of future cash flows based on market rates and prices at the valuation date. For long-term debt, an increase in interest rates results in a decline in the fair value of debt.

The sensitivity analysis assumes an instantaneous 100 basis point change in interest rates in all currencies from their levels at 31 December 2021, with all other variables held constant. Based on the composition of our long-term debt portfolio as at 31 December 2021, a 1% increase in interest rates would result in an additional $54m in interest expense being incurred per year due to new floating rate debt issued during the year. The exchange rate sensitivity analysis assumes an instantaneous 10% change in foreign currency exchange rates from their levels at 31 December 2021, with all other variables held constant. The +10% case assumes a 10% strengthening of the US dollar against all other currencies and the -10% case assumes a 10% weakening of the US dollar.

Each incremental 10% movement in foreign currency exchange rates would have approximately the same effect as the initial 10% detailed in the table below and each incremental 1% change in interest rates would have approximately the same effect as the 1% detailed in the table below.

	Interest rates		Exchange rates	
31 December 2019	+1%	-1%	+10%	-10%
Increase/(decrease) in fair value of financial instruments ($m)	1,417	(1,521)	(4)	(36)
Impact on profit: (loss)/gain ($m)	–	–	(174)	172
Impact on equity: gain/(loss) ($m)	–	–	170	(208)

	Interest rates		Exchange rates	
31 December 2020	+1%	-1%	+10%	-10%
Increase/(decrease) in fair value of financial instruments ($m)	1,696	(1,758)	114	(132)
Impact on profit: (loss)/gain ($m)	–	–	(57)	74
Impact on equity: gain/(loss) ($m)	–	–	171	(206)

	Interest rates		Exchange rates	
31 December 2021	**+1%**	**-1%**	**+10%**	**-10%**
Increase/(decrease) in fair value of financial instruments ($m)	**1,978**	**(2,106)**	**82**	**(85)**
Impact on profit: gain/(loss) ($m)	**–**	**–**	**24**	**(9)**
Impact on equity: gain/(loss) ($m)	**–**	**–**	**58**	**(76)**

Credit risk

The Group is exposed to credit risk on financial assets, such as cash investments, derivative instruments, and Trade and other receivables. The Group is also exposed in its Net asset position to its own credit risk in respect of the 2023 debentures which are accounted for at fair value through profit or loss. Under IFRS 9, the effect of the losses and gains arising from own credit risk on the fair value of bonds designated at fair value through profit or loss are recorded in Other comprehensive income.

Financial counterparty credit risk

The majority of the AstraZeneca Group's cash is centralised within the Group treasury entity and is subject to counterparty risk on the principal invested. The level of the Group's cash investments and hence credit risk will depend on the cash flow generated by the Group and the timing of the use of that cash. The credit risk is mitigated through a policy of prioritising security and liquidity over return and, as such, cash is only invested in high credit-quality investments. Counterparty limits are set according to the assessed risk of each counterparty and exposures are monitored against these limits on a regular basis.

The Group's principal financial counterparty credit risks at 31 December 2021 were as follows:

Current assets

	2021 $m	2020 $m	2019 $m
Cash at bank and in hand	**1,461**	1,182	755
Money market liquidity funds	**4,772**	6,602	4,110
Collateralised repurchase agreement	**–**	–	400
Other short-term cash equivalents	**96**	48	104
Total Cash and cash equivalents (Note 17)	**6,329**	7,832	5,369
Fixed income securities at fair value through profit and loss (Note 12)	**16**	118	811
Fixed deposits (Note 12)	**53**	42	38
Total derivative financial instruments (Note 13)	**83**	142	36
Current assets subject to credit risk	**6,481**	8,134	6,254

Non-current assets

	2021 $m	2020 $m	2019 $m
Fixed income securities at fair value through profit and loss (Note 12)	**–**	–	62
Derivative financial instruments (Note 13)	**102**	171	61
Non-current assets subject to credit risk	**102**	171	123

The majority of the Group's cash is invested in US dollar AAA rated money market liquidity funds. The money market liquidity fund portfolios are managed by five external third-party fund managers to maintain an AAA rating. The Group's investments represent no more than 10% of each overall fund value. There were no other significant concentrations of financial credit risk at the reporting date.

The short-term repurchase agreements were fully collateralised investments. The Group closed out its repurchase agreements during 2020. The value of the cash deposited in repurchase agreements at 31 December 2021 was $nil (2020: $nil; 2019: $401m).

The fixed income securities were managed by four external third-party fund managers. During 2020, the securities were sold and re-invested in money market funds. The long-term rating of these securities was BBB- or better.

All financial derivatives are transacted with commercial banks, in line with standard market practice. The Group has agreements with some bank counterparties whereby the parties agree to post cash collateral, 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 at 31 December 2021 was $93m (2020: $288m; 2019: $71m) and the carrying value of such cash collateral posted by the Group at 31 December 2021 was $47m (2020: $11m; 2019: $10m).

The impairment provision for other financial assets at 31 December 2021 was immaterial.

Trade receivables

Trade receivable exposures are managed locally in the operating units where they arise and credit limits are set as deemed appropriate for the customer. The Group is exposed to customers ranging from government-backed agencies and large private wholesalers to privately owned pharmacies, and the underlying local economic and sovereign risks vary throughout the world. Where appropriate, the Group endeavours to minimise risks by the use of trade finance instruments such as letters of credit and insurance. The Group applies the expected credit loss approach to establish an allowance for impairment that represents its estimate of expected losses in respect of Trade receivables.

The Group applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for all Trade receivables. To measure expected credit losses, Trade receivables have been grouped based on shared credit characteristics and the days past due.

The expected loss rates are based on payment profiles over a period of 36 months before 31 December 2021, 31 December 2020 or 31 December 2019 respectively and the corresponding historical credit losses experienced within this period. The historical loss rates are adjusted to reflect current and forward-looking information on macroeconomic factors affecting the ability of the customer to settle the receivables.

28 Financial risk management objectives and policies *continued*

On that basis, the loss allowance was determined as follows:

31 December 2019	Current	0-90 days past due	90-180 days past due	Over 180 days past due	Total
Expected loss rate	0.1%	0.8%	2.0%	44.0%	
Gross carrying amount ($m)	3,178	312	82	34	3,606
Loss allowance ($m)	2	2	2	15	21

31 December 2020	Current	0-90 days past due	90-180 days past due	Over 180 days past due	Total
Expected loss rate	0.1%	1.6%	19.4%	60.6%	
Gross carrying amount ($m)	3,659	124	21	25	3,829
Loss allowance ($m)	2	2	4	15	23

31 December 2021	**Current**	**0-90 days past due**	**90-180 days past due**	**Over 180 days past due**	**Total**
Expected loss rate	0.1%	1.2%	22.6%	11.0%	
Gross carrying amount ($m)	5,617	328	18	91	6,054
Loss allowance ($m)	5	4	4	10	23

Trade receivables are written off where there is no reasonable expectation of recovery.

Impairment losses on Trade receivables are presented as net impairment losses within Operating profit, any subsequent recoveries are credited against the same line.

In the US, sales to three wholesalers accounted for approximately 94% of US sales (2020: three wholesalers accounted for approximately 95%; 2019: three wholesalers accounted for approximately 94%).

The movements of the Group expected credit losses provision are as follows:

	2021 $m	2020 $m	2019 $m
At 1 January	23	21	38
Net movement recognised in income statement	(2)	3	(13)
Amounts utilised, exchange and other movements	2	(1)	(4)
At 31 December	**23**	23	21

Given the profile of our customers, including large wholesalers and government-backed agencies, no further credit risk has been identified with the Trade receivables not past due other than those balances for which an allowance has been made. The income statement credit or charge is recorded in Operating profit.

29 Employee costs and share plans for employees

Employee costs

The monthly average number of people, to the nearest hundred, employed by the Group is set out in the table below. In accordance with the Companies Act 2006, this includes part-time employees.

	2021	2020	2019
Employees			
UK	8,900	7,900	7,400
Rest of Europe	18,300	16,600	15,500
The Americas	18,800	17,300	16,600
Asia, Africa & Australasia	33,600	33,000	27,800
Continuing operations	79,600	74,800	67,300

Geographical distribution described in the table above is by location of legal entity employing staff. Certain staff will undertake some or all of their activity in a different location.

The number of people employed by the Group at the end of 2021 was 83,100 (2020: 76,100; 2019: 70,600).

The costs incurred during the year in respect of these employees were:

	2021 $m	2020 $m	2019 $m
Wages and salaries	7,633	6,273	5,648
Social security costs	886	726	658
Pension costs	564	435	491
Other employment costs	1,192	813	771
Total	10,275	8,247	7,568

Severance costs of $238m are not included above (2020: $116m; 2019: $158m).

The Directors believe that, together with the basic salary system, the Group's employee incentive schemes provide competitive and market-related packages to motivate employees. They should also align the interests of employees with those of shareholders, as a whole, through long-term share ownership in the Company. The Group's current UK, Swedish and US schemes are described below; other arrangements apply elsewhere.

Bonus plans

The AstraZeneca UK Performance Bonus Plan

Employees of participating AstraZeneca UK companies are invited to participate in this bonus plan, which rewards strong individual performance. Bonuses are paid in cash.

The AstraZeneca Executive Annual Bonus Scheme

This scheme is a performance bonus scheme for Directors and senior employees who do not participate in the AstraZeneca UK Performance Bonus Plan. Annual bonuses are paid in cash and reflect both corporate and individual performance measures. The Remuneration Committee has discretion to reduce or withhold bonuses if business performance falls sufficiently short of expectations in any year such as to make the payment of bonuses inappropriate.

The AstraZeneca Deferred Bonus Plan

This plan was introduced in 2006 and is used to defer a portion of the bonus earned under the AstraZeneca Executive Annual Bonus Scheme into Ordinary Shares in the Company for a period of three years. The plan currently operates only in respect of Executive Directors and members of the SET (with awards granted as AstraZeneca ADSs for members of SET employed within the US). Awards of shares under this plan are typically made in March each year, the first award having been made in February 2006.

Sweden

In Sweden, an all-employee performance bonus plan is in operation, which rewards strong individual performance. Bonuses are paid 50% into a fund investing in AstraZeneca equities and 50% in cash. The AstraZeneca Executive Annual Bonus Scheme, the AstraZeneca Performance Share Plan and the AstraZeneca Global Restricted Stock Plan all operate in respect of relevant AstraZeneca employees in Sweden.

US

In the US, there are two all-employee short-term or annual performance bonus plans in operation to differentiate and reward strong individual performance. Annual bonuses are paid in cash. There is also one senior staff long-term incentive scheme, under which 129 participants may be eligible for awards granted as AstraZeneca ADSs. AstraZeneca ADSs necessary to satisfy the awards are purchased in the market or funded via a share trust. The AstraZeneca Performance Share Plan and the AstraZeneca Global Restricted Stock Plan operate in respect of relevant employees in the US.

Share plans

The charge for share-based payments in respect of share plans is $615m (2020: $277m; 2019: $259m). Payments made to the Employee Benefit Trust upon vesting of share awards are recognised within operating cash flows, reflecting the substance of the arrangement in place between the group and the Trust. The plans are equity settled.

The AstraZeneca UK All-Employee Share Plan

The Company offers UK employees the opportunity to buy Partnership Shares (Ordinary Shares). Employees may invest up to £150 a month to purchase Partnership Shares in the Company at the current market value. In 2010, the Company introduced a Matching Share element, the first award of which was made in 2011. Currently one Matching Share is awarded for every four Partnership Shares purchased. Partnership Shares and Matching Shares are held in the HM Revenue & Customs (HMRC)-approved All-Employee Share Plan. At the Company's AGM in 2002, shareholders approved the issue of new shares for the purposes of the All-Employee Share Plan.

The AstraZeneca 2014 Performance Share Plan

This plan was approved by shareholders in 2014 for a period of 10 years and replaces the AstraZeneca Performance Share Plan. Generally, awards can be granted at any time, but not during a closed period of the Company. The first grant of awards was made in May 2014. Awards granted under the plan vest after three years, or in the case of Executive Directors and members of the SET, after an additional two-year holding period, and can be subject to the achievement of performance conditions. For awards granted to all participants in 2021, vesting is subject to a combination of measures focused on scientific leadership, revenue growth and financial performance. The Remuneration Committee has responsibility for agreeing any awards under the plan and for setting the policy for the way in which the plan should be operated, including agreeing performance targets and which employees should be invited to participate.

	Ordinary Shares '000	WAFV[1] pence	ADR Shares '000	WAFV[1] $
Outstanding at 1 January 2019	2,682	2295	6,963	15.65
Granted	1,018	3147	1,978	21.06
Forfeited	(350)	2317	(1,900)	16.80
Exercised	(491)	1983	(1,835)	14.17
Outstanding at 31 December 2019	2,859	2649	5,206	17.80
Granted	932	3702	1,767	24.02
Forfeited	(191)	3088	(478)	19.57
Cancelled	(3)	2234	–	–
Exercised	(552)	2426	(1,704)	15.43
Outstanding at 31 December 2020	3,045	2985	4,791	20.76
Granted	1,275	2485	2,082	17.18
Forfeited	(220)	3005	(494)	20.53
Cancelled	(9)	3653	–	–
Exercised	(632)	2332	(1,201)	17.40
Outstanding at 31 December 2021	3,459	2919	5,178	20.12

[1] Weighted average fair value.

29 Employee costs and share plans for employees *continued*

The AstraZeneca Investment Plan

This plan was introduced in 2010 and approved by shareholders at the 2010 AGM. The final grant of awards under this plan took place in March 2016. Awards granted under the plan vest after eight years and are subject to performance conditions measured over a period of four years.

The AstraZeneca Global Restricted Stock Plan

This plan was introduced in 2010. This plan provides for the grant of restricted stock unit (RSU) awards to selected below SET-level employees and is used in conjunction with the AstraZeneca Performance Share Plan to provide a mix of RSUs and performance shares. Awards typically vest on the third anniversary of the date of grant and are contingent on continued employment with the Company. The Remuneration Committee has responsibility for agreeing any awards under the plan and for setting the policy for the way in which the plan should be operated.

	Ordinary Shares '000	WAFV pence	ADR Shares '000	WAFV $
Outstanding at 1 January 2019	1,001	4598	10,493	31.57
Granted	759	6313	3,685	42.06
Forfeited	(115)	5438	(1,199)	35.44
Cancelled	–	–	(1)	32.39
Exercised	(317)	4028	(3,408)	28.82
Outstanding at 31 December 2019	1,328	5640	9,770	36.22
Granted	689	7408	3,671	47.71
Forfeited	(113)	6204	(1,077)	41.08
Cancelled	–	7280	(9)	36.93
Exercised	(278)	4929	(3,180)	31.47
Outstanding at 31 December 2020	1,626	6471	9,175	41.89
Granted	**902**	**6893**	**4,509**	**47.75**
Forfeited	**(158)**	**6865**	**(1,254)**	**45.77**
Cancelled	**(1)**	**7244**	**(8)**	**45.89**
Exercised	**(341)**	**4980**	**(2,881)**	**35.11**
Outstanding at 31 December 2021	**2,028**	**6879**	**9,541**	**46.19**

The AstraZeneca Restricted Share Plan

This plan was introduced in 2006 and provides for the grant of restricted share awards to key employees, excluding Executive Directors. Awards are made on an ad hoc basis with variable vesting dates. The plan has been used four times in 2021 to make awards to 111 employees. The Remuneration Committee has responsibility for agreeing any awards under the plan and for setting the policy for the way in which the plan should be operated.

	Ordinary Shares '000	WAFV pence	ADR Shares '000	WAFV $
Outstanding at 1 January 2019	92	4952	1,062	30.79
Granted	105	6894	176	43.91
Forfeited	(7)	5907	(141)	31.17
Cancelled	–	–	(2)	28.19
Exercised	(14)	5244	(446)	30.12
Outstanding at 31 December 2019	176	6051	649	34.70
Granted	80	7931	295	52.92
Forfeited	(6)	7168	(79)	39.26
Exercised	(89)	5166	(359)	31.05
Outstanding at 31 December 2020	161	7434	506	47.20
Granted	**139**	**7415**	**481**	**53.96**
Forfeited	**(18)**	**7562**	**(42)**	**44.73**
Exercised	**(27)**	**7643**	**(182)**	**41.87**
Outstanding at 31 December 2021	**255**	**7393**	**763**	**52.88**

The AstraZeneca Extended Incentive Plan

This plan was introduced in 2018 and provides for the grant of awards to key employees, excluding Executive Directors. Awards are made on an ad hoc basis and 50% of the award will normally vest on the fifth anniversary of grant, with the balance vesting on the tenth anniversary of grant. The award can be subject to the achievement of performance conditions. The Remuneration Committee has responsibility for agreeing any awards under the plan and for setting the policy for the way in which the plan should be operated, including agreeing performance targets (if any) and which employees should be invited to participate.

	Ordinary Shares '000	WAFV pence	ADR Shares '000	WAFV $
Outstanding at 1 January 2019	238	5239	65	38.46
Granted	44	7301	–	–
Outstanding at 31 December 2019	282	5563	65	38.46
Granted	18	8386	–	–
Outstanding at 31 December 2020	300	5730	65	38.46
Granted	–	–	**175**	**56.83**
Forfeited	**(18)**	**8386**	**(45)**	**38.46**
Outstanding at 31 December 2021	**282**	**5563**	**195**	**54.92**

Alexion employee share award plan

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.

	Ordinary Shares '000	WAFV pence	ADR Shares '000	WAFV $
Outstanding at 1 January 2021	–	–	–	–
Granted	–	–	20,189	57.54
Forfeited	–	–	(838)	57.54
Exercised	–	–	(4,131)	57.54
Outstanding at 31 December 2021	–	–	15,220	57.54

The fair values for the market-based performance conditions of the AstraZeneca 2014 Performance Share Plan were determined using a modified version of the Monte Carlo model. This method incorporated market inputs in addition to expected dividends. The fair values of all other plans are set using the market price at the point of award. The grant date fair values of share awards disclosed in this section do not take account of service and non-market related performance conditions.

30 Commitments and contingent liabilities

Commitments	2021 $m	2020 $m	2019 $m
Contracts placed for future capital expenditure on Property, plant and equipment and software development costs not provided for in these financial statements	**388**	689	396

Guarantees and contingencies arising in the ordinary course of business, for which no security has been given, are not expected to result in any material financial loss.

Research and development collaboration payments

The Group has various ongoing collaborations, including in-licensing and similar arrangements with development partners. Such collaborations may require the Group to make payments on achievement of stages of development, launch or revenue milestones, although the Group generally has the right to terminate these agreements at no cost. The Group recognises research and development milestones as an intangible asset once it is committed to payment, which is generally when the Group reaches set trigger points in the development cycle. Revenue-related milestones are recognised as intangible assets on product launch at a value based on the Group's long-term revenue forecasts for the related product. The table below indicates potential development and revenue-related payments that the Group may be required to make under such collaborations.

	Total $m	Under 1 year $m	Years 1 and 2 $m	Years 3 and 4 $m	Years 5 and greater $m
Future potential research and development milestone payments	12,764	1,047	1,958	3,382	6,377
Future potential revenue milestone payments	17,769	68	420	1,452	15,829

The table includes all potential payments for achievement of milestones under ongoing research and development arrangements. Revenue-related milestone payments represent the maximum possible amount payable on achievement of specified levels of revenue as set out in individual contract agreements, but exclude variable payments that are based on unit sales (e.g. royalty-type payments) which are expensed as the associated sale is recognised. The table excludes any payments already capitalised in the Financial Statements for the year ended 31 December 2021.

The future payments we disclose represent contracted payments and, as such, are not discounted and are not risk-adjusted. As detailed in the Risk section from page 48, the development of any pharmaceutical product candidate is a complex and risky process that may fail at any stage in the development process due to a number of factors (including items such as failure to obtain regulatory approval, unfavourable data from key studies, adverse reactions to the product candidate or indications of other safety concerns). The timing of the payments is based on the Group's current best estimate of achievement of the relevant milestone.

Environmental costs and liabilities

The Group's expenditure on environmental protection, including both capital and revenue items, relates to costs that are necessary for implementing internal systems and programmes, and meeting legal and regulatory requirements for processes and products. This includes investment to conserve natural resources and otherwise minimise the impact of our activities on the environment.

They are an integral part of normal ongoing expenditure for carrying out the Group's research, manufacturing and commercial operations and are not separated from overall operating and development costs. There are no known changes in legal, regulatory or other requirements resulting in material changes to the levels of expenditure for 2019, 2020 or 2021.

In addition to expenditure for meeting current and foreseen environmental protection requirements, the Group incurs costs in investigating and cleaning up land and groundwater contamination. In particular, AstraZeneca has environmental liabilities at some currently or formerly owned, leased and third-party sites.

In the US, Zeneca Inc., and/or its indemnitees, have been named as potentially responsible parties (PRPs) or defendants at a number of sites where Zeneca Inc. is likely to incur future environmental investigation, remediation, operation and maintenance costs under federal, state, statutory or common law environmental liability allocation schemes (together, US Environmental Consequences). Similarly, Stauffer Management Company LLC (SMC), which was established in 1987 to own and manage certain assets of Stauffer Chemical Company acquired that year, and/or its indemnitees, have been named as PRPs or defendants at a number of sites where SMC is likely to incur US Environmental Consequences.

30 Commitments and contingent liabilities *continued*

AstraZeneca has also given indemnities to third parties for a number of sites outside the US. These environmental liabilities arise from legacy operations that are not currently part of the Group's business and, at most of these sites, remediation, where required, is either completed or in progress. AstraZeneca has made provisions for the estimated costs of future environmental investigation, remediation, operation and maintenance activity beyond normal ongoing expenditure for maintaining the Group's R&D and manufacturing capacity and product ranges, where a present obligation exists, it is probable that such costs will be incurred and they can be estimated reliably. With respect to such estimated future costs, there were provisions at 31 December 2021 in the aggregate of $90m (2020: $100m; 2019: $96m), mainly relating to the US. Where we are jointly liable or otherwise have cost-sharing agreements with third parties, we reflect only our share of the obligation. Where the liability is insured in part or in whole by insurance or other arrangements for reimbursement, an asset is recognised to the extent that this recovery is virtually certain.

It is possible that AstraZeneca could incur future environmental costs beyond the extent of our current provisions. The extent of such possible additional costs is inherently difficult to estimate due to a number of factors, including: (i) the nature and extent of claims that may be asserted in the future; (ii) whether AstraZeneca has or will have any legal obligation with respect to asserted or unasserted claims; (iii) the type of remedial action, if any, that may be selected at sites where the remedy is presently not known; (iv) the potential for recoveries from or allocation of liability to third parties; and (v) the length of time that the environmental investigation, remediation and liability allocation process can take. As per our accounting policy on page 144, Provisions for these costs are made when there is a present obligation and where it is probable that expenditure on remedial work will be required and a reliable estimate can be made of the cost. Notwithstanding and subject to the foregoing, we estimate the potential additional loss for future environmental investigation, remediation, remedial operation and maintenance activity above and beyond our provisions to be, in aggregate, between $99m and $165m (2020: $95m and $158m; 2019: $86m and $143m) which relates mainly to the US.

