AstraZeneca

What science can do

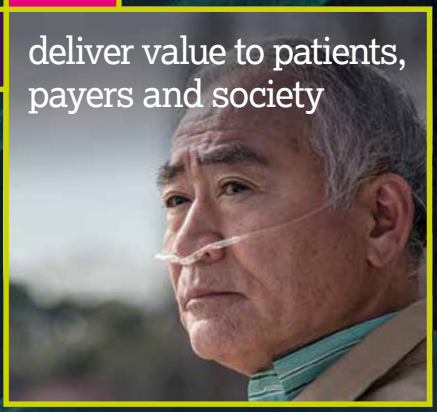
AstraZeneca Annual Report and Form 20-F Information 2018

Welcome

We are a global, science-led pharmaceutical business, and in this Annual Report we report on the progress we made in 2018 in pushing the boundaries of science to deliver life-changing medicines and demonstrating what science can do.

Science *can*

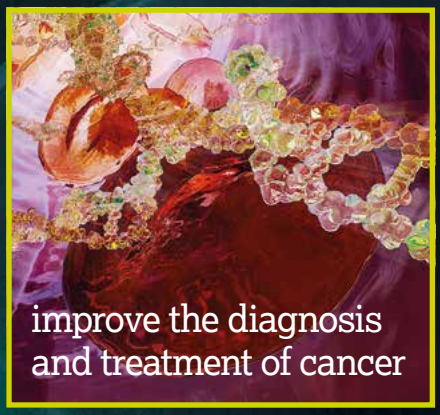
deliver value to patients, payers and society



Innovative Value Strategies and indication-based pricing
See page 17

deliver complete disease management in China

Innovative ideas in healthcare
See page 37



improve the diagnosis and treatment of cancer

Pioneering the use of circulating tumour DNA
See page 28

Searching for new treatment options
See page 49

help find a cure for ovarian cancer

help people undergoing heart bypass surgery

New ways of treating heart disease
See page 61

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.

Front cover image: Circulating tumour DNA
AstraZeneca has pioneered the use of circulating tumour DNA (ctDNA) in the diagnosis of cancer. Pieces of DNA break off from a tumour and circulate in the bloodstream where they can be analysed to give genetic information about a patient's tumour. This allows healthcare professionals to determine the right treatment for the patient using a minimally invasive blood test.

Contents

Financial highlights

Total Revenue*
Down 2% to $22,090 million at actual rate of exchange (down 2% at CER), comprising Product Sales of $21,049 million (up 4%; 4% at CER) and Externalisation Revenue of $1,041 million (down 55%; 55% at CER)

2018	**$22,090m**
2017	$22,465m
2016	$23,002m

$22.1bn

Net cash flow from operating activities
Down 27% at actual rate of exchange to $2,618 million

2018	**$2,618m**
2017	$3,578m
2016	$4,145m

$2.6bn

Reported operating profit
Down 8% at actual rate of exchange to $3,387 million (down 7% at CER)

2018	**$3,387m**
2017	$3,677m
2016	$4,902m

$3.4bn

Core operating profit
Down 17% at actual rate of exchange to $5,672 million (down 17% at CER)

2018	**$5,672m**
2017	$6,855m
2016	$6,721m

$5.7bn

Reported EPS
Down 28% at actual rate of exchange to $1.70 (down 29% at CER)

2018	**$1.70**
2017	$2.37
2016	$2.77

$1.70

Core EPS
Down 19% at actual rate of exchange to $3.46 (down 19% at CER)

2018	**$3.46**
2017	$4.28
2016	$4.31

$3.46

// 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 74.

* As detailed on page 154, Total Revenue consists of Product Sales and Externalisation Revenue.

For more information within this Annual Report

For more information, see www.astrazeneca.com

This Annual Report is also available on our website, www.astrazeneca.com/annualreport2018

AstraZeneca at a glance

A global science-led business delivering medicines to patients through innovative science and excellence in development and commercialisation.

Our Purpose is to push the boundaries of science to deliver life-changing medicines. We want to be valued and trusted by our stakeholders as a source of great medicines over the long term.

Our strategic priorities

Reflect how we are working to achieve our Purpose

- 1. Achieve Scientific Leadership
- 2. Return to Growth
- 3. Be a Great Place to Work

A science-led innovation strategy

Strategy from page 18 and Key Performance Indicators from page 20.

Distinctive R&D capabilities:
Small molecules, oligonucleotides and other emerging drug platforms, as well as biologic medicines, including immunotherapies, and innovative delivery devices

8
new molecular entities (NMEs) in Phase III/ pivotal Phase II or under regulatory review, covering 15 indications

Broad R&D platform in three main areas

Achieve Scientific Leadership from page 25 and Therapy Area Review from page 50.

Oncology
Our ambition is to push the boundaries of science to change the practice of medicine, transform the lives of patients living with cancer, and ultimately eliminate cancer as a cause of death

Cardiovascular, Renal and Metabolism
As science uncovers commonalities between cardiovascular, renal and metabolic diseases and their associated complications, we aim to transform how they are understood and treated

Respiratory
Our research focuses on the underlying causes of respiratory diseases, using new modalities to pursue previously hard-to-reach targets, with the ambition of achieving remission or even cures for patients

Other Disease Areas
We are also selectively active in the areas of autoimmunity, neuroscience and infection

Portfolio of specialty and primary care products (Product Sales)

$6,028m
29% of total
2017: $4,024m
2016: $3,383m

Sales growth of 50% (49% at CER), including:

Imfinzi sales of $633 million, reflecting ongoing launches

Lynparza sales of $647 million, representing growth of 118% (116% at CER), driven by expanded use in the treatment of ovarian cancer and first approvals for breast cancer

Tagrisso sales of $1,860 million, representing growth of 95% (93% at CER)

$6,710m
32% of total
2017: $7,266m
2016: $8,116m

Sales decline of 8% (8% at CER), including:

Crestor sales of $1,433 million, down 39% (40% at CER) reflecting generic competition

Brilinta sales of $1,321 million, representing growth of 22% (21% at CER), due to continued market penetration

Farxiga sales of $1,391 million, with growth of 30% (30% at CER), including a sales increase of 45% in Emerging Markets (52% at CER) to $336 million

$4,911m
23% of total
2017: $4,706m
2016: $4,753m

Sales growth of 4% in the year (3% at CER), including:

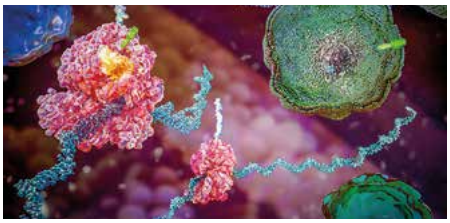
Fasenra sales of $297 million, performing exceptionally well in the countries where it was launched

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

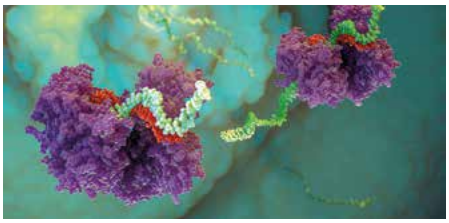
Symbicort sales decline of 9% (10% at CER) to $2,561 million, as competitive price pressures in the US continued

$3,400m
16% of total
2017: $4,156m
2016: $5,067m

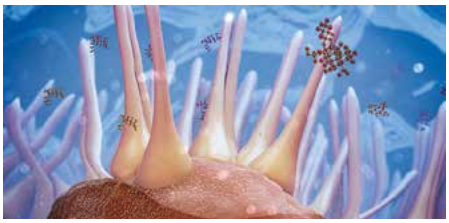
Product Sales declined by 18% (19% at CER) and represented 16% of total Product Sales, down from 21% in 2017



Oncology. See page 50.



Cardiovascular, Renal and Metabolism. See page 56.



Respiratory. See page 62.

Global commercial presence, with strength in Emerging Markets (Product Sales)

Return to Growth from page 29.

Emerging Markets

$6,891m
33% of total
2017: $6,149m
2016: $5,794m

Product Sales increased by 12% (13% at CER). New Medicines represented 15% of Emerging Market sales in the year, up from 10% in 2017

US

$6,876m
33% of total
2017: $6,169m
2016: $7,365m

Product Sales increased by 11%. New Medicines represented 48% of Product Sales, up from 26% in 2017

Europe

$4,459m
21% of total
2017: $4,753m
2016: $5,064m

Product Sales declined by 6% (10% at CER), reflecting the entry of generic *Crestor* medicines in various markets in 2017 and continued competitive and price pressures

Established Rest of World

$2,823m
13% of total
2017: $3,081m
2016: $3,096m

Product Sales declined by 8% (9% at CER). New Medicines represented 24% of sales in the year, up from 13% in 2017. Performance reflected, in particular, the success of *Tagrisso* and *Forxiga*

Our talented employees

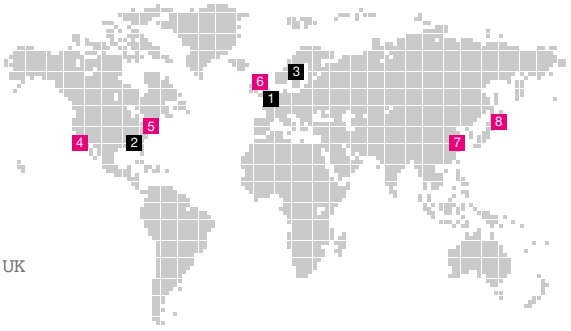
Committed to attracting, retaining and developing a talented and diverse workforce united in the pursuit of our Purpose and living our Values

Be a Great Place to Work from page 38.

64,600
employees
2017: 61,100
2016: 59,700

44.6%
of our senior roles are filled by women

102
manuscripts published by our scientists in high-impact peer-reviewed journals



Strategic R&D centres
1. Cambridge, UK (HQ)
2. Gaithersburg, MD, US
3. Gothenburg, Sweden

Other R&D centres
4. California, US
5. Boston, MA, US
6. Alderley Park and Macclesfield, UK
7. Shanghai, China
8. Osaka, Japan

A sustainable business

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

Sustainability from page 42.

Priority 1

Broadening access to healthcare

Priority 2

Furthering ethics and transparency

Priority 3

Protecting the environment

100%
of employees trained in Code of Ethics

CDP DRIVING SUSTAINABLE ECONOMIES

MEMBER OF Dow Jones Sustainability Indices In Collaboration with RobecoSAM

access to medicine index

Our capital allocation priorities

Striking a balance between the interests of the business, our financial creditors and shareholders, and supporting our progressive dividend policy

Financial Review from page 74.

Distributions to shareholders

Dividends

$3,484m
2017: $3,519m
2016: $3,561m

Proceeds from issue of shares

$(34)m
2017: $(43)m
2016: $(47)m

Total

$3,450m
2017: $3,476m
2016: $3,514m

Dividend per Ordinary Share for 2018

1st interim dividend

$0.90
Pence: 68.4
SEK: 7.92
Payment date:
10 September 2018

2nd interim dividend

$1.90
Pence: 146.8
SEK: 17.46
Payment date:
27 March 2019

Total

$2.80
Pence: 215.2
SEK: 25.38
2017: $2.80
2016: $2.80

Chairman's Statement

In 2013, your Board chose a very clear strategic route to follow. It was a strategy rooted in our heritage as a company focused on innovative science to deliver great medicines.

"We succeeded because we have been true to our Value of following the science. We also succeeded because we put patients first."

In 2018, under the leadership of Pascal Soriot, and together with the entire talented AstraZeneca team, we delivered on our promise and returned a reinvigorated AstraZeneca to Product Sales growth.

Delivering for patients

We succeeded because we have been true to our Value of following the science. We also succeeded because we put patients first. This will become increasingly important as more people take an active role in managing their health and new technologies empower them to make their own health choices. In visits around the world, I have seen how digital technology is transforming the way we work and has the potential to help us develop better medicines, faster and with clearer benefits for patients and value for society.

A changing world

We also need to show leadership in responding to other ways in which our world is changing: the increasing burden of non-communicable diseases, especially in poorer parts of the world; growing and ageing populations; and, notably, society's growing expectations of business. At the same time, we face more immediate challenges: the uncertainties surrounding the UK's impending departure from the EU, the trade dispute between the US and China, and other countries where we see a rise in disruptive politics.

Sustainable health

I believe that being a sustainable business is fundamental to overcoming these challenges, as well as our ability to deliver innovative medicines to patients and ensure people have access to them. We are committed to our role in delivering sustainable health and maximising the benefit of what we do for patients, broader society and the planet. I'm pleased that, once again, our efforts have been recognised by, for example, the Dow Jones Sustainability and World Indices and Access to Medicine Index.

Returns to shareholders and outlook

While we returned to Product Sales growth in 2018, that has yet to be reflected in our profitability, with Reported earnings per share (EPS) of $1.70 representing a decline of 28% (29% at CER) compared with 2017. This reflected a decline in Total Revenue and the Reported Gross Margin. Core EPS declined by 19% to $3.46, also driven by the investments we made in launching our new medicines. Core EPS for the final quarter rose, however, by 22% compared with the prior year quarter, reflecting Product Sales growth, higher ongoing Externalisation Revenue and a favourable adjustment to deferred taxes arising from recently announced reductions in Dutch and Swedish corporate income tax rates. Our guidance for 2019 is for an increase in Core EPS at CER to $3.50-3.70 as we anticipate a high single-digit percentage increase in Product Sales to underpin improved profitability.

In light of this, the Board reaffirmed its commitment to the progressive dividend policy, with a second interim dividend for 2018 of $1.90 per share, taking the unchanged full-year dividend per share to $2.80.

Appreciation

I would like to thank Pascal and everyone at AstraZeneca for all they have done to bring us to this point in our strategic journey. I am looking forward to the coming years when, by continuing to push the boundaries of science, we can bring more medicines to more patients and make a difference to more lives.

Leif Johansson
Chairman

Chief Executive Officer's Review

As we enter the next phase in our journey, the fundamentals of our strategy and plans remain unchanged, with Product Sales growth driving improved profitability and the generation of increasing levels of cash.

"…in 2018, after the previous six years in which revenues had fallen by more than one third, we turned the corner and returned to Product Sales growth."

New medicines launched since 2013

Oncology
- *Imfinzi* for lung and bladder cancer
- *Lynparza* for ovarian and breast cancer
- *Tagrisso* for lung cancer
- *Calquence* for mantle cell lymphoma
- *Lumoxiti* for hairy cell leukaemia

CVRM
- *Lokelma* for hyperkalaemia
- *Qtern* for diabetes

Respiratory
- *Fasenra* for severe asthma
- *Bevespi Aerosphere* for chronic obstructive pulmonary disease

In March 2013, shortly after I joined AstraZeneca, we set out our strategy to Achieve Scientific Leadership, Return to Growth and ensure we are a Great Place to Work. Five years on, thanks to the great work of every single one of my colleagues, we have made remarkable progress: our science-led strategy and our open and entrepreneurial culture are underpinning a resurgence in innovation that is fuelling sustainable Product Sales growth and delivering medicines that patients and society value and can access.

Product Sales growth

The first phase in our journey provided focus and galvanised the organisation behind rebuilding our pipeline. Having regained our scientific edge, the second stage was crucial as we drove our Growth Platforms forward, launched new medicines and made them available to patients. I am pleased to report that, in 2018, after the previous six years in which revenues had fallen by more than one third, we turned the corner and returned to Product Sales growth, driven by a new generation of medicines from our therapy areas.

As we look ahead through 2019 and beyond, continued investment in our product launches and pipeline should keep us on track to deliver sustainable and profitable growth in line with our targets. Consistent with this, we are reshaping the way we undertake research and development to bring new focus and impetus, accelerate the launches of new medicines and consolidate what is already one of the most exciting and productive pipelines in the industry. We are also reorganising our commercial operations to reflect our therapy area focus, maximise collaboration with our R&D organisation, and strengthen strategic planning and field force integration to support delivery of our medicines to patients.

Achieve Scientific Leadership

Our first priority for achieving scientific leadership was to focus on innovative science in three main therapy areas: Oncology; Cardiovascular, Renal and Metabolism (CVRM); and Respiratory. This has been our driving force all along, a focus reinforced by our recent organisational changes. In other disease areas, we have sought to maximise the value of our portfolio through licensing, collaboration and externalisation activity.

We also said we would rebuild our pipeline and, by 2015, had 15 new molecular entities (NMEs) in Phase III/Pivotal Phase II or under regulatory review compared with a target, set in 2013, of 10 by the end of 2016. In 2018, we had eight NMEs in Phase III/Pivotal Phase II or under regulatory review. The same year, we also made 28 regulatory submissions in major markets and received 23 approvals for our medicines. Both are record numbers for AstraZeneca. Of course, we know that in pushing the boundaries of science we will sometimes experience setbacks. In 2018, for example, there were disappointing Phase III trial results for six projects, including the MYSTIC trial of *Imfinzi* and tremelimumab in stage 4 non-small cell lung cancer (NSCLC). However, we remain confident in *Imfinzi* as the cornerstone of our immuno-oncology (IO) programme and continue to evaluate its potential in ongoing NSCLC trials, including *Imfinzi* and *Imfinzi* plus tremelimumab in combination with chemotherapy. Overall, we are on target for sustainably delivering two NMEs annually by 2020.

Chief Executive Officer's Review *continued*

23

23 NME and major LCM regional approvals – a record

84%

Five Growth Platforms represent 84% of Total Revenue

84%

84% of employees understand how they can contribute to our sustainability priorities

"...we are well on our way to exceeding our target of launching 10 major new medicines by 2020."

Finally, we are well on our way to exceeding our target of launching 10 major new medicines by 2020. The panel on the previous page shows how, since 2013, nine medicines have been launched from our three main therapy areas which are making a real difference to the lives of patients around the world. In 2018 alone, we delivered three new medicines – *Lumoxiti*, *Lokelma* and roxadustat. Roxadustat, for the treatment of chronic kidney disease (CKD) anaemia, is particularly noteworthy as it is the first time that a first-in-class medicine has been approved first in China. We expect it to be launched later in 2019.

Above all, we believe in what science can do. And it is a testament to the strength of our science that, in 2018, AstraZeneca scientists published 102 manuscripts (another record number) in 'high-impact' peer-reviewed journals – a 14-fold increase since 2012.

Return to Growth

In support of our Return to Growth priority, we said we would focus on five Growth Platforms: Oncology, New CVRM, Respiratory, Japan and Emerging Markets. In 2013, they represented less than half of sales and this had grown to 84% of Total Revenue by 2018. Overall, as shown in the table opposite, Product Sales in 2018 increased by 4% to $21,049 million (4% at CER), driven by strong growth in the last two quarters of the year – 8% and 5% respectively (9% and 8% at CER). This reflected the performance of our New Medicines[1], up by 81% (at CER) and adding $2.8 billion in incremental sales, as well as the sustained strength of Emerging Markets, up by 12% (13% at CER). Product Sales in China increased by 28% (25% at CER) in the year. Externalisation Revenue declined by 55% in the year to $1,041 million, partly driven by the impact of $1,247 million of income received during 2017 as part of our collaboration with MSD for *Lynparza*. Total Revenue declined by 2% (2% at CER) to $22,090 million.

We also said that we would leverage our global commercial presence and our strength in Emerging Markets. After four years of decline, the US returned to sales growth in 2018 while Product Sales in Emerging Markets, which represented 21% of sales in 2013, amounted to 33% of Product Sales. Emerging Markets now represent our largest Region by Product Sales.

[1] *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Lumoxiti*, *Brilinta*, *Farxiga*, *Lokelma*, *Bevespi* and *Fasenra*. These New Medicines are pillars in the three main therapy areas and important platforms for future growth.

Additionally, we wanted to shift to a balance of specialty and primary care medicines. Specialty care medicines now comprise all our Oncology medicines and *Fasenra*. They represented 30% of Product Sales in 2018 and sales increased by 57% in the year (56% at CER) to $6,325 million.

Be a Great Place to Work

Underpinning everything is our dedication to being a great place to work, with a talented and diverse team committed to living our Values and supported by an inclusive, learning culture. It is that team of people who drive our progress, and our employee (Pulse) surveys show that 94% of employees understand our strategy, 89% believe in it and 83% would recommend AstraZeneca as a great place to work – all statistics that place us among the leading companies in the world.

While there is always more we can do, 2018 also saw continued employee development and an increase in the representation of women in senior roles. More generally, we have implemented numerous initiatives, such as unconscious bias training, across the globe as part of our commitment to inclusion and diversity. We are therefore particularly proud to have been recognised as the only pharmaceutical company selected for the 2019 Bloomberg Gender-Equality Index which distinguishes companies committed to transparency in gender reporting and advancing women's equality.

More widely, 84% of employees understand how they can contribute to our sustainability priorities where our achievements include reaching 12 million people through our access to healthcare programmes and winning Ethical Corporation's Community Investment Program of the year award for Young Health – our global disease prevention programme. We know we can't achieve our goals alone. As a sustainable organisation we have an unwavering commitment to being a trusted partner for stakeholders, an excellent investment for shareholders, and an indispensable ally in the quest to meet the global healthcare challenge.

Global Product Sales by therapy area

	2018			2017			2016		
	Sales $m	**Actual growth %**	**CER growth %**	Sales $m	Actual growth %	CER growth %	Sales $m	Actual growth %	CER growth %
Oncology	**6,028**	**50**	**49**	4,024	19	19	3,383	20	20
Cardiovascular, Renal & Metabolism	**6,710**	**(8)**	**(8)**	7,266	(10)	(10)	8,116	(14)	(13)
Respiratory	**4,911**	**4**	**3**	4,706	(1)	(1)	4,753	(5)	(3)
Other Disease Areas	**3,400**	**(18)**	**(19)**	4,156	(18)	(17)	5,067	(20)	(19)
Total	**21,049**	**4**	**4**	20,152	(5)	(5)	21,319	(10)	(8)

Seizing the opportunities ahead

As we enter the next phase in our journey, the fundamentals of our strategy and plans remain unchanged, with Product Sales growth driving improved profitability and the generation of increasing levels of cash. Our focus will continue to be on innovative science and leadership in our three main therapy areas. And we will carry on leveraging our global presence and strength in emerging markets, while pursuing the development of strong, balanced portfolios of both specialty and primary care medicines.

As the Chairman indicated, the world around us is changing, so we too are shifting the way in which we deliver our strategy. Our emphasis is on growth through innovation – being more patient-centric, doing more with digital technology and data, and advancing more innovative science.

The new organisational structure we announced in January 2019 supports the next phase in our journey and is intended to enhance scientific innovation and commercial success. The changes further increase focus on our main therapy areas, integrate R&D functions for agile decision making and more flexible resource allocation, as well as increasing collaboration between our R&D and commercial units.

My colleagues

At the same time as making these changes, we announced the appointment of Dr José Baselga to lead our R&D unit for Oncology. José is an outstanding oncology leader with vast experience in the development of innovative cancer therapies. His research and clinical achievements have led to the development of several innovative medicines, and he is an international thought leader in cancer care and clinical research. José's expertise adds further scientific and leadership excellence to our already strong team and will help us to continue building a world-class R&D unit for Oncology.

Before this, we said goodbye to Bahija Jallal, EVP MedImmune, and Mark Mallon, EVP Global Product and Portfolio Strategy, Global Medical Affairs and Global Corporate Affairs, whose moves to become CEOs at two exciting biotech companies illustrated the talent that we have in AstraZeneca and how highly other companies regard our people. Sean Bohen, EVP for Global Medicines Development and Chief Medical Officer will also be leaving following the leadership structure changes. I would like to thank Bahija, Mark and Sean for the important roles they played in AstraZeneca's return to growth.

Finally, my thanks go to all my colleagues in AstraZeneca. We have been on an incredible journey. None of this would have been possible without the talented people we have in the organisation. I thank them all for everything they have done as, together, we embark on the next phase in this great Company's journey.

Pascal Soriot
Chief Executive Officer

Business model and life-cycle of a medicine

AstraZeneca at a glance summarises our business. In this section, we review our business model – how we create financial value and the resources we need in order to bring benefits to patients.

Why AstraZeneca

We are a global pharmaceutical business which has:

> A science-led innovation strategy
> An R&D platform across small molecules and biologics
> Three main therapy areas: Oncology; Cardiovascular, Renal and Metabolism; and Respiratory
> A portfolio of specialty care and primary care medicines
> A global footprint

Who we are

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

We follow the science.
We put patients first.
We play to win.
We do the right thing.
We are entrepreneurial.

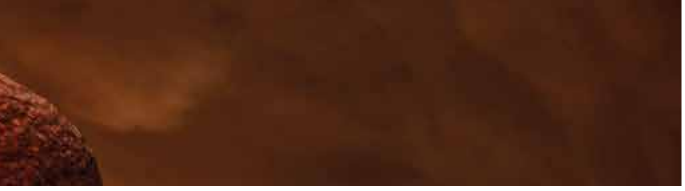
Our Values determine how we work together and the behaviours that drive our success. Our Values guide our decision making, define our beliefs and foster a strong AstraZeneca culture.

Our Sustainability

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 priorities in health, ethics and the environment support the delivery of our business strategy.

Business Review from page 24.



What we do

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

How we create financial value

Investment

We invest in the discovery, development, manufacturing and commercialisation of our pipeline of innovative small molecule and biologic prescription medicines, including targeted business development through collaboration, in-licensing and acquisitions.

Revenue generation

We generate revenue from Product Sales of our existing medicines and Growth Platform launches, as well as from our externalisation activities. Our focus is on creating products 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 Growth Platforms that provide the platform for future sources of revenue in the face of recent losses of key patents.

Life-cycle of a medicine

Research and development phases 5–15 years

1. Find potential medicine
> Identify unmet medical need aligned with our three therapy areas and undertake scientific research to identify potential new medicines.
> Initiate process of seeking patent protection.

2. Pre-clinical studies
> Conduct laboratory and animal studies to understand if the potential medicine is safe to introduce into humans and in what quantities.
> Determine likely efficacy, side effect profile and maximum dose estimates.

3. Phase I studies
> Begin clinical studies with small groups of healthy human volunteers (small molecules) or patients (biologics) to understand how the potential medicine is absorbed into the body, distributed around it and excreted.
> Determine approximate dosage and identify side effects.

4. Phase II studies
> Conduct studies on small- to medium-sized groups of patients to test effectiveness and tolerability of the medicine and determine optimal dose.
> Design Phase III studies to generate data needed for regulatory approvals and pricing/reimbursement globally.

5. Phase III studies
> Engage in studies in a larger group of patients to gather information about effectiveness and safety of the medicine and evaluate the overall benefit/risk profile.
> Initiate branding for the new medicine in preparation for its launch.

6. Regulatory submission and pricing
> Seek regulatory approvals for manufacturing, marketing and selling the medicine.
> Submit clinical data to regulatory authorities (and, if requested, generate further data increasingly in real-world settings) to demonstrate the safety and efficacy of the medicine to enable them to decide on whether to grant regulatory approvals.

Launch phase 5–15 years

7. Launch new medicine
> Raise awareness of patient benefit and appropriate use, market and sell medicine.
> Clinicians begin to prescribe medicines and patients begin to benefit.
> Continuously monitor, record and analyse reported side effects. Review need to update the side effect warnings to ensure that patients' wellbeing is maintained.
> Assess real-world effectiveness, and opportunities to support patients and prescribers, to achieve maximum benefit from the medicine.

8. Post-launch research and development
> Conduct studies to further understand the benefit/risk profile of the medicine in larger and/or additional patient populations.
> Life-cycle management activities to broaden understanding of a medicine's full potential.
> Consider additional diseases or aspects of disease to be treated by or better ways of administering the medicine.
> Submit data packages with requests for life-cycle management to regulatory authorities for review and approval.

Post-exclusivity 20+ years

9. Post-exclusivity
> Patent expiry and generic entry.
> Reinvestment of returns.

Note: This is a high-level overview of a medicine's life-cycle and is illustrative only. It is neither intended to, nor does it, represent the life-cycle of any particular medicine or of every medicine discovered and/or developed by AstraZeneca, or the probability of success or approval of any AstraZeneca medicine.

Business model and life-cycle of a medicine *continued*

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 united in pursuit of our Purpose and Values and fostering a strong AstraZeneca culture.

See Employees from page 38.

64,600
employees

A leadership position in science
We need to achieve scientific leadership if we are to deliver life-changing medicines. To that end, we need to focus on innovative science, prioritise and accelerate our pipeline and transform our innovation and culture model.

See Achieve Scientific Leadership from page 25.

$5.9bn
invested in our science

Effective partnerships
We need business development, specifically partnering, which is an important element of our business model. It supplements and strengthens our pipeline and our efforts to achieve scientific leadership.

See Partnering on page 35.

>630
collaborations worldwide

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

See Return to Growth from page 29.

>100
countries in which we are active

Intellectual property (IP)
We need to create and protect our IP rights. Developing a new medicine requires significant investment over many years, with no guarantee of success. For our investments to be viable, we seek to protect new medicines from being copied for a reasonable period of time through patent protection.

See Intellectual Property from page 35.

>100
countries where we obtain patent protection

A robust supply chain
We need a supply of high-quality medicines, whether from one of the 29 Operations sites in 17 countries in which we manufacture or the $13 billion we spend on the purchase of goods, services and active pharmaceutical ingredients (APIs).

See Operations and Supply chain management from page 33.

$13bn
spent with suppliers

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

See Financial Review from page 74.

$2.6bn
net cash flow from operating activities

How we add value

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

- improving health outcomes and transforming patients' lives
- 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 externalisation activities generates cash flow, which helps us:

- fund our investment in science and Growth Platforms to drive long-term value
- follow our progressive dividend policy
- meet our debt service obligations.

This involves balancing the interests of our business, financial creditors and shareholders.

See Financial Review from page 74.

Marketplace

Economic growth, an expanding global population and technological change are expected to contribute to growth in the pharmaceutical industry. However, social, economic and political challenges remain in meeting unmet medical need.

A changing world

> NCDs kill 41 million people each year, disproportionately affecting low- and middle-income countries
> Growing and ageing populations, with increasing urbanisation
> Breakthroughs in digital and other technologies transforming the pharmaceutical industry

Increasing demand for healthcare

> The US is the largest pharmaceutical market, with 47% of global sales
> Pharmaceutical sales growth of 4.4% in 2018, led by emerging markets
> Expected growth to 2022 will be led by the US and developing markets but with slower growth in China

Pharmaceutical sector opportunities and challenges

> Pricing, regulation and patent exclusivity present opportunities as well as challenges
> The sector is reshaping itself at the same time as it seeks to develop trust with key stakeholders

A changing world

Society is changing

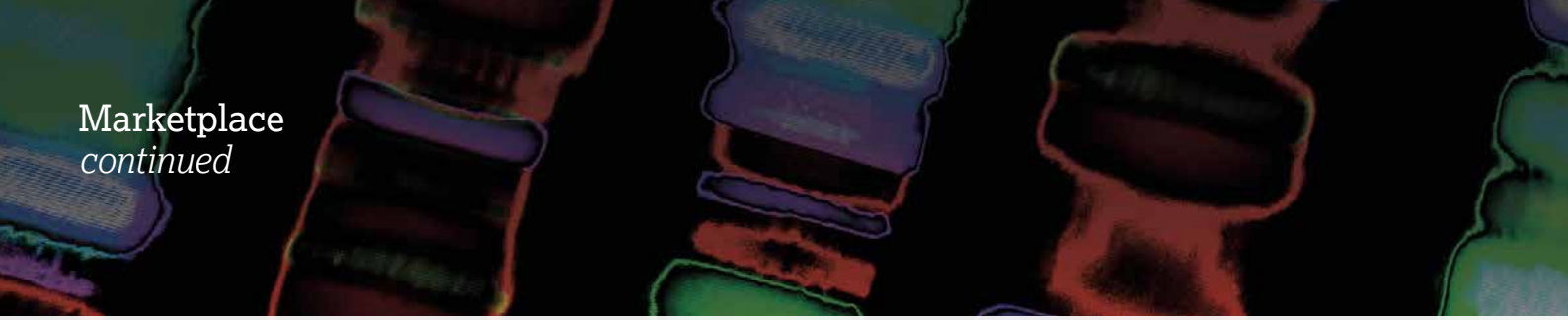
Increasing burden of chronic disease
An ageing population and changes in society are contributing to steady increases in non-communicable diseases (NCDs) with developing countries particularly affected as their populations grow. As the burden of NCDs grows, so do public expectations while governments' ability to meet them is constrained as finances are under stress. Low- and middle-income countries are also disproportionately affected by issues such as air pollution and climate change, thereby exacerbating social, economic and demographic inequalities.

Growing societal expectation of businesses
Society's views of business are changing with organisations no longer valued solely on the quality of products and services and financial performance, but also their engagement with employees, customers, communities and society as a whole. Workforce dynamics are also changing for many as working for a single employer is replaced by working independently in a number of different roles.

$47tn
The WHO estimates that NCDs kill 41 million people each year and could cost the global economy $47 trillion by 2030.

75%
NCDs disproportionately affect people in low- and middle-income countries where more than three quarters of global NCD deaths – 32 million – occur.

57%
Between 2001 and 2020, the WHO estimates that chronic diseases will have increased by 57%.

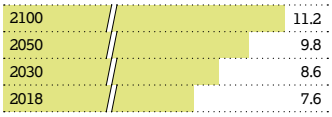


Global growth is shifting

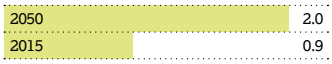
Growing and ageing populations, increasing urbanisation
As shown on the right, patient populations are expanding. For example, the world's population is rising and more people are living in cities, with an estimated three million people a week moving to cities in 2015. Urbanisation presents opportunities, such as greater wealth and access to better healthcare, but also new hazards and healthcare challenges, such as an increase in the prevalence of NCDs. These diseases include cancer and cardiovascular, metabolic and respiratory diseases which are often associated with urban lifestyle choices, including smoking, diet and lack of exercise. NCDs are also associated with ageing and, with the majority of the world's workforce rapidly ageing, healthcare costs are rising as people are living longer. In many markets, ageing populations mean the size of the labour force will stagnate or decline, resulting in a potential shortage of labour compared with the abundance of labour that has fuelled growth since the 1970s. On the other hand, and as outlined below, technology is transforming the workplace.