Legal proceedings

AstraZeneca is involved in various legal proceedings considered typical to its business, including actual or threatened litigation and actual or potential government investigations relating to employment matters, product liability, commercial disputes, pricing, sales and marketing practices, infringement of IP rights, and the validity of certain patents and competition laws. The more significant matters are discussed below.

Most of the 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.

There is one matter, which is considered probable that an outflow will be required, but for which we are unable to make an estimate of the possible loss or range of possible losses at this stage.

We do not believe that disclosure of the amounts sought by plaintiffs, if known, would be meaningful with respect to these legal proceedings. This is due to a number of factors, including (i) the stage of the proceedings (in many cases trial dates have not been set) and the overall length and extent of pre-trial discovery; (ii) the entitlement of the parties to an action to appeal a decision; (iii) clarity as to theories of liability, damages and governing law; (iv) uncertainties in timing of litigation; and (v) the possible need for further legal proceedings to establish the appropriate amount of damages, if any.

While there can be no assurance regarding the outcome of any of the legal proceedings referred to in this Note 30, based on management's current and considered view of each situation, we do not currently expect them to have a material adverse effect on our financial position including within the next financial year. This position could of course change over time, not least because of the factors referred to above.

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 other similar forms of relief), or where a loss is probable and we are able to make a reasonable estimate of the loss, we generally indicate the loss absorbed or make a provision for our best estimate of the expected loss.

Where it is considered that the Group is more likely than not to prevail, legal costs involved in defending the claim are charged to profit as they are incurred.

Where it is considered that the Group has a valid contract which provides the right to reimbursement (from insurance or otherwise) of legal costs and/or all or part of any loss incurred or for which a provision has been established, and we consider recovery to be virtually certain, the best estimate of the amount expected to be received is recognised as an asset.

KJ Assessments as to whether or not to recognise provisions or assets, and of the amounts concerned, usually involve a series of complex judgements about future events and can rely heavily on estimates and assumptions. AstraZeneca believes that the provisions recorded are adequate based on currently available information and that the insurance recoveries recorded will be received. However, given the inherent uncertainties involved in assessing the outcomes of these cases, and in estimating the amount of the potential losses and the associated insurance recoveries, we could in the future incur judgments or insurance settlements that could have a material adverse effect on our results in any particular period.

IP claims include challenges to the Group's patents on various products or processes and assertions of non-infringement of patents. A loss in any of these cases could result in loss of patent protection on the related product. The consequences of any such loss could be a significant decrease in Product Sales, which could have a material adverse effect on our results. The lawsuits filed by AstraZeneca for patent infringement against companies that have filed abbreviated new drug applications (ANDAs) in the US, seeking to market generic forms of products sold by the Group prior to the expiry of the applicable patents covering these products, typically also involve allegations of non-infringement, invalidity and unenforceability of these patents by the ANDA filers. In the event that the Group is unsuccessful in these actions or the statutory 30-month stay expires before a ruling is obtained, the ANDA filers involved will also have the ability, subject to FDA approval, to introduce generic versions of the product concerned.

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

Over the course of the past several years, including in 2021, a significant number of commercial litigation claims in which AstraZeneca is involved have been resolved, particularly in the US, thereby reducing potential contingent liability exposure arising from such litigation. Similarly, in part due to patent litigation and settlement developments, greater certainty has been achieved regarding possible generic entry dates with respect to some of our patented products. At the same time, like other companies in the pharmaceutical sector and other industries, AstraZeneca continues to be subject to government investigations around the world.

Patent litigation

Calquence

US patent proceedings

In February 2022, in response to Paragraph IV notices from multiple ANDA filers, AstraZeneca filed patent infringement lawsuits in the US District Court for the District of Delaware.

In its complaint, AstraZeneca alleged that a generic version of *Calquence*, if approved and marketed, would infringe patents listed in the US FDA Orange Book with reference to *Calquence* that are owned or licensed by AstraZeneca. No trial date has been set.

Tagrisso

US patent proceedings

In February 2020, in response to Paragraph IV notices from multiple ANDA filers, AstraZeneca filed patent infringement lawsuits in the US District Court for the District of Delaware. In its complaint, AstraZeneca alleged that a generic version of *Tagrisso*, if approved and marketed, would infringe a US Orange Book-listed *Tagrisso* patent. In the fourth quarter of 2021, AstraZeneca entered into settlement agreements with Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Limited (collectively, Zydus) and MSN Laboratories Pvt. Ltd. and MSN Pharmaceuticals Inc. (collectively, MSN), resolving all US patent litigation with Zydus and MSN relating to *Tagrisso*. The trial with the remaining defendant, Alembic Pharmaceuticals Limited, is scheduled for May 2022.

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 authorisation 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.

Faslodex

Patent proceedings outside the US

In Japan, in April 2021, AstraZeneca received notice from the Japan Patent Office that Sandoz K.K. filed a Request for Invalidation of the *Faslodex* formulation patent. In October 2021, AstraZeneca received notice that Sun Pharma Japan Ltd. requested to intervene in the Request for Invalidation brought by Sandoz K.K seeking invalidation of the *Faslodex* formulation patent. The Japan Patent Office has permitted the intervention. AstraZeneca is defending the challenged patent.

Farxiga/Forxiga

US patent proceedings

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 the asserted claims of 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 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.

Brilinta

US patent proceedings

In 2015 and subsequently, in response to Paragraph IV notices from ANDA filers, AstraZeneca filed patent infringement lawsuits in the US District Court for the District of Delaware (the District Court) relating to patents listed in the FDA Orange Book with reference to *Brilinta*. In 2020, AstraZeneca entered into three separate settlements and the District Court entered consent judgments to dismiss each of the corresponding litigations. Additional proceedings are ongoing in the District Court. No trial date has been set.

Roxadustat

US patent proceedings

In April 2021, Akebia Therapeutics, Inc. and Otsuka America Pharmaceutical, Inc. served AstraZeneca with a complaint seeking a declaration of invalidity and non-infringement for several of FibroGen, Inc's (FibroGen) method of use patents related to HIF prolylhydroxylase inhibitors. AstraZeneca is the exclusive licensee of FibroGen in the United States. AstraZeneca filed a motion to dismiss in June 2021.

Patent proceedings outside the US

In Canada, in May 2018, Akebia Therapeutics, Inc. filed an impeachment action in the Federal Court of Canada alleging invalidity of several of FibroGen, Inc.'s (FibroGen) method of use patents related to HIF prolylhydroxylase inhibitors. AstraZeneca is the exclusive licensee of FibroGen in Canada. AstraZeneca and FibroGen were defending the action. The parties have resolved the action.

Symbicort

US patent proceedings

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 US Court of Appeals for the Federal Circuit (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 Federal Circuit. In December 2021, the Federal Circuit affirmed the decision by the District Court determining that the asserted patent claims were nonobvious. However, the Federal Circuit reversed the District Court's claim construction decision, vacated the stipulated judgment of infringement by Mylan and Kindeva and remanded the matter back to the District Court for determination of whether their ANDA product infringes the asserted patent claims under the Federal Circuit's claim construction. In January 2022, AstraZeneca filed a Combined Petition for Panel Rehearing and Rehearing En Banc with the Federal Circuit.

Daliresp

US patent proceedings

In 2015 and subsequently, in response to Paragraph IV notices from ANDA filers, AstraZeneca filed patent infringement lawsuits in the US District Court for the District of New Jersey (the District Court) relating to patents listed in the FDA Orange Book with reference to *Daliresp*. In 2020, AstraZeneca entered into a settlement and the District Court entered a consent judgment to dismiss the corresponding litigation. Additional proceedings are ongoing in the District Court. No trial date has been set.

Movantik

US patent proceedings

In March 2020, Aether Therapeutics, Inc. filed a patent infringement lawsuit in the US District Court for the District of Delaware against AstraZeneca, Nektar Therapeutics and Daiichi Sankyo, Inc., relating to *Movantik*. A trial has been set for March 2023.

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.

30 Commitments and contingent liabilities *continued*

Enhertu

US patent proceedings

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 alleging that *Enhertu* infringes US Patent No. 10,808,039 (the '039 patent). AstraZeneca Pharmaceuticals LP co-commercialises *Enhertu* with Daiichi Sankyo, Inc. (Daiichi Sankyo) in the US. In July 2021, AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited intervened in the Texas action in support of Daiichi Sankyo. 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 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 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 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.

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 US patent held by Chugai. Upon issuance of another US 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. Trial scheduled to occur in January 2022 has been postponed until February 2022 due to COVID-19.

Patent proceedings outside the US

In Japan, 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. In 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

Farxiga and *Xigduo* XR

In several jurisdictions in the US, AstraZeneca has been named as a defendant in lawsuits involving plaintiffs claiming physical injury, including Fournier's Gangrene and necrotising fasciitis, from treatment with *Farxiga* and/or *Xigduo* XR. A majority of these claims are filed in Delaware state court and remain pending.

One case, filed in state court in Minnesota, is scheduled for trial in January 2023.

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.

Onglyza and *Kombiglyze*

In the US, AstraZeneca is defending various lawsuits alleging heart failure, cardiac injuries, and/or death from treatment with *Onglyza* or *Kombiglyze*. In February 2018, the Judicial Panel on Multidistrict Litigation ordered the transfer of various pending federal actions to the US District Court for the Eastern District of Kentucky (District Court) for consolidated pre-trial proceedings with the federal actions pending in the District Court. In the previously disclosed California State Court coordinated proceeding, AstraZeneca submitted its motion for summary judgment in December 2021.

Nexium and *Losec/Prilosec*

US proceedings

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 previously scheduled for January 2022 has been rescheduled to October 2022. In addition to the MDL cases, there are cases filed in several state courts around the US: a trial in Delaware state court previously scheduled for February 2022 is being rescheduled.

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 scheduled a trial for November 2022.

Canada proceedings

In Canada, in July and August 2017, AstraZeneca was served with three putative class action lawsuits. Two of the lawsuits have been dismissed, one in 2019 and one in 2021. The third lawsuit, filed in Saskatchewan, seeks authorisation to represent individual residents in Canada who allegedly suffered kidney injuries from the use of proton pump inhibitors, including *Nexium* and *Losec*.

Commercial litigation

Amplimmune

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. This matter is now concluded.

Array BioPharma
In December 2017, AstraZeneca was served with a complaint filed in New York State court by Array BioPharma, Inc. (Array) alleging breaches of contractual obligations relating to a 2003 collaboration agreement between AstraZeneca and Array. In June 2020, an appeal court denied AstraZeneca's motion for an early dismissal of the case, allowing the case to continue towards trial. No trial date has been set.

Ocimum lawsuit
In the US, in December 2017, AstraZeneca was served with a complaint filed by Ocimum Biosciences, Ltd. (Ocimum) in the Superior Court for the State of Delaware that alleged, among other things, breaches of contractual obligations and misappropriation of trade secrets, relating to a now terminated 2001 licensing agreement between AstraZeneca and Gene Logic, Inc. (Gene Logic), the rights to which Ocimum purports to have acquired from Gene Logic. In February 2021, the Delaware Supreme court affirmed the grant of AstraZeneca's motion for summary judgment. This matter is now concluded.

Seroquel XR (Antitrust Litigation)
In the US in 2019, AstraZeneca was named in several related complaints brought in the US District Court for the Southern District of New York (the Court), including several putative class action lawsuits that were purportedly brought on behalf of classes of direct purchasers or end payors of *Seroquel XR*, that allege AstraZeneca and generic drug manufacturers violated antitrust laws when settling patent litigation related to *Seroquel XR*. In August 2020, the Court granted AstraZeneca's motions to transfer all such lawsuits to the US District Court for the District of Delaware. AstraZeneca has filed motions to dismiss the complaints, which remain pending.

Anti-Terrorism Act Civil Lawsuit
In the US, in October 2017, AstraZeneca and certain other pharmaceutical and/or medical device companies were named as defendants in a complaint filed in federal court in the District of Columbia (the District Court) by US nationals (or their estates, survivors, or heirs) who were killed or wounded in Iraq between 2005 and 2013. The plaintiffs allege 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. In July 2020, the District Court granted AstraZeneca's and the other defendants' motion and dismissed the lawsuit, and the plaintiffs appealed to the DC Circuit Court of Appeals (the Appellate Court). In January 2022, a panel of the Appellate Court reversed the dismissal and remanded the case back to the District Court. AstraZeneca and the other defendants have filed petitions requesting en banc review by the entire Appellate Court.

AZD1222 Securities litigation
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.

Defiriens
In Germany, in July 2020, AstraZeneca received a notice of arbitration filed with the German Institution of Arbitration from the sellers of Defiriens AG (the Sellers) regarding the 2014 Share Purchase Agreement (SPA) between AstraZeneca and the Sellers. The Sellers claim they are owed approximately $140m in earn-outs under the SPA. AstraZeneca disputes the claims of the Sellers. An oral hearing is scheduled for July 2022.

Alexion shareholder litigation
In March 2021, several shareholders of Alexion Pharmaceuticals, Inc. (Alexion) filed individual lawsuits against Alexion, its management, and/or AstraZeneca and affiliates in federal district court in New York. The complaints generally alleged that the preliminary registration statement filed with the SEC on 19 February 2021, omitted certain allegedly material information in connection with AstraZeneca's proposed acquisition of Alexion (the Acquisition), and one of the complaints further alleged that the Alexion directors breached their fiduciary duties in connection with the Acquisition and that AstraZeneca and the other entity defendants aided and abetted the alleged breaches. In May 2021, all such complaints were withdrawn and dismissed. This matter is now concluded.

PARP inhibitor royalty dispute
In October 2012, Tesaro, Inc. (now wholly owned by GlaxoSmithKline plc, "GSK") entered into two worldwide, royalty-bearing patent license agreements with AstraZeneca related to GSK's product niraparib. In May 2021, AstraZeneca filed a lawsuit against Tesaro in the Commercial Court of England and Wales alleging that GSK has failed to pay all of the royalties due on niraparib sales under our license agreements. While a case schedule has not yet been set, trial is anticipated in H2 2022.

Portola shareholder litigation
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 for December 2022.

Shareholder litigation – Alexion (US)
In December 2016, putative securities class action lawsuits were filed in the US District Court for the District of Connecticut (the District Court) 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 District Court issued a decision denying in part Defendants' motion to dismiss the matter.

Syntimmune
In connection with Alexion's prior acquisition of Syntimmune, Inc. (Syntimmune), a clinical-stage biotechnology company developing an antibody therapy targeting the FcRn, in the US, in December 2020, Alexion was served with a lawsuit filed by the stockholders' representative for Syntimmune in Delaware State Court that alleged, among other things, breaches of contractual obligations relating to the 2018 merger agreement. The stockholders' representative alleges that Alexion failed to meet its obligations under the merger agreement to use commercially reasonable efforts to achieve the milestones, and the plaintiff has requested payment of all milestone obligations. Alexion also filed a claim for breach of the representations in the 2018 merger agreement regarding unusable drug product and drug substance that Alexion acquired from Syntimmune. Trial in the matter is scheduled for November 2022.

30 Commitments and contingent liabilities *continued*

Government investigations/proceedings

Toprol-XL Louisiana Attorney General litigation
In July 2020, the Louisiana First Circuit Court of Appeals (the Appellate Court) reversed and remanded a Louisiana state trial court (the Trial Court) ruling that had granted AstraZeneca's motion for summary judgment and dismissed a state court complaint, brought by the Attorney General for the State of Louisiana (the State), alleging that AstraZeneca engaged in unlawful monopolisation and unfair trade practices in connection with the enforcement of its *Toprol-XL* patents. In August 2020, AstraZeneca petitioned the Louisiana Supreme Court (the Supreme Court) to review the decision of the Appellate Court and reinstate the Trial Court's summary judgment ruling. In April 2021, the Supreme Court granted a motion to dismiss all of the State's claims with prejudice and vacate the decisions of the Trial Court and Appellate Court. This matter is now closed.

Vermont US Attorney Investigation
In April 2020, AstraZeneca received a Civil Investigative Demand from the US Attorney's Office in Vermont and the Department of Justice, Civil Division, seeking documents and information relating to AstraZeneca's relationships with electronic health record vendors. AstraZeneca is co-operating with this enquiry.

US 340B Litigations and Proceedings
AstraZeneca is involved in several matters relating to its contract pharmacy recognition policy under the 340B Drug Pricing Program in the US. In 2020, three lawsuits 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 to an unlimited number of contract pharmacies. AstraZeneca has sought to intervene in the lawsuits. Two of the three cases are currently stayed pending further proceedings and the third case has been dismissed. Administrative Dispute Resolution 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 contract pharmacy recognition policy under the 340B Drug Pricing Program. AstraZeneca has cooperated with the inquiry.

In January 2021, AstraZeneca filed a separate lawsuit in federal court in Delaware alleging that an 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 antitrust 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 in the diabetes market through contract pharmacies.

US Congressional
In January 2019, AstraZeneca received a letter from the US House of Representatives Committee on Oversight and Reform (Committee) seeking information related to pricing practices for *Crestor*. Similar letters were sent to 11 other pharmaceutical manufacturers. AstraZeneca cooperated with the inquiry and produced certain responsive information. In December 2021, the Committee issued a final report culminating the Committee's pharmaceutical pricing investigation. AstraZeneca's products are not the subject of the findings in the final report.

European Commission claim regarding AZD1222
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 was 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
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.

Tagrisso
In India, in June 2021, the National Pharmaceutical Pricing Authority (NPPA) issued a demand notice (Demand Notice) to AstraZeneca Pharma India Limited (AZPIL), regarding the pricing of *Tagrisso*. The NPPA has alleged that AZPIL has overcharged *Tagrisso*, claiming approximately $21m plus interest. AZPIL has challenged the Demand Notice in the Delhi High Court.

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 US Securities & Exchange Commission (SEC) 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 $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 (PMPRB) 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 $71.4m in escrow pending the final resolution of all appeals in this matter.

Brazilian operations investigation
In May 2017, Brazilian authorities seized records and data from Alexion's São Paulo, Brazil offices as part of an investigation being conducted into Alexion's Brazilian operations. AstraZeneca are cooperating with this inquiry.

Brazilian tax assessment matter
In connection with an ongoing matter, in August 2019, the Brazilian Federal Revenue Service provided a Notice of Tax and Description of the Facts (the Tax Assessment) to two Alexion subsidiaries (the Brazil Subsidiaries), as well as to two additional entities, a logistics provider utilized by Alexion and a distributor. The Tax Assessment focuses on the importation of *Soliris* vials pursuant to Alexion's free drug supply to patients program (referred to as Global Access to Medicines, or GATM) in Brazil. In September 2019, the Brazil Subsidiaries filed defences to the Tax Assessment disputing the basis for liability under the Tax Assessment, based on, among others, the following: in connection with the operation of GATM, during the period from September 2014 to June 2019: (i) the importers responsible for the importation of the GATM *Soliris* vials into Brazil were correctly identified and (ii) the correct customs value was utilised for the purpose of importing the GATM *Soliris* vials provided to the patients free of charge. Alexion prevailed in the first level of administrative appeals in the Brazilian federal administrative proceeding system based on a deficiency in the Brazil Tax Assessment. The decision was subject to an automatic (ex officio) appeal to the second level of the administrative courts, which is pending. There are three separate levels of administrative appeals within the Brazilian federal administrative proceeding system and, if the outcome of these administrative appeals is unfavourable, the final decision of the federal administrative proceeding system can be disputed to the federal court systems in Brazil (at this time, AstraZeneca intends to appeal the Tax Assessment if it is not overturned in the course of administrative appeals). Given the early stage of these proceedings, AstraZeneca is unable to predict the duration, scope or outcome of this matter, but we expect that a final resolution will take three years or more. While it is possible that a loss related to the Tax Assessment may be incurred, given its ongoing nature, we cannot reasonably estimate the potential magnitude of any such possible loss or range of loss, or the cost of the ongoing administrative appeals (and potential appeals to the federal court system) of the Tax Assessment. Any determination that any aspects of the importation of free of charge medications into Brazil as set forth in the Tax Assessment are not, or were not, in compliance with existing laws or regulations could result in the imposition of fines, civil penalties and, potentially criminal penalties, and/or other sanctions against the Group, and could have an adverse impact on the Group's Brazilian operations.

Additional government inquiries
As is true for most, if not all, major prescription pharmaceutical companies, AstraZeneca is currently involved in multiple inquiries into drug marketing and pricing practices. In addition to the investigations described above, various law enforcement offices have, from time to time, requested information from the Group. There have been no material developments in those matters.

Tax

KJ 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 with respect to the ultimate outcome of current and potential future tax audits, and actual results could vary from these estimates.

Transfer pricing and other international tax contingencies
The total net accrual included in the Group Financial Statements to cover the worldwide exposure to transfer pricing audits is $77m (2020: $287m; 2019: $140m), a decrease of $210m compared with 2020 mainly as a result of reduction of tax liabilities arising from updates to estimates of prior period tax liabilities following settlements with tax authorities. These positions can be complex and judgemental. Therefore in determining the accrual, management has assessed their expectation of the ultimate resolution of the uncertainty, including settlement or litigation.

Management continues to believe that AstraZeneca's positions on all its transfer pricing and other international tax audits and disputes are robust, and that AstraZeneca is appropriately provided, including consideration of whether corresponding relief will be available under Mutual Agreement procedures or unilaterally.

HMRC communicated to the Group that they do not consider that the Group is a beneficiary of state aid following the European Commission's (EC) decision on the state aid review of UK Controlled Foreign Company Group Financing Exemption therefore this matter is now closed.

For transfer pricing and other international tax matters where AstraZeneca and the tax authorities are in dispute, AstraZeneca estimates the potential for additional liabilities above the amount provided where the possibility of the additional liabilities falling due is more than remote, to be up to $48m (2020: $251m; 2019: $76m) including associated interest. Management believes that it is unlikely that these additional liabilities will arise. It is possible that some of these contingencies may change in the future to reflect progress in tax authority reviews, to the extent that any tax authority challenge is concluded, or matters lapse including following expiry of the relevant statutes of limitation resulting in a reduction in the tax charge in future periods.

SE AstraZeneca considers whether it is probable that a taxation authority will accept an uncertain tax treatment. If it is concluded that it is not probable that the taxation authority will accept an uncertain tax treatment, where tax exposures can be quantified, an accrual is made based on either the most likely amount method or the expected value method depending on which method management expects to better predict the resolution of the uncertainty. Accruals can be built up over a long period of time, but the ultimate resolution of tax exposures usually occurs at a point in time, and given the inherent uncertainties in assessing the outcomes of these exposures (which sometimes can be binary in nature), we could, in future periods, experience adjustments to these accruals that have a material positive or negative effect on our results in any particular period. Details of the movements in relation to material tax exposures are discussed below.