Strong global economic growth, driven by Eastern economies
With the rapid urbanisation of developing markets, such as China and India, economic growth is shifting east and away from advanced economies such as North America, Western Europe and Japan. By some estimates, Africa could represent the fourth largest economy in the world by 2040 and, by 2050, India could overtake the US as the second largest economy. So far as shorter-term economic trends are concerned, the October 2018 World Economic Outlook of the International Monetary Fund (IMF) continued to forecast strong economic growth. However, it cautioned that "the balance of risks… has shifted to the downside in a context of elevated policy uncertainty".

Estimated world population (UN, bn)



Estimated population over the age of 60 (WHO, bn)



// Denotes a scale break.

3m
Three million people per week estimated to have moved to cities in 2015.

80%
By 2050, 80% of all older people will live in low- and middle-income countries.

Digital and technical breakthroughs

Advances in digitisation, analytics, artificial intelligence (AI) and automation are redefining how business and industries work. They will transform the workplace and business processes as people interact with increasingly smarter machines.

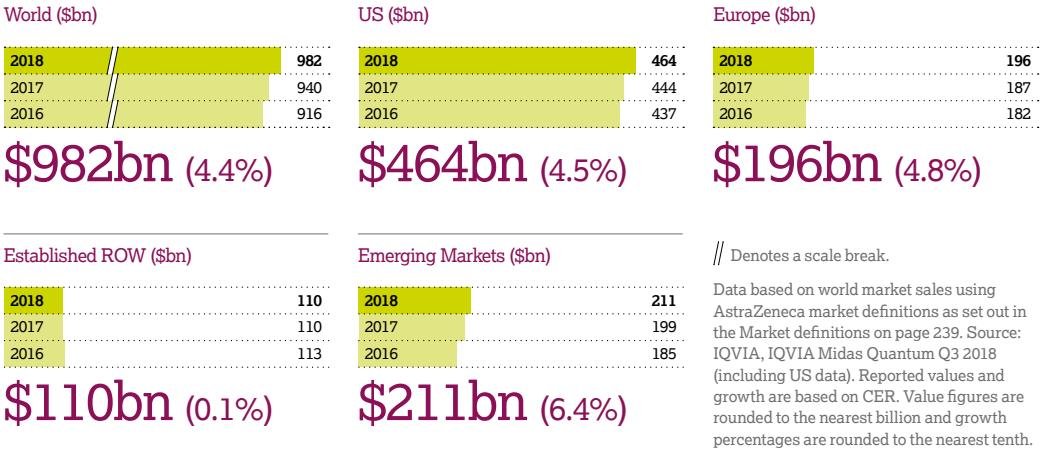
New entrants from the technology sector are bringing different competencies to healthcare, applying their knowledge to accelerate scientific discovery, improve health through technology and better understanding the consumer. At the same time, and enabled by technology, patients are becoming more engaged and willing to take greater control of their health and treatment choices.

"New entrants from the technology sector are bringing different competencies to healthcare… and enabled by technology, patients are becoming more engaged and willing to take greater control of their health and treatment choices."

Increasing demand for healthcare

Global pharmaceutical sales

As shown in the chart on the right, global pharmaceutical sales grew by 4.4% in 2018. Established Markets saw an average revenue increase of 3.9% and Emerging Markets revenue grew at 6.4%. The US, China, Japan, Germany and France are the world's top five pharmaceutical markets by 2018 sales. In 2018, the US had 47.2% of global sales (2017: 47.2%; 2016: 47.7%).



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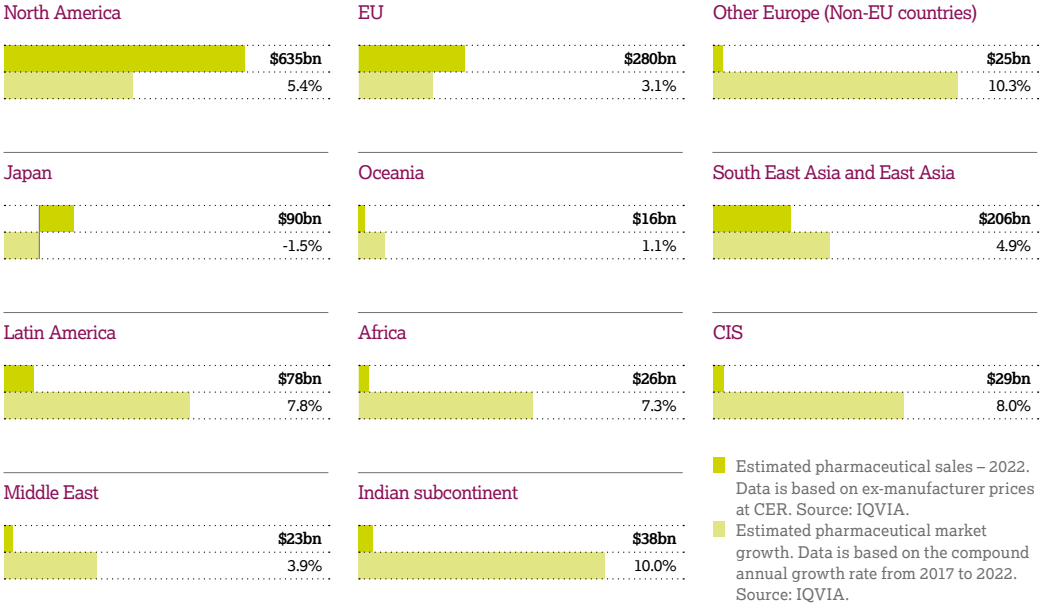
Data based on world market sales using AstraZeneca market definitions as set out in the Market definitions on page 239. Source: IQVIA, IQVIA Midas Quantum Q3 2018 (including US data). Reported values and growth are based on CER. Value figures are rounded to the nearest billion and growth percentages are rounded to the nearest tenth.

Estimated pharmaceutical sales and market growth – 2022

The table on estimated pharmaceutical sales and market growth to 2022 on the right also illustrates that we expect the established markets in North America and developing markets, including Africa, CIS, 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 4.6%. This is due to the continued slowdown of the major hospital sector.



Estimated pharmaceutical sales – 2022. 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 2017 to 2022. Source: IQVIA.

Marketplace
continued

Pharmaceutical sector opportunities and challenges

In addition to the global trends set out on the previous pages, we also face a number of opportunities and challenges within the pharmaceutical sector, as set out below. Our strategy reflects our response to this environment and, where applicable, the relevant strategic response to each trend is highlighted below.

For more information, see Strategy from page 18, Key Performance Indicators from page 20, Achieve Scientific Leadership from page 25, Return to Growth from page 29 and Be a Great Place to Work from page 38.

Advances in science and medicine

Scientific innovation is critical to addressing unmet medical need. The delivery of new medicines will rely on a more advanced understanding of the underlying biology of the disease, and the use of new technology and approaches. These include genomics and digital healthcare. Scientific and technological breakthroughs in small molecules and in biologics are also helping accelerate innovation. Innovation will be accelerated through the use of large volumes of biological data from disease biology and genomics which is driving precision medicine, while advances in data management and data integration are improving the speed and quality of clinical trial processes. Such advances have resulted in increased numbers of FDA Priority Reviews and Breakthrough designations.

The cost of developing new medicines continues to rise with annual global R&D investment estimated to be $150-160 billion. Regulators and payers are demanding greater evidence of the comparative effectiveness of medicines. On the other hand, a greater emphasis on Proof of Concept is helping to improve productivity and reduce costs by showing the potential efficacy of drugs earlier in the development process. Against this background, the FDA approved 59 novel drugs in 2018 compared with 46 in 2017 and 22 in 2016. Nevertheless, the risk of any products failing at the development or launch stages, or not securing regulatory approvals, continues.

$150-160bn
Annual global R&D investment estimated to be $150-160 billion.

59
The FDA approved 59 novel drugs in 2018 compared with 46 in 2017 and 22 in 2016.

Link to strategy
Achieve Scientific Leadership

For more information, see Risk from page 220.

Regulatory environment

The public's expectation of safe, effective and high-quality medicines is reflected in a highly regulated biopharmaceutical industry. At the same time, we are seeing instances of government policy and regulation being introduced to stimulate innovation in drug development, and of regulatory health authorities implementing programmes intended to speed up patient access to transformative medicines. Examples include the 21st Century Cures Act of 2016 and the FDA Reauthorization Act of 2017 in the US, a new conditional early approval system in Japan and proposed changes to regulations in China.

In addition, international harmonisation of regulatory requirements is being advanced in many areas through organisations such as the International Council for Harmonization (ICH), the Pharmaceutical Inspection Cooperation Scheme (PIC/S), the Pan American Network for Drug Regulatory Harmonization (PANDRH), and the International Conference of Drug Regulatory Authorities (ICDRA).

There are also uncertainties. In Europe, they include how the UK will work with the EU regulatory system following its planned exit from the EU, the approach the UK will take to establishing its own regulatory system outside the EU, and the relocation of the EMA from London to Amsterdam, Netherlands (and the likely disruption this will cause to regulatory processes).

The implementation of the EU Clinical Trials Regulation has also been delayed. Nevertheless, paediatrics and use of digital tools in clinical development, as well as patients' access to innovative medicines and stakeholders' interactions to improve drug development, are high on the EU agenda.

In biosimilar development, regulatory requirements for the registration of biosimilar products are becoming better defined. However, significant areas of regulatory policy are still evolving. Among these are transparency of data regarding the level of evidence to support approval of claims for biosimilarity in labelling, standards for interchangeability and pharmaceutical substitution, and traceability of pharmacovigilance reports through naming conventions that permit differentiation of products.

Increased transparency of data used for regulatory decision making continues to be an area of interest to regulatory authorities in the EU and the US. It has recently attracted interest elsewhere, such as in Canada. We believe that transparency enhances the scientific understanding of how our medicines work and is in the medical interest of our patients.

"We believe that transparency enhances the scientific understanding of how our medicines work and is in the medical interest of our patients."

Link to strategy
Achieve Scientific Leadership

For more information, see Risk from page 220. For more information about biosimilars, see Loss of exclusivity and genericisation opposite.

Pricing of medicines

Pricing and reimbursement remain challenging in many markets. We continue to see examples where healthcare services (including pharmaceuticals) are highly regulated by governments, insurers and other private payers through various controls on pricing and reimbursement. Implementation of cost-containment reforms and shifting market dynamics are further constraining healthcare providers, while difficult economic conditions burden patients who have out-of-pocket expenses relating to their medicines. Pharmaceutical companies are now expending significant resources to demonstrate the economic as well as the therapeutic value of their medicines.

The need and desire for payers to manage drug expenditure has been heightened by the shift over the last decade from a primary care to a specialty care focus. Specialty drugs are used for the treatment of complex, chronic or rare conditions such as cancers, and 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.

Pricing controls and transparency measures remain a priority in key markets such as China, where the National Reimbursement Drug List (NRDL) was updated in 2017. In Europe, governments continue to implement and expand price control measures for medicines, and the EU has committed to introducing a harmonised HTA review. In other markets, there has been a trend towards rigorous and consistent application of pricing regulations, including reference pricing and group/alliance purchasing.

There is also pressure on pricing in the US. For example, federal and state policymakers are considering legislative and regulatory efforts to lower drug prices and to implement transparency measures. While legislative efforts to repeal and replace the Affordable Care Act (ACA) have not been successful, the current administration and members of Congress remain focused on healthcare policy priorities, including efforts to increase competition and generic drug use in government programmes, which could create downward pressure on pricing. The healthcare industry may also be used as a means to offset government spending. US federal agencies continue to propose and implement policies and programmes with the goal of reducing costs, increasing transparency, transforming the delivery system, and improving quality and patient outcomes.

"We continue to see examples where healthcare services (including pharmaceuticals) are highly regulated by governments, insurers and other private payers through various controls on pricing and reimbursement."

Link to strategy
Return to Growth

For more information, see Risk from page 220.

Loss of exclusivity and genericisation

Patent protection for pharmaceutical products is finite and, after protection expires, payers, physicians and patients gain greater access to generic alternatives (both substitutable and analogue) in many important drug classes. These generic alternatives are primarily lower priced because generic manufacturers are largely spared the costs of R&D and market development. As a result, demand for generics is high. For prescriptions dispensed in the US in 2018, generics constituted 84.8% of the market by volume (2017: 84.9%).

Generic competition can also result from patent disputes or challenges before patent expiry. Increasingly, generics companies are launching products 'at risk', for example, before resolution of the relevant patent litigation. This trend, which is likely to continue, creates significant market presence for the generic version while the litigation remains unresolved. Given the unpredictable nature of patent litigation, some companies have settled such challenges on terms acceptable to the innovator and generic manufacturer. While competition authorities generally accept such agreements as a legitimate way to settle these disputes, they have questioned some settlements as being anti-competitive.

Biologics typically retain exclusivity for longer than traditional small molecule pharmaceuticals, with less generic competition. With limited experience to date, the substitution of biosimilars for the original branded product has not followed the same pattern as generic substitution in small molecule products and, as a result, erosion of the original biologic's branded market share has not been as rapid. This is due to biologics' complex manufacturing processes and the inherent difficulties in producing a biosimilar, which could require additional clinical trials. However, with regulatory authorities in Europe and the US continuing to implement abbreviated approval pathways for biosimilar versions, innovative biologics are likely to face increased competition. Like biologics, some small molecule pharmaceutical products are in complex formulations and/or require technically challenging manufacturing and thus may not follow the pattern of generic market erosion seen with traditional, tableted pharmaceuticals. For those products, the introduction of generic alternatives (both substitutable and analogue) can be slower.

84.8%

For prescriptions dispensed in the US in 2018, generics constituted 84.8% of the market by volume (2017: 84.9%).

Link to strategy
Return to Growth

For more information, see Intellectual Property from page 35.

Marketplace
continued

Pharmaceutical sector opportunities and challenges *continued*

Trust

The pharmaceutical industry continues to face challenges in building and maintaining its reputation and the trust of its stakeholders. This reflects past sales and marketing practices, pricing practices by some, as well as legal disputes between pharmaceutical companies and government and regulatory authorities.

Companies, including those in the pharmaceutical industry, have been investigated by the China Public Security Bureau following allegations of bribery, and criminal and financial penalties have been imposed. In the US, investigations by the US Department of Justice (DOJ) and Securities and Exchange Commission (SEC) under the Foreign Corrupt Practices Act continue, as do investigations by the UK Serious Fraud Office under the UK Bribery Act.

To address these challenges, companies are seeking to:

> embed a culture of ethics and integrity
> adopt higher governance standards
> promote sustainability programmes, particularly focused on access to healthcare
> improve relationships with employees, shareholders and other stakeholders.

Companies are also adopting more 'patient-centric' approaches that go 'beyond the pill' to encompass all aspects of disease management – prevention, screening, diagnosis, treatment and rehabilitation.

More generally, to be trusted by stakeholders, companies need to operate in a way that meets their expectations.

"The pharmaceutical industry continues to face challenges in building and maintaining its reputation and the trust of its stakeholders."

Link to strategy

Be a Great Place to Work

For more information, see Ethics and transparency from page 43.

Reshaping of the sector

Our competitors include large, research-based pharmaceutical companies (like AstraZeneca) that discover, develop and sell innovative, patent-protected prescription medicines and vaccines, smaller biotechnology and vaccine businesses, and companies that produce generic medicines. The pharmaceutical market is highly competitive. For example, the global respiratory market is likely to see changes with new branded or generic products with new combinations and devices. In immuno-oncology, the large number of clinical trials being carried out highlight the competitive nature of this area.

While our peers face similar challenges and opportunities, they approach them in different ways. Some companies have pursued a strategy focused on branded prescription pharmaceuticals. Others have diversified by acquiring or building branded generics businesses or consumer portfolios, or have looked to geographic expansion, especially in Emerging Markets. Companies are also focused on improving R&D productivity and operational efficiency. Across the industry, consolidation, business development deals (including licensing and collaborations) and competition for business development opportunities have continued.

The speed of technological change may also transform current business models. Existing and new entrants to the sector, for example from the technology sector, are focusing on patient outcomes rather than just products and services, prediction and prevention rather than just diagnosis and treatment. This may also entail new ways of competing.

The sustainability and growth of a more 'patient-centric' pharmaceutical industry is predicated on organisations being able to take full advantage of these breakthroughs in digital and other technologies.

"Existing and new entrants to the sector are focusing on patient outcomes rather than just products and services, prediction and prevention rather than just diagnosis and treatment."