30 Commitments and contingent liabilities *continued*

Other tax contingencies

Included in the tax accrual is $691m (2020: $727m; 2019: $887m) relating to a number of other tax contingencies, a decrease of $36m mainly due to releases of tax contingencies following the expiry of the relevant statute of limitations and on the conclusion of tax authority review and exchange rate effects, partially offset by the inclusion of provisions for tax contingencies relating to Alexion. The majority of the accrual relates to tax contingencies which are estimated using the expected value method and depend on AstraZeneca's assessment of the likelihood of the approach taken by the tax authorities and could change in the future to reflect progress in tax authority reviews, the extent that any tax authority challenge is concluded, or matters lapse including following expiry of the relevant statutes of limitation resulting in a reduction in the tax charge in future periods.

For these other tax contingencies, AstraZeneca estimates the potential for additional liabilities above the amount provided where the possibility of the additional liabilities falling due is more than remote, to be up to $598m (2020: $517m; 2019: $327m) including associated interest. It is possible that some of these contingencies may reduce in the future if any tax authority challenge is concluded or matters lapse following expiry of the relevant statutes of limitation, resulting in a reduction in the tax charge in future periods.

Timing of cash flows and interest

It is not possible to estimate the timing of tax cash flows in relation to each outcome. It is anticipated that tax payments may be required in relation to a number of significant disputes which may be resolved over the next one to two years. AstraZeneca considers the accruals set out above to appropriately reflect the expected value of any final settlement. Some of the items discussed above are not currently within the scope of tax authority audits and may take longer to resolve.

Included within other receivables and payables is a net amount of interest arising on tax contingencies of $85m (2020: $82m; 2019: $90m).

31 Statutory and other information

	2021 $m	2020 $m	2019 $m
Fees payable to PricewaterhouseCoopers LLP and its associates:			
Group audit fee	**10.5**	6.3	3.9
Fees payable to PricewaterhouseCoopers LLP and its associates for other services:			
The audit of subsidiaries pursuant to legislation	**15.2**	10.8	8.3
Attestation under s404 of Sarbanes-Oxley Act 2002	**2.0**	2.0	2.0
Audit-related assurance services	**4.5**	0.7	0.3
Other assurance services	**3.4**	0.2	0.1
Fees payable to PricewaterhouseCoopers Associates in respect of the Group's pension schemes:			
The audit of subsidiaries' pension schemes	**0.3**	0.3	0.3
	35.9	20.3	14.9

$0.4m of fees payable in 2021 are in respect of the Group audit and audit of subsidiaries related to prior years (2020: $0.8m in respect of the 2019 Group audit and audit of subsidiaries).

$0.3m of audit fees and $0.7m of Audit-related and Other assurance services relate to pre-acquisition fees incurred by Alexion.

Included in Audit-related and Other assurance services are $6.1m of services provided in relation to the acquisition of Alexion and related debt issuance.

Related party transactions

The Group had no material related party transactions which might reasonably be expected to influence decisions made by the users of these Financial Statements.

Key management personnel compensation

Key management personnel are defined for the purpose of disclosure under IAS 24 'Related Party Disclosures' as the members of the Board and the members of the SET.

	2021 $'000	2020 $'000	2019 $'000
Short-term employee benefits	**32,985**	29,126	31,329
Post-employment benefits	**1,378**	1,602	1,766
Share-based payments	**45,234**	27,666	19,210
	79,597	58,394	52,305

Total remuneration is included within employee costs (see Note 29).

32 Subsequent events

On 4 January 2022, AstraZeneca completed the sale of the global rights to *Tudorza* and *Duaklir* to Covis Pharma GmbH for an upfront payment of $270m, which will be recorded within Other operating income and expense. The intangible assets of $368m associated with this transaction were classified as Assets held for sale as at 31 December 2021 (Note 18).

Group Subsidiaries and Holdings

In accordance with section 409 of the Companies Act 2006 a full list of subsidiaries, partnerships, associates, joint ventures and joint arrangements, the country of incorporation, registered office address, and the effective percentage of equity owned as at 31 December 2021 are disclosed below. Unless otherwise stated the share capital disclosed comprises ordinary shares which are indirectly held by AstraZeneca PLC.

Unless otherwise stated the accounting year ends of subsidiaries are 31 December. The Group Financial Statements consolidate the Financial Statements of the Company and its subsidiaries at 31 December 2021.

At 31 December 2021	Group Interest
Wholly owned subsidiaries	
Algeria	
AAPM Sarl	100%
20 Zone Macro-Economique, Hydra, Dar El Medina, Algiers, Algeria	
Argentina	
AstraZeneca S.A.	100%
Nicolas de Vedia 3616, Piso 8, Ciudad Autónoma de Buenos Aires, Argentina	
Alexion Pharma Argentina SRL	100%
Avenida Leandro N. Alem 592 Piso 6, Buenos Aires, Argentina	
Australia	
AstraZeneca Holdings Pty Limited	100%
AstraZeneca PTY Limited	100%
66 Talavera Road, Macquarie Park, NSW 2113, Australia	
Alexion Pharmaceuticals Australasia Pty Ltd	100%
Building A Suite 401 Level 4, 20 Rodborough Road, Frenchs Forest, NSW 2086, Australia	
Austria	
AstraZeneca Österreich GmbH	100%
Landstraßer Hauptstraße 1A, A-1030 Wien, Österreich	
Alexion Pharma Austria GmbH	100%
Donau-City-Straße 7, 30. Stock, DC Tower, Vienna 1220, Austria	
Belgium	
AstraZeneca S.A. / N.V.	100%
Alfons Gossetlaan 40 bus 201 at 1702 Groot-Bijgaarden, Belgium	
Alexion Pharma Belgium Sprl	100%
Alexion Services Europe Srl	100%
de Meeûssquare 37 Bruxelles 1000 Belgium	
Bermuda	
Alexion Bermuda Holding ULC	100%
Alexion Bermuda Limited	100%
Canon's Court, 22 Victoria St., Hamilton, Bermuda	

At 31 December 2021	Group Interest
Brazil	
AstraZeneca do Brasil Limitada	100%
Rod. Raposo Tavares, KM 26, 9, Cotia, Brazil	
Alexion Farmacêutica América Latina Serviços de Administração de Vendas Ltda.	100%
Alexion Farmacêutica Brasil Importação e Distribuição de Produtos e Serviços de Administração de Vendas Ltda	100%
Avenida Dr. Chucri Zaidan, 1240, 15th floor, Morumbi Corporate Golden Tower, São Paulo, SP, 04711-130, Brazil	
Bulgaria	
AstraZeneca Bulgaria EOOD	100%
36 Dragan Tzankov Blvd., District Izgrev, Sofia, 1057, Bulgaria	
Canada	
AstraZeneca Canada Inc.[1]	100%
Suite 5000, 1004 Middlegate Road, Ontario, L4Y 1M4, Canada	
Alexion Pharma Canada Corporation	100%
1300-1969 ST; Upper Water; Halifax, NS B3J3R7, Canada	
Cayman Islands	
AZ Reinsurance Limited	100%
18 Forum Lane, 2nd Floor, Camana Bay, Grand Cayman, P.O. BOX 69, Cayman Islands	
Chile	
AstraZeneca S.A.	100%
AstraZeneca Farmaceutica Chile Limitada	100%
Av. Isidora Goyenechea 3477, 2nd Floor, Las Condes, Santiago, Chile	
China	
AstraZeneca Pharmaceuticals Co., Limited	100%
No. 2, Huangshan Road, Wuxi, Jiangsu Province, China	
AstraZeneca (Wuxi) Trading Co. Ltd	100%
Building E, Huirong Plaza, Jinghui Road East, Xinwu District, Wuxi, Jiangsu Province, China	
AstraZeneca Investment (China) Co., Ltd	100%
199 Liangjing Road, China (Shanghai) Pilot Free Trade Zone, Shanghai, China	
AstraZeneca Pharmaceutical (China) Co. Ltd	100%
No. 9 Medical Avenue, Jiangsu Province, Taizhou, China	
AstraZeneca Pharmaceutical (Beijing) Co., Ltd	100%
1F, Building No.4, No.8 Courtyard, No.1 Kegu Street, Beijing Economic-Technological Development Area, Beijing 100176, China	

At 31 December 2021	Group Interest
AstraZeneca (Guangzhou) Pharmaceutical Consulting Co., Ltd.	100%
Room 406-178, No. 1, Yichuang Street, (China-Singapore Guangzhou Knowledge City) Huangpu District, Guangzhou City, China	
AstraZeneca Investment Consulting (Wuxi) Co., Ltd	100%
Room 808, 8F, Building 99-2 Linghu Avenue, Xinwu District, Wuxi, Jiangsu, China	
AstraZeneca Pharmaceutical (Hangzhou) Co., Ltd	100%
12F & 14F, Building 1, Shuli Plaza, 758 Fei Jia Tang Road, Gongshu District, Hangzhou, Zhejiang Province, China	
AstraZeneca Global R&D (China) Co., Ltd	100%
16F, 88 Xizang North Road, Jing'an District, Shanghai, China	
AstraZeneca Pharmaceutical (Chengdu) Co., Ltd.	100%
10th Floor, Building 11 (Building E11), No. 366, Hemin Street, Chengdu High-tech Zone, China (Sichuan) Pilot Free Trade Zone	
AstraZeneca Pharmaceutical (Shanghai) Co., Ltd	100%
B1F, 8F & 9F, 88 Xizang North Road, Jing'an District, Shanghai, China	
Alexion Pharmaceuticals (Shanghai) Company Limited	100%
Room 702, Level, No. 1539 West Nanjing Road, Jing'an District, Shangai, China	
Colombia	
AstraZeneca Colombia S.A.S.	100%
Carrera 7 No. 71-21, Torre A, Piso 19, Bogota, D.C., Colombia	
Alexion Pharma Colombia S.A.S.	100%
Carrera 9 No. 115 – 06 /30 Edificio Tierra Firme Oficina 2904 Bogota D.C., Colombia	
Costa Rica	
AstraZeneca CAMCAR Costa Rica, S.A.	100%
Escazu, Guachipelin, Centro Corporativo Plaza Roble, Edificio Los Balcones, Segundo Nivel, San Jose, Costa Rica	
Croatia	
AstraZeneca d.o.o.	100%
Radnicka cesta 80, 10000 Zagreb, Croatia	
Czech Republic	
AstraZeneca Czech Republic, s.r.o.	100%
U Trezorky 921/2, 158 00 Prague 5, Czech Republic	
Alexion Pharma Czech s.r.o.	100%
Novodvorská 994/138, Branik, 142 00 Prague, Czech Republic	

Group Subsidiaries and Holdings
continued

At 31 December 2021	Group Interest
Denmark	
AstraZeneca A/S	100%
World Trade Center Ballerup, Borupvang 3, DK- 2750 Ballerup, Denmark	
Egypt	
AstraZeneca Egypt for Pharmaceutical Industries SAE	100%
6th of October City, 6th Industrial Zone, Plot 2, Giza, Egypt	
AstraZeneca Egypt LLC	100%
47 St. 270 New Maadi, Maddi, Cairo, Egypt	
Drimex LLC	100%
Plot 133, Banks' District, 5th Settlement, New Cairo, Cairo, Egypt	
Estonia	
AstraZeneca Eesti OÜ	100%
Valukoja 8, Ülemiste City, Tallinn 11415, Estonia	
Finland	
AstraZeneca OY.	100%
Itsehallintokuja 4, Espoo, 02600, Finland	
France	
AstraZeneca S.A.S.	100%
Tour Carpe Diem-31, Place des Corolles, 92400 Courbevoie, France	
AstraZeneca Dunkerque Production SCS	100%
224 Avenue de la Dordogne, 59640 Dunkerque, France	
AstraZeneca Reims Production	100%
Chemin de Vrilly Parc, Industriel de la Pompelle, 51100, Reims, France	
Alexion Europe S.A.S.	100%
Alexion Pharma France S.A.S.	100%
103-105 Rue Anatole France 92300 Levallois-Perret	
Germany	
AstraZeneca Holding GmbH	100%
AstraZeneca GmbH	100%
Tinsdaler Weg 183, Wedel, D-22880, Germany	
Sofotec GmbH	100%
Benzstrasse 1-3, 61352, Bad Homburg v.d. Hohe, Germany	
AstraZeneca Computational Pathology GmbH[2]	100%
Bernhard-Wicki-Straße 5, 80636, Munich, Germany	
Portola FRG GmbH	100%
Fraunhoferstraße 12Planegg 82152 Germany	
Alexion Pharma Germany GmbH	100%
Landsberger Straße 300, 80687 Munich, Germany	
Greece	
AstraZeneca S.A.	100%
Agisilaou 6-8 str., Marousi-Athens, 15123, Greece	

At 31 December 2021	Group Interest
Hong Kong	
AstraZeneca Hong Kong Limited	100%
Unit 1 - 3, 11/F., 18 King Wah Road, North Point, Hong Kong	
Hungary	
AstraZeneca Kft	100%
1st floor, 4 building B, Alíz str., Budapest, 1117, Hungary	
India	
AstraZeneca India Private Limited[3]	100%
Block A, Neville Tower, 11th Floor, Ramanujan IT SEZ, Taramani, Chennai, Tamil Nadu, PIN 600113, India	
Alexion Business Services Private Limited	100%
9th Floor, Platina, G BlockPlot No. C-59, Bandra-Kurla Complex Bandra (East), Mumbai 400051 India	
Iran	
AstraZeneca Pars Company	100%
Suite 1, 1st Floor No. 39, Alvand Ave., Arganlin Sq., Tehran 1516673114, Iran	
Ireland	
AstraZeneca Pharmaceuticals (Ireland) Designated Activity Company	100%
4th Floor, South Bank House, Barrow Street, Dublin, 4, Republic of Ireland	
Alexion Pharma Holding UC	100%
Alexion Pharma International Operations UC	100%
Alexion Pharma Development UC	100%
College Business & Technology Park, Blanchardstown Road, North Dublin 15, Ireland	
Israel	
AstraZeneca (Israel) Ltd	100%
6 Hacharash St., Hod Hasharon, 4524075, Israel	
Alexion Pharma Israel Ltd	100%
4 Weizmann Str., Tel-Aviv-Jaffa, Israel	
Italy	
Simesa SpA	100%
AstraZeneca SpA	100%
Viale Decumano 39 20157 Milan, Italy	
Alexion Pharma Italy Srl	100%
Via Melchiorre Gioia 8 Milano 20124, Italy	
Japan	
AstraZeneca K.K.	100%
Grand Front Osaka Tower B, 3-1, Oluka-cho, Kita-ku, Osaka, 530-0011, Japan	
Alexion Pharma GK	100%
Ebisu First Square, 18-14, Ebisu 1-chome, Shibuya-ku, Tokyo, Japan	
Kenya	
AstraZeneca Pharmaceuticals Limited	100%
L.R. No.1/1327, Avenue 5, 1st Floor, Rose Avenue, Nairobi, Kenya	

At 31 December 2021	Group Interest
Latvia	
AstraZeneca Latvija SIA	100%
Skanstes iela 50, Riga, LV-1013, Latvia	
Lithuania	
AstraZeneca Lietuva UAB	100%
Spaudos g., Vilnius, LT-05132, Lithuania	
Luxembourg	
AstraZeneca Luxembourg S.A.	100%
Rue Nicolas Bové 2A – L-1253 Luxembourg	
Malaysia	
AstraZeneca Asia-Pacific Business Services Sdn Bhd	100%
12th Floor, Menara Symphony, No. 5 Jalan Prof. Khoo Kay Kim, Seksyen 13, 46200 Petaling Jaya, Selangor Darul Ehsan, Malaysia	
AstraZeneca Sdn Bhd	100%
Nucleus Tower, Level 11 & 12, No. 10 Jalan PJU 7/6, Mutiara Damansara, 47800 Petaling Jaya, Selangor Darul Ehsan, Malaysia	
Mexico	
AstraZeneca Health Care Division, S.A. de C.V.	100%
AstraZeneca, S.A. de C.V.	100%
Av. Periferico Sur 4305 interior 5, Colonia Jardines en la Montaña, Mexico City, Tlalpan Distrito Federal, CP 14210, Mexico	
Alexion Pharma Mexico S. de R.L. de C.V.	100%
Paseo de los Tamarindos 90 Torre 1piso 6 - ACol. Bosques de la Lomas CP 05120 D.F Mexico	
Morocco	
AstraZeneca Maroc SARLAU	100%
92 Boulevard Anfa ETG 2, Casablanca 20000, Morocco	
The Netherlands	
AstraZeneca B.V.	100%
AstraZeneca Continent B.V.	100%
AstraZeneca Gamma B.V.	100%
AstraZeneca Holdings B.V.	100%
AstraZeneca Jota B.V.	100%
AstraZeneca Rho B.V.	100%
AstraZeneca Sigma B.V.	100%
AstraZeneca Treasury B.V.	100%
AstraZeneca Zeta B.V.	100%
Alexion Holding B.V.	100%
Alexion Pharma Foreign Holdings, B.V.	100%
Prinses Beatrixlaan 582, 2595BM, The Hague, The Netherlands	
AstraZeneca Nijmegen B.V.	100%
Lagelandseweg 78, 6545 CG Nijmegen, The Netherlands	
Acerta Pharma B.V.	100%
Aspire Therapeutics B.V.	100%
Kloosterstraat 9, 5349 AB, Oss, The Netherlands	

At 31 December 2021	Group Interest
Portola Netherlands B.V.	100%
Prins Bernhardplein 200 JB Amsterdam 1097, The Netherlands	
Alexion Pharma Netherlands B.V.	100%
Herengracht 282 Amsterdam 1016 BX, The Netherlands	
New Zealand	
AstraZeneca Limited	100%
Pharmacy Retailing (NZ) Limited t/a Healthcare Logistics, 58 Richard Pearse Drive, Mangere, Auckland, 1142, New Zealand	
Nigeria	
AstraZeneca Nigeria Limited	100%
11A, Alfred Olaiya Street, Awuse Estate, Off Salvation Street, Opebi, Ikeja, Lagos, Nigeria	
Norway	
AstraZeneca AS	100%
Fredrik Selmers vei 6 NO-0663 Oslo, Norway	
Pakistan	
AstraZeneca Pharmaceuticals Pakistan (Private) Limited[4]	100%
Office No. 1, 2nd Floor, Sasi Arcade, Block 7, Main Clifton Road, Karachi, Pakistan	
Panama	
AstraZeneca CAMCAR, S.A.	100%
Bodega #1, Parque Logistico MIT, Carretera Hacia Coco Solo, Colon, Panama	
Peru	
AstraZeneca Peru S.A.	100%
Calle Las Orquideas No. 675, Int. 802, Edificio Pacific Tower, San Isidro, Lima, Peru	
Philippines	
AstraZeneca Pharmaceuticals (Phils.) Inc.	100%
16th Floor, Inoza Tower, 40th Street, Bonifacio Global City, Taguig 1634, Philippines	
Poland	
AstraZeneca Pharma Poland Sp.z.o.o.	100%
Postepu 14, 02-676, Warszawa, Poland	
Portugal	
Astra Alpha Produtos Farmaceuticos Lda	100%
AstraZeneca Produtos Farmaceuticos Lda	100%
Novastra Promoção e Comércio Farmacêutico Lda	100%
Novastuart Produtos Farmaceuticos Lda	100%
Stuart-Produtos Farmacêuticos Lda	100%
Zeneca Epsilon – Produtos Farmacêuticos Lda	100%
Zenecapharma Produtos Farmaceuticos, Unipessoal Lda	100%
Rua Humberto Madeira, No 7, Queluz de Baixo, 2730-097, Barcarena, Portugal	
Puerto Rico	
IPR Pharmaceuticals, Inc.	100%
Road 188, San Isidro Industrial Park, Canóvanas, Puerto Rico 00729	

At 31 December 2021	Group Interest
Romania	
AstraZeneca Pharma S.R.L.	100%
12 Menuetului Street, Bucharest Business Park, Building D, West Wing, 1st Floor, Sector 1, Bucharest, 013713, Romania	
Russia	
AstraZeneca Industries, LLC	100%
249006, 1st Vostochniy proyezd, 8, Dobrino village, Borovskiy district, Russian Federation	
AstraZeneca Pharmaceuticals, LLC	100%
Building 1, 21 First Krasnogvardeyskiy lane, floor 30, Moscow, Russia	
Alexion Pharma OOO LLC	100%
4th Lesnoy Pereulok, Floor 5, Office 529, Moscow, 125047, Russian Federation.	
Singapore	
AstraZeneca Singapore Pte Limited	100%
10 Kallang Avenue #12-10, Aperia Tower 2, 339510, Singapore	
South Africa	
AstraZeneca Pharmaceuticals (Pty) Limited	100%
17 Georgian Crescent West, Northdowns Office Park, Bryanston, 2191, South Africa	
South Korea	
AstraZeneca Korea Co.-Ltd	100%
21st Floor, Asem Tower, 517, Yeongdong-daero, Gangnam-gu, Seoul, 06164, South Korea	
Alexion Pharma Korea LLC	100%
41 FL., 152 Teheran-ro (Yeoksam-dong Gangnam Finance Center), Gangnam-gu, Seoul, South Korea	
Spain	
AstraZeneca Farmaceutica Holding Spain, S.A.	100%
AstraZeneca Farmaceutica Spain S.A.	100%
Fundación AstraZeneca	100%
Laboratorio Beta, S.A.	100%
Laboratorio Lailan, S.A.	100%
Laboratorio Tau S.A.	100%
Parque Norte, Edificio Álamo, C/Serrano Galvache no 56., 28033 Madrid, Spain	
Alexion Pharma Spain S.L.	100%
Av Diagonal Num. 601 P.1 Barcelona 08028, Spain	
Sweden	
Astra Export & Trading Aktiebolag	100%
Astra Lakemedel Aktiebolag	100%
AstraZeneca AB	100%
AstraZeneca Biotech AB	100%
AstraZeneca BioVentureHub AB	100%
AstraZeneca Holding Aktiebolag[5]	100%
AstraZeneca International Holdings Aktiebolag[5]	100%
AstraZeneca Nordic AB	100%
AstraZeneca Pharmaceuticals Aktiebolag	100%
AstraZeneca Södertälje 2 AB	100%
Stuart Pharma Aktiebolag	100%
Tika Lakemedel Aktiebolag	100%
SE-151 85 Södertälje, Sweden	