Link to strategy

Global, science-led pharmaceutical company

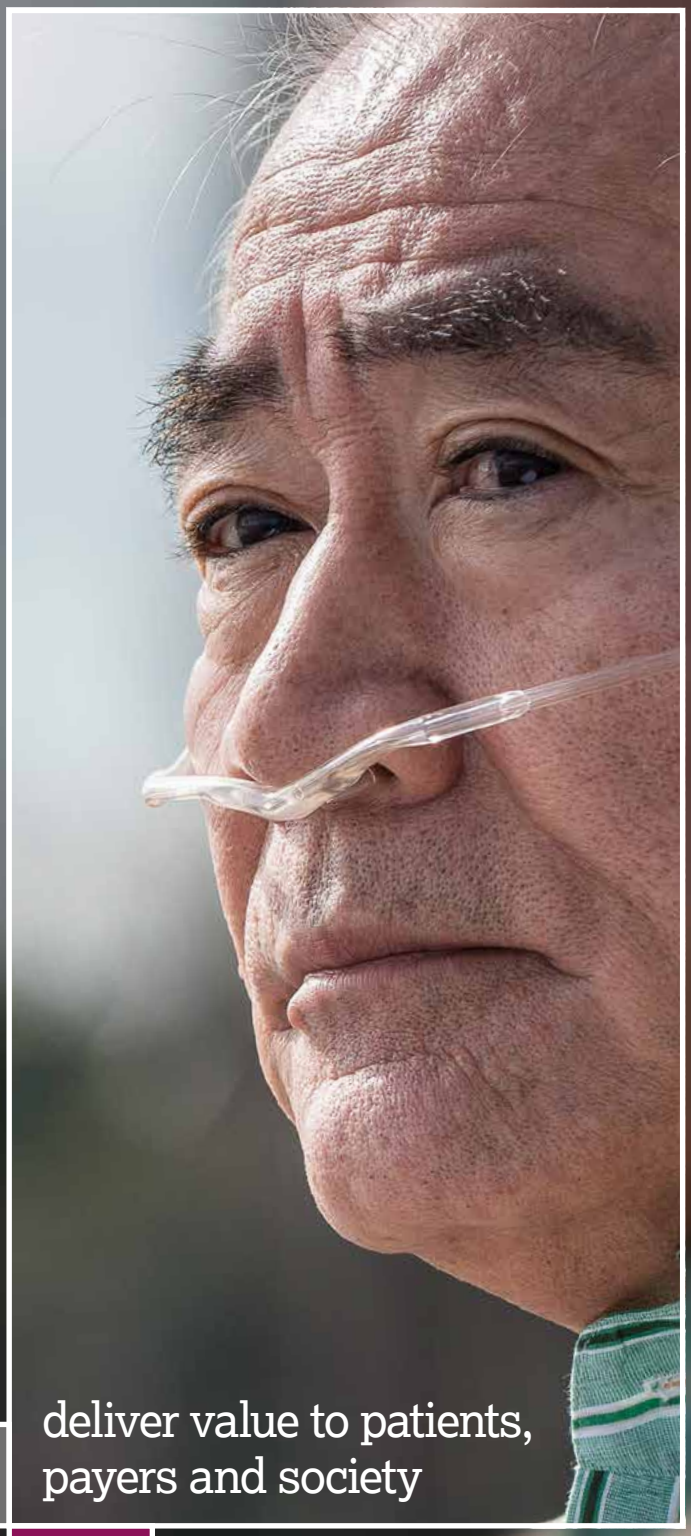
For more information, see Risk from page 220.

One of the approaches we are adopting to payment for our medicines is the implementation of Innovative Value Strategies, which link payment for a medicine to its effectiveness and the outcomes it achieves for patients, payers and society. For example, in the US we have entered into 37 agreements that span across each of our main therapy areas.

Scientific advances have led to a new era of medicines that have the potential to be used across different disease areas and patient populations. Value delivered by a medicine may differ across different indications and may not align to a single price. Additive pricing of combinations may also present an access challenge for health systems.

As part of our Innovative Value Strategies, we are working with payers and healthcare systems to introduce indication-based pricing (IBP) which aligns payment to value at the indication level. This development is part of our commitment to working with all stakeholders to improve patient health and adding value to the health system through innovative personalised medicines that are both accessible and affordable.

IBP requires three elements: a system of value assessment at the individual indication level; appropriate evidence that allows usage per indication to be linked to payment; and an ability to implement confidential commercial agreements that recognise the different value of individual indications. A number of countries have already implemented various IBP approaches, including the US, Australia, Italy and Switzerland.



Science *can* deliver value to patients, payers and society

~75%
of oncology medicines are expected to have multiple indications by 2020

50%
this is a 50% increase vs 2014

For more information on the principles on which we base the price of our medicines, see page 30.

Strategy

We announced our strategy for returning to growth in 2013. The first phase in our journey was focused on rebuilding our pipeline. The second stage was crucial as we drove our Growth Platforms forward, continued to launch new medicines and made them available to patients. We returned to Product Sales growth in 2018 and, as we look ahead to 2020 and beyond, continued investment in our product launches and pipeline will keep us on track to deliver sustainable growth in line with our targets.

Our strategic priorities

We are a 'pure-play', global, science-led pharmaceutical company. We are focused on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of unmet medical need in three main therapy areas: Oncology; Cardiovascular, Renal and Metabolism; and Respiratory. In 2018, our strategic priorities were focused under the three pillars listed below.

1. Achieve Scientific Leadership

We are focusing our science on three therapy areas and accelerating our pipeline. We are also transforming our way of working.

2. Return to Growth

We are focusing on our Growth Platforms and transforming the business through specialty care, devices and biologic medicines. Targeted business development reinforces our efforts.

3. Be a Great Place to Work

We are evolving our culture and simplifying our business. We want to attract and retain the best talent.

We also want to do business sustainably.

Achieve Group Financial Targets

Effective delivery of our three strategic pillars will help us achieve our financial targets. We aim to deliver great medicines to patients while maintaining cost discipline and a flexible cost base. We wish to maintain a progressive dividend policy and a strong balance sheet.

How we report our progress

Key Performance Indicators (KPIs)
The following pages present our KPIs for 2018. Our KPIs are aligned to our three strategic priorities and are the indicators against which we measure our productivity and success. We also monitor financial targets, which indicate whether we have delivered our strategy in a way that allows us to continue to operate as a successful business.

Our remuneration arrangements are also aligned to our strategic priorities as set out in our Group scorecard and reflected in our KPIs. Achieve Scientific Leadership, Return to Growth and Achieve Group Financial Targets are included in the annual bonus targets.

For more information, see the Directors' Remuneration Report from page 120.

Strategic Report
Our operating model comprises key business functions that are aligned to delivery of our strategy. In addition, our therapy areas provide strategic direction for each of our disease areas all the way from early-stage development to commercialisation. Our Strategic Report therefore encompasses two types of review and our Principal Risks:

Business Review
Provides information on key activities and progress within each of the three strategic pillars. Within this section we report on our pipeline, the key business functions that are integral to delivering our strategy (R&D and Commercial), as well as those that we see as vital strategic enablers (Partnering and Operations) or which underpin our business model (Intellectual Property). We also report on our employees and how we do business sustainably.

Therapy Area Review
Looks at each of our therapy areas, their developments and focus for 2018, as well as what is in the pipeline.

Risks
We also review the risks that might challenge the delivery of our strategy.

For more information, see Business Review from page 24, Therapy Area Review from page 50 and Risk Overview from page 70.

How our current strategy responds to market trends

Our strategy reflects the way we have chosen to respond to the opportunities and challenges posed by the environment in which we operate, together with our competition, as outlined in Marketplace from page 11.

Strategic Priority	How are we responding to our environment?
1. Achieve Scientific Leadership	> Focus on innovative science in three therapy areas, a range of drug modalities, emerging drug platforms and new technologies. > Strengthen our ability to match targeted medicines to patients who need them most. > Drive R&D productivity by focusing on quality rather than quantity at all stages of drug discovery and development, and leveraging technology including the provision of enhanced data and clinical insights. > Partner with academia, governments, industry and scientific organisations to: – allow us to access the best and most advanced science and technology, and drive innovation – streamline regulatory processes, define and clarify approval requirements for innovative drug and biologic products. > Maintain effective working relationships with health authorities worldwide, including the FDA in the US, the EMA in the EU, the PMDA in Japan, ANVISA in Brazil and the NMPA in China. > Make information about our clinical research publicly available and work with regulators and other stakeholders to ensure the appropriate level of data transparency.
2. Return to Growth	> Engage 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 and wellness to deliver better patient outcomes more efficiently. > Enable our Emerging Markets to deliver better and broader patient access through innovative and targeted equitable pricing strategies and practices. > Partner with industry, governments and academia to find ways to bring new medicines to market more quickly and efficiently. > Evaluate the use of real-world evidence to further bolster the evidence base around therapeutic and economic value. > Base pricing policy on four principles: value, sustainability, access and flexibility. > Consider innovative outcomes contracts with payers as a mechanism to pay for value. > Pursue a strong patent strategy – from building robust patent estates that protect our pipeline and products to defending and enforcing our patent rights.
3. Be a Great Place to Work	> Our Code of Ethics is built on a refusal to tolerate bribery or any other form of corruption. > Further ethics and transparency, and broaden access to healthcare: two of our sustainability priorities. > As a values-led organisation, we are able to recruit the best talent which underpins our innovation and growth. > Engender a high-performing culture and lifelong learning. > Harness different perspectives, talents and ideas as well as ensuring that our employees reflect the diversity of the communities in which we operate.

Looking ahead – Beyond 2020

As we deliver the science-led transformation of our Company, developments are taking place that are changing the world in which our patients and employees live, and the environment and sector in which we operate. Looking to the future, we are considering the opportunities and challenges that these developments present and factoring them into our plans. For example, how do we:

> respond to an increased prevalence in NCDs, urbanisation and economic growth shifting east?
> maximise the opportunities arising from changing workforce dynamics and improve productivity with an ageing workforce?
> capitalise on digital and technological advances?
> connect better with patients who are taking a more active role in managing their own health?
> meet the challenges posed by the rise of social enterprise and sustainable development?

Questions such as these were among those discussed at our Board's formal annual strategy review day as they considered the fitness for purpose of our strategy beyond 2020. The preparation for this year's review included the crowdsourcing of ideas from employees as an input into those deliberations.

For more information on Board engagement with employees, see page 99.

Key Performance Indicators

Strategic priorities

Key Performance Indicators

Achieve Scientific Leadership

Focus on innovative science in three main therapy areas
Focus on Oncology; Cardiovascular, Renal and Metabolism; and Respiratory. We are also selectively active in autoimmunity, infection and neuroscience.

Work across small molecules, oligonucleotides and other emerging drug platforms, as well as biologic medicines, including immunotherapies, and innovative delivery devices that can offer choice to patients.

Prioritise and accelerate our pipeline
Accelerate and invest in key R&D programmes. At the end of 2018, eight NMEs were in Phase III/pivotal Phase II or under regulatory review, covering 15 indications.

Three NMEs were approved in 2018. Having met the targets for 2016 we had set ourselves in 2013, we are now on target to meet our longer-term goal of sustainably delivering two NMEs annually by 2020.

Strengthen our early-stage pipeline through novel science and technology.

Transform our innovation and culture model
Focus on novel science, such as immune-mediated therapy combinations and precision medicine.

Co-location near bioscience clusters at three strategic centres in Cambridge, UK; Gaithersburg, MD, US; and Gothenburg, Sweden helps to leverage our capabilities and foster collaboration with leading scientists and research organisations.

Accelerate through business development
Work to reinforce our therapy areas and strengthen our portfolio and pipeline through targeted business development, including collaborations, in-licensing and acquisitions.

Collaborate strategically to broaden and accelerate the development of pipeline assets (externalisation) and divest non-core assets to realise value.

NME Phase II starts/progressions

9

2018	**9**
2017	14
2016	16[1]

[1] 15 for determining annual bonus.
See from page 127.

Phase III investment decisions

19

2018	**19**
2017	9
2016	7

NME or LCM project regulatory submissions in major markets

28

2018	**28[1]**
2017	18[2]
2016	14[3]

[1] 24 for determining annual bonus.
[2] 13 for determining annual bonus.
[3] 13 for determining annual bonus.
See from page 127.

NME and major LCM regional approvals

23

2018	**23**
2017	19
2016	11

Note: The Clinical-stage strategic transactions KPI, covering acquisition, licensing and divestment deals, has been removed from Achieve Scientific Leadership. The impact of this activity is captured in the Group financial targets which better reflects the results, rather than a separate measure for the number of deals.

Achieve Scientific Leadership from page 25; Therapy Area Review from page 50; Development Pipeline from page 212.

"We delivered three new molecular entities (NMEs) in 2018 and are on target to meet our goal of sustainably delivering two NMEs annually by 2020."

Strategic priorities

Key Performance Indicators

Return to Growth

Focus on Growth Platforms

Emerging Markets – Focus on delivering innovative medicines by investing in Emerging Markets' capabilities, with a focus on China and other leading markets, such as Brazil and Russia. The ongoing transformation of our capabilities is supporting new medicines and improving access and affordability.

Respiratory – Work to maximise pipeline value, devices and medicines to fulfil unmet medical need and improve patient outcomes in asthma and COPD. Includes all respiratory brands.

New CVRM – Since 2017, New CVRM Growth Platform includes *Brilinta*, *Onglyza* franchise (*Onglyza* and *Kombiglyze*), *Farxiga* franchise (*Farxiga* and *Xigduo*), Exenatide Total (*Byetta* and *Bydureon*), *Symlin*, *Qtern*, roxadustat, *Epanova* and *Lokelma*.

Japan – Strengthen our Oncology franchise and work to maximise the success of our Diabetes medicines.

Oncology – Aim to deliver six new cancer medicines to patients by 2020. Since 2014, we have delivered five Oncology medicines to date: *Lynparza*, *Tagrisso*, *Imfinzi*, *Calquence* and *Lumoxiti* that make a meaningful difference to patients.

Transform through specialty care, devices and biologics

Biologic medicines now account for about half of our NMEs in development, potentially enhancing asset longevity. A greater focus on innovative and differentiated delivery devices affords patients choice while ensuring product durability. Our new specialty care portfolio is expected to balance our strength in primary care medicines.

Emerging Markets

$6,891m
Product Sales

2018	**$6,891m**
2017	$6,149m
2016	$5,794m

Actual growth	CER growth
2018 +12%	2018 +13%
2017 +6%	2017 +8%
2016 0%	2016 +6%

Respiratory

$4,911m
Product Sales

2018	**$4,911m**
2017	$4,706m
2016	$4,753m

Actual growth	CER growth
2018 +4%	2018 +3%
2017 -1%	2017 -1%
2016 -5%	2016 -3%

New CVRM

$4,004m
Product Sales

2018	**$4,004m**
2017	$3,567m
2016	$3,266m

Actual growth	CER growth
2018 +12%	2018 +12%
2017 +9%	2017 +9%
2016 +15%	2016 +17%

Japan

$2,004m
Product Sales

2018	**$2,004m**
2017	$2,208m
2016	$2,184m

Actual growth	CER growth
2018 -9%	2018 -11%
2017 +1%	2017 +4%
2016 +8%	2016 -3%

Oncology[2]

$6,028m
Product Sales

2018	**$6,028m**
2017	$4,024m
2016	$3,383m

Actual growth	CER growth
2018 +50%	2018 +49%
2017 +19%	2017 +19%
2016 +20%	2016 -20%

[1] Total removes the effect of certain Product Sales which are included in more than one Growth Platform. Reconciliation to the number used for calculating annual bonus is shown from page 127.

[2] In 2018, Oncology Growth Platform included the entire Oncology portfolio. Prior years have been revised on this basis.

Return to Growth from page 29; Therapy Area Review from page 50.

$18,464m

Revenue from Growth Platforms of $18,464 million[1] in 2018 represented 84% of Total Revenue

Key Performance Indicators *continued*

Strategic priorities | Key Performance Indicators

Be a Great Place to Work*

Evolve our culture
Improve our employees' engagement with our Purpose and Values and promote greater understanding of, and belief in, our strategy.

Simplify our business
Develop simpler, more efficient processes and flatten our organisational structure to improve productivity, encourage accountability and improve decision making and communication.

Attract and retain the best talent
An inclusive environment that enhances our ability to attract and retain diverse talent with critical capabilities.

Be a Great Place to Work from page 38.

Employee belief in our strategy

89%

2018	89%[1]
2017	88%[2]
2016	80%[3]

[1] Source: December 2018 Pulse survey across a sample of the organisation.
[2] Source: December 2017 Pulse survey across a sample of the organisation.
[3] Source: December 2016 Pulse survey across a sample of the organisation.

Organisational structure – % of employees within six management steps of the CEO

72%

2018	72%
2017	70%
2016	82%

Employees who would recommend AstraZeneca as a great place to work

83%

2018	83%[1]
2017	81%[2]
2016	74%[3]

[1] Source: December 2018 Pulse survey across a sample of the organisation.
[2] Source: December 2017 Pulse survey across a sample of the organisation.
[3] Source: December 2016 Pulse survey across a sample of the organisation.

Do business sustainably†

Making science accessible
Deliver our business strategy in a way that brings wider benefits to society and the planet.

Focus on:

- increasing access to healthcare for more people
- furthering ethics and transparency in everything we do
- reducing environmental impacts on human health and the natural world.

Connect our work with the UN Sustainable Development Goals and integrate our commitments into day-to-day business activities.

Sustainability from page 42.

Ethics: Non-compliance with our Code of Ethics

56.6
per 1,000 employees in Commercial Regions

2018	56.6
2017	41.4
2016	50.7

There were 2,042 instances, most of them minor, of non-compliance with our Code of Ethics or supporting requirements in our Commercial Regions by employees and third parties.

Health: Reaching people through our Access to Healthcare programmes

12.0m
people

2018	12.0m
2017	7.2m
2016	4.2m

Our Access to Healthcare programmes, including Healthy Heart Africa, Healthy Lung, and Phakamisa, have reached 12.0 million people through education, screenings, diagnosis and treatment cumulatively since the start of each programme.

Environmental protection: Operational greenhouse gas (GHG) footprint[1]

1,769 kt CO_2e

2018	1,769 kt CO_2e
2017	1,705 kt CO_2e
2016	1,684 kt CO_2e

[1] Operational GHG footprint is emissions from all Scope 1, 2 and selected Scope 3 sources. See page 231.

Our 2018 operational GHG footprint met our target of progressing our Science Based Targets and represents a 0.4% reduction from our 2015 baseline.

* We will review the Be a Great Place to Work KPIs in 2019 to evaluate appropriate representation of the strategy. Where possible, we will continue to make updates on current indicators publicly available.

† As disclosed in the 2017 Annual Report, we reassessed our Do business sustainably KPIs in 2018:

- We added an Ethics & Transparency KPI to measure progress for our third sustainability focus area.
- We expanded the Access to Healthcare KPI to incorporate more of our programmes.
- We changed the title of our Environmental protection KPI. In line with World Resources Institute GHG Protocol, a carbon dioxide equivalent (CO_2e) number can be used to report on GHGs, and it is commonly called 'carbon'. At AstraZeneca, the majority of our operational GHG footprint is from non-CO_2 GHGs so we are now using the better representation of 'GHG'. There is no change in the content of our CO_2e reporting.
- The retired KPIs are reported for continuity in the 2018 Sustainability Report on www.astrazeneca.com/sustainability. The retired KPIs are the Dow Jones Sustainability Index rating and number of people reached through only our Healthy Heart Africa programme.

"Our achievements are only made possible by a skilled and talented team who live our Values and are true to our Purpose."

Strategic priorities | Key Performance Indicators

Achieve Group Financial Targets

Cost discipline
Our aim is to deliver great medicines for patients while maintaining cost discipline and a flexible cost base.

Maintain a progressive dividend
Policy is to maintain or grow dividend per share.

Maintain a strong balance sheet
Target a strong, investment-grade credit rating and optimal cash generation.

Product Sales[1,2]

$21,049m

Actual growth	CER growth
2018 +4%	2018 +4%
2017 -5%	2017 -5%
2016 -10%	2016 -8%

// Denotes a scale break.

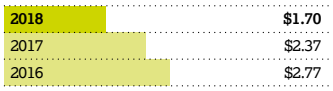
Net cash flow from operating activities[2]

$2,618m

Actual growth
2018 -27%
2017 -14%
2016 +25%

Reported EPS

$1.70



Actual growth	CER growth
2018 -28%	2018 -29%
2017 -14%	2017 -15%
2016 +24%	2016 +9%

Core EPS[2]

$3.46

Actual growth	CER growth
2018 -19%	2018 -19%
2017 -1%	2017 -2%
2016 +1%	2016 -5%

Dividend per share[3]

$2.80

"The Board reaffirms its commitment to the progressive dividend policy."

[1] The Total Revenue KPI has been replaced by Product Sales which aligns with our external guidance and focus on commercial execution to drive Product Sales growth. Product Sales and Externalisation Revenue make up Total Revenue.
[2] Reconciliation to the number used for calculating annual bonus is shown from page 127.
[3] First and second interim dividend for the year.

Financial Review from page 74.

The first phase in AstraZeneca's strategy focused on strengthening and accelerating our pipeline. In the second phase, it was on driving our Growth Platforms and launching new products. Following our return to Product Sales growth, our focus is now on delivering sustainable growth through innovation.

In this Business Review, we report on how the elements of our business are delivering against our strategic priorities which are to:

1. Achieve Scientific Leadership
2. Return to Growth
3. Be a Great Place to Work

Our operating model includes our Research & Development (R&D), Commercial and Operations functions, together with our Enabling Units. It is outlined below.

In January 2019, we announced organisational changes to support continued scientific innovation and commercial success as we enter the next phase in our strategic development. The changes are designed to further integrate R&D and accelerate decision making and the launches of new medicines, consolidating what we believe is already one of the most exciting and productive pipelines in the industry.

We are also enhancing our commercial functions to increase collaboration with our R&D organisation, enabling greater commitment to our main therapy areas. We want AstraZeneca to be more agile, collaborative and focused on bringing innovative medicines to patients.

The functions will share many common areas, including basic biology and science platforms as well as medicine supply, manufacturing and IT infrastructure to improve efficiency. These resources will continue to be allocated on a Group-wide basis, according to the overall therapy-area considerations and strategy.

Since 2007, we have made significant efforts to restructure and reshape our business to control costs and improve long-term competitiveness.

Full details are provided in the Financial Review from page 74.

Research & Development

Our R&D activities focus on three strategic R&D centres: Gaithersburg, MD, US; Gothenburg, Sweden; and Cambridge, UK, which is also our global HQ.

In 2018, we managed our R&D activities with two discovery and early-stage biotech units (Innovative Medicines and Early Development, and MedImmune) and one late-stage development unit (Global Medicines Development – GMD).

From January 2019, we are creating therapy area-focused R&D units that are responsible for discovery through to late-stage development – one for BioPharmaceuticals (CVRM and Respiratory) and one for Oncology. This is designed to enable us to follow the science by accelerating promising early-stage assets and life-cycle management programmes, as well as providing new opportunities for combinations.

Operations

Our Operations function plays a key role in development, manufacturing, testing and delivery of our medicines to our customers.

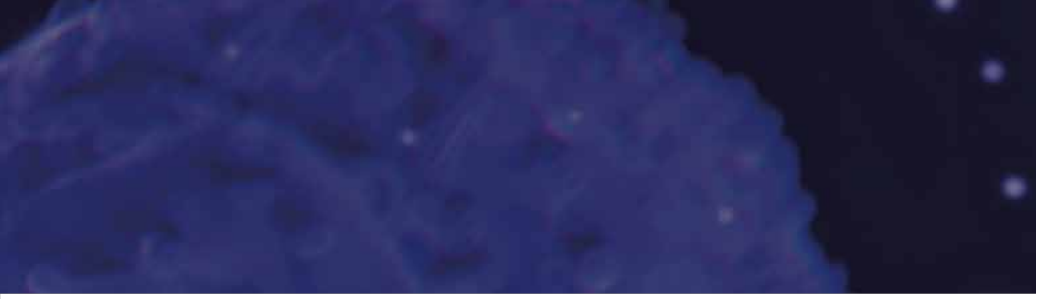
Commercial

In 2018, our sales and marketing functions were grouped into regions: North America (US and Canada); Europe; and International (Emerging Markets, including China, and Australia and New Zealand).

From January 2019, we are creating two commercial units – one for BioPharmaceuticals and one for Oncology. The creation of the BioPharmaceuticals commercial unit aligns product strategy, previously undertaken by our Global Product and Portfolio Strategy group (GPPS), and commercial delivery across CVRM and Respiratory in the US and Europe. These responsibilities mirror the Oncology Business Unit, formed in April 2017, and sharpen our focus on our main therapy areas as we bring new medicines to patients. The International commercial organisation remains unchanged and Japan is categorised separately, being one of our Growth Platforms.

Enabling Units

Finance, Human Resources, Legal, Sustainability, Information Technology.



1. Achieve Scientific Leadership

We are using our distinctive scientific capabilities, as well as investing in key programmes and focused business development, to deliver a pipeline of life-changing medicines.

Overview

During 2018, we had:

- 23 approvals of NMEs or major LCM projects in major markets
  - 13 Oncology approvals for *Imfinzi*, *Lumoxiti*, *Lynparza* and *Tagrisso*
  - 6 CVRM approvals for *Bydureon*, *Bydureon BCise*, *Lokelma* and roxadustat
  - 3 Respiratory approvals for *Bevespi* and *Fasenra*
  - 1 Other approval for *Nexium*
- 28 NME or major LCM regulatory submissions in major markets
- 19 Phase III NME investment decisions
- 9 Phase II starts
- Accelerated reviews included
  - 1 Breakthrough Therapy designation
  - 3 Orphan Drug designations
  - 3 Priority Review designations
- 18 projects discontinued

Scientific leadership and collaboration

AstraZeneca's Purpose is to push the boundaries of science to deliver life-changing medicines. It underpins everything we do. However, as we seek to achieve scientific leadership, we know that we cannot do so alone. We want the way we work to be inclusive, open and collaborative. We believe our operating model gives us access to the best science, both internal and external, and we are open to exploring new and different kinds of collaborations.

One of the measures of our success in achieving scientific leadership and demonstrating the quality of research conducted in our laboratories is the number of publications in high-quality and 'high-impact' journals. It is also critical for recruiting and retaining the best scientists from around the world. Scientists from IMED, MedImmune and GMD have published 102 manuscripts (up by 20 compared with 2017, a record number) in 'high-impact' peer-reviewed journals, each with an impact factor exceeding 15 (Thomson Reuters 5yr IF score) and a score exceeding 955 in total. This represents a fourteen-fold improvement since 2012.

Early science

During 2018, both IMED and MedImmune worked to strengthen our early-stage product portfolio by exploring novel biology across our disease areas and developing the best molecules to address unmet medical need. The diversity of technologies applied in our early pipeline is exemplified by the increased number of new modalities entering clinical development: 12 in 2018 compared to six in 2012. For example, our collaboration with Moderna is exploring the use of modified ribonucleic acid (mRNA) for cardiac regeneration in patients undergoing coronary artery bypass graft surgery (AZD8601) as well as an additional programme where we are evaluating anti-cancer T cell responses with mRNA therapies in patients with solid tumours. With Ionis Pharmaceuticals, Inc., we are investigating an antisense oligonucleotide in immuno-oncology (danvatersin), in combination with *Imfinzi*. With Pieris Pharmaceuticals, AZD1402 entered clinical development in 2018 as a novel inhaled drug for asthma based on its proprietary bicyclic peptide platform. In addition, we continue evaluation of our DNA-based cancer vaccine targeting HPV-16 and HPV-18 (MEDI0457) in collaboration with Inovio Pharmaceuticals, Inc.

Since 2014, we have had 26 diagnostic tests approved in the US, EU and Japan. They support four precision medicines for patients with some of the most challenging diseases of our time, including three for lung and ovarian cancers: therapies that target the epidermal growth factor receptor (EGFR), including the T790M resistance mutation; the poly ADP ribose polymerase (PARP) pathway; and the programmed death-ligand (PD-L1) pathway. Approximately 90% of our pipeline now has a precision medicine approach and reflects the broad range of cutting-edge technologies, tissue diagnostics, next-generation sequencing and point of care diagnostics we have introduced.

For more information, see Therapy Area Review from page 50.

Transforming medical science

We are determined to advance our understanding of disease biology to uncover novel drivers for the diseases we aim to treat, prevent, and even cure. We aim to foster an environment where our scientists can freely share their ideas and collaborate with the best external partners. Our approach to science is exemplified by the number of joint research facilities we have established with leading scientific centres, such as the Karolinska Institutet in Sweden and the CRUK Cancer Institute in Cambridge. In 2018, we extended our joint research facility at the Max Planck Institute to include the Chemical Genomics Centre III, focused on novel basic research in the biosciences and chemical biology. With the Swedish Innovation Bridge Company (SWIBCo), we established a partnership with Procella Therapeutics and Smartwise to develop novel stem cell-based therapies for heart failure. The Blue-Sky fund we established with the MRC Laboratory of Molecular Biology (LMB) is now in its fourth year of funding projects which involve 40% of LMB's Principal Investigators. A recent project breakthrough uncovered the first protein structures for human ataxia telangiectasia mutated (ATM), a key trigger protein in the DNA damage response (DDR) and a prime therapeutic target in cancer. In 2018, we announced a collaboration to develop and commercialise a gene therapeutic for patients with chronic lung disease, utilising 4D Molecular Therapeutics' novel discovery platform to generate optimised adeno-associated virus (AAV) vectors. We also continue to advance our strategic research collaboration with Ethris GmbH where we are evaluating mRNA-based therapies in pulmonary diseases.

Innovating in drug discovery

We are also exploring emerging technologies to accelerate the design and testing of tomorrow's medicines. For example, artificial intelligence (AI) is being used increasingly in the pharmaceutical sector building on the emergence of novel computing technologies, the exponential increase in data and deep learning algorithms. Our teams are looking across the discovery and development process, from target identification to clinical trials, to understand where we can harness new technologies and further automate processes, freeing up more time for discovering and delivering as many new medicine programmes as we can from our pipeline. In Drug Discovery, our teams are facilitating rapid, unbiased drug design and speeding up compound synthesis through improvements in AI algorithmic processes. In the previous two years, our scientists have published more than 20 scientific publications showing improvements in algorithmic processes in drug design. We are also collaborating with the University of Bern and University of Bonn in ExCAPE, an EC-funded project that harvests the power of supercomputers to speed up drug discovery using machine learning. Through the acquisition of Definiens in 2014, we are

developing new AI approaches to evaluate complex morphology, such as in the tumour microenvironment. In Early Development, we are starting to connect high-density datasets, from imaging, biosensors, multiomics and quality-of-life information, to inform earlier decision making in clinical trials. In a recent publication in *Lancet Respiratory Medicine*, we describe a novel modelling tool that has the potential to reduce the time of Phase II trials in respiratory by half.

Late-stage development

During 2018, GMD delivered clinical trial data and submissions that resulted in 23 approvals for new medicines in the US, EU, China and Japan. As shown in the table opposite, our pipeline includes 149 projects, of which 131 are in the clinical phase of development, and we are making significant progress in advancing our late-stage programmes through regulatory approval with 28 NME or major LCM regulatory submissions during 2018.

At the end of the year, we had eight NME projects in pivotal studies or under regulatory review (covering 15 indications), compared with 11 at the end of 2017.

Also in 2018, 20 NMEs progressed to their next phase of development and 18 projects were discontinued: 15 for poorer than anticipated safety and efficacy results; and three as a result of a strategic shift in the environment or portfolio prioritisation.

As is to be expected when we are investigating treatments for diseases that are hard to treat, we also had some setbacks during the year. These included disappointing Phase III data results. For example, the results of the MYSTIC trial showed that *Imfinzi* in combination with tremelimumab for 1st line non-small cell lung cancer (NSCLC) did not meet the primary endpoint of overall survival (OS), and the Phase III EAGLE trial of *Imfinzi* and tremelimumab did not meet the primary endpoints of improving OS in advanced head and neck cancer relative to standard of care chemotherapy. Along with Lilly, we also discontinued development of lanabecestat for Alzheimer's disease after an independent data monitoring committee concluded that the trials were unlikely to meet their primary endpoints and recommended the trials be stopped for futility.

Accelerating the pipeline

GMD is prioritising its investment in specific programmes to accelerate them so that new treatments get to patients more quickly but still safely. As a result, we had numerous study read-outs in 2018, including *Lynparza* in 1st line BRCA-mutated advanced ovarian cancer (SOLO-1), *Imfinzi* OS results in unresectable stage 3 NSCLC, the *Farxiga* cardiovascular outcomes trial in adults with type-2 diabetes (DECLARE) and the *Fasenra* Phase III extension trial evaluating long-term safety and efficacy (BORA). Our teams have also been quick to turn positive clinical trial data into regulatory submissions. In 2018, we made submissions in the US, EU, Japan and China for *Lynparza* for 1st line maintenance treatment for advanced BRCA-mutated ovarian cancer, and *Bevespi* for Chronic Obstructive Pulmonary Diseases (COPD) in the EU, Japan and China. We also received approval in the US and EU for *Lokelma* for the treatment of adults with hyperkalaemia, *Lumoxiti* in the US for the treatment of adults with relapsed or refractory hairy cell leukaemia (HCL), roxadustat for the treatment of anaemia in Chronic Kidney Disease (CKD) in China, *Fasenra* for severe asthma in the EU and Japan, and US approval for *Lynparza* for 1st line maintenance treatment for advanced BRCA-mutated ovarian cancer.

In 2018, we presented scientific rationale that resulted in four regulatory designations for Breakthrough Therapy or Priority Review for new medicines which offer the potential to address unmet medical need in certain diseases, including tezepelumab in patients with severe asthma, *Lynparza* for ovarian cancer (SOLO-1), *Tagrisso* in 1st line EGFR mutated NSCLC (FLAURA) and *Lumoxiti* in 3rd line HCL (PLAIT). We also secured Orphan Drug designation for the development of three medicines to treat very rare diseases including *Lynparza* for treatment of pancreatic cancer (POLO), selumetinib for the treatment of neurofibromatosis type 1 (SPRINT) and *Fasenra* for the treatment of eosinophilic granulomatosis with polyangitis (EGPA).

We also collaborate to advance our clinical research – from strategic alliances with contract research organisations (CROs) for the delivery of clinical trials, to academic collaborations.

Life-cycle management

We also drive an extensive life-cycle management programme for already-approved medicines to pursue further indications and label updates to expand the potential for our products to help more patients. For example, this year we made regulatory submissions for *Lynparza* in the EU to extend treatment into breast cancer; *Farxiga* for type-1 diabetes in the US, EU and Japan; and saxagliptin + dapagliflozin + metformin for type-2 diabetes in the US and EU. We also secured approvals for important life-cycle programmes such as *Imfinzi* in the US, EU and Japan for 1st line treatment of stage 3 NSCLC; *Lynparza* for BRCA-mutated metastatic breast cancer in the US and Japan; *Lynparza* for platinum-sensitive relapsed ovarian cancer in the EU, China and Japan; *Tagrisso* for 1st line treatment of EGFR mutated NSCLC; and *Bydureon BCise*, a new formulation of once-weekly *Bydureon* in a single-dose, pen-filled device.