At 31 December 2021	Group Interest
Aktiebolaget Hassle	100%
Symbicom Aktiebolag[6]	100%
431 83 Molndal, Sweden	
Astra Tech International Aktiebolag	100%
Box 14, 431 21 Molndal, Sweden	
Alexion Pharma Nordics Holding AB	100%
Alexion Pharma Nordics AB	100%
TTM Europe Development AB	100%
Wilson Therapeutics AB	100%
Wilson Therapeutics Incentive AB	100%
Kungsgatan 3, 111 43 Stockholm, Sweden	
Switzerland	
AstraZeneca AG	100%
Neuhofstrasse 34, 6340 Baar, Switzerland	
Spirogen Sarl[6]	100%
Rue du Grand-Chêne 5, CH-1003 Lausanne, Switzerland	
Portola Schweiz GmbH	100%
c/o Tom Schaffner Schärer Rechtsanwälte Hintere Bahnhofstrasse 6, 5000 Aarau, Switzerland	
Alexion Pharma GmbH	100%
Giesshübelstrasse 30, Zürich, 8045, Switzerland	
Taiwan	
AstraZeneca Taiwan Limited	100%
21st Floor, Taipei Metro Building 207, Tun Hwa South Road, SEC 2 Taipei, Taiwan	
Alexion Pharma Taiwan Ltd	100%
Room 1153, 11F, No.1, SongZhi Rd Taipei, 11047 Taiwan	
Thailand	
AstraZeneca (Thailand) Limited	100%
Asia Centre 19th floor, 173/20, South Sathorn Rd, Khwaeng Thungmahamek, Khet Sathorn, Bangkok, 10120, Thailand	
Tunisia	
AstraZeneca Tunisie SaRL	100%
Lot No. 1.5.5 les jardins du lac, bloc B les berges du lac Tunis, Tunisia	
Turkey	
AstraZeneca Ilac Sanayi ve Ticaret Limited Sirketi	100%
YKB Plaza, B Blok, Kat:3-4, Levent/ Besiktas, Istanbul, Turkey	
Zeneca Ilac Sanayi Ve Ticaret Anonim Sirketi	100%
Büyükdere Cad., Y.K.B. Plaza, B Blok, Kat:4, Levent/Besiktas, Istanbul, Turkey	
Alexion Ilac Ticaret Limited Sirketi	100%
Içerenköy Mahallesi Umut Sok. AND Ofis Sit. No. 1012/73 Atasehir Istanbul, Turkey	
Ukraine	
AstraZeneca Ukraina LLC	100%
54 Simi Prakhovykh street, Kiev, 01033, Ukraine	

Group Subsidiaries and Holdings
continued

At 31 December 2021	Group Interest
United Arab Emirates	
AstraZeneca FZ-LLC	100%
P.O. Box 505070, Block D, Dubai Healthcare City, Oud Mehta Road, Dubai, United Arab Emirates	
Alexion Pharma Middle East FZ-LLC	100%
Dubai Science Park, 501, Floor 5, EIB Building No. 2, Dubai, United Arab Emirates	
United Kingdom	
Ardea Biosciences Limited	100%
Arrow Therapeutics Limited	100%
Astra Pharmaceuticals Limited	100%
AstraPharm[6]	100%
AstraZeneca China UK Limited	100%
AstraZeneca Death In Service Trustee Limited	100%
AstraZeneca Employee Share Trust Limited	100%
AstraZeneca Finance Limited	100%
AstraZeneca Intermediate Holdings Limited[5]	100%
AstraZeneca Investments Limited	100%
AstraZeneca Japan Limited	100%
AstraZeneca Nominees Limited	100%
AstraZeneca Quest Limited	100%
AstraZeneca Share Trust Limited	100%
AstraZeneca Sweden Investments Limited	100%
AstraZeneca Treasury Limited[6]	100%
AstraZeneca UK Limited	100%
AstraZeneca US Investments Limited[5]	100%
AZENCO2 Limited	100%
AZENCO4 Limited	100%
Cambridge Antibody Technology Group Limited	100%
KuDOS Horsham Limited	100%
KuDOS Pharmaceuticals Limited	100%
Zenco (No. 8) Limited	100%
Zeneca Finance (Netherlands) Company	100%
1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge, CB2 0AA, United Kingdom	
MedImmune Limited	100%
Milstein Building, Granta Park, Cambridge, CB21 6GH, United Kingdom	
MedImmune U.K. Limited	100%
Plot 6, Renaissance Way, Boulevard Industry Park, Liverpool, L24 9JW, United Kingdom	
Syntimmune Limited	100%
21 Holborn Viaduct, London, EC1A 2DY, United Kingdom	
Alexion Pharma UK Limited	100%
Portola Pharma UK Limited	100%
3 Furzeground Way, Stockley Park, Uxbridge, Middlesex, UB11 1EZ, United Kingdom	

At 31 December 2021	Group Interest
United States	
Amylin Ohio LLC[7]	100%
Amylin Pharmaceuticals, LLC[7]	100%
AstraZeneca Collaboration Ventures, LLC[7]	100%
AstraZeneca Pharmaceuticals LP[8]	100%
Atkemix Nine Inc.	100%
Atkemix Ten Inc.	100%
BMS Holdco, Inc.	100%
Corpus Christi Holdings Inc.	100%
Ornthera Pharmaceuticals, Inc.	100%
Optein, Inc.	100%
Stauffer Management Company LLC[7]	100%
Zeneca Holdings Inc.	100%
Zeneca Inc.	100%
Zeneca Wilmington Inc.[6]	100%
AstraZeneca Finance LLC	100%
AstraZeneca Finance and Holdings Inc.[5]	100%
1800 Concord Pike, Wilmington, DE 19803, United States	
ZS Pharma Inc.	100%
1100 Park Place, Suite 300, San Mateo, CA 94403, United States	
AlphaCore Pharma, LLC[7]	100%
333 Parkland Plaza, Suite 5, Ann Arbor, MI 48103, United States	
AZ-Mont Insurance Company	100%
76 St Paul Street, Suite 500, Burlington, VT 05401, United States	
Definiens Inc.	100%
1808 Aston Avenue, Suite 190, Carlsbad, CA 92008, United States	
MedImmune, LLC[7]	100%
MedImmune Ventures, Inc.	100%
One MedImmune Way, Gaithersburg, MD 20878, United States	
Pearl Therapeutics, Inc.	100%
200 Cardinal Way, Redwood City, CA 94063, United States	
Caelum Biosciences Inc.	100%
1200 Florence Columbus Road, Bordentown, NJ 08505, United States	
Alexion Services Latin America Inc.	100%
600 Brickell Ave, Miami, FL 33131, United States	
Portola USA, Inc.	100%
Portola Pharmaceuticals LLC	100%
270 East Grand Avenue, South San Francisco, CA 94080, United States	
Achillion Pharmaceuticals, Inc.	100%
Alexion Delaware Holding LLC	100%
Alexion Holding LLC	100%
Alexion Pharma LLC	100%
Alexion Pharmaceuticals, Inc.	100%
Syntimmune, Inc.	100%
Alexion US Holdings LLC	100%
Alexion US1 LLC	100%
Savoy Therapeutics Corp	100%
Wilson Therapeutics USA, Inc.	100%
121 Seaport Boulevard, Boston, MA 02210, United States	

At 31 December 2021	Group Interest
Acerta Pharma LLC[7]	100%
121 Oyster Point Boulevard, South San Francisco, CA 94080, United States	
Cider Merger Sub, Inc.	100%
1209 Orange Street, City of Wilmington, County of New Castle, Delaware 19801, United States	
Uruguay	
AstraZeneca S.A.	100%
Yaguarón 1407 of 1205, 11.100, Montevideo, Uruguay	
Venezuela	
AstraZeneca Venezuela S.A.	100%
Gotland Pharma S.A.	100%
Av. La Castellana, Torre La Castellana, Piso 5, Oficina 5-G, 5-H, 5-I, Urbanización La Castellana, Municipio Chacao, Estado Bolivariano de Miranda, Venezuela	
Vietnam	
AstraZeneca Vietnam Company Limited	100%
18th Floor, A&B Tower, 76 Le Lai, Ben Thanh Ward, District 1, Ho Chi Minh City, Vietnam	

At 31 December 2021	Group Interest
Subsidiaries where the effective interest is less than 100%	
India	
AstraZeneca Pharma India Limited[3]	75%
Block N1, 12th Floor, Manyata Embassy Business Park, Rachenahalli, Outer Ring Road, Bangalore-560 045, India	
Indonesia	
P.T. AstraZeneca Indonesia	95%
Perkantoran Hijau Arkadia Tower F, 3rd Floor, Jl. T.B. Simatupang Kav. 88, Jakarta, 12520, Indonesia	
Joint Ventures	
Hong Kong	
WuXi MedImmune Biopharmaceutical Co., Limited	50%
Room 1902, 19/F, Lee Garden One, 33 Hysan Avenue, Causeway Bay, Hong Kong	
IHP HK Holdings Limited	50%
Unit 5805, 58/F., Two International Finance Centre 8 Finance Street, Central, Hong Kong	
United Kingdom	
Archigen Biotech Limited[3]	50%
Centus Biotherapeutics Limited[3]	50%
1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge, CB2 0AA, United Kingdom	
United States	
Montrose Chemical Corporation of California	50%
Suite 380, 600 Ericksen Ave N/E, Bainbridge Island, United States	

At 31 December 2021	Group Interest
Significant Holdings	
Australia	
Armaron Bio Ltd[10]	24.60%
MPR Group, HWT Tower, Level 19, 40 City Rd, Southbank, VIC 3006, Australia	
China	
Dizal (Jiangsu) Pharmaceutical Co., Ltd.[11]	26.95%
199 Liangjing Rd, Zhangjiang Hi-Tech Park, Pudong District, Shanghai, China, 201203	
Wuxi AstraZeneca-CICC Venture Capital Partnership (Limited Partnership)	22.13%
Room 808, 8F, Building 99-2 Linghu Avenue, Xinwu District, Wuxi, Jiangsu, China	
United Kingdom	
Apollo Therapeutics LLP[7]	25%
Stevenage Biosciences Catalyst, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2FX, United Kingdom	
VaxEquity[14]	40%
The Mansion, Chesterford Research Park, Little Chesterford, Essex, CB10 1XL, United Kingdom	
United States	
C.C. Global Chemicals Company[8]	37.5%
PO Box 7, MS2901, Texas, TX76101-0007, United States	

At 31 December 2021	Group Interest
Associated Holdings	
France	
Medetia SAS[9]	10%
Institute Imagine 24, Boulevard du Montparnasse 75015, Paris, France	
Sweden	
Swedish Orphan Biovitrum AB (publ)	9.9%
Tomtebodavägen 23A, Stockholm, Sweden	
Ondosis[8]	19.9%
BioVentureHub, Pepparedsleden 1, 431 83 Mölndal, Sweden	
United Kingdom	
Circassia Pharmaceuticals PLC	17%
Northbrook House, Robert Robinson Avenue, Oxford Science Park, Oxford, OX4 4GA, United Kingdom	
United States	
AbMed Corporation[12]	18%
66 Cummings Park Drive, Woburn, MA 01801, United States	
Aristea Therapeutics, Inc.[13]	11.85%
122770 High Bluff Drive, #380, San Diego, CA 92130, United States	
Baergic Bio, Inc.	19.95%
2 Gansevoort Street, 9th Floor, New York, NY 10014, United States	
Employee Benefit Trust	
The AstraZeneca Employee Benefit Trust	

[1] Ownership held in ordinary and class B special shares.
[2] Ownership held in common shares, preferred shares 2003, preferred shares 2003 ex (A), preferred shares 2003 ex (B), preferred shares Series D, preferred shares Series E and preferred shares Series F.
[3] Accounting year end is 31 March.
[4] Accounting year end is 30 June.
[5] Directly held by AstraZeneca PLC.
[6] Ownership held in Ordinary A shares and Ordinary B shares.
[7] Ownership held as membership interest.
[8] Ownership held as partnership interest.
[9] Ownership held in class A preference shares.
[10] Ownership held in class B preference shares.
[11] Voting rights and percentages vary depending on the subject matter and business to be voted on.
[12] Ownership held in common shares and series A preferred shares.
[13] Ownership held in series A-1 preferred stock and series B preferred stock.
[14] Ownership held in series A preferred stock.

Company Balance Sheet
at 31 December

AstraZeneca PLC

	Notes	2021 $m	2020 $m
Fixed assets			
Fixed asset investments	1	65,624	33,268
Other receivables		–	4
		65,624	33,272
Current assets			
Debtors – other		9	26
Debtors – amounts owed by Group undertakings		6,321	7,011
		6,330	7,037
Creditors: Amounts falling due within one year			
Other payables	3	(198)	(192)
Interest-bearing loans and borrowings	2	(1,249)	(1,535)
		(1,447)	(1,727)
Net current assets		4,883	5,310
Total assets less current liabilities		70,507	38,582
Creditors: Amounts falling due after more than one year			
Amounts owed to Group undertakings	2	(283)	(283)
Interest-bearing loans and borrowings	2	(20,781)	(17,161)
Other payables	3	(32)	–
		(21,096)	(17,444)
Net assets		49,411	21,138
Capital and reserves			
Called-up share capital	4	387	328
Share premium account		35,126	7,971
Capital redemption reserve		153	153
Other reserves		2,182	2,382
Profit and loss account		11,563	10,304
Shareholders' funds		49,411	21,138

$m means millions of US dollars.

The Company's profit for the year was $5,141m (2020: $1,974m).

The Company Financial Statements from pages 202 to 208 were approved by the Board and were signed on its behalf by

Pascal Soriot
Director
10 February 2022

Aradhana Sarin
Director

DocuSigned by:
Aradhana Sarin
D0A6952019FE443...

Company's registered number 02723534

DocuSigned by:
Pascal Soriot
D7EA08B4526C4C7...

Company Statement of Changes in Equity

for the year ended 31 December

	Share capital $m	Share premium account $m	Capital redemption reserve $m	Other reserves[1] $m	Profit and loss account[2] $m	Total equity $m
At 1 January 2020	328	7,941	153	2,441	11,998	22,861
Total comprehensive income for the period						
Profit for the period	–	–	–	–	1,974	1,974
Total comprehensive income for the period	–	–	–	–	1,974	1,974
Transactions with owners, recorded directly in equity						
Dividends	–	–	–	–	(3,668)	(3,668)
Capital contributions for share-based payments	–	–	–	(59)	–	(59)
Issue of Ordinary Shares	–	30	–	–	–	30
Total contributions by and distributions to owners	–	30	–	(59)	(3,668)	(3,697)
At 31 December 2020	328	7,971	153	2,382	10,304	21,138
Total comprehensive income for the period						
Profit for the period	–	–	–	–	5,141	5,141
Total comprehensive income for the period	–	–	–	–	5,141	5,141
Transactions with owners, recorded directly in equity						
Dividends	–	–	–	–	(3,882)	(3,882)
Capital contributions for share-based payments	–	–	–	(200)	–	(200)
Issue of Ordinary Shares	59	27,155	–	–	–	27,214
Total contributions by and distributions to owners	59	27,155	–	(200)	(3,882)	23,132
At 31 December 2021	387	35,126	153	2,182	11,563	49,411

1 The Other reserves arose from the cancellation of £1,255m share premium by the Company in 1993 and the redenomination of share capital of $157m in 1999. Included within Other reserves at 31 December 2021 is $341m (31 December 2020: $541m) in respect of cumulative share-based payment awards, which are not available for distribution.

2 At 31 December 2021, the Profit and loss account reserve of $11,563m (31 December 2020: $10,304m) was available for distribution, subject to filing these Financial Statements with Companies House. When making a distribution to shareholders, the Directors determine profits available for distribution by reference to guidance on realised and distributable profits under the Companies Act 2006 issued by the Institute of Chartered Accountants in England and Wales and the Institute of Chartered Accountants of Scotland in April 2017. The profits of the Company have been received in the form of receivables due from subsidiaries. The availability of distributable reserves in the Company is dependent on those receivables meeting the definition of qualifying consideration within the guidance, and in particular on the ability of subsidiaries to settle those receivables within a reasonable period of time. The Directors consider that, based on the nature of these receivables and the available cash resources of the Group and other accessible sources of funds, at 31 December 2021, all (31 December 2020: all) of the Company's profit and loss reserves were available for distribution.

Company Accounting Policies

Basis of presentation of financial information

These financial statements were prepared in accordance with FRS 101 'Reduced Disclosure Framework'.

In preparing these financial statements, the Company applied the recognition, measurement and disclosure requirements of International Financial Reporting Standards as adopted by the UK (UK-adopted International Accounting Standards), but made amendments where necessary in order to comply with the Companies Act 2006 and to take advantage of FRS 101 disclosure exemptions.

In these financial statements, the Company has applied the exemptions available under FRS 101 in respect of the following disclosures:

- Statement of Cash Flows and related notes
- disclosures in respect of transactions with wholly owned subsidiaries
- disclosures in respect of capital management
- the effects of new but not yet effective IFRSs
- disclosures in respect of the compensation of Key Management Personnel.

As the Group Financial Statements (presented on pages 134 to 201) include the equivalent disclosures, the Company has also taken the exemptions under FRS 101 available in respect of the following disclosures:

- IFRS 2 'Share-based Payment' in respect of Group settled share-based payments
- certain disclosures required by IFRS 13 'Fair Value Measurement' and the disclosures required by IFRS 7 'Financial Instruments: Disclosures'.

No individual profit and loss account is prepared as provided by section 408 of the Companies Act 2006.

UK-adopted International Accounting Standards

On 31 December 2020, EU-adopted IFRS was brought into UK law and became UK-adopted International Accounting Standards, with future changes to IFRS being subject to endorsement by the UK Endorsement Board. In preparing these financial statements in accordance with FRS 101, the Company Financial Statements transitioned to UK-adopted International Accounting Standards (as described above) on 1 January 2021. There is no impact on recognition, measurement or disclosure in the period reported as a result of this change.

Basis of accounting

The Company Financial Statements are prepared under the historical cost convention and on a going concern basis, in accordance with the Companies Act 2006.

The following paragraphs describe the main accounting policies, which have been applied consistently.

Estimates and judgements

The preparation of the Company Financial Statements in conformity with generally accepted accounting principles requires management to make estimates and judgements that affect the reported amounts of assets and liabilities at the date of the Financial Statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. There are no key judgements or significant estimates.

Foreign currencies

Profit and loss account items in foreign currencies are translated into US dollars at average rates for the relevant accounting periods. Monetary assets and liabilities are translated at exchange rates prevailing at the date of the Company Balance Sheet. Exchange gains and losses on loans and on short-term foreign currency borrowings and deposits are included within net Finance expense. Exchange differences on all other foreign currency transactions are recognised in Operating profit.

Taxation

The current tax payable is based on taxable profit for the year. Taxable profit differs from reported profit because taxable profit excludes items that are either never taxable or tax deductible or items that are taxable or tax deductible in a different period. The Company's current tax assets and liabilities are calculated using tax rates that have been enacted or substantively enacted by the reporting date.

Deferred tax is provided using the balance sheet liability method, providing for temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. Deferred tax assets are recognised to the extent that it is probable that taxable profit will be available against which the asset can be utilised. This requires judgements to be made in respect of the availability of future taxable income.

No deferred tax asset or liability is recognised in respect of temporary differences associated with investments in subsidiaries and branches where the Company is able to control the timing of reversal of the temporary differences and it is probable that the temporary differences will not reverse in the foreseeable future.

The Company's deferred tax assets and liabilities are calculated using tax rates that are expected to apply in the period when the liability is settled or the asset realised based on tax rates that have been enacted or substantively enacted by the reporting date.

Accruals for tax contingencies require management to make judgements of potential exposures in relation to tax audit issues. Tax benefits are not recognised unless the tax positions will probably be accepted by the authorities. This is based upon management's interpretation of applicable laws and regulations and the expectation of how the tax authority will resolve the matter. Once considered probable of not being accepted, management reviews each material tax benefit and reflects the effect of the uncertainty in determining the related taxable result.

Accruals for tax contingencies are measured using either the most likely amount or the expected value amount depending on which method the Company expects to better predict the resolution of the uncertainty.

Investments
Fixed asset investments, including investments in subsidiaries, are stated at cost and reviewed for impairment if there are indications that the carrying value may not be recoverable.

Debtors
Amounts owed by Group undertakings are recognised initially at fair value. Subsequent to initial recognition they are measured at amortised cost using the effective interest method, less any impairment losses.

The recoverability of these balances has been assessed in accordance with IFRS 9 and no impairment has been identified. The amounts owed by Group undertakings are considered to have low credit risk, due to timely payment of interest and settlement of principal amounts on agreed due dates, limiting the loss allowance to 12-month expected credit losses.

Amounts owed by Group undertakings are written off where there is no reasonable expectation of recovery. Impairment losses are presented as net impairment losses within Operating profit, any subsequent recoveries are credited against the same line.

Other payables
Liabilities included in Other payables are recognised initially at fair value. Subsequent to initial recognition they are re-measured at fair value using an expected credit loss model.

Share-based payments
The issuance by the Company to employees of its subsidiaries of a grant of awards over the Company's shares, represents additional capital contributions by the Company to its subsidiaries. An additional investment in subsidiaries results in a corresponding increase in shareholders' equity. The additional capital contribution is based on the fair value of the grant issued, allocated over the underlying grant's vesting period, less the market cost of shares charged to subsidiaries in settlement of such share awards.

Financial instruments
Interest-bearing loans are initially measured at fair value (with direct transaction costs being amortised over the life of the loan) and are subsequently measured at amortised cost using the effective rate method at each reporting date. Changes in carrying value are recognised in profit.

Litigation
Through the normal course of business, the AstraZeneca Group is involved in legal disputes, the settlement of which may involve cost to the Company. Provision is made where an adverse outcome is probable and associated costs can be estimated reliably. In other cases, appropriate descriptions are included.

Notes to the Company Financial Statements

1 Fixed asset investments

	Investments in subsidiaries		
	Shares $m	Loans $m	Total $m
At 1 January 2020	15,861	15,664	31,525
Additions during the year	–	2,971	2,971
Transfer to Debtors – amounts owed by Group undertakings	–	(1,451)	(1,451)
Capital reimbursement	(44)	–	(44)
Exchange	–	254	254
Amortisation	–	13	13
At 31 December 2020	15,817	17,451	33,268
Additions during the year	33,745	290	34,035
Transfer to Debtors – amounts owed by Group undertakings	–	(1,249)	(1,249)
Capital reimbursement	(13)	–	(13)
Exchange	–	(172)	(172)
Amortisation	–	13	13
Disposals and other movements	32	(290)	(258)
At 31 December 2021	49,581	16,043	65,624

Loans to subsidiaries consists of bonds which are issued externally and are issued back to Group undertakings with comparable terms on interest rates and are repayable on maturity, details of which are disclosed in Note 2. The recoverability of these inter-company loans has been assessed in accordance with IFRS 9 with no impairment identified. The inter-company balances are considered to have low credit risk due to timely payment of interest and settlement of principal amount on agreed due dates, limiting the loss allowance to 12-month expected credit losses. In 2021, there have been no credit losses (2020: $nil).

Included within Additions during the year of inter-company loans, are the distribution in specie received from subsidiary undertakings in the form of a loan receivable from Group companies for $290m. The loan was settled during the year and recorded as disposed in the same year. The other movements include $32m representing fair value of a guarantee provided to Group companies as explained in Notes 2 and 3.