R&D resources

We have approximately 8,900 employees in our R&D organisation, working in various sites around the world. We have three strategic R&D centres: Cambridge, UK; Gaithersburg, MD, US; and Gothenburg, Sweden. Other R&D centres are located in the UK (Alderley Park and Macclesfield), the US (Waltham, MA and California), Japan (Osaka) and China (Shanghai). We also have a site in Poland (Warsaw) that focuses on late-stage development.

In 2018, R&D expenditure was $5,932 million (2017: $5,757 million; 2016: $5,890 million), including Core R&D costs of $5,266 million (2017: $5,412 million; 2016: $5,631 million). In addition, we spent $476 million on acquiring product rights (such as in-licensing) (2017: $404 million; 2016: $821 million). We also invested $94 million on the implementation of our R&D restructuring strategy (2017: $201 million; 2016: $178 million). The allocations of spend by early-stage and late-stage development are presented in the R&D spend analysis table below.

R&D spend analysis

	2018	2017	2016
Discovery and early-stage development	**37%**	36%	36%
Late-stage development	**63%**	64%	64%

Development pipeline overview (as at 31 December 2018)

Phase I	Phase II	Late-stage development*	Life-cycle management projects*
38	43	22	46
> 38 projects in Phase I, including: – 26 NMEs – 12 oncology combination projects	> 43 projects in Phase II, including: – 25 NMEs – 6 significant additional indications for projects that have reached Phase III – 12 oncology combination projects	> 22 projects in late-stage development, either in Phase III/ pivotal Phase II studies or under regulatory review: – 8 NMEs not yet approved in any market – 7 projects exploring additional indications for these NMEs – 7 NMEs already approved or launched in the EU, China, Japan and/or the US * NMEs and significant additional indications.	> 46 LCM projects* * Only includes material projects where first indication is launched in all markets.

Cambridge

Cambridge, UK, is a world-leading academic and life sciences hub, and is where we are building our new strategic R&D centre and global corporate headquarters. With around 2,500 AstraZeneca and MedImmune staff now located in the city, we are already seeing the impact of significant scientific and strategic collaborations within the Cambridge cluster.

Construction began in April 2015 and during 2018, the focus of our activities at the site on the Cambridge Biomedical Campus (CBC) shifted from the base building infrastructure and exterior towards the fit-out of laboratory and scientific support spaces, interior design of the office areas and landscaping. Reflecting this shift of focus, we changed construction manager with effect from November 2018.

We remain committed to the design principles of the site and making it a great place to work. The complexity of the building project is reflected in the updated schedule, in which we are expected to start occupation of the building from 2020 rather than have it fully operational in that year as reported in our previous Annual Report. We believe that with our staff in Cambridge already delivering the strategic goals around our decision to locate ourselves in the city, we do not need to press for earlier occupation by adjusting the building programme.

Costs for the project have risen since our original cost projection due to the complexity of the build, construction cost inflation, including the impact of a weakening pound sterling, and increased investment in new technologies and equipment (for example genomics, screening lab) as part of our ongoing investment in R&D in the UK. The new construction manager is reviewing cost estimates but our current cost projection for the project is in the region of £750 million. The project is being funded out of operational cash flows.

Our longer-term vision is to have our non-laboratory-based Cambridge colleagues co-located on the CBC and near our key scientific, research and clinical partners. We are now updating the overall master plan for the site and the next stage will be the development of an office building opposite our R&D centre that can accommodate an additional 1,000 people.

8,900

We have approximately 8,900 employees in our R&D organisation

$5.9bn

$5,932 million invested in our science

"AstraZeneca is partnering with world-leading diagnostic developers to deliver complete disease profiling with a single ctDNA test continuing to improve outcomes for patients."

can

Science

improve the diagnosis and treatment of cancer

30%

Some 30% of biopsies can 'fail'

AstraZeneca has pioneered the use of circulating tumour DNA (ctDNA) for the detection of biomarkers in cancer. Pieces of DNA are shed from a tumour and circulate in the bloodstream where they can be analysed to give genetic information about a patient's tumour. The world's first ctDNA diagnostic test was associated with *Iressa* for specific mutations in the epidermal growth factor receptor (EGFR), namely Exon 19 deletions and L858R in patients with non-small cell lung cancer. It is an approach that allows healthcare professionals to determine the right treatment for a patient using a minimally invasive blood test in place of a biopsy, a more invasive method that can 'fail' in some 30% of cases. AstraZeneca is partnering with world-leading diagnostic developers to deliver complete disease profiling with a single ctDNA test continuing to improve outcomes for patients.

Circulating tumour DNA also has an important role to play if we are to realise our ambition of eliminating cancer as a cause of death. We believe it has the potential to improve drug development by identifying patients who are at risk of relapse and enabling rapid changes in therapy to address this. For example, in early-stage lung cancer, the majority of patients are cured by surgery and chemoradiation therapy. The key to improving overall survival in these stages is to identify those patients at high risk of early relapse and an emerging potential way to do this is by detecting the failure to clear ctDNA from the blood once curative intent treatment has been completed. Investigating the clinical utility and validity of ctDNA in this setting is an active area of research. For example, for these high risk patients, we can test in a minimally invasive manner whether three months' intervention with investigational compounds removes residual disease as evidenced by the clearance of ctDNA, and whether this ultimately impacts long-term outcomes.

Circulating tumour DNA – see caption on inside front cover.

2. Return to Growth

Our return to Product Sales growth was underpinned by our focus on our Growth Platforms and leveraging our strong global commercial presence, particularly in Emerging Markets, to ensure the right medicines are available and that patients have access to them.

Overview

> Product Sales of $21,049 million (up 4% at actual rate of exchange; 4% at CER) and Externalisation Revenue of $1,041 million (down 55%; 55% at CER), resulting in Total Revenue of $22,090 million (down 2%; 2% at CER)
> Growth Platforms revenue of $18,464 million, up 13% (12% at CER)
  – Emerging Markets: Sales growth of 12% (13% at CER) to $6,891 million. China sales in the year grew by 28% (25% at CER), supported by the launches of new medicines
  – Respiratory: Sales grew by 4% (3% at CER). *Symbicort* sales declined by 9% (10% at CER), *Pulmicort* sales rose by 9% (8% at CER) and *Fasenra* performed well in the countries where it had been launched
  – New CVRM: Sales growth of 12% (12% at CER). Strong performances from *Farxiga* and *Brilinta*, with sales of each exceeding $1.3 billion in 2018
  – Japan: Sales decline of 9% (11% at CER). The impact of generic *Crestor* was felt faster than expected and the biennial price reduction also impacted sales
  – Oncology: Sales growth of 50% (49% at CER). Sales of *Tagrisso* reached $1,860 million to become AstraZeneca's largest-selling Oncology medicine
> US revenue was up by 11% to $6,876 million; Europe was down by 6% (10% at CER) to $4,459 million; and Established ROW was down by 8% (9% at CER) to $2,823 million
> 81% increase in New Medicines[1] revenue (81% at CER), contributing 30% of Total Revenue

[1] *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Lumoxiti*, *Brilinta*, *Farxiga*, *Lokelma*, *Bevespi* and *Fasenra*.

Our plans for growth

Our Commercial teams, which comprised around 36,100 employees at the end of 2018, are active in more than 100 countries. In most countries, 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.

Our return to Product Sales growth was underpinned by our Growth Platforms. As shown on page 21 and above, these comprise our three main therapy areas, together with Emerging Markets and Japan. In 2018 they grew by 13% (12% at CER) and represent 84% of Total Revenue.

Sales of our New Medicines[1] generated incremental sales of $2.8 billion at CER and represented 30% of Total Revenue. These New Medicines are important platforms for future growth. In Emerging Markets, they represented 15% of sales, up from 10% in 2017 and, in the US, they represented 48% of Product Sales, up from 26%. US performance reflected, in particular, the success of the new Oncology medicines plus the strong performance of *Fasenra*. In Europe, the decline in Product Sales reflected the impact of generic *Crestor* medicines in various markets in 2017 and continued competitive and price pressures. New Medicines represented 28% of Product Sales, up from 18% in 2017. In Established Rest of World, New Medicines represented 24% of sales in the year, up from 13% in 2017.

However, the pharmaceutical market is highly competitive. For example, our Diabetes franchise continues to see pricing pressure. In immuno-oncology, the large number of clinical trials that are being carried out highlight the competitive nature of this area and renders speed to market critical.

Regional Product Sales

1. Emerging Markets
12%
12% growth in the year (13% at CER) to $6,891m

2. US
11%
11% growth in the year (11% at CER) to $6,876m

3. Europe
(6)%
6% decline in the year (10% at CER) to $4,459m

4. Established Rest of World
(8)%
8% decline in the year (9% at CER) to $2,823m

All numbers as at 31 December 2018.

Pricing and delivering value

Our medicines help treat unmet medical need, improve health and create economic benefits. Effective treatments can lower healthcare costs by reducing the need for more expensive care, preventing more serious and costly diseases and increasing productivity. We are committed to a pricing policy for our medicines based on four principles:

- We determine the price of our medicines while considering their full **value** for patients, payers and society. The agreement on price involves many national, regional and local stakeholders, reflecting factors such as clinical benefit, cost effectiveness, improvement to life expectancy and quality of life.
- We aim to ensure the **sustainability** of both the healthcare system and our research-led business model. We believe we share a collective responsibility with healthcare providers and other stakeholders to work together to enable an efficient healthcare system for patients today and support a pipeline of new medicines for patients tomorrow.
- We seek to ensure appropriate patient **access** to our medicines. We work closely with payers and providers to understand their priorities and requirements, and play a leading role in projects to align better the requirements of regulatory and health technology assessment (HTA) agencies or other organisations that provide value assessment of medicines. For example, we have a leading role in the European IMI ADAPT-SMART programme for exploring adaptive licensing.
- We pursue a **flexible** pricing approach that reflects the wide variation in global healthcare systems. We have developed patient access programmes that are aligned with the ability to pay of patients and healthcare systems. We are committed to the appropriate use of managed entry schemes and the development of real-world evidence and we are investigating innovative approaches to the pricing of medicines, such as payment for outcomes received by the patient and healthcare system.

By way of example of our approach, we apply Tiered Pricing Principles globally. This defines price levels commensurate with affordability based on a country's ability to pay. We believe that this approach to pricing is sustainable and fair, and that it will increase access and improve patient outcomes in Emerging Markets.

More generally, we remain committed to exploring innovative solutions to improve patient access and affordability, focusing on the value our medicines bring to patients and the healthcare system. We are collaborating with payers to conclude value-based pricing solutions that improve patient outcomes and have entered into 37 such agreements across our therapy areas. For more information, see the case study on page 17.

US

As the sixteenth largest prescription-based pharmaceutical company in the US, we have a 2.5% market share of US pharmaceuticals by sales value. In 2018, Product Sales in the US increased by 11% to $6,876 million (2017: $6,169 million).

The US healthcare system is complex with multiple payers and intermediaries exerting pressure on patient access to branded medicines through regulatory and voluntary rebates. Regulatory rebates are statutorily mandated chargebacks and discounts paid on government-funded programmes such as Medicaid, Department of Defense (including TRICARE) and Department of Veteran's Affairs. Voluntary rebates are paid to managed care organisations and pharmacy benefit managers for commercially insured patients, including Medicare Part D patients. In the Medicare Part D programme, in addition to voluntary negotiated rebates, branded pharmaceutical manufacturers are statutorily required to pay a percentage of the patient's out-of-pocket costs during the 'coverage gap' portion of their benefit design. From the beginning of 2019, the mandatory coverage gap discount increased to 70% from its former amount of 50%, as a result of the passage of legislation in 2018. As part of the Affordable Care Act (ACA), we also pay a portion of an overall industry Patient Protection and Affordable Care Act Branded Prescription Drug Fee.

In 2018, the overall measurable reduction in our profit before tax for the year due to discounts on branded pharmaceuticals in the Medicare Part D Coverage Gap and an industry-wide HealthCare Reform Fee was $432 million (2017: $119 million; 2016: $471 million).

In the US, there is significant pricing pressure driven by payer consolidation, restrictive reimbursement policies and cost control tools, such as exclusionary formularies and price protection clauses. Many formularies, which specify particular medicines that are approved to be prescribed in a healthcare system, or under a health insurance policy, employ 'generic first' strategies and/or require physicians to obtain prior approval for the use of a branded medicine where a generic alternative exists. These mechanisms can be used by intermediaries to limit the use of branded products and put pressure on manufacturers to reduce net prices. In 2018, 84.8% of prescriptions dispensed in the US were generic, compared with 84.9% in 2017. In addition, patients are seeing changes in the design of their health plan benefits and may experience variation, including increases, in both premiums and out-of-pocket payments for their branded medications. The patient out-of-pocket spend is generally in the form of a co-payment or co-insurance, but there is a growing trend towards high-deductible health plans which require patients to pay the full list price until they meet certain out-of-pocket thresholds.

Ongoing scrutiny of the US pharmaceutical industry, focused largely on pricing, has been the basis of multiple policy proposals in the US. In May 2018, the Trump Administration issued its 'Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs', which included a wide range of policy proposals that would impact the US pharmaceutical industry if implemented. Proposed changes under consideration include, but are not limited to, fundamentally changing the role of rebates in the pharmaceutical supply chain, reforms to the 340B Drug Pricing Program, and policies to increase competition in the Medicare programme and encourage generic drug use. The Trump Administration has already taken action on several of the policies discussed in the Blueprint, and more policy actions are pending. In addition, lawmakers at both the federal and state level have sought increased drug pricing transparency and have proposed and implemented policies that include measures relating to the submission of proprietary manufacturer data, establishment of price parameters that are indexed to certain federal programmes, and reporting of changes in pricing beyond certain thresholds.

Though widespread adoption of a broad national price control scheme in the near future is unlikely, we continue to comply with new state-level regulations in this area and we recognise the sustained potential for substantial changes to laws and regulations regarding drug pricing that could have a significant impact on the pharmaceutical industry.

We understand that our medicines will not benefit patients if they are unable to afford them and that is why we offer a number of resources and programmes that can help increase patients' access to medication and reduce their out-of-pocket costs. We focus our formulary access on affordability for patients through rebate payments as well as savings cards for eligible patients when the out-of-pocket costs are not affordable. AstraZeneca has one of the longest-standing patient assistance programmes in the industry, AZ&Me, which provides eligible patients with AstraZeneca medicines at no cost. AstraZeneca has provided prescription savings to four million patients across the US and Puerto Rico over the past 10 years.

For more information, see Community investment on page 48.

Europe

The total European pharmaceutical market was worth $196 billion in 2018. We are the fifteenth largest prescription-based pharmaceutical company in Europe (see Market definitions on page 239) with a 2.0% market share of pharmaceutical sales by value.

In 2018, our Product Sales in Europe decreased by 6% at actual rate of exchange (10% at CER) to $4,459 million (2017: $4,753 million). Key drivers of the decline, leaving aside the impact of divestments such as *Seloken*, *Atacand*, *Nexium* and *Zomig*, were continued competition from *Symbicort* analogues, loss of exclusivity for *Crestor*, and the continued impact of early generic entry in certain markets for *Faslodex*, which we expect to continue in 2019. The continued macroeconomic environment, pricing pressure from payers and parallel trade across markets also affected sales.

Despite these conditions, we continued to launch innovative medicines across Europe and saw encouraging performance for certain products across our Growth Platforms, in particular with *Forxiga*, *Brilinta*, *Fasenra*, *Lynparza* and *Tagrisso*. Oncology sales in Europe grew by 19% (14% at CER), partly driven by the approval of *Tagrisso* for the treatment of patients in the 1st line EGFRm setting in June 2018. *Lynparza* sales grew by 46% (41% at CER), partly benefiting from the approval in May 2018 for its use as a tablet-based treatment for platinum-sensitive ovarian cancer, regardless of BRCA status. *Brilique* sales growth of 18% (13% at CER) was accompanied by *Forxiga* sales growth of 30% (24% at CER). *Fasenra* was successfully launched in several European countries, with a strong initial uptake.

Established Rest of World (ROW)*

In 2018, Product Sales in Japan decreased by 9% at actual rate of exchange (11% at CER) to $2,004 million (2017: $2,208 million), as a result of the biennial government price cuts and increased intervention from the government to rapidly increase the volume share of generic products. In September 2017, a *Crestor* authorised generic entered the market and in December 2017 we saw more than 20 generic companies enter the Japanese statin market with generic rosuvastatin which has strongly impacted *Crestor* Product Sales with a decrease of 60%. Leaving aside these generic restraints, Japan is presenting strong growth from the brands in our Growth Platforms and *Nexium*. In addition, there were particularly strong performances from *Tagrisso*, *Fasenra*, *Imfinzi*, *Lynparza* and the Diabetes franchise. We now hold twelfth position in the ranking of pharmaceutical companies by sales of medicines in Japan. Japan remains an attractive market for innovative pharmaceuticals.

Canada has a mixed public/private payer system for medicines that is funded by the provinces, insurers and individual patients. It has also now become common for public payers to negotiate lower non-transparent prices after they have gone through a review by the Canadian Agency for Drugs and Technology in Health, a health technology assessment body. Most private insurers pay full price, although there is increasing pressure to achieve lower pricing. Overall, the split for AstraZeneca's portfolio is 62% funded by private payers and 38% by public plans.