2 Loans and borrowings

		Repayment dates	2021 $m	2020 $m
Amounts due within one year				
Interest-bearing loans and borrowings (unsecured)				
0.25% Callable bond	euros	2021	–	614
0.875% Non-callable bond	euros	2021	–	921
Floating rate notes	US dollars	2022	250	–
2.375% Callable bond	US dollars	2022	999	–
			1,249	1,535
Amounts due after more than one year				
Amounts owed to Group undertakings (unsecured)				
7.2% Loan	US dollars	2023	283	283
Interest-bearing loans and borrowings (unsecured)				
Floating rate notes	US dollars	2022	–	250
2.375% Callable bond	US dollars	2022	–	996
Floating rate notes	US dollars	2023	400	400
0.3% Callable bond	US dollars	2023	1,397	–
3.5% Callable bond	US dollars	2023	848	847
0.75% Callable bond	euros	2024	1,014	1,102
2024 Floating bank loan	US dollars	2024	1,997	–
3.375% Callable bond	US dollars	2025	1,988	1,985
0.7% Callable bond	US dollars	2026	1,193	1,192
3.125% Callable bond	US dollars	2027	745	744
1.25% Callable bond	euros	2028	896	973
0.375% Callable bond	euros	2029	898	–
4% Callable bond	US dollars	2029	994	993
1.375% Callable bond	US dollars	2030	1,292	1,291
5.75% Non-callable bond	pounds sterling	2031	470	475
6.45% Callable bond	US dollars	2037	2,724	2,722
4% Callable bond	US dollars	2042	988	988
4.375% Callable bond	US dollars	2045	980	980
4.375% Callable bond	US dollars	2048	737	737
2.125% Callable bond	US dollars	2050	486	486
3% Callable bond	US dollars	2051	734	–
Total amounts due after more than one year			21,064	17,444
Total loans and borrowings			22,313	18,979

	2021 $m	2020 $m
Loans and borrowings are repayable:		
After five years from balance sheet date	**11,944**	11,581
From two to five years	**6,192**	4,617
From one to two years	**2,928**	1,246
Within one year	**1,249**	1,535
Total unsecured	**22,313**	18,979

All bonds are issued with fixed interest rates with the exception of two bonds, the 2022, the 2023 floating rate notes and the $2bn USD 2024 floating rate loan. The $2bn USD 2024 floating rate loan pays interest linked to 1 month LIBOR. As the loan is held at amortised cost, changes in interest rates and the credit rating of the Company do not have any effect on the Company's net assets. The other two floating rate notes are not impacted by LIBOR reference as they either use non-LIBOR fixings or will mature before the withdrawal of relevant LIBOR rate.

In addition, the Company acts as guarantor for bonds issued by its wholly owned subsidiaries, AstraZeneca Finance LLC and AstraZeneca Finance and Holdings Inc. AstraZeneca Finance LLC is the issuer of $1,600m 0.700% Notes due 2024, $1,250m 1.200% Notes due 2026, $1,250m 1.750% Notes due 2028 and $750m 2.250% Notes due 2031 (the 'AstraZeneca Finance Notes'). AstraZeneca Finance and Holdings Inc. has a $2bn bank loan due 2023. Each series of AstraZeneca Finance Notes has been fully and unconditionally guaranteed by the Company. Each of the guarantees by the Company is full and unconditional and joint and several.

The guarantee by the Company of the AstraZeneca Finance Notes is the senior unsecured obligation of the Company and ranks equally with all of the Company's existing and future senior unsecured and unsubordinated indebtedness. Each guarantee by the Company is effectively subordinated to any secured indebtedness of the Company 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 the Company, none of which guarantee the AstraZeneca Finance Notes.

3 Other payables

	2021 $m	2020 $m
Amounts due within one year		
Other creditors	**187**	185
Deferred income	**4**	–
Amounts owed to Group undertakings	**7**	7
	198	192
Amounts due after more than one year		
Other creditors	**32**	–
	32	–

Non-current other creditors include an amount representing the fair value of the guarantee provided by the Company to its subsidiary for the bonds issued externally as explained in Note 2. As at 31 December 2021, the fair value of the guarantee was $32m (2020: $nil).

4 Called-up share capital

Details of share capital movements in the year are included in Note 24 to the Group Financial Statements.

5 Contingent liabilities

The Company has guaranteed the external borrowing of a subsidiary in the amount of $286m (2020: $286m), and no amount of undrawn borrowing facility of a subsidiary was guaranteed (2020: $17.5bn) in relation to the acquisition of Alexion.

Vermont US Attorney Investigation

In the US, in April 2020, AstraZeneca received a Civil Investigative Demand from the US Attorney's Office in Vermont and the Department of Justice, Civil Division, seeking documents and information relating to AstraZeneca's relationships with electronic health-record vendors. AstraZeneca is co-operating with this enquiry.

AZD1222 Securities Litigation

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.

5 Contingent liabilities *continued*

Alexion Shareholder Litigation

In March 2021, several shareholders of Alexion Pharmaceuticals, Inc. (Alexion) filed individual lawsuits against Alexion, its management, and/or AstraZeneca and affiliates in federal district court in New York. The complaints generally allege that the preliminary registration statement filed with the SEC on 19 February 2021, omitted certain allegedly material information in connection with AstraZeneca's proposed acquisition of Alexion (the Acquisition), and one of the complaints further alleges that the Alexion directors breached their fiduciary duties in connection with the Acquisition and that AstraZeneca and the other entity defendants aided and abetted the alleged breaches. In May 2021, all such complaints were withdrawn and dismissed. This matter is now closed.

US Congressional

In January 2019, AstraZeneca received a letter from the US House of Representatives Committee on Oversight and Reform (Committee) seeking information related to pricing practices for *Crestor*. Similar letters were sent to 11 other pharmaceutical manufacturers. AstraZeneca cooperated with the inquiry and produced certain responsive information. In December 2021, the Committee issued a final report culminating the Committee's pharmaceutical pricing investigation. AstraZeneca's products are not the subject of the findings in the final report.

6 Statutory and other information

The Directors of the Company were paid by another Group company in 2021 and 2020.

7 Subsequent events

No subsequent events having material impact on the financial statements were identified after the balance sheet date.

Group Financial Record

For the year ended 31 December	2017 $m	2018 $m	2019 $m	2020 $m	2021 $m
Revenue and profits					
Product Sales	20,152	21,049	23,565	25,890	**36,541**
Collaboration Revenue	2,313	1,041	819	727	**876**
Cost of sales	(4,318)	(4,936)	(4,921)	(5,299)	**(12,437)**
Distribution costs	(310)	(331)	(339)	(399)	**(446)**
Research and development expense	(5,757)	(5,932)	(6,059)	(5,991)	**(9,736)**
Selling, general and administrative expense	(10,233)	(10,031)	(11,682)	(11,294)	**(15,234)**
Other operating income and expense	1,830	2,527	1,541	1,528	**1,492**
Operating profit	3,677	3,387	2,924	5,162	**1,056**
Finance income	113	138	172	87	**43**
Finance expense	(1,508)	(1,419)	(1,432)	(1,306)	**(1,300)**
Share of after tax losses in associates and joint ventures	(55)	(113)	(116)	(27)	**(64)**
Profit/(loss) before tax	2,227	1,993	1,548	3,916	**(265)**
Taxation	641	57	(321)	(772)	**380**
Profit for the period	2,868	2,050	1,227	3,144	**115**
Other comprehensive income/(loss) for the period, net of tax	639	(1,059)	(611)	1,608	**(145)**
Total comprehensive income/(loss) for the period	3,507	991	616	4,752	**(30)**
Profit attributable to:					
Owners of the Parent	3,001	2,155	1,335	3,196	**112**
Non-controlling interests	(133)	(105)	(108)	(52)	**3**
Earnings per share					
Basic earnings per $0.25 Ordinary Share	$2.37	$1.70	$1.03	$2.44	**$0.08**
Diluted earnings per $0.25 Ordinary Share	$2.37	$1.70	$1.03	$2.44	**$0.08**
Dividends	$2.80	$2.80	$2.80	$2.80	**$2.80**

At 31 December	2017 $m	2018 $m	2019 $m	2020 $m	2021 $m
Statement of Financial Position					
Property, plant and equipment, right-of-use assets, goodwill and intangible assets	45,628	41,087	40,836	41,709	**72,555**
Other non-current assets	2,387	1,594	2,260	2,038	**2,234**
Deferred tax assets	2,189	2,379	2,718	3,438	**4,330**
Current assets	13,150	15,591	15,563	19,544	**26,244**
Total assets	63,354	60,651	61,377	66,729	**105,363**
Current liabilities	(16,383)	(16,292)	(18,117)	(20,307)	**(22,594)**
Deferred tax liabilities	(3,995)	(3,266)	(2,490)	(2,918)	**(6,206)**
Other non-current liabilities	(26,334)	(27,029)	(26,174)	(27,866)	**(37,276)**
Net assets	16,642	14,044	14,596	15,638	**39,287**
Share capital	317	317	328	328	**387**
Reserves attributable to equity holders of the Company	14,643	12,151	12,799	15,294	**38,881**
Non-controlling interests	1,682	1,576	1,469	16	**19**
Total equity and reserves	16,642	14,044	14,596	15,638	**39,287**

For the year ended 31 December	2017 $m	2018 $m	2019 $m	2020 $m	2021 $m
Cash flows					
Net cash inflow/(outflow) from:					
Operating activities	3,578	2,618	2,969	4,799	**5,963**
Investing activities	(2,328)	963	(657)	(285)	**(11,058)**
Financing activities	(2,936)	(2,044)	(1,765)	(2,203)	**3,649**
	(1,686)	1,537	547	2,311	**(1,446)**

Additional Information

Shareholder information 211

Directors' report 213

Sustainability supplementary information 216

Task force on Climate-related Financial Disclosures Statement 217

Trade Marks 223

Glossary 224

Cautionary statement regarding forward-looking statements 228



Shareholder information

This section of the Annual Report contains information for shareholders that is required by regulation in the UK. Further information that may be of use to shareholders is available on the Shareholder information page of our website at www.astrazeneca.com. Additional information required by SEC regulations is included in AstraZeneca's Form 20-F filing for 2021, which is available on the SEC website at www.sec.gov.

The principal markets for trading in AstraZeneca shares are the London Stock Exchange, Nasdaq Stockholm and the Nasdaq Global Select Market (Nasdaq). AstraZeneca shares were listed on Nasdaq on 25 September 2020, prior to which they were listed on the New York Stock Exchange. Ordinary Shares of $0.25 each in AstraZeneca PLC are listed on the London Stock Exchange and the shareholder register is maintained by Equiniti Limited, the Ordinary Share registrar. Shares listed on Nasdaq Stockholm are issued under the Euroclear Services Agreement by Euroclear Sweden AB, the Swedish Central Securities Depositary. Shares listed on Nasdaq are in the form of American Depositary Shares (ADSs), evidenced by American Depositary Receipts (ADRs) issued by the Company's ADR depositary, Deutsche Bank Trust Company Americas (Deutsche Bank). Two ADSs are equivalent to one Ordinary Share. Before 27 July 2015, the ratio was one ADS per one Ordinary Share. Shares are listed on all three markets under the stock symbol AZN.

Ordinary Share registrar

Equiniti Limited
Aspect House
Spencer Road
Lancing
West Sussex
BN99 6DA
UK
Tel (Freephone in UK): +44 (0)800 389 1580
Tel (outside UK): +44 (0)121 415 7033

Swedish Central Securities Depositary

Euroclear Sweden AB
PO Box 191
SE-101 23 Stockholm
Sweden
Tel: +46 (0)8 402 9000

ADR depositary

Deutsche Bank Trust Company Americas
c/o American Stock Transfer & Trust Company, LLC
6201 15th Avenue
Brooklyn NY 11219
USA
Tel (toll free in the US): +1 (888) 697 8018
Tel (outside US): +1 (718) 921 8137
db@astfinancial.com

Annual General Meeting (AGM)

The 2022 AGM will be held on 29 April 2022 and further details will be set out in the Notice of Meeting. If you hold shares listed in Stockholm or hold ADRs, information relating to voting and attendance will be included in the relevant Notice of AGM. If you hold your shares through a nominee, your nominee provider will be able to advise you of their arrangements in relation to voting and attendance.

Dividends

Dividend dates for 2022 are shown in the financial calendar below. A first interim dividend is normally announced in July/August and paid in September and a second interim dividend is normally announced in January/February and paid in March. Dividends are paid in GBP, SEK and USD, depending on where the eligible shares are listed.

For further information on dividends declared, see the Shareholder information section of our website, www.astrazeneca.com.

Financial calendar

Event	Provisional date
Second interim dividend for 2021	
Ex-dividend date	24 February 2022
Record date	25 February 2022
Payment date	28 March 2022
Announcement of first quarter results for 2022	29 April 2022
Annual General Meeting (AGM)	29 April 2022
Announcement of second quarter and half-year results for 2022	29 July 2022
First interim dividend for 2022	
Ex-dividend date	11 August 2022
Record date	12 August 2022
Payment date	12 September 2022
Announcement of third quarter results for 2022	10 November 2022
Financial year end	31 December 2022

Related party transactions

During the period 1 January 2022 to 31 January 2022, there were no transactions, loans, or proposed transactions between the Company and any related parties which were material to either the Company or the related party, or which were unusual in their nature or conditions (see also Note 31 to the Financial Statements on page 196).

Conflicts of interest

The Articles enable the Directors to authorise any situation in which a Director has an interest that conflicts or has the potential to conflict with the Company's interests and which would otherwise be a breach of the Director's duty, under Section 175 of the Companies Act 2006. The Board has a formal system in place for Directors to declare such situations to be considered for authorisation by those Directors who have no interest in the matter being considered.

In deciding whether to authorise a situation, the non-conflicted Directors must act in the way they consider, in good faith, would be most likely to promote the success of the Company, and they may impose limits or conditions when giving the authorisation, or subsequently, if they think this is appropriate. Situations considered by the Board and authorisations given are recorded in the Board minutes and in a register of conflicts maintained by the Company Secretary and are reviewed annually by the Board. The Board believes that this system operates effectively.

Shareholder fraud warning

Shareholders of AstraZeneca and many other companies have reported receiving unsolicited calls and correspondence relating to their shareholdings and investment matters. Shareholders are advised to be very cautious of any unsolicited approaches and to note that reputable firms authorised by the Financial Conduct Authority (FCA) are very unlikely to make such approaches. Such approaches are likely to be part of a 'boiler room scam' attempting to defraud shareholders.

Shareholders are advised to familiarise themselves with the information on scams available on the FCA website, www.fca.org.uk/consumers and within the FAQs in the Investors section of our website, www.astrazeneca.com.

Any suspected scams or fraudulent approaches should be reported to the FCA via its website and to AstraZeneca's Ordinary Share registrar, using the contact details on this page.

Shareholder information
continued

Issued share capital, shareholdings and share prices

At 31 December 2021, the Company had 74,520 registered holders of 1,549,400,665 Ordinary Shares. There were 167,902 holders of Ordinary Shares held under the Euroclear Services Agreement, representing 10.9% of the issued share capital of the Company and 1,700 registered holders of ADSs, representing 19.0% of the issued share capital of the Company.

Information on the Company's share price, including historical closing prices and volumes, and an interactive share price graph can be found on the Investor Relations page on our website, www.astrazeneca.com.

Ordinary Shares in issue

	2021	2020	2019
Ordinary Shares in issue – millions			
At year end	1,549	1,313	1,312
Weighted average for year	1,418	1,312	1,301
Stock market closing price per Ordinary Share (London Stock Exchange)			
Highest (pence)	9444.0	9320.0	7808.0
Lowest (pence)	6794.0	6221.0	5325.0
At year end (pence)	8678.0	7324.0	7607.0

Analysis of shareholdings as a percentage of issued share capital at 31 December

Number of Ordinary Shares[1]	2021 %	2020 %	2019 %
1 – 250	0.3	0.4	0.4
251 – 500	0.3	0.4	0.5
501 – 1,000	0.4	0.5	0.5
1,001 – 5,000	0.6	0.7	0.7
5,001 – 10,000	0.2	0.2	0.2
10,001 – 50,000	1.1	1.1	1.0
50,001 – 1,000,000	1.1	11.2	11.2
Over 1,000,000	96.0	85.5	85.5

[1] Includes Euroclear and ADR holdings.

US holdings

At 31 January 2022, the proportion of Ordinary Shares represented by ADSs was 19.0% of the issued share capital of the Company. At 31 January 2022, there were 74,257 registered holders of Ordinary Shares, of which 646 were based in the US and there were 1,696 record holders of ADRs, of which 1,672 were based in the US.

Exchange controls and other limitations affecting security holders

There are no governmental laws, decrees or regulations in the UK restricting the import or export of capital or affecting the remittance of dividends, interest or other payments to non-resident holders of Ordinary Shares or ADRs.

There are no limitations under English law or the Articles on the right of non-resident or foreign owners to be the registered holders of, or to exercise voting rights in relation to, Ordinary Shares or ADRs or to be registered holders of notes or debentures of the Company or its wholly owned subsidiaries, Zeneca Wilmington Inc. and AstraZeneca Finance LLC.

Directors' Report

The Directors' Report includes information required to be given in accordance with the Companies Act 2006.

Relevant information below, which is contained elsewhere in the Annual Report, is incorporated by cross reference herein.

Subsidiaries and principal activities

The Company is the holding company for a group of subsidiaries whose principal activities are described in this Annual Report. The Group's subsidiaries and their locations are set out in Group Subsidiaries and Holdings in the Financial Statements from page 197.

Branches and countries in which the Group conducts business

In accordance with the Companies Act 2006, we disclose below countries of our representative, scientific or branch offices outside the UK established through various subsidiaries of the Company:

Algeria, Angola, Costa Rica, Cuba, Denmark, Egypt, Georgia, Ghana, Jordan, Kazakhstan, Lebanon, Norway, Portugal, Romania, Russia, Saudi Arabia, Serbia, Slovakia, Slovenia, Syria, Ukraine, United Arab Emirates, United States (a branch effective 1 January 2022), Vietnam, Yemen.

Disclosure of information to auditors

The Directors who held office at the date of approval of this Annual Report confirm that, so far as they are each aware, there is no relevant audit information of which the Company's auditors are unaware; and each Director has taken all the steps that he or she ought to have taken as a Director to make himself or herself aware of any relevant audit information and to establish that the Company's auditors are aware of that information.

Going concern accounting basis

Information on the business environment in which AstraZeneca operates, including the factors underpinning the industry's future growth prospects, is included in the Strategic Report. Details of the product portfolio of the Group are contained in the Strategic Report (in the Disease Area Review from page 16). For information on patent expiry dates for key marketed products, see the Patent Expiries Supplement on our website, www.astrazeneca.com/annualreport2021. Our approach to product development is covered in detail with additional information by disease area in the Strategic Report. For information on our development pipeline, see the Development Pipeline Supplement on our website, www.astrazeneca.com/annualreport2021.

The financial position of the Group, its cash flows, liquidity position and borrowing facilities are described in the Financial Review from page 52. In addition, Note 28 to the Financial Statements from page 180 includes the Group's objectives, policies and processes for managing capital; financial risk management objectives; details of its financial instruments and hedging activities; and its exposures to credit, market and liquidity risk. Further details of the Group's cash balances and borrowings are included in Notes 17 and 19 to the Financial Statements from page 163.

Having assessed the Principal Risks and other matters considered in connection with the Viability statement on page 49, the Board considers it appropriate to adopt the going concern basis of accounting in preparing the Annual Report and Financial Statements.

Shares

For more information, see Issued share capital, shareholdings and share prices on page 212.

A shareholders' resolution was passed at the 2021 AGM authorising the Company to purchase its own shares. The Company did not purchase any of its own shares in 2021. On 31 December 2021, the Company did not hold any shares in treasury.

Rights, preferences and restrictions attaching to shares

As at 31 December 2021, the Company had 1,549,400,665 Ordinary Shares and 50,000 Redeemable Preference Shares in issue. The Ordinary Shares represent 99.98% and the Redeemable Preference Shares represent 0.02% of the Company's total share capital (these percentages have been calculated by reference to the 8am WM/Reuters USD/GBP exchange rate on 31 December 2021).

As agreed by the shareholders at the Company's AGM held on 29 April 2010, the Articles were amended with immediate effect to remove the requirement for the Company to have an authorised share capital, the concept of which was abolished under the Companies Act 2006. Each Ordinary Share carries the right to vote at general meetings of the Company.

The rights and restrictions attaching to the Redeemable Preference Shares differ from those attaching to Ordinary Shares as follows:

- The Redeemable Preference Shares carry no rights to receive dividends.
- The holders of Redeemable Preference Shares have no rights to receive notices of attend or vote at general meetings except in certain limited circumstances. They have one vote for every 50,000 Redeemable Preference Shares held.
- On a distribution of assets of the Company, on a winding-up or other return of capital (subject to certain exceptions), the holders of Redeemable Preference Shares have priority over the holders of Ordinary Shares to receive the capital paid up on those shares.
- Subject to the provisions of the Companies Act 2006, the Company has the right to redeem the Redeemable Preference Shares at any time on giving not less than seven days' written notice.

There are no specific restrictions on the transfer of shares in the Company, which is governed by the Articles and prevailing legislation.

The Company is not aware of any agreements between holders of shares that may result in restrictions on the transfer of shares or that may result in restrictions on voting rights. The Company is also not aware of any arrangements under which financial rights are held by a person other than the holder of the shares.

Action necessary to change the rights of shareholders

In order to vary the rights attached to any class of shares, the consent in writing of the holders of three quarters in nominal value of the issued shares of that class or the sanction of a special resolution passed at a general meeting of such holders is required.

Changes in share capital

Changes in the Company's Ordinary Share capital during 2021, including details of the allotment of new shares under the Company's share plans and as partial consideration for the Alexion acquisition, are given in Note 24 and Note 27 to the Financial Statements from page 176.

Employee share trust ownership rights

The trustee of the AstraZeneca Employee Benefit Trust (the EBT, the Trustee) will not exercise voting rights attached to shares held in the EBT (Shares). Any decision as to acceptance or rejection of an offer for Shares subject to subsisting awards would be made by the Trustee, having regard to the interests of award holders.

Major shareholdings

At 31 December 2021, the following persons had disclosed an interest in the issued Ordinary Share capital of the Company in accordance with the requirements of rules 5.1.2 or 5.1.5 of the UK Listing Authority's Disclosure Guidance and Transparency Rules.

Changes in the percentage ownerships disclosed by major shareholders are set out below. Major shareholders do not have different voting rights.

			Number of Ordinary Shares disclosed as a percentage of issued share capital at:				
Shareholder	Date of the latest disclosure to the Company[1]	Number of Ordinary Shares disclosed	Date of the latest disclosure to the Company	31 December 2019	31 December 2020	31 December 2021	31 January 2022
BlackRock, Inc.	4 December 2009	100,885,181	6.96	7.69	7.69	6.51	6.51
Investor AB	3 April 2019	51,567,810	3.93	3.93	3.93	3.33	3.33
The Capital Group Companies, Inc.	17 July 2018	63,802,495	5.04	4.86	4.86	4.12	4.12
Wellington Management Group LLP[2]	21 July 2020	65,120,892	4.96	5.89[3]	4.96	4.20	4.20
Wellington Management Company LLP[2]	21 July 2020	65,118,411	4.96	5.88[4]	4.96	4.20	4.20

[1] Since the date of disclosure to the Company, the interest of any person listed above in Ordinary Shares may have increased or decreased. No requirement to notify the Company of any increase or decrease arises unless the holding passes a notifiable threshold in accordance with rules 5.1.2 or 5.1.5 of the UK Listing Authority's Disclosure Guidance and Transparency Rules.
[2] The Company was notified at the time of the disclosure that Wellington Management Company LLP was a subsidiary of Wellington Management Group LLP and that the shareholding percentage notified by Wellington Management Company LLP was included within the aggregate shareholding percentage notified by Wellington Management Group LLP.
[3] Based on the most recent shareholding disclosed to the Company prior to 31 December 2019, being a holding of 77,360,227 Ordinary Shares disclosed on 4 October 2019.
[4] Based on the most recent shareholding disclosed to the Company prior to 31 December 2019, being a holding of 77,153,687 Ordinary Shares disclosed on 4 October 2019.

So far as the Company is aware, no other person held a notifiable interest in the issued Ordinary Share capital of the Company. No changes to major shareholdings were disclosed to the Company between 31 December 2021 and 31 January 2022.

So far as the Company is aware, it is neither directly nor indirectly owned or controlled by one or more corporations or by any government.

The Company does not know of any arrangements, the operation of which might result in a change in the control of the Company

Directors', officers' and SET shareholdings

At 31 January 2022, the total amount of the Company's voting securities owned by Directors and officers of the Company and other SET members was:

Title of class	Amount owned	Percentage of class
Ordinary Shares	**614,738**	**0.04**

Options to purchase securities from registrant or subsidiaries

(a) At 31 January 2022, options outstanding to subscribe for Ordinary Shares were:

Number of shares	Subscription price (pence)	Normal expiry date
1,212,060	**3597-6903**	2022-2027

The weighted average subscription price of options outstanding at 31 January 2022 was 6035 pence. All options were granted under Company employee share schemes.

(b) Included in paragraph (a) are options granted to officers of the Company and SET members as follows:

Number of shares	Subscription price (pence)	Normal expiry date
526	**6839**	2024

(c) During 2021, no options were held by Directors.

During the period 1 January 2022 to 31 January 2022, no Director was granted or exercised any options.

Distributions to shareholders – dividends for 2021

Details of our distribution policy are set out in the Financial Review from page 52 and Notes 24 and 25 to the Financial Statements from page 176.

The Company's dividend for 2021 of $2.87 (210.1 pence, SEK 25.77) per Ordinary Share is estimated to amount to, in aggregate, a total dividend payment to shareholders of $4,445 million. Two employee share trusts, AstraZeneca Employee Benefit Trust and AstraZeneca Share Retention Trust, waived their rights to a dividend on the Ordinary Shares they hold and instead received nominal dividends.

For more information, see Financial calendar on page 211

Articles of Association

AstraZeneca PLC's current Articles were adopted by shareholders at the Company's AGM held on 18 May 2018. Any amendment to the Articles requires the approval of shareholders by a special resolution at a general meeting of the Company.

Objects

The Company's objects are unrestricted.

Directors

The Board has the authority to manage the business of the Company, for example, through powers to allot and repurchase its shares, subject where required to shareholder resolutions. Subject to certain exceptions, Directors do not have power to vote at Board meetings on matters in which they have a material interest.

The quorum for meetings of the Board is a majority of the full Board, of whom at least four must be Non-Executive Directors. In the absence of a quorum, the Directors do not have power to determine compensation arrangements for themselves or any member of the Board.

The Board may exercise all the powers of the Company to borrow money. Variation of these borrowing powers would require the passing of a special resolution of the Company's shareholders.

All Directors must retire from office at the Company's AGM each year and may present themselves for election or re-election. Directors are not prohibited, upon reaching a particular age, from submitting themselves for election or re-election.

For more information on the Directors, see Board of Directors on pages 74 and 75.

General meetings

AGMs require 21 clear days' notice to shareholders. Subject to the Companies Act 2006, other general meetings require 14 clear days' notice.

For all general meetings, a quorum of two shareholders present in person or by proxy, and entitled to vote on the business transacted, is required unless each of the two persons present is a corporate representative of the same corporation, or each of the two persons present is a proxy of the same shareholder.

Shareholders and their duly appointed proxies and corporate representatives are entitled to be admitted to general meetings.

Limitations on the rights to own shares

There are no limitations on the rights to own shares.

Gender diversity

	Directors of the Company's subsidiaries*
Men	262 (61%)
Women	170 (39%)
Total	432

	Senior Executive Team*
Men	7 (58%)
Women	5 (42%)
Total	12

All numbers as at 31 December 2021.

For the purposes of section 414C(8)(c)(ii) of the Companies Act 2006, 'Senior Managers' are the Senior Executive Team (SET), the Directors of all of the subsidiaries of the Company and other individuals holding named positions within those subsidiaries.

Stakeholder engagement

The discussion on stakeholder engagement and the impact of these interactions is contained in Connecting with our Stakeholders from page 80 and throughout the Strategic Report. This includes engagement with our employees, suppliers and other stakeholders, as well as the impact of our operations on the community and environment.

Information on how we encourage employee involvement in the Company's performance is set out in Our people on page 41. Details of some of the employee share plans are described in the Directors' Remuneration Report from page 98, and in Note 29 to the Financial Statements from page 186. All employees are provided with information on matters of concern to them through regular meetings and updates on the Group's intranet and internal social media. Townhall meetings and Q&A sessions are hosted regularly by members of senior management, including the SET, including global and targeted broadcasts on internal social media. During 2021, these broadcasts included business updates, as well as information on the Group's response to the COVID-19 pandemic and working arrangements. In addition, information about the Group's quarterly results is shared with employees. These updates inform employees of the financial and economic factors which affect the performance of the Company.

Political donations

Neither the Company nor its subsidiaries made any EU political donations or incurred any EU political expenditure in 2021 and they do not intend to do so in the future in respect of which shareholder authority is required, or for which disclosure in this Annual Report is required, under the Companies Act 2006. However, to enable the Company and its subsidiaries to continue to support interest groups or lobbying organisations concerned with the review of government policy or law reform without inadvertently breaching the Companies Act 2006, which defines political donations and other political expenditure in broad terms, a resolution will be put to shareholders at the 2022 AGM, similar to that passed at the 2021 AGM, to authorise the Company and its subsidiaries to:

> make donations to political parties or independent election candidates
> make donations to political organisations other than political parties
> incur political expenditure, up to an aggregate limit of $250,000.

Corporate political contributions in the US are permitted in defined circumstances under the First Amendment of the US Constitution and are subject to both federal and state laws and regulations. In 2021, the Group's US legal entities made contributions amounting in aggregate to $1,142,260 (2020: $1,016,550) to national political organisations, state-level political party committees and to campaign committees of various state candidates. No corporate donations were made at the federal level and all contributions were made only where allowed by US federal and state law. We publicly disclose details of our corporate US political contributions, which can be found on our website, www.astrazeneca-us.com/sustainability/corporate-transparency.

The annual corporate contributions budget is reviewed and approved by the US Vice-President, Corporate Affairs and the President of our US business to ensure robust governance and oversight. US citizens or individuals holding valid green cards exercised decision making over the contributions and the funds were not provided or reimbursed by any non-US legal entity. Such contributions do not constitute political donations or political expenditure for the purposes of the Companies Act 2006 and were made without any involvement of persons or entities outside the US.

Significant agreements

There are no significant agreements to which the Company is a party that take effect, alter or terminate on a change of control of the Company following a takeover bid. There are no persons with whom we have contractual or other arrangements, who are deemed by the Directors to be essential to our business.

Use of financial instruments

The Notes to the Financial Statements, including Note 28 from page 180, include further information on our use of financial instruments.

Insurance and indemnities

The Company maintained Directors' and officers' liability insurance cover throughout 2021. The Directors are also able to obtain independent legal advice at the expense of the Company, as necessary, in their capacity as Directors.

The Company has entered into a deed of indemnity in favour of each Board member since 2006. These deeds of indemnity are still in force and provide that the Company shall indemnify the Directors to the fullest extent permitted by law and the Articles, in respect of all losses arising out of, or in connection with, the execution of their powers, duties and responsibilities as Directors of the Company or any of its subsidiaries. This is in line with current market practice and helps us attract and retain high-quality, skilled Directors.

Compliance requirements under Listing Rule 9.8.4

The only matter to report is the shareholder waiver of dividends on page 214.

Directors' Report

The Directors' Report, which has been prepared in accordance with the requirements of the Companies Act 2006, comprises the following sections:

> Chair's Statement
> Chief Executive Officer's Review
> Disease Area Review
> Business Review
> Risk Overview
> Financial Review: Financial risk management
> Corporate Governance: including the Corporate Governance Overview, Corporate Governance Report, Nomination and Governance Committee Report, Science Committee Report, Sustainability Committee Report and Audit Committee Report
> Directors' responsibility statement
> Shareholder information
> Sustainability supplementary information

and has been approved by the Board and signed on its behalf.

On behalf of the Board

A C N Kemp
Company Secretary
10 February 2022

DocuSigned by:
AWKG
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Sustainability
supplementary information

External assurance
Bureau Veritas has provided independent external assurance to a limited level on the following sustainability information contained within this Annual Report:

- Commitment to society, see page 3.
- Key Performance Indicators, including Our sustainability and Be a Great Place to Work, see pages 12 to 15.
- Our sustainability approach, including Sustainability strategy, see pages 30 and 31.
- Bioethics, including Clinical trial transparency, Research use of human biological samples and Animal research, see page 34.
- Healthcare in low- and middle-income countries, see page 37.
- Responsible sales and marketing, see page 37.
- Anti-bribery and anti-corruption, see page 37.
- Responsible supply chain, see page 38.
- Human rights, see page 42.
- Employee relations, see page 43.
- Workplace safety and health, see page 43.
- Sustainability, including Driving the sustainability agenda, see page 44.
- Access to healthcare, including Equitable access, Affordability and pricing, Health system resilience, see pages 44 and 45.
- Environmental protection, including Ambition Zero Carbon, Product sustainability, Natural resources, see pages 45 and 46.
- Ethics and transparency, see page 47.
- Greenhouse gas reporting, see page 216.
- Task Force on Climate-related Financial Disclosures Statement, see pages 217 to 222.

BV Used throughout this Annual Report to denote the sustainability information listed above, which has been independently assured by Bureau Veritas.

Based on the evidence provided and subject to the scope, objectives and limitations defined in the full assurance statement, nothing has come to the attention of Bureau Veritas causing them to believe that the sustainability information contained within this Annual Report is materially misstated. Bureau Veritas is a professional services company that has a long history of providing independent assurance services in environmental, health, safety, social and ethical management and disclosure.

The full assurance statement, which includes Bureau Veritas' scope of work, methodology, overall opinion, and limitations and exclusions, is available on our website, www.astrazeneca.com.

Greenhouse gas (GHG) reporting BV

We have reported on all of the emission sources required under the Quoted Companies GHG Emissions (Directors' Reports) Regulations 2013. These sources fall within our consolidated Financial Statements. We do not have responsibility for any emission sources that are not included in our consolidated Financial Statements.

We have used the GHG Protocol Corporate Accounting and Reporting Standard (revised edition). Emission factors for electricity have been derived from the International Energy Agency, USEPA eGRID, US Green-e and the Association of Issuing Bodies databases and for all other fuels and emission sources from the 2006 IPCC Guidelines for National Greenhouse Gas Inventories.

During 2021, the acquisition of Alexion was completed and Scopes 1, 2 and 3 emissions data has been integrated to our reported footprint for 2021 and all previous years to 2015.

Global GHG emissions data for the period 1 January 2021 to 31 December 2021[1]

	Tonnes CO_2e		
	2021	2020	2019
Emissions from:			
Scope 1: Combustion of fuel and operation of facilities[2,5]	**245,882**	240,052	269,647
Scope 2 (Market-based): Electricity (net of market instruments), heat, steam and cooling purchased for own use[3,5]	**21,135**	32,218	138,261
Scope 2 (Location-based): Electricity, heat, steam and cooling purchased for own use[3,5]	**207,005**	228,727	246,054
Company's chosen intensity measurement: Scope 1 + Scope 2 (Market-based) emissions reported above normalised to million US dollar revenue	**7**	8	14
Scope 3 Total: Emissions from all 15 GHG Protocol Scope 3 Categories	**6,581,749**	5,985,733	5,716,412
Scope 3 intensity measurement: Scope 3 emissions from all 15 GHG Protocol Scope 3 Categories normalised to million US dollar revenue	**161**	183	195
	MegaWatt hours (MWh)		
Total energy consumption[4,5]	**1,737,124**	1,699,480	1,848,804

1 Regular review of the data is carried out to ensure accuracy, consistency and reflect major business changes. This has led to changes in the data from previous years. The majority of adjustments made are not material individually, except for: (i) Scope 3 category 1 purchased goods and services (methodology update to transition from a global emissions factor database for estimating emissions based on spend, to a country-based database, thereby improving accuracy, method updates applied to current and previous years); and (ii) Scope 1, 2 and 3 emissions from Alexion that was acquired during 2021 (reporting boundary expansion to include the acquired business, calculate the emissions across all scopes in a consistent manner, and integrate to previous years reporting).

2 Included in this section are GHGs from direct fuel combustion, process and engineering emissions at our sites and from fuel use in our vehicle fleet.
GHGs from imported electricity are calculated using the GHG Protocol Scope 2 Guidance (January 2015) requiring dual reporting using two emissions factors for each site – Market-based and Location-based. Our corporate emissions reporting and targets follow the Market-based approach.

3 The aggregate of: (i) the annual quantity of energy consumed from activities for which the Company is responsible, including the combustion of fuel at a facility or the operation of any facility and (ii) the annual quantity of energy consumed resulting from the purchase of electricity, heat, steam or cooling by the Company for its own use.
Under the Companies (Directors' Report) and Limited Liability Partnerships (Energy and Carbon Report) Regulations 2018, the Company needs to disclose what proportion of this figure relates to energy use in the UK and offshore area. For 2021, the proportion of total global energy and emissions originating from AstraZeneca's UK and offshore area footprint were as follows: energy use 371 GWh (21 %); Scope 1 site energy and road fleet emissions 60 ktCO$_2$e (24 %); Scope 2 site imported energy emissions using Market-based accounting 0 ktCO$_2$e (0 %); Scope 2 site imported energy emissions using Location-based accounting 12 ktCO$_2$e (6 %).

For more information, see Environmental protection from page 45.

For more information, see our 2021 Sustainability Report on our website, www.astrazeneca.com/sustainability.

Task Force on Climate-related Financial Disclosures Statement

Our commitment to climate change

The COVID-19 pandemic has demonstrated the need to build resilience across society, economies and healthcare systems globally. In similar ways to the pandemic, the threat that climate change poses also places societies at higher risk financially, socially and environmentally, with many of its impacts disproportionately affecting vulnerable communities and emerging economies still struggling to recover from the pandemic. The climate crisis also poses risks to public health, with rising global temperatures increasing the prevalence of respiratory and cardiovascular disease, changes in water-borne illnesses, allergen distribution and concentration, as well as mental health effects. Health system resilience across the entire value chain, from disease prevention to treatment, has never been more important.

The commitments we have made through our flagship $1 billion Ambition Zero Carbon programme ensure that we are playing our part in tackling the climate crisis as well as the opportunities that transitioning to a low-carbon economy could mean for our business.

We support the Task Force on Climate-related Financial Disclosures (TCFD) framework and we have made disclosures consistent with the four TCFD recommendations and the 11 recommended disclosures. The bullet point list on Page 222 set outs the required disclosures and explains where in this Annual Report (or other relevant document) the various disclosures can be found. We first adopted the TCFD framework in our 2020 Annual Report, and continue to apply it this year to describe activities conducted in the year to 31 December 2021.

All our business operations worldwide are in scope, unless otherwise stated. The framework has been introduced with a risk-based approach focusing on the most material risks and opportunities. Future priorities to broaden the scope to medium- and low-risk areas are indicated in each section.

For further information relating to our TCFD disclosures, see our website www.astrazeneca.com.

Our Carbon Disclosure Project (CDP) response provides further disclosures (2020 performance) on our approach to climate change and is available at www.cdp.net/en.

Climate change and our strategy for physical risks

Understanding the potential impact of future climate scenarios, together with proactive mitigation, intervention plans and targeted investment, will future proof our business and build resilience to ensure our long-term financial sustainability and continued supply of medicines to patients. It is critical to understand the physical climate change risks to our workforce, local communities, our assets and supply to patients. Working in a preventive way, we want to minimise reactive behaviour and minimise interruptions from extreme weather events across our operations and value chain.

In 2020, we screened climate impacts across our operations and in 2021 we added our strategic suppliers (defined by cost of interruption and strategic role to AstraZeneca) to assess what a worst-case scenario (Representative Concentration Pathway (RCP) 8.5) will look like in 2030, 2050 and 2100. In addition, two more optimistic scenarios (RCP 2.6 and 4.5) were modelled. By combining the results of the climate assessments with business criticality, we prioritised 12 potentially 'at risk' sites for further assessment in 2021.

For further information, see the scenario table on page 218.

Physical climate assessments will be expanded in 2022 and 2023 to include a deep-dive analysis of all strategic sites irrespective of risk. We will also focus on strategic upstream and downstream partners to understand their resilience to climate change e.g. bulk drug manufacturing, batch/QA/QC testing, distribution centres etc.

As the work progresses, we will increase our knowledge base with regard to the potential financial impact of extreme weather events, and appropriate mitigation and intervention plans. Financial impacts, such as stranded assets, cost of interruptions of supply, and capital investments, will be further assessed and, where material, they will be disclosed.

Climate change and our strategy for transition risks and opportunities

The nature of the risks and opportunities we face depends not only on the physical aspects of climate change, but also regulatory and commercial changes in the markets in which we operate, pressures to reduce the carbon footprints of specific medicines, and our ability to shape a culture of climate action focused on de-carbonising our value chain.

To respond to the identified climate risks and opportunities, we are taking enterprise-wide actions, and are committed to:

> Achieving net-zero greenhouse gas (GHG) emissions by maximising our energy efficiency, shifting to renewable energy sources, and investing in nature-based removals to compensate for any residual GHG footprint.
> Building resilience by managing the physical (sites, supply chain) and transitional (regulatory, market and product) risks and opportunities from climate change in the value chain through adaptation and business continuity planning.

Through our Ambition Zero Carbon programme we are on track to reduce GHG emissions from our global operations by 98% by the beginning of 2026 and halve our entire value chain footprint by 2030, on the way to a 90% reduction by 2045. Our emission reduction targets have been verified by the Science Based Targets initiative and we were one of the first seven companies worldwide to have our net-zero, science-based Scopes 1 to 3 targets verified under their new Net-Zero Corporate Standard. We were also an early supporter of the UN-backed Race to Zero.

Near-term targets

> achieve 98% reduction in Scope 1 and Scope 2 GI IG emissions by the beginning of 2026 from 2015 baseline
> switch to a 100% fully electric vehicle fleet (EV100) by the end of 2025
> use 100% renewable energy (RE100) for power and heat by the end of 2025
> double energy productivity (EP100) from 2015 to 2025
> launch first next-generation respiratory inhalers with near-zero climate impact
> align supplier spend to companies with approved science-based targets by end of 2025
> plant and steward over 50 million trees by end of 2025 as a nature-based solution to enhance climate, ecological and community resilience through our AstraZeneca Forest Global Initiative.

Long-term targets

> achieve 50% reduction in total Scope 3 emissions by 2030 and 90% reduction by 2045, from 2019 baseline
> become carbon negative for all residual emissions from 2030 and science-based net-zero by 2045
> transition to next-generation respiratory inhalers with near-zero climate impact by 2030.

Recognising that the healthcare system represents approximately 4% of global GHG emissions, AstraZeneca continues to identify and exploit opportunities to deliver patient-centric, net-zero healthcare. In 2021, AstraZeneca established the Sustainable Healthcare Round Table under HRH The Prince of Wales' Sustainable Markets Initiative (SMI). This SMI Sustainable Healthcare Round Table was launched at COP26 and focuses on the environmental and clinical benefits that can be delivered through digital health, proactive supply chain management and taking a patient care pathways approach that integrates clinical and environmental considerations to accelerate the provision of net-zero healthcare.

Governance

In October 2021, the Board established the Sustainability Committee to monitor the execution of our sustainability strategy, oversee communication of our sustainability activities with stakeholders and provide input to the Board and other Committees on sustainability matters. The members of the Committee are Nazneen Rahman (Chair of the Committee), Sheri McCoy, Andreas Rummelt and Marcus Wallenberg. The launch of the Sustainability

Task force on Climate-related Financial Disclosures Statement *continued*

Committee is an important next step in advancing and delivering our sustainability goals. The Sustainability Committee met once in December 2021 for an update on progress regarding our Climate Strategy and TCFD.

For more information on the Sustainability Committee and other Committees, see from page 86.

Our CEO is responsible to the Board for the management, development and performance of our business, including AstraZeneca's Ambition Zero Carbon and climate-related risks and opportunities. Reporting to the CEO, the Executive Vice-President (EVP), Sustainability and Chief Compliance Officer (CCO), is responsible for the delivery of AstraZeneca's sustainability strategy, including our climate-related strategy.

A number of strategic groups have been established to support delivery of our sustainability and climate strategies:

- In 2020, we established an Ambition Zero Carbon Governance Group with executive-level ownership, accountable for the delivery of our Ambition Zero Carbon programme. The group includes AstraZeneca's CEO; CFO; the EVP for Sustainability and CCO; and EVP for Operations and IT. The Ambition Zero Carbon Governance Group met six times in 2021.
- In 2020, a TCFD steering group was also established with cross-functional membership (Corporate Affairs, Investor Relations, Finance Risk and Reporting, R&D, Operations and Global Sustainability) to identify and proactively manage the physical and transition risks and opportunities posed to AstraZeneca by climate change. In 2021, members of the group undertook training on climate change and principles for future climate scenarios.

The outcomes from the specialist groups are reported regularly to the Board. The Audit Committee was updated on progress in April and the Sustainability Committee was updated in December 2021. The TCFD steering group met eight times in 2021 with a focus on the (i) execution of climate risk assessments at priority sites in AstraZeneca's supply chain, (ii) mapping of transition risks and opportunities, (iii) integrating the management of climate risks and opportunities within the current governance structure and (iv) how to structure the TCFD Disclosure in the annual reporting process.

Execution
At a site level, the execution of roadmaps to deliver against our climate strategy and to manage the physical risks posed by climate change are led by the accountable site lead, executing control measures (technical or organisational) as an integrated part of their existing risk management system.

On a commercial level, each franchise lead is accountable for integrating transition risks in their strategies and financial forecasts for each brand. By managing the risks posed by a low-carbon economy and healthcare system, each business can unlock potential opportunities to support the transition to a low-carbon, patient-centric healthcare system.

Remuneration
In 2021, to incentivise delivery of our environmental, social and governance priorities, delivery of our Ambition Zero Carbon commitment was included in our executive incentive arrangements for the Performance Share Plan (PSP), with a weighting of 10%. This underlines the importance we place on reducing our Scope 1 and Scope 2 GHG emissions by 98% by 2026.