Our sales in Australia and New Zealand declined by 16% at actual rate of exchange (14% at CER) in 2018. This was primarily due to the continued erosion of *Nexium* and *Seroquel* by generic medicines, further price reductions on established brands and entry of an analogue for *Symbicort* in Australia, which had an impact on both price and volume. Consequently, sales in 2018 declined at a greater rate compared to that seen in 2017. However, the pace of generic erosion has moderated notably with *Crestor* and *Atacand*, while the sales growth from new products such as *Brilinta*, *Lynparza* and the Diabetes portfolio has continued. *Brilinta*, *Lynparza* and the Diabetes portfolio grew by 4% at actual rate of exchange (6% at CER), 41% at actual rate of exchange (43% at CER) and 4% at actual rate of exchange (6% at CER), respectively.

* Established ROW comprises Australia and New Zealand, Canada and Japan.

11%

11% increase in Product Sales in the US in 2018 (11% at CER) to $6,876 million

28%

28% increase in Product Sales in China in 2018 (25% at CER) to $3,795 million

"AstraZeneca was the fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2018."

Emerging Markets

Emerging Markets, as defined in Market definitions on page 239, comprise various countries with dynamic, growing economies. As outlined in Marketplace from page 11, these countries represent a major growth opportunity for the pharmaceutical industry due to high unmet medical need and sound economic fundamentals. Emerging Markets are not immune, however, to economic downturn. Market volatility is higher than in Established Markets, and various political and economic challenges exist. These include regulatory and government interventions. In selected markets, governments are encouraging local manufacturing by offering more favourable pricing legislation and pricing is increasingly controlled by governments with price referencing regulations.

Growth drivers for Emerging Markets include new medicines across our Oncology, CVRM and Respiratory portfolios. To educate physicians about our broad portfolio, we are selectively investing in sales capabilities where opportunities from unmet medical need exist. We are also expanding our reach through multi-channel marketing and external partnerships.

With revenues of $6,891 million, AstraZeneca was the fourth largest multinational pharmaceutical company, as measured by prescription sales, and the fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2018.

China

In China, AstraZeneca is the second largest pharmaceutical company by value in the hospital sector, as measured by sales. Sales in China in 2018 increased by 28% at actual rate of exchange (25% at CER) to $3,795 million (2017: $2,955 million). We delivered sales growth above the growth rate of the hospital market sector through strategic brand investment, systematic organisational capability improvements and long-term channel expansion programmes in our main therapy areas. In addition, *Tagrisso* was listed in the National Reimbursed Drug List (NRDL) and we launched *Lynparza* during 2018. Pricing practices remain a priority for regulators, and new national regulations, in addition to provincial and hospital tenders, continue to put increasing pricing pressures on pharmaceutical companies in China. In addition, the planned roll-out of the Generics Quality Consistency Evaluation (GQCE) will have an impact on pharmaceuticals budgets and pricing through setting new standards for bioequivalence that generic products must adhere to. The outcome of the latest round of tenders involving *Crestor* and *Iressa* were announced in December 2018 with implementation from early 2019. This is expected to result in a level of sales decline for both brands in 2019. This evaluation is being applied retrospectively, so several existing generic products may fail and be withdrawn which could lead to a consolidation in the sector. This would leave fewer, higher-quality generics in the market thereby putting pressure on any originator brand price premiums and driving a reduction in overall medical costs.

The industry-wide growth rate is expected to be a moderate single digit percentage, following the updates of the NRDL and expanding health insurance coverage. Nevertheless, the healthcare environment in China remains dynamic. Opportunities are arising from incremental healthcare investment, strong underlying demand for our more established medicines and the emergence of innovative medicines such as *Tagrisso* and *Lynparza*.

For more information on our work in China, see page 37.

Emerging market healthcare

We continue to make our medicines affordable to more people on a commercially and socially sustainable basis. As, on average, almost half of medicine funding in emerging countries is paid for by the patient or their families, we base our approach in these markets on an understanding of their economic circumstances and the burden placed on them by health costs. We are aiming to enable our Emerging Markets to deliver better and broader patient access through innovative and targeted equitable pricing strategies and practices.

We have a variety of access programmes around the world, each tailored to meet the needs of the local community, which include a patient's ability to pay. These include patient assistance programmes, such as Terapia Plus in Ukraine, Karta Zdorovia in Russia and FazBem in Brazil. Through these programmes, we help qualifying patients with discounts and donations. We provide these programmes in markets with limited or no public reimbursement system, no coverage beyond the most basic therapies, or where it is unlikely or only after an extended period that public reimbursement is a possible consideration.

AstraZeneca also aims to partner with countries' healthcare systems to optimise access to healthcare. For example, in South Africa, Phakamisa supports the healthcare system by bringing together different organisations to strengthen healthcare capabilities and improve access to treatment and support networks. It aims to reduce the burden of breast and prostate cancer through the promotion of primary prevention and early detection.

In 2017, we launched the Healthy Lung Asia programme, focusing on improving care for asthma, COPD and lung cancer across nine Asian countries (India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam). The Healthy Lung initiative aims to support: increased awareness; earlier diagnosis; improved treatment; better disease management; and establishing standards of care and initiatives in line with international best practice.

So far, we have initiated 28 formal partnerships and signed 13 memoranda of understanding with national and regional governments, professional organisations and NGOs to drive care improvement, which has enabled Healthy Lung to:

> Support the training of more than 25,000 healthcare professionals.
> Enable diagnosis of more than 500,000 cases of asthma.
> Activate more than 900 Respiratory Centres.
> Align 10 national care guidelines and care pathways to international best practice (GINA).

In 2018, the programme was extended with launches in Latin America, the Middle East and Africa.

Healthy Heart Africa was launched in Kenya in 2014, Ethiopia in 2016 and Tanzania in 2018, supporting the countries to address the burden of NCDs. Since launching, the programme has:

> Conducted 9.97 million blood pressure screenings in the community and in healthcare facilities.
> Trained over 5,800 healthcare workers, including doctors, nurses, community health volunteers and pharmacists, to provide education and awareness, screening and treatment services for hypertension.
> Activated over 700 healthcare facilities in Africa to provide hypertension services, including the establishment of a secure supply chain for low-cost, high-quality antihypertensive medicines.
> Identified over 1.86 million people living with high blood pressure.

In 2018, AstraZeneca began a pilot of clean biogas cooking in Western Kenya. This is enabling the local community to process waste into clean energy, while improving respiratory health of nearby communities by replacing wood-burning fires with alternative fuel sources. The pilot is in partnership with the Cambridge Institute for Sustainability Leadership who will study the environmental impact of this intervention.

For more information on Broadening access to healthcare as one of our sustainability priorities, see page 43.

Operations

Our manufacturing and supply function supports our Return to Growth, and our Operations 2020 plan provides a focus for our investments. They will help ensure we are able to respond to patient and market needs for our medicines.

Operations 2020 was launched in 2015 to enhance supply capabilities in order to respond better to patient and market needs. It focuses on supporting the delivery of our new product launches, strengthening our science and technology capabilities across the globe, creating a more agile and flexible supply chain, and embedding Lean principles throughout our network. Our goal is to be recognised as a leader in the pharmaceutical supply chain by 2020.

Quality, regulation and compliance

We are committed to high product quality, which underpins the safety and efficacy of our medicines. We maintain a comprehensive quality management system to assure compliance and quality. Similarly, we set strict standards for safety, health and environment at each of our sites. Manufacturing facilities and processes are subject to rigorous and continuously evolving regulatory standards. They are subject to inspections by regulatory authorities, who are authorised to mandate improvements to facilities and processes, halt production and impose conditions for production to resume.

To ensure compliance with global Good Manufacturing Practice regulations, the Operations Quality team continuously reviews and strengthens the Quality Systems at our manufacturing sites through internal audit programmes, external intelligence and sharing learnings between sites. In 2018, these measures helped us successfully achieve zero critical observations from 48 independent inspections. We reviewed observations from these inspections together with the outcomes of internal audits and, where necessary, implemented improvement actions.

We are committed to maintaining the highest ethical standards and compliance with internal policies, laws and regulations. We review and comment upon evolving national and international compliance regulations through our membership of industry associations, including IFPMA, EFPIA and PhRMA.

Pharmaceutical Technology & Development

The integration of our Pharmaceutical Technology & Development (PT&D) group into our Operations organisation has been completed, ensuring a seamless transfer of manufacturing technology and processes from our late-stage development group to our commercial manufacturing sites and external partners. PT&D now has a physical presence at our major manufacturing facilities supporting successful product launches, including *Lokelma*, *Bydureon BCise* and *Lynparza* tablets and providing technical leadership for our commercial portfolio throughout the product life-cycle. PT&D is also accountable for the development and introduction of new manufacturing, packaging and analytical technologies across the AstraZeneca small molecule network.

In collaboration with our R&D groups, PT&D is accountable for the development of commercial pharmaceutical products across our pipeline of innovative, small molecule projects. PT&D's core capabilities in chemical development, and oral, inhaled and sterile product development, and digital therapeutics are focused on the development of sustainable processes for medicines designed to meet patients' needs. The clinical operations capability in PT&D works closely with our partners in R&D to design and supply early- and late-stage clinical material and is accountable for the worldwide supply of 260 AstraZeneca sponsored studies.

Supply chain management

We need an uninterrupted supply of high-quality raw materials and active pharmaceutical ingredients (APIs) and, with most of our API manufacturing outsourced, we place great importance on our global external sourcing and procurement organisations and policies, as well as our integrated risk management processes. We purchase materials from a wide range of suppliers and work to mitigate supply risks, such as natural or man-made disasters that disrupt supply chains or the unavailability of raw materials. Contingency plans include using dual or multiple suppliers where appropriate, maintaining adequate stock levels and working to mitigate the effect of pricing fluctuations in raw materials.

As a consequence of the UK's decision to leave the EU, which is anticipated to become effective from 29 March 2019, we have also been working closely with our suppliers on their readiness for the impact this will have, with a view to mitigating the effect on our business.

Since late 2017, we have completed a detailed assessment of approximately 400 suppliers across all areas of our supply chain, including our major and critical suppliers. During 2018, we saw a decline in the overall level of supplier-related risk due to various mitigations, including revised logistics channels, additional warehousing, the potential to move clinical trial related activities, stock building of product and manufacturing related goods, movement of

stock locations, and assessment of the opportunity for supplier substitution. We continue to consider further mitigation activities with a focus on clinical trials and manufacturing given the risk arising from the mix of goods and services, and the associated cross-border UK/EU and EU/UK movements. While we continue to make progress, it is possible that adverse events will impact supplier activities. Issue management may therefore play a key element in our ability to maintain safe supply of our medicines and ongoing business operations more generally.

In addition, as part of our planning to manage the impact of the UK leaving the EU, we have engaged with regulators and government to ensure they have a clear view on the potential impact on pharmaceutical supply chains. We have made significant efforts to duplicate our UK testing capability within the EU and to implement system changes necessary to facilitate compliance with EU law once the UK becomes a third country. Furthermore, we have revised our logistics plans (including shipping routes) and built additional inventory in anticipation of some level of border congestion to reduce the risk of disruption of supply to patients.

Supply chain financing

AstraZeneca has a supply chain finance programme to support the cash flow of its supply base. This programme, in partnership with Taulia Inc. and Greensill Capital, provides suppliers with visibility of invoices and payment dates. Suppliers can access this platform free of charge and have full optionality and flexibility on an invoice by invoice basis to request early payment of invoices. 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 paid by Greensill Capital, and AstraZeneca settles the original invoice amount with Greensill Capital at maturity of the original invoice due date.

We believe this programme offers a benefit to our suppliers, as it provides visibility and flexibility to manage their cash flow, and the rates offered can be preferential to their cost of funding. The programme is currently live in the US, UK, Sweden and Germany. As of December 2018, the programme had 2,548 suppliers enrolled, and a potential early payment balance of $166 million.

For more information on supply chain financing, see Note 19 on page 177.

For more information on Ethical supply chain management, see from page 45.

Manufacturing capabilities

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, Germany, 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 that is complemented by internal capability in Sweden.

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. In Sweden, our new biologics drug product manufacturing facility became available at the end of 2018.

As part of our ongoing review of manufacturing capabilities and capacity, in January 2019, we made the decision to discontinue operations at the Boulder and Longmont, CO manufacturing facilities to increase efficiencies in our global biologics supply chain. This step will consolidate our biologic drug substance manufacturing network to one large-scale drug substance facility, the Frederick Manufacturing Center, MD. The closure of the sites is expected to be completed by the end of 2019 and will not impact the supply or global availability of any of our biologic medicines. We will be working with the impacted employees to provide outplacement and transition support.

For small molecules we have constructed a new small-scale development and launch facility alongside our existing manufacturing facility in Wuxi, China. This investment supports the acceleration of delivery of new innovative medicines to patients in China and completes our ability to execute across the whole life-cycle of medicines from discovery to commercialisation.

At the end of 2018, approximately 13,000 people were employed at 29 Operations sites in 17 countries.

29

We have 29 Operations sites in 17 countries

260

Completed more than 260 major or strategically important business transactions in the last three years, including 80 in 2018

630

We have more than 630 collaborations worldwide

"As part of our planning to manage the impact of the UK leaving the EU, we have engaged with regulators and government to ensure they have a clear view on the potential impact on pharmaceutical supply chains."

Partnering

Business development, specifically partnering, is an important element of our business. It supplements and strengthens our pipeline and our efforts to achieve scientific leadership. We partner with others around the world, including academia, governments, industry, scientific organisations and patient groups, as well as other pharmaceutical companies, to access the best science to stimulate innovation and accelerate the delivery of new medicines to target unmet medical need. We currently have more than 630 collaborations around the world.

More generally, our business development activity takes many forms and can be broadly grouped into:

- alliances, collaborations and acquisitions to enhance our portfolio and pipeline in our main therapy areas
- externalisation activity to maximise the value of our assets
- divestments of non-priority medicines.

We continue to assess opportunities to make strategic, value-enhancing additions to our portfolio and pipeline in our main therapy areas, including through in-licensing and acquisitions. No acquisitions were completed in 2018.

Over the past three years, we have completed more than 260 major or strategically important business development transactions, including some 80 in 2018. Of these transactions, eight were related to pre-clinical assets or programmes and 38 to precision medicine and biomarkers associated with small molecule and biologics programmes. Thirteen transactions helped expand our biologics capabilities.

Of particular note, we announced a new agreement with Innate Pharma under which we will exercise our existing option to obtain full oncology rights to monalizumab, a first-in-class humanised anti-NKG2A antibody which has demonstrated positive Phase II results in head and neck cancer and presents opportunities in colorectal cancer and haematological malignancies as well (see Oncology therapy area review, from page 50 for further details). The agreement also provides us with access to Innate Pharma's anti-CD39 mAb, IPH5201, plus four additional immuno-oncology molecules, increasing the breadth and depth of our immuno-oncology portfolio. As part of this transaction, we also licensed US commercial rights for *Lumoxiti* to Innate Pharma.

In addition, we entered into an agreement under which AstraZeneca will gain the exclusive rights from Zambon to import, distribute and promote *Fluimucil* ampoules, a medicine which treats respiratory disease, for inhalation in China (excluding Hong Kong, Macau and Taiwan).

Externalisation is a core component of our strategy and has an important role to play in the delivery of our ambition as we continue to sharpen our focus on developing key assets within our main therapy areas. This activity creates additional value from our existing medicines as well as recurring Externalisation Revenue and falls broadly into two categories:

- collaborations that help us access therapy area expertise
- collaborations that help us increase the number of patients and the reach of medicines in which we maintain an ongoing interest, but which typically sit outside our main therapy areas.

Details of significant business development transactions which give rise to Externalisation Revenue are included in the Financial Review from page 74. The Externalisation Revenue generated in 2018 is provided in Note 1 from page 160. There were no significant transactions during 2018.

We also divest medicines that typically sit outside our main therapy areas and that can be deployed better by a partner, in order to redirect investment and resource in our main areas of focus, while ensuring continued or expanded patient access. For example, in 2018, we divested European rights for *Atacand* to Cheplapharm; European rights for *Nexium* to Grünenthal; rights for *Seroquel* in all except the US and European markets to Luye Pharma; rights for *Vimovo*, excluding the US and Japan, to Grünenthal; and rights to *Alvesco*, *Omnaris* and *Zetonna* in all markets except the US to Covis. We also entered into an agreement with Sobi to divest the US rights for *Synagis*, the agreement was signed in November 2018 and the transaction completed in January 2019. In addition, we spun out six molecules from our early-stage inflammation and autoimmunity programmes into an independent biotech company, Viela Bio (see Other Disease Areas therapy area review, from page 67 for further details). These agreements will enable us to concentrate our resources on bringing multiple new medicines to patients.

The resulting revenue from these activities supports our R&D investments in our main therapy areas. A total of 15 transactions that contribute to Externalisation Revenue or generate income through divestment or out-licensing were completed in 2018.

More information on our partnering activity in 2018 can be found in the Financial Review from page 74 and Notes 1 and 2 to the Financial Statements from page 160.

Intellectual Property

Our industry's principal economic safeguard is a well-functioning system of patent and related protection that recognises our efforts and rewards innovation with appropriate protection – and allows time to generate the revenue we need to reinvest in pharmaceutical innovation. Patent rights are limited by territory and duration.

A significant portion of a patent's term can be spent during R&D, before it is possible to launch the protected product. Therefore, we commit significant resources to establishing and defending our patent and related IP protections for inventions.