For more information, see Directors' Remuneration Report from page 98.

Physical risks and temperature scenarios by 2100		Transition risks & opportunities and scenarios used	
+2°C (RCP 2.6)	> RCP 2.6 lays out a pathway and emissions trajectory that is generally aligned with the objectives of the Paris Agreement to limit global warming to well below 2°C, preferably to 1.5°C by 2100, compared to pre-industrial levels.	> 1.65°C (IEA WEO Sustainable Development Scenario (SDS) – equivalent to RCP 2.6).	> The IEA WEO SDS was used as the primary low-carbon future scenario within the Climate Financial Driver Analysis (CFDA). Renewable Electricity Generation and Transport Oil Demand figures were used from the SDS. As a 'well below 2°C' pathway, the SDS represents a gateway to the outcomes targeted by the Paris Agreement. The SDS is based on a surge in clean energy policies and investment that puts the energy system on track for key Sustainable Development Goals (SDGs).
		> 1.5°C (IEA WEO Net-Zero Emissions by 2050 scenario (NZE) – equivalent to RCP 1.9).	> Within the CFDA, sensitivity analysis was carried out using carbon prices from the IEA NZE emissions scenario, to ascertain the impact that carbon prices higher than in Stated Policies Scenario (STEPS) would have. The NZE is a normative IEA scenario that shows a narrow but achievable pathway for the global energy sector to achieve net-zero CO_2 emissions by 2050, with advanced economies reaching NZE in advance of others.
+2.5°C (RCP 4.5)	> RCP 4.5 is an intermediate scenario with emissions peaking in 2040 and falling rapidly thereafter until 2080.	> 2.5°C (IEA WEO Stated Policies Scenario – STEPS) – equivalent to RCP 4.5.	> The IEA WEO STEPS was used as the primary high carbon future scenario within the CFDA. Carbon prices from STEPS were used as the primary carbon price regime. Renewable Electricity Generation and Transport Oil Demand figures were also used. STEPS provides a more conservative benchmark for the future, because it does not take it for granted that governments will reach all announced goals.
+4°C (RCP 8.5)	> RCP 8.5 is a worst-case scenario consistent with no policy changes to reduce emissions, where CO_2 concentrations in the atmosphere are roughly doubled by 2050 and continue on that path until 2100.	> 4°C (IEA WEO business as usual) equivalent to RCP 8.5.	> This high emissions 'business as usual' scenario was not modelled in detail but is expected to give rise to more significant physical impacts and delayed but more uncertain/disruptive transition, potentially leading to higher overall costs and representing failure to implement stated policies.
Time horizons	> Present day, 2030, 2050, 2100.		> Present day, 2025, 2030, 2035 and 2040.

Identifying and managing climate risk and opportunity

To inform the wider enterprise risk management process of any specific risks and opportunities posed by climate change and/or the transition to a low-carbon economy, we have integrated climate assessments into the overall enterprise risk management process.

Our overall approach to risk management and a summary of our Principal Risks can be found from page 48.

Scope and definitions

Scenario analysis helps us to understand the potential impact of climate change on our business to inform our business strategy and financial planning. In line with the TCFD guidance, we decided to use a low/medium/high case scenario based on Representative Concentration Pathway shared by The Intergovernmental Panel on Climate Change.

For more information, see the table on page 218.

Assessment of physical risks

In 2020, working with environmental resource management experts, ERM Group, Inc. (ERM), we conducted a screening study of two future climate scenarios to explore our physical climate-related risks (floods, water scarcity, extreme heat, cyclones and wildfires). These scenarios were applied to material AstraZeneca sites with predictions out from 2020 to 2030, 2050 and 2100. The evaluated sites included all business-critical operations sites, R&D hubs, IT centres and other strategic hubs. The outcome of these screening studies was combined with a revenue-based assessment for each site to identify mid- to long-term risks. A similar study was conducted in 2021 to cover Alexion R&D and Operations sites, and their strategic suppliers with support from AECOM Limited. This has now been integrated into the AstraZeneca approach to assessing physical climate risks at sites.

During 2021, we extended our access to climate scenario data by using Jupiter, Inc. for screening of risks from climate hazards to all AstraZeneca sites in future scenarios (RCP 2.6, 4.5 and 8.5). We also used the WWF Water Risk Filter to assess site risks for droughts in water stressed areas and how these could be amplified by climate change.

For further information relating to the screening assessments for material sites, see our website www.astrazeneca.com.

Priorities for 2022 include:

> Identify opportunities to take collective actions in hot spot regions, together with stakeholders, including peers, to manage water stress in a systemic way.

In 2021, we conducted a deep dive at 12 sites with high business criticality and potential exposure to climate change impacts in a worst-case scenario (RCP 8.5) by 2030 and 2050. The assessments cover:

> inventory of hazards
> risk analysis
> risk evaluation
> identification of mitigation measures.

Global Subject Matter Experts coordinated these assessments together with local representation from Manufacturing, Facilities Management, Safety, Health and Environment and the Risk Management Network. Where appropriate, the risk mitigation measures and interventions were escalated to site management and captured on the local risk register. Measures and actions to address these risks are included in the site master plans and business continuity plans as they are developed, and captured under the mid- and long-term financial planning for that site and function.

Priorities for 2022/23 include all material sites in scope for the initial climate risk screening and the Alexion sites will be subject to detailed site level physical climate impact assessments.

During 2021, we included nearly 350 strategic suppliers in a screening assessment for physical climate risks. Suppliers with a 12 month cost of interruption of more than $200 million and with a critical role in patient supply will be prioritised for further assessment in 2022.

In 2021, we included vulnerability to climate change as a formal decision criteria for the establishment of future internal or external manufacturing capacity.

Assessment of transition risks and opportunities

To meet the Paris Agreement commitments to be net-zero and restrict global warming to 1.5°C, we need to take a product, company and healthcare system perspective to proactively manage the risks and opportunities posed by the transition to a low-carbon economy and healthcare system.

To deliver our 2030 carbon negative ambition, our products as well as our business will need to become carbon neutral. However, we also need to recognise that, given the limited period of exclusivity we have for innovative medicines, the GHG footprint of our current portfolio of products will not fully reflect our 2030 footprint. Many innovative treatments that will make up our 2030 portfolio are still in development and we can prioritise sustainability and efficiency in design, both in terms of process and product design, as well as the supplier network for manufacture and delivery. That means we are responsible for our choices in raw material sourcing, manufacture and formulation of APIs, along with device and packaging selection.

In November 2021, we launched a supplier-focused Power Purchase Agreement (PPA) programme (Energize) with peers in the pharmaceutical industry to accelerate access to renewable power for our suppliers.

We believe our patients and society will require products that have the smallest possible environmental impact, without sacrificing medical efficacy or safety. As technologies and healthcare systems evolve, so too should circular solutions to:

> design out waste and pollution
> keep products and materials in use
> regenerate natural systems.

For this to happen, our scientists embrace carbon neutral design, migrate away from fossil fuels (where possible) and embrace a circular mindset to use materials (minimise by design, reuse, recycle, recover). To help our scientists prioritise what environmental aspects to focus on, we use life-cycle assessments to look at the environmental impact of our products. The GHG footprint for most medicines lies in our upstream supply chain; the exception is for the respiratory pMDI portfolio where the GHG footprint lies with the patient use.

As the wider healthcare system looks to deliver patient-centric net-zero healthcare, this will present some risks for AstraZeneca to manage, as well as some opportunities to deliver better patient and societal outcomes with a lower GHG footprint for the healthcare sector. AstraZeneca is part of the Scope 3 emissions of healthcare providers; we are part of their purchased goods and services footprint. Some healthcare providers have already set out their net-zero ambitions. For example, the NHS has established targets to procure medicines only from suppliers with climate targets aligned with, or more ambitious than their own, and they have goals to reduce the footprint of respiratory products by 50% over the next seven years. Therefore, the transition to next-generation propellants with a near-zero global warming potential within our Ambition Zero Carbon strategy is not only reducing our GHG footprint, it is also mitigating some of the transition risks we face in the market and will protect our revenue.

To better understand the financial consequences of the transition into a low-carbon economy to our business, we started to work with ERM. Risks and opportunities were assessed at an enterprise level and product-specific level for the top 10 brands where life-cycle assessment (LCA) data is available, representing approximately 50% of Total Revenue with examples from all our disease areas.

Task Force on Climate-related Financial Disclosures Statement *continued*

Key

○ Low risk	**Time horizon for impact**
○ Medium risk	Short-term: 1–3 years
● High risk	Mid-term: 3–7 years
● Opportunity	Long-term: 7–25 years

Risk or opportunity	Time horizon Short/Mid/Long	Potential impact	How it is managed
Physical risks			
Increased frequency of extreme weather and climate-related natural disasters.	○ ○ ○	> Detailed site-level climate risk assessments have now been conducted at 12 sites (Wuxi, Södertälje, Maihara, Chennai, Westchester, Guadalajara, Gothenburg, Cairo, Canovanas, Mount Vernon, Bensalem and Taizhou) to verify the screening results from 2020. Outcomes indicate potential for: > increased exposure to extreme heat events and an increased need for cooling to maintain GMP compliance > heavy rainfall causing local flooding and/or inducing landslides > high wind events that can damage site structures. > Potential risks relate primarily to disruption or delays in a single manufacturing site, product distribution, and/or product impairment due to broken cold chain logistics, along with associated increased liability insurance premiums and reputational damage. However, investment in at-risk sites, the design of our supply chains and levels of inventory held mean that we do not currently foresee a material business impact arising from these short-term events. > Three case studies underpin this conclusion by exemplifying some typical risks, the consequences and associated mitigations: Södertälje in Sweden, Maihara in Japan and Canovanas in Puerto Rico. For more information, see www.astrazeneca.com/sustainability/resources.html > We will continue to expand our site assessments and business impact assessments in 2022.	> Identified risks have been addressed in the local business continuity plans or planning of technical mitigations integrated into the site master plans. Any investments required are integrated into the normal mid- and long-term financial planning process. Mitigation examples include increased cooling capacity to cover periods of extreme heat, drainage systems to handle increased volumes of precipitation or strengthening of building resilience to stand up against increased wind speed. > Business resilience has been increased to mitigate our exposure to extreme weather events like hurricane Maria at Canovanas (Puerto Rico, 2017), an extended period of heat in Södertälje (Sweden, 2018) and water scarcity in Chennai (India, 2019). > For example, our site in Canovanas has taken proactive steps to increase its resilience and mitigate the risks posed to our business operations by installing its own heat and power plant to reduce reliance on the local power network complemented with on-site solar panels and emergency generators ($12 million) and renovations of the two main manufacturing and warehouse buildings to comply with the latest building code ($9 million). > In 2021, physical risks have been mapped in the broader supply chain based on location and then matched with climate scenarios of RCP 2.6, 4.5 and 8.5. Suppliers with high criticality (cost of 12 month interruption more than $200 million) and exposure to significant future climate hazards will be contacted in 2022 to ensure that they build climate resilience within their business continuity plans. > Climatic risk assessments have been included in the site evaluation criteria for investment in new operations in 2021.
Transition risks and opportunities			
Increased demand for sustainable low Global Warming Potential (GWP) products and services from healthcare providers in some countries may result in the potential for green substitution of medicinal products with a high GWP (e.g. anaesthetics and respiratory products). Business opportunities will exist with increased future demand for low GWP alternatives and where earlier diagnosis and clinical intervention can reduce the carbon footprint of healthcare pathways.	○ ○	> Some healthcare providers and professionals are actively looking to substitute medicinal products based on their GHG footprint to reduce their own Scope 3 footprint, as part of their net-zero targets. > One example is NHS England and its target for net-zero by 2045, with an ambition to reach an 80% reduction by 2036 to 2039. This could impact market access and revenue in some countries for high GWP products where alternatives with a lower GHG footprint exist. Future revenue from our pMDI inhaled medicines portfolio could be 'at risk' should substitution become widespread before the transition to our next-generation near-zero GWP pMDIs. These risks are currently low, limited to a few countries, and any impact is likely to occur in a timeframe when we have lost exclusivity for some 'at risk' brands. > Transitioning to low GWP respiratory products as part of AstraZeneca Ambition Zero Carbon, and understanding the positive impacts that disease prevention, digital, early diagnosis and clinical intervention can have on the carbon footprint of specific patient care pathways, will provide business opportunities to improve the standard of care and clinical outcomes with a lower environmental footprint.	> As part of our $1 billion AstraZeneca Ambition Zero Carbon commitment, we will transition to near-zero GWP propellants across our asthma and COPD products between 2025 and 2030. > AstraZeneca has life-cycle assessments (LCAs) in place for key brands (respiratory and wider) that includes the GHG footprint to help assess and manage risks and target interventions to reduce the environmental footprint of our products. > In 2021, we have also launched an internal Product Sustainability Index (PSI) to proactively assess and manage the environmental footprint of our products. The PSI captures GHG and water intensity metrics per product, per patient and per annum, as well as measures of % renewable power and resource efficiency used to make that product. > Patients whose treatment is optimised are more likely to have a lower climate impact overall, through reduced reliever pMDI use and fewer unscheduled healthcare interventions. We are working with academics and healthcare agencies to understand the environmental impact of respiratory care pathways for patients with controlled and uncontrolled asthma and the opportunities for improved clinical care with a lower environmental footprint. The output of these environmental and clinical studies was communicated at scientific conferences and via peer-reviewed literature in 2021. > Early diagnosis and clinical intervention can provide business opportunities to improve the standard of care and clinical outcomes with a lower environmental footprint. In 2021, at COP26, AstraZeneca launched the Sustainable Healthcare Round Table under HRH The Prince of Wales' Sustainable Markets Initiative (SMI). The initiative focuses on the environmental and clinical benefits that can be delivered through digital health, proactive supply chain management and taking a patient care pathways approach that integrates clinical and environmental considerations to accelerate the provision of net-zero healthcare.

Key

○ Low risk	Time horizon for impact
○ Medium risk	Short-term: 1–3 years
● High risk	Mid-term: 3–7 years
● Opportunity	Long-term: 7–25 years

Risk or opportunity	Time horizon Short/Mid/Long	Potential impact	How it is managed
Transition risks and opportunities *continued*			
Review of the US, EU, UK and other national F-Gas Regulations and their impact on respiratory medicines used to treat asthma and COPD.	○ ●	> The US and EU F-Gas reviews carry the potential risk that some F-gases used in pMDI-based respiratory products could be subject to emission restrictions from which they are currently exempt (EU: 70% phase down target by 2030). The loss of the medicinal exemption, or lack of a long-term phased transition, could prevent or limit availability of products in our pMDI-inhaled medicines portfolio should these restrictions apply before the transition to our next-generation near-zero GWP pMDIs. > Inhaler device selection is a critical consideration as patient need or preference for a specific device type will influence adherence to treatment which in turn impacts clinical outcomes. Failure to maintain a patient-centric approach in the short- to mid-term could result in unnecessary adverse respiratory events and hospitalisations that could come with an increased GHG footprint.	> Patient advocacy assesses both clinical and environmental outcomes: > As part of the $1 billion AstraZeneca Ambition Zero Carbon commitment, AstraZeneca will transition to low GWP propellants in its asthma and COPD products between 2025 and 2030. > We are advocating a phased transition period to at least 2030 if the medicinal exemption is lifted to ensure patient safety and provide sufficient time for the regulatory approval and transition to alternative low GWP propellants.
Carbon pricing and future environmental taxation.	○ ●	> There is uncertainty over the future environmental policy and fiscal landscape in many countries where we operate. We anticipate increased regulation and other developments related to carbon pricing, broader adjustment taxes, and broader environmental taxation over the medium to long term. > Carbon pricing based on the IEA Net-Zero economy forecast which follows the 1.5°C warming pathway ($130/$tCO_2$ by 2030).	> Our AstraZeneca Ambition Zero Carbon commitment will help to mitigate some exposure to future carbon pricing and environmental taxation for our operations and our wider value chain. Managed correctly, this presents a commercial opportunity where peers have yet to establish a path to deep decarbonisation and net-zero. > We are being positive advocates for science-based targets to address climate change across our industry and supply chain via trade associations and networks. We continue to monitor regulatory and market developments in carbon pricing to inform our strategy.
Supply-demand of renewable energy (power and heat).	○ ●	> Access to clean heat alternatives to natural gas e.g. biomethane generally requires higher investment. > Participation in renewable energy programmes and adoption of energy efficiency measures to reduce operating costs and exposure to future fossil fuel price/carbon price increases.	> AstraZeneca invests approximately $25 million per annum in natural resource reduction programmes, including those that improve energy efficiency. Absolute natural resource reductions, including those that reduce our GHG emissions, are a primary metric alongside return on investment. Since 2015, we have invested $130 million and delivered a 9% reduction in energy use and 59% reduction in our GHG emissions. This reduces our exposure to incremental costs associated with some renewable alternatives. > Renewable power implemented by 2020 at all sites with a 2% premium. In 2021, the premium increased to 3.5%. > We joined the Renewable Thermal Collaborative in 2020 to unlock opportunities for renewable biomethane in the US and UK markets to prepare for a transition by 2025. > Project started with peers in pharmaceutical industry (Energize) to enable access to renewable energy in supply chains with a start in the US and the EU, and plans to expand into less mature markets.
Change in raw material or sourcing cost.	○ ●	> Costs associated with new low-carbon technology as the business needs to comply with expected new and emerging legislation for lower emissions technology (and meet stakeholder expectations for proactively decreasing emissions). > Similar increased operational costs in the supply chain may also have an effect on pricing and costs of raw materials including packaging. > There could be a significant risk associated with increased costs for using high carbon transport modes. > More efficient buildings will reduce costs: improved facilities management will lead to lower costs for repair and replacements. > Use of lower-emission sources of energy will reduce costs and will reduce exposure to fossil fuel and carbon price changes. > Use of more efficient production and distribution processes will reduce operational and logistical costs from using more efficient processes.	> Carbon costs are properly factored into engineering feasibility, options appraisal and capital expenditure decision making. Engagement with contract manufacturing organisations (CMOs) and other supply chain partners covers issues such as their transition to the low-carbon economy. > Ensuring the early opportunities for gaining regulatory approvals for new and emerging transport modes and technologies so that logistics continuity is maintained > Ensuring the costing for drugs considers potential increases associated with transition risks (such as cost of fuels and changes to approval mechanisms) > Many of the risks associated with incremental cost exposure are not unique to AstraZeneca. They will also be faced by our peers and the wider healthcare sector. > Engagement ensuring that sustainable performance is positively recognised within procurement is being explored.

Task Force on Climate-related Financial Disclosures Statement *continued*

In 2021, we have focused on a pMDI product in our respiratory portfolio due to its relative high carbon intensity, strategic importance to the business, and being the initial focus for the next-generation propellant transition as part of our Ambition Zero Carbon strategy. In an initial Climate Financial Driver Analysis, risks and opportunities were identified during the transition phase where the current propellant will be substituted to a low-carbon alternative by end of 2025. The financial implications of transitioning to next-generation propellants are included in our financial forecasts, which inform our impairment assessments.

Priorities for 2022 include:

- Define a methodology for ensuring that the climate risks associated with the franchise are fully integrated into business planning.
- Determine the transition risks for other high carbon intensity products based on the pilot assessment.
- Consolidate into Climate Financial Driver Analysis report (quantitative) to be included in the annual reporting process for 2022.
- Initiate work to understand carbon intensity for Alexion products, their potential exposure to transition risks, and identify potential opportunities where their use can reduce the environmental footprint of existing healthcare pathways.
- Conduct a study on how climate change impacts different disease areas and any future needs from patient groups.

Outcome of the physical and transitional assessments

In many cases mitigation measures are already in place to address the risks and opportunities presented by climate change, including those posed by the transition to a low-carbon economy and the provision of net-zero healthcare.

For more information, see the Risk supplement available on our website, www.astrazeneca.com/annualreport2021.

As a result of the analysis, the risk 'Failure to meet regulatory expectations on environmental impact, including climate change' is managed as a standalone risk to the Group's risk landscape. Based on current assessments, climate risk is not expected to have a material impact on our current business model. Therefore climate change is not seen as a Principal Risk for the Group and is not disclosed as a Principal Risk in the earlier Risk Overview section. This TCFD statement has been shared with the Board and Audit Committee.

For more information, see our Sustainability Report available on our website, www.astrazeneca.com/sustainability

Monitoring our progress

The climate emergency is a public health emergency. It is changing our planet irreversibly, with warming reaching critical tolerance thresholds for health. Human health and the health of the planet are deeply interconnected. We have an opportunity now to reset how we live and create a more sustainable world – together and without delay.

We report on our GHG emissions and progress towards mid- and long-term targets in line with the World Resources Institute GHG Protocol guidance for defining and calculating our GHG footprint, which is disclosed separately in the Sustainability Data Summary Report.

Full details of our GHG footprint are disclosed in our Sustainability Data Summary Report 2021, www.astrazeneca.com/sustainability/resources.html

The performance report is reflecting how well we have been able to decarbonise the business and by that, reduce exposure to transition risks and unlock future opportunities for the Company and the wider healthcare sector.

During 2021, we were recognised for our efforts in sustainability across our strategic priorities. This included the following:

- Inaugural 2021 Terra Carta Seal award
- Dow Jones Sustainability Index constituent
- FTSE4Good Index Series constituent
- Financial Times 2021 European Climate Leader for reduction of GHG emissions
- CDP Double A List for Climate and Water Security for the sixth consecutive year
- Corporate Knights Global 100 Most Sustainable Corporations in the World.

For more information, see our Sustainability Report available on our website, www.astrazeneca.com/sustainability

The bullet points below provide an explanation of where in this Annual Report (or other relevant document or location in respect of supplementary information) the various TCFD recommended disclosures can be found:

- Governance
  - Is the Board's oversight of climate-related risks and opportunities described? Pages 73, 89, 90 and 217. Sustainability Report pages 8 and 19.
  - Is management's role in assessing and managing climate-related risks and opportunities disclosed? Pages 6, 15, and 217. Sustainability Report pages 8 and 19.
- Strategy
  - Are climate-related risks and opportunities the organisation has identified over the short, medium and long term disclosed? Pages 8, 30, 45 to 46, 220 to 221. Sustainability Report pages 20 to 22. Sustainability Data Summary pages 5 to 8.
  - Is the impact of the climate-related risks and opportunities on the organisation's business, strategy, and financial planning described? Pages 48, 217, 219, 220 to 222.
  - Is the resilience of the organisation's strategy described, taking into consideration different climate-related scenarios, including a 2°C or lower scenario? Pages 48, 218 and www.astrazeneca.com/sustainability/resources.html
- Risk management
  - Are the organisation's processes for identifying and assessing climate-related risks described? Pages 48, 91, 217 to 222. Sustainability Report pages 8 and 19.
  - Is the organisation's process for managing climate-related risks disclosed? Pages 217 to 222. Risk Supplement page 5. Sustainability Report pages 8 and 19.
  - Is it described how the organisation's process for identifying and managing climate-related risks is integrated into the organisation's overall risk management? Pages 217 to 222. Sustainability Report pages 8 and 19.
- Metrics and Targets
  - Is there disclosure of the metrics used by the organisation to assess climate-related risks and opportunities in line with its strategy and risk management process? Pages 48 and 90.
  - Does the organisation disclose its Scope 1, Scope 2 and, if appropriate, Scope 3 greenhouse gas (GHG) emissions, and related risks? Page 216. Sustainability Report pages 20 to 22. Sustainability Data Summary pages 5 to 7.
  - Does the organisation describe the targets used to manage climate-related risks and opportunities and performance against targets? Pages 45 to 46, 48 and 216. Sustainability Report pages 20 to 22. Sustainability Data Summary pages 5 to 8.

For more information, see our Sustainability Report and Sustainability Data Summary available on our website, www.astrazeneca.com/sustainability.

Trade Marks

AstraZeneca, the AstraZeneca logotype, and the AstraZeneca symbol are all trade marks of the Group.

The following medicine names which appear in italics in this Annual Report are trade marks of the Group:

Trade mark			
Andexxa	*Daliresp*	*Losec*[4]	*Soliris*
Arimidex[1]	*Daxas*	*Lokelma*	*Strensiq*
Atacand[3]	*Epanova*	*Lumoxiti*	*Symbicort*
Atacand HCT[3]	*Evusheld*	*Lynparza*	*Symbicort Turbuhaler*
Atacand Plus[3]	*Farxiga*	*Movantik*	*Symlin*
BCise	*Fasenra*	*Moventig*	*Synagis*[4]
Bevespi Aerosphere	*Faslodex*	*Nexium*	*Tagrisso*
Breztri	*Fluenz*	*Ondexxya*	*Toprol-XL*
Breztri Aerosphere	*FluMist*	*Onglyza*	*Turbuhaler*
Brilinta	*Forxiga*	*Orpathys*	*Ultomiris*
Brilique	*Genuair*	*Prilosec*	*Vaxzevria*
Bydureon	*Imfinzi*	*Pulmicort*	*Vimovo*[5]
Byetta	*Iressa*	*Qtern*	*Xigduo*
Calquence	*Kanuma*	*Saphnelo*	*Zoladex*
Casodex[1]	*Kombiglyze*	*Seloken*	
Cosudex	*Komboglyze*	*Seroquel*[2]	
Crestor	*Koselugo*	*Seroquel XR*[2]	

1 AstraZeneca divested these trade marks in a number of European, African and other markets to Juvisé Pharmaceuticals effective 19 December 2019.
2 AstraZeneca divested these trade marks in Europe to Cheplapharm effective 28 September 2018, and in more than 70 other markets effective 31 December 2020.
3 AstraZeneca divested these trade marks in Europe and Russia to Cheplapharm effective 13 December 2019.
4 Effective 25 January 2019, AstraZeneca sold its rights to *Synagis* in the US to Sobi, aka Swedish Orphan Biovitrum AB (publ). AbbVie transferred its ownership rights to this trademark to MedImmune LLC, effective 1 July 2021.
5 AstraZeneca divested the global rights (excluding the US and Japan) for this trade mark to Grünenthal, effective 3 December 2018.

The following medicine names, which appear in italics in this Annual Report, are trade marks licensed to the Group by the entities set out below:

Trade mark	Licensor or Owner
Anticalin	Pieris AG
Duaklir	Almirall, S.A.
Eklira	Almirall, S.A.
Enhertu	Daiichi Sankyo Company, Limited
Linzess	Ironwood Pharmaceuticals, Inc.
Tezspire	Amgen, Inc.
Tudorza	Almirall, S.A.

The following medicine names, which appear in italics in this Annual Report, are not owned by or licensed to the Group and are owned by the entities set out below:

Trade mark	Owner
messenger RNA Therapeutics	Moderna
Covushield	Serum Institute of India

Glossary

Market definitions

Region	Country				
US	US				
Europe	Albania*	Czech Republic	Hungary	Luxembourg*	Serbia and Montenegro*
	Austria*	Denmark	Iceland*	Malta*	Slovakia*
	Belgium	Estonia*	Ireland	Netherlands	Slovenia*
	Bosnia and Herzegovina*	Finland	Israel*	Norway	Spain
	Bulgaria*	France	Italy	Poland	Sweden
	Croatia	Germany	Latvia*	Portugal	Switzerland
	Cyprus*	Greece	Lithuania*	Romania	UK
Established ROW	Australia	Canada	Japan	New Zealand	
Emerging Markets	Algeria	Costa Rica	Iraq*	Pakistan*	Syria*
	Argentina	Cuba*	Jamaica*	Palestine*	Taiwan
	Aruba*	Dominican Republic*	Jordan	Panama	Thailand
	Bahamas*	Ecuador*	Kazakhstan	Peru	Trinidad and Tobago*
	Bahrain*	Egypt	Kuwait*	Philippines	Tunisia*
	Barbados*	El Salvador	Lebanon*	Qatar*	Turkey
	Belarus*	Georgia*	Libya*	Russia	Ukraine
	Belize*	Guatemala	Malaysia	Saudi Arabia	United Arab Emirates
	Bermuda*	Honduras	Mexico	Singapore	Uruguay*
	Brazil	Hong Kong	Morocco*	South Africa	Venezuela*
	Chile	India	Nicaragua	South Korea	Vietnam
	China	Indonesia	Oman*	Sri Lanka*	Yemen*
	Colombia	Iran*	Other Africa*	Sudan*	

* Q3 2021 IQVIA. IQVIA Midas Quantum Q3 2021 data are not available or AstraZeneca does not subscribe for IQVIA quarterly data for these countries. The above table is not an exhaustive list of all the countries in which AstraZeneca operates, and excludes countries with revenue in 2021 of less than $2 million.

Established Markets means US, Europe and Established ROW.

North America means US.

Other Established ROW means Australia and New Zealand.

Other Emerging Markets means all Emerging Markets except China.

Other Africa includes Angola, Botswana, Ethiopia, Ghana, Kenya, Mauritius, Mozambique, Namibia, Nigeria, Eswatini, Tanzania, Uganda, Zambia and Zimbabwe.

Asia Area comprises India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand and Vietnam.

US equivalents

Terms used in this Annual Report	US equivalent or brief description
Accruals	Accrued expenses
Called-up share capital	Issued share capital
Creditors	Liabilities/payables
Debtors	Receivables and prepaid expenses
Earnings	Net income
Employee share schemes	Employee stock benefit plans
Fixed asset investments	Non-current investments
Freehold	Ownership with absolute rights in perpetuity
Loans	Long-term debt
Prepayments	Prepaid expenses
Profit	Income
Share premium account	Additional paid-in capital or paid-in surplus (not distributable)
Short-term investments	Redeemable securities and short-term deposits

The following abbreviations and expressions have the meanings given below when used in this Annual Report:

AbbVie – AbbVie Inc.

Acerta Pharma – Acerta Pharma B.V.

Actavis – Actavis plc.

ADC – antibody drug conjugate(s).

ADRs – American Depositary Receipts.

ADSs – American Depositary Shares.

AGM – an Annual General Meeting of the Company.

AI – artificial intelligence.

Alexion – Alexion Pharmaceuticals, Inc.

Almirall – Almirall, S.A.

Amgen – Amgen Inc.

Amplimmune – Amplimmune, Inc.

ANDA – an abbreviated new drug application, which is a marketing approval application for a generic drug submitted to the FDA.

Annual Report – this Annual Report and Form 20-F Information 2021.

API – active pharmaceutical ingredient.

Ardea – Ardea Biosciences, Inc.

Articles – the Articles of Association of the Company.

Astellas – Astellas Pharma Inc.

Astra – Astra AB, being the company with whom the Company merged in 1999.

AstraZeneca – the Company and its subsidiaries.

AstraZeneca HealthCare Foundation – a Delaware, US not-for-profit corporation and a 501(c)(3) entity, separate from AstraZeneca Pharmaceuticals, organised for charitable purposes, including to promote public awareness and education of healthcare issues and support eligible non-profit organisations in alignment with its mission. The Foundation has received $30 million in contributions to date from AstraZeneca to support the *Connections for Cardiovascular Health*℠ programme.

Atnahs – Atnahs Pharma UK Ltd.

biologic(s) or biologic medicine(s) – a class of drugs that are produced in living cells.

BMS – Bristol-Myers Squibb Company.

Board – the Board of Directors of the Company.

Bureau Veritas – Bureau Veritas UK Limited.

Caelum – Caelum Biosciences, Inc.

CDP (formerly the Carbon Disclosure Project) – a not-for-profit organisation that runs the global disclosure system for investors, companies, cities, states and regions to manage their environmental impacts.

CEO – the Chief Executive Officer of the Company.

CER – constant exchange rates.

CFO – the Chief Financial Officer of the Company.

Cheplapharm – Cheplapharm Arzneimittel GmbH.

Circassia – Circassia Pharmaceuticals PLC

CKD – chronic kidney disease.

CLL – chronic lymphocytic leukaemia.

Code of Ethics – the Group's Code of Ethics, see page 47.

Company or Parent Company – AstraZeneca PLC (formerly Zeneca Group PLC (Zeneca)).

Complement-biology platform – capabilities to translate the biology of the complement system, a part of the immune system comprised of proteins that is essential to the body's defence against infection, into innovative medicines that target and inhibit the dysregulated complement system cascade that is a key driver of many devastating diseases.

COPD – chronic obstructive pulmonary disease.

COVAX – the vaccines pillar of the Access to COVID-19 Tools (Act) Accelerator. COVAX is co-led by CEPI, the Coalition for Epidemic Preparedness Innovations; Gavi, the Vaccines Alliance; and the WHO, working in collaboration with developed and developing country vaccine manufacturers, UNICEF, the World Bank and others.

COVID-19 – the official WHO name for the disease caused by the 2019 novel coronavirus.

Covis – Covis Pharma B.V.

CV – cardiovascular.

CVRM – Cardiovascular, Renal & Metabolism.

Daiichi Sankyo – Daiichi Sankyo, Inc. or a company within the Daiichi Sankyo group of companies.

DDR – DNA damage response.

Definiens – Definiens AG.

Director – a director of the Company.

DOJ – the United States Department of Justice.

DTR – UK Disclosure Guidance and Transparency Rules.

earnings per share (EPS) – profit for the year after tax and non-controlling interests, divided by the weighted average number of Ordinary Shares in issue during the year.

EBITDA – Reported Profit before tax plus net finance expense, share of after tax losses of joint ventures and associates and charges for depreciation, amortisation and impairment.

EFPIA – European Federation of Pharmaceutical Industries and Associations.

EGFR – epidermal growth factor receptor.

EMA – European Medicines Agency.

ESG – environmental, social and governance.

ESMO – European Society for Medical Oncology.

EVP – Executive Vice-President.

EU – the European Union.

Glossary
continued

FDA – the US Food and Drug Administration, which is part of the US Department of Health and Human Services Agency, which is the regulatory authority for all pharmaceuticals (including biologics and vaccines) and medical devices in the US.

FibroGen – FibroGen, Inc.

FRC – the UK Financial Reporting Council.

GAAP – Generally Accepted Accounting Principles.

GHG – greenhouse gas.

GLP1 – glucagon-like peptide-1.

gross margin – the margin, as a percentage, by which sales exceed the cost of sales, calculated by dividing the difference between the two by the sales figure.

Group – AstraZeneca PLC and its subsidiaries.

Grünenthal – Grünenthal Group.

GSK – GlaxoSmithKline plc.

GWP – global warming potential.

HCPs – healthcare practitioners.

HF – heart failure.

HMRC – Her Majesty's Revenue & Customs, the UK tax authority.

HTA – health technology assessment.

IA – the Group's Internal Audit Services function.

IAS – International Accounting Standards.

IASB – International Accounting Standards Board.

ICS – inhaled oral corticosteroid.

IFPMA – International Federation of Pharmaceutical Manufacturers and Associations.

IFRS – International Financial Reporting Standards or International Financial Reporting Standard, as the context requires.

Innate Pharma – Innate Pharma S.A.

IO – immuno-oncology.

IP – intellectual property.

IQVIA – IQVIA Solutions HQ Limited.

For more information, see page 228.

Ironwood – Ironwood Pharmaceuticals, Inc.

IS – information services.

ISAs – International Standards on Auditing.

IT – information technology.

KPI – key performance indicator.

krona or SEK – references to the currency of Sweden.

Kyowa Kirin – Kyowa Kirin International plc, a subsidiary of Kyowa Hakko Kirin Co., Ltd.

LABA – long-acting beta2-agonist.

LAMA – long-acting muscarinic antagonist.

LCM projects – significant life-cycle management projects (as determined by potential revenue generation), or line extensions.

Lilly – Eli Lilly and Company.

Luye Pharma – Luye Pharma Group.

mAb – monoclonal antibody, a biologic that is specific, meaning it binds to and attacks one particular antigen.

major market – US, Europe, Japan and China.

MAT – moving annual total.

MedImmune – MedImmune, LLC (formerly MedImmune, Inc.).

mRNA – Messenger RNA.

MI – myocardial infarction.

Moderna – Moderna Therapeutics, Inc.

MSD – Merck & Co., Inc., which is known as Merck in the US and Canada, and MSD in other territories.

n/m – not meaningful.

Nasdaq – Nasdaq Global Select Market.

Nasdaq Stockholm – previously the Stockholm Stock Exchange.

New Medicines – Roxadustat, *Koselugo*, *Enhertu*, *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Farxiga*, *Brilinta*, *Lokelma*, *Fasenra*, *Bevespi* and *Breztri*.

NME – new molecular entity.

Novartis – Novartis Pharma AG.

NRDL – National Reimbursement Drug List, China.

NSCLC – non-small cell lung cancer.

NYSE – the New York Stock Exchange.

OECD – the Organisation for Economic Co-operation and Development.

OMICs – refers to a field of study in biology ending in 'omics', such as genomics, proteomics or metabolomics.

operating profit – sales, less cost of sales, less operating costs, plus operating income.

Ordinary Share – an ordinary share of $0.25 each in the share capital of the Company.

Orphan Drug – a drug that has been approved for use in a relatively low-incidence indication (an orphan indication) and has been rewarded with a period of market exclusivity; the period of exclusivity and the available orphan indications vary between markets.

Paediatric Exclusivity – in the US, a six-month period of exclusivity to market a drug which is awarded by the FDA in return for certain paediatric clinical studies using that drug. This six-month period runs from the date of relevant patent expiry. Analogous provisions are available in certain other territories (such as European Supplementary Protection Certificate (SPC) paediatric extensions).

PARP – an oral poly ADP-ribose polymerase.

PD-L1 – an anti-programmed death-ligand 1.

Pearl Therapeutics – Pearl Therapeutics, Inc.

PFS – progression-free survival. The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease without it getting worse.

PhRMA – Pharmaceutical Research and Manufacturers of America.

Phase I – the phase of clinical research where a new drug or treatment is tested in small groups of people (20 to 80) to check that the drug can achieve appropriate concentrations in the body, determine a safe dosage range and identify side effects. This phase includes healthy volunteer studies.

Phase II – the phase of clinical research which includes the controlled clinical activities conducted to evaluate the effectiveness of the drug in patients with the disease under study and to begin to determine the safety profile of the drug. Phase II studies are typically conducted in small- or medium-sized groups of patients and can be divided into Phase IIa studies, which tend to be designed to assess dosing requirements, and Phase IIb studies, which tend to assess safety and efficacy.

Phase III – the phase of clinical research which is performed to gather additional information about effectiveness and safety of the drug, often in a comparative setting, to evaluate the overall benefit/risk profile of the drug. Phase III studies usually include between several hundred and several thousand patients.

Pieris Pharmaceuticals – Pieris Pharmaceuticals, Inc.

pMDI – pressurised metered-dose inhaler.

pound sterling, £, GBP or pence – references to the currency of the UK.

primary care – general healthcare provided by physicians who ordinarily have first contact with patients and who may have continuing care for them.

Proof-of-Concept – data demonstrating that a candidate drug results in a clinical change on an acceptable endpoint or surrogate in patients with the disease.

ProTACs – a proteolysis targeting chimera, which is a heterobifunctional small molecule composed of two active domains and a linker capable of removing specific unwanted proteins.

PTE – Patent Term Extension, an extension of up to five years in the term of a US patent relating to a drug which compensates for delays in marketing resulting from the need to obtain FDA approval. The analogous right in the EU is an SPC.

Pulse Survey – an AstraZeneca employee opinion survey, which seeks employees' views of the business.

PwC – PricewaterhouseCoopers LLP.

R&D – research and development.

R&I – Respiratory & Immunology.

Rare Disease – the EU defines a disease or condition as rare if it affects fewer than 1 in 2,000 people within the general population and in the US, the Orphan Drug Act defines a rare disease as a disease or condition that affects less than 200,000 people in the United States.

Redeemable Preference Share – a redeemable preference share of £1 each in the share capital of the Company.

Regulatory Exclusivity – any of the IP rights arising from generation of clinical data and includes Regulatory Data Protection, Paediatric Exclusivity and Orphan Drug status.

RNA – ribonucleic acid.

Roche – F. Hoffmann-La Roche AG.

ROW – rest of world.

RSV – respiratory syncytial virus.

RWE – Real-World Evidence.

SABA – short-acting beta2-agonist.

Samsung Biologics – Samsung Biologics Co., Ltd.

sales platforms – previously referred to as Growth Platforms, consisting of Emerging Markets, Japan, Oncology, CVRM, Respiratory & Immunology, Oncology and Rare Disease.

Sanofi – Sanofi S.A./Sanofi Pasteur, Inc.

Sarbanes-Oxley Act – the US Sarbanes-Oxley Act of 2002.

SEC – the US Securities and Exchange Commission, the governmental agency that regulates the US securities industry and stock markets.

SEK – Swedish krona (or kronor).

SET – Senior Executive Team.

SG&A costs – selling, general and administrative costs.

Sobi – Swedish Orphan Biovitrum AB.

SPC – supplementary protection certificate.

specialty care – specific healthcare provided by medical specialists who do not generally have first contact with patients.

Spirogen – Spirogen Sàrl.

SoC – standard of care. Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals.

Takeda – Takeda Pharmaceutical Company Limited.

TCFD – Task Force on Climate-related Financial Disclosures.

TerSera – TerSera Therapeutics LLC.

Total Revenue – the sum of Product Sales and Collaboration Revenue.

TSR – total shareholder return, being the total return on a share over a period of time, including dividends reinvested.

UK – United Kingdom of Great Britain and Northern Ireland.

UK Corporate Governance Code – the UK Corporate Governance Code published by the FRC in July 2018 that sets out standards of good practice in corporate governance for the UK.

US – United States of America.

US dollar, US$, USD or $ – references to the currency of the US.

Vaxzevria – COVID-19 Vaccine AstraZeneca.

VBP – value-based procurement.

Viela Bio – Viela Bio, Inc.

WHO – World Health Organization, the United Nations' specialised agency for health.

ZS Pharma – ZS Pharma, Inc.

Important information for readers of this Annual Report

Cautionary statement regarding forward-looking statements

The purpose of this Annual Report is to provide information to the members of the Company. The Company and its Directors, employees, agents and advisers do not accept or assume responsibility to any other person to whom this Annual Report is shown or into whose hands it may come and any such responsibility or liability is expressly disclaimed. In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act of 1995 and the UK Companies Act 2006, we are providing the following cautionary statement:

This Annual Report contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Forward-looking statements are statements relating to the future which are based on information available at the time such statements are made, including information relating to risks and uncertainties. Although we believe that the forward-looking statements in this Annual Report are based on reasonable assumptions, the matters discussed in the forward-looking statements may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of the preparation of this Annual Report and the Company undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things:

- the risk of failure or delay in delivery of pipeline or launch of new medicines
- the risk of failure to meet regulatory or ethical requirements for medicine development or approval
- the risk of failures or delays in the quality or execution of the our commercial strategies
- the impact of pricing, affordability and competitive pressures
- the risk of failure to maintain supply of compliant, quality medicines
- the risk of illegal trade in our medicines
- the impact of reliance on third-party goods and services
- the risk of failure in information technology or cybersecurity
- the risk of failure of critical processes
- the risk of failure to collect and manage data in line with legal and regulatory requirements and strategic objectives
- the risk of failure to attract, develop, engage and retain a diverse, talented and capable workforce
- the risk of failure to meet regulatory or ethical expectations on environmental impact, including climate change
- the risk of the safety and efficacy of marketed medicines being questioned
- the risk of adverse outcome of litigation and/or governmental investigations
- the risks related to IP protection of our products
- the risk of failure to achieve strategic plans or meet targets or expectations
- the risk of failure in financial control or the occurrence of fraud
- the risk of unexpected deterioration in our financial position
- the impact that the COVID-19 global pandemic may have or continue to have on these risks, on the Group's ability to continue to mitigate these risks, and on the Group's operations, financial results or financial condition.

Certain of these factors are discussed in more detail, without limitation, in the Risk Supplement (at www.astrazeneca.com/annualreport2021) and reproduced in AstraZeneca's Form 20-F filing for 2021 (available on the SEC website www.sec.gov). Nothing in this Annual Report should be construed as a profit forecast.

Inclusion of Reported performance, Core financial measures and constant exchange rate growth rates

AstraZeneca's determination of non-GAAP measures together with our presentation of them within our financial information may differ from similarly titled non-GAAP measures of other companies.

Statements of competitive position, growth rates and sales

In this Annual Report, except as otherwise stated, market information regarding the position of our business or products relative to its or their competition is based upon published statistical sales data for the 12 months ended 30 September 2021 obtained from IQVIA, a leading supplier of statistical data to the pharmaceutical industry. Unless otherwise noted, for the US, dispensed new or total prescription data and audited sales data are taken, respectively, from IQVIA National Prescription Audit and IQVIA National Sales Perspectives for the 12 months ended 31 December 2021; such data are not adjusted for Medicaid and similar rebates. Except as otherwise stated, these market share and industry data from IQVIA have been derived by comparing our sales revenue with competitors' and total market sales revenues for that period, and except as otherwise stated, growth rates are given at CER.

For the purposes of this Annual Report, unless otherwise stated, references to the world pharmaceutical market or similar phrases are to the 50 countries contained in the IQVIA database, which amounted to approximately 93% (in value) of the countries audited by IQVIA. Changes in data subscriptions, exchange rates and subscription coverage, as well as restated IQVIA data, have led to the restatement of total market values for prior years.

AstraZeneca websites

Information on or accessible through our websites, including www.astrazeneca.com, and www.astrazenecaclinicaltrials.com and on any websites referenced in this Annual Report, does not form part of and is not incorporated into this Annual Report.

External/third-party websites

Information on or accessible through any third-party or external website does not form part of and is not incorporated into this Annual Report.

Figures

Figures in parentheses in tables and in the Financial Statements are used to represent negative numbers.

Supplements

For detailed information on our Development Pipeline, Patent Expiries and Key Marketed Products, and Risk, see our website, www.astrazeneca.com/annualreport2021.

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