Patent process

We file patent protection applications for our inventions to safeguard the large investment required to obtain marketing approvals for potential new drugs. As we further develop a product and its uses, these new developments may necessitate new patent filings. We apply for patents through government patent offices around the world. These assess whether our inventions meet the strict legal requirements for a patent to be granted. Our competitors can challenge our patents in patent offices and/or courts. We may face challenges early in the patent application process and throughout a patent's life. The grounds for these challenges could be the validity of a patent and/or its effective scope and are based on ever-evolving legal precedents. We are experiencing increased challenges in the US and elsewhere in the world (such as in Australia, Brazil, Canada, China, Europe and Japan), and there can be no guarantee of success for either party in patent proceedings.

For information about third-party challenges to patents protecting our products, see Note 29 to the Financial Statements from page 194.

For more information on the risks relating to patent litigation and early loss and expiry of patents, see Risk from page 220.

The basic term of a patent is typically 20 years from the filing of the patent application with the relevant patent office. However, a product protected by a pharmaceutical patent may not be marketed for several years after filing, due to the duration of clinical trials and regulatory approval processes. Patent Term Extensions (PTEs) are available in certain major markets, including the EU and the US, to compensate for these delays. The term of the PTE can vary from zero to five years, depending on the time taken to obtain any marketing approval. The maximum patent term, when including PTE, cannot exceed 15 years (EU) or 14 years (US) from the first marketing authorisation.

Patent expiries
The table on pages 217 to 219 sets out certain patent expiry dates and sales for our key marketed products.

Other exclusivities
Regulatory data protection (RDP or 'data exclusivity') is an important additional form of exclusivity which is separate from, but runs in parallel to, patent exclusivity. RDP arises in respect of data which is required to be submitted to regulatory authorities to obtain marketing approvals for our medicines. Significant investment is required to generate such data (for example, through conducting global clinical trials) and this proprietary data is protected from use by third parties (such as generic manufacturers) for a number of years in a limited number of countries. The period of such protection, and the extent to which it is respected, differs significantly among countries and varies depending on whether an approved drug is a small or large molecule compound. RDP is an important protection for our products, and we strive to enforce our rights to it, particularly as patent rights are increasingly being challenged.

The RDP period starts from the date of the first marketing approval from the relevant regulatory authority and runs parallel to any patent protection. For small molecule drugs, RDP generally expires prior to patent expiry in all major markets.

If a product takes an unusually long time to secure marketing approval, or if patent protection has not been secured, has expired or has been lost, then RDP may be the sole right protecting a product from copying. Generic manufacturers, we believe, should not be allowed to rely on AstraZeneca's data to support the generic product's approval or marketing until the RDP right has expired. In the EU, the RDP period is eight years followed by two years' market exclusivity.

In the US, new chemical entities (NCEs) are entitled to a period of five years of RDP under the Federal Food, Drug and Cosmetic Act. This period of RDP runs parallel to any pending or granted patent protection and starts at the approval of the new application. There are circumstances where RDP could be the sole layer of exclusivity protecting a product from being copied. Further, under the Biologics License Application process, the FDA will grant 12 years' data RDP for a new biologic to an innovator manufacturer.

Under Orphan Drug laws in the EU and US, market exclusivity is granted to an innovator who gains approval for a pharmaceutical product developed to treat a rare disease. What qualifies as a rare disease differs between the EU and US. Qualifying Orphan Drugs are granted 10 years' market exclusivity in the EU and seven years' market exclusivity in the US.

Compulsory licensing
Compulsory licensing (where a Patent Authority imposes a licence on the Patentee) is on the increase in certain markets in which we operate. We recognise the right of developing countries to use the flexibilities in the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (including the Doha amendment) in certain circumstances, such as a public health emergency. We believe this should apply only when all other ways of meeting the emergency needs have been considered and where healthcare frameworks and safeguards exist to ensure the medicines reach those who need them.

Information technology and information services resources
In 2018, we continued to sharpen our focus on running IT with high quality performance – improving IT cost efficiency, systems performance and delivering higher levels of support for business priorities.

With the IT foundation now firmly in place and operating at high levels of efficiency, we have started to shift our focus to drive more transformative and digital capabilities to support the evolving needs of the business. We have a growing programme portfolio which will see us take advantage of data and analytics, artificial intelligence, digital and the Internet of Things – all of which are key to support our overall business transformation. In order to deliver on these commitments, IT has actively been strengthening its capabilities through recruiting key external talent into the organisation, as the expertise to succeed in some of these technologies was not internally present at the levels needed. In addition to recruiting leaders in new technologies, the IT organisation continues to harness internal capabilities, enabling us to accelerate drug development, revenue growth and profitability.

Cybersecurity
The cybersecurity threat landscape continues to grow in both volume and complexity, with the healthcare industry increasingly becoming a target of cyber criminals. Protecting our IT systems, IP and confidential information against cyber crimes continues to be a critical area of focus and investment. Our implementation of the National Institute of Standards & Technology (NIST) risk framework allows us to understand cyber resilience and risk positioning, improving our ability to prevent attacks and minimise damage and data loss should a breach occur. We have seen success with our mandatory employee cybersecurity awareness training programme, which helps employees recognise and defend against common and high-risk cyber threats.

Our 'Defense in depth' strategy has focused on enhancing multiple levels of protection and detection as well as introducing additional third-party cybersecurity intelligence with an appropriate response from our 24x7 Security Operations Centre. Cybersecurity testing via both internal and external cybersecurity teams will continue to validate our cyber maturity and risk. We continue to develop our relationships with government agencies, third-party cybersecurity professionals, and many cybersecurity-related peer groups. Cybersecurity within our third-party vendors and supply chains is a focus area for AstraZeneca. As an ongoing process, we are evaluating reasonable levels of security and associated controls, requiring contractors, vendors and critical supply chain partners to meet or exceed our cybersecurity standards.

For more details, including the risks relating to information technology and cyber threats, see Risk from page 220.

can

Science deliver complete disease management in China

Opened in 2017, and jointly developed with partners from government, industry and academia, as well as with research and medical institutions, our China Commercial Innovation Centre in Wuxi in Jiangsu Province is designed as a showcase for innovative ideas in healthcare. It uses the Internet of Things (IoT), big data, artificial intelligence and other digital technologies to meet the needs of patients in disease prevention, screening, diagnosis, treatment and rehabilitation.

We collaborate with companies who use advanced technologies to make diagnosis more precise, effectively combine drugs with medical devices for better treatment, and integrate online and offline healthcare resources to make information more accessible. In this way, we can develop complete disease management solutions that deliver better outcomes for patients, make healthcare more accessible, and improve the understanding and management of diseases.

We currently have eight models for disease management which continue to be rolled out, not only across Wuxi, but across the whole of China:

- Chronic disease management – 42 centres
- China chest pain – 783 centres
- Metabolic management – 200 centres
- Gastrointestinal cancer – 66 centres
- Integrated centre for lung cancer treatment – 20 centres
- Integrated centre for prostate cancer diagnosis and treatment – 200 centres
- Paediatric nebulisation – 15,000 centres, including 4,200 smart centres
- Pulmonary and critical care medicine – 593 centres

593
Pulmonary and critical care medicine centres

3. Be a Great Place to Work

Great people are central to our success and being a great place to work is at the heart of our efforts to foster the talents of our people. We promote a culture, both for employees and those third parties with whom we work, that delivers sustainable good performance and long-term business success.

Overview

- Encouraging improvements in scores in our employee survey (Pulse)
- Continued development of women and increase in the representation of women in senior roles
- Published new Global Standards on inclusion and diversity, sexual harassment and bullying, reinforced by training
- Continued focus on workforce planning to attract critical capabilities and manage retention risks
- Maintained listing in Pharmaceuticals, Biotechnology and Life Sciences industry group of Dow Jones Sustainability Index
- Materiality assessment reaffirmed focus and used to refine our sustainability priorities
- Sustainability Advisory Board met twice in 2018 to guide, recommend opportunities and provide external feedback
- Continued progress towards our target to source 100% renewable power by 2025

Employees

To achieve our strategic priorities, we continue to attract, retain and develop a talented and diverse workforce united in the pursuit of our Purpose and living our Values.

We value the talents and skills of our employees and our people strategy supports our strategic priority of being a Great Place to Work.

Build and develop organisations and capabilities

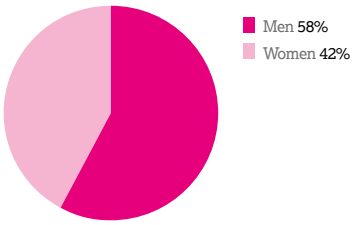
We are developing strategic workforce plans to ensure we can attract the critical capabilities required to deliver our long-term strategic priorities. These plans are underpinned by predictive analytics, meaning workforce decisions are data-driven. We also use workforce analytics to ensure that we manage our global workforce optimally. In addition, we have implemented a significant number of automation initiatives to allow our workforce to spend a higher proportion of their time on higher-value activity.

We have implemented a talent scout model to enhance our ability to attract key talent into senior roles. This has been successful, demonstrating our ability to hire best-in-class critical capability at a reduced cost. This has been supported by an enhanced employee referral scheme, which has become an increasingly important source of hire. This scheme won a significant external award.

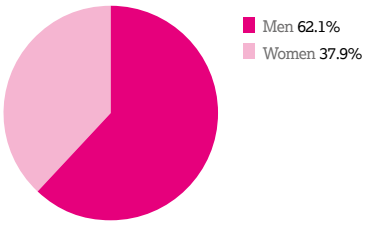
We are working to attract emerging talent, as well as investing in internships and recruitment opportunities globally. For example, we conduct a global programme to hire recent graduates for pharmaceutical technology and development, procurement, quality, engineering, IT, supply chain, and biometrics and information sciences functions. We also ran a graduate programme for IMED, which complements our established IMED Post Doctorate Programme for researcher recruitment. Additionally, we offer a 12-week internship opportunity for business school students to contribute to key initiatives in our Oncology therapy area.

Gender diversity

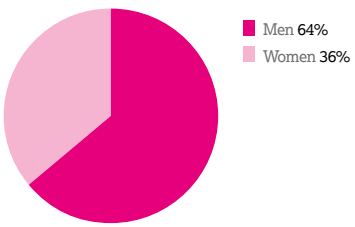
Board of Directors of the Company



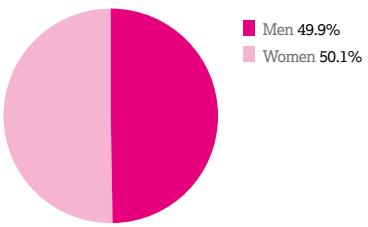
Directors of the Company's subsidiaries*



Senior Executive Team*



AstraZeneca employees



* 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.

All numbers as at 31 December 2018.

During 2018, we hired 13,000 permanent employees. Hiring over recent years means that employees with less than two years' service now represent 33% of our global workforce (up from 20% in 2012). This provides a greater balance in terms of refreshing talent and retaining organisational experience. The majority of this hiring has been focused in our Emerging Markets, in particular China, as we continue to reshape our workforce footprint to support our strategic objectives and to position us well for the future. Our data indicates that these recent hires are performing strongly, although in some areas of the business retention of this population is challenging.

Voluntary employee turnover increased slightly to 10.2% (2017: 9.7%). The voluntary employee turnover rate among our high performers decreased in 2018 to 6.6% (2017: 7.1%), while the voluntary employee turnover of recent hires increased to 14.5% (2017: 12.2%). We seek to reduce regretted turnover through more effective hiring and induction, exit interviews, risk assessments and retention plans.

The uncertainty faced by individuals and their families following the UK's decision to leave the EU could have an impact on hiring and retaining staff in some business-critical areas. Consequently, we are providing extensive support and information to employees who might be impacted, monitoring trends in recruitment and resignation closely, and also guiding new hires through our recruitment process.

Drive a vibrant, high-performing culture

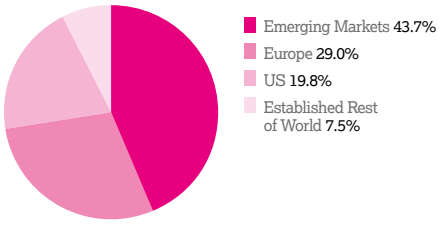
Continuing our emphasis on high performance, in 2018, our high performers were promoted at twice the rate of the wider employee population. We require every employee to have high-quality objectives, aligned to our strategy, which we monitor closely. Managers are accountable for working with their employees to develop individual and team performance targets, and for ensuring employees understand how they contribute to our overall business objectives. Through increased investment in technology, we have also extended our global annual salary and incentive review process to cover 90% of employees (2017: 87%). We encourage participation in various employee share plans, some of which are described in the Directors' Remuneration Report from page 120, and also in Note 28 to the Financial Statements from page 192. Additionally, in the UK, we are making changes to the way we reward, provide benefits and support our people. These changes are designed to rebalance the reward mix, improve understanding of benefits and simplify our processes.

Our salary and bonus budgets are distributed in line with our principles, allowing us to clearly differentiate reward according to performance.

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 discrimination on any grounds (including disability) and cover recruitment and selection, performance management, career development and promotion, transfer, training, retraining (including retraining, if needed, for people who have become disabled), and reward. Our Global Standard for Inclusion and Diversity sets out how we

A global business

Employees by reporting region



64,600
employees

Co-locating around three strategic R&D centres

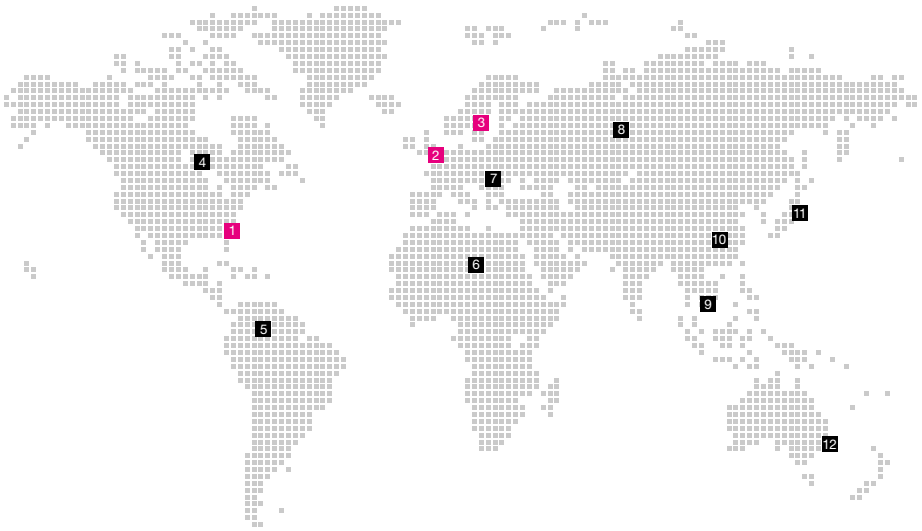
1. Gaithersburg, MD, US
3,200

2. Cambridge, UK
2,500

3. Gothenburg, Sweden
2,200

All numbers as at 31 December 2018.

By geographical area



1. US
12,800
19.8%

2. UK
7,400
11.4%

3. Sweden
6,300
9.8%

4. Canada
800
1.3%

5. Central and South America
3,100
4.9%

6. Middle East and Africa
1,700
2.6%

7. Other Europe
7,400
11.5%

8. Russia
1,000
1.6%

9. Other Asia Pacific
6,900
10.6%

10. China
13,200
20.5%

11. Japan
3,000
4.6%

12. Australia and New Zealand
1,000
1.6%

foster an inclusive and diverse workforce where everyone feels valued and respected because of their individual ability and perspective. It describes the principles of our commitment and provides a framework for developing and implementing the people plans needed to ensure we deliver these principles consistently worldwide. More information on our Global Policy framework can be found on page 43, our Code of Ethics on page 105, and our Global Policies and Standards can be found on our website, www.astrazeneca.com/sustainability.

Employee opinion surveys help us measure employee satisfaction and engagement, and progress in our aim of being a great place to work. Comparing our most recent survey (December 2018) to the previous year (December 2017), of the 17 items common to both surveys, we improved in 11 items, remained stable for four and saw minor reductions (-1%) in the score for two items. Importantly, we scored highly for 'understanding of the future direction and strategy', and we saw good progress in 'opportunities for personal development and growth' and items around inclusion and diversity (where we are above the global high-performing norm). We also exceeded our scorecard target for 'I would recommend AstraZeneca as a great place to work'. Despite progress in the latest survey, there remains further opportunity for improvement around leadership communication and prioritisation.

Develop a strong and diverse pipeline of leaders

To foster innovation, we seek to harness different perspectives, talents and ideas as well as ensuring that our employees reflect the diversity of the communities in which we operate.

As part of our commitment to inclusion and diversity, we have implemented numerous initiatives across the globe, such as unconscious bias training, the formation of various employee resource groups (such as an LGBT+ network) and updated recruitment standards to ensure diverse candidate lists.

Our commitments include a goal to increase the number of women on our leadership teams. As shown in the gender diversity figure on page 38, women comprise 50.1% of our global workforce. There were five women on our Board (42% of the total) at the end of 2018 (Shriti Vadera retired with effect from 1 January 2019). Below Board level, the representation of women in senior roles (ie roles at Career Level F or above which constitute the six highest bands of our employee population) increased to 44.6% in 2018 (2017: 44.4%), which exceeded our scorecard target of 44.4% for this measure and compares favourably to external benchmarks. Women are also currently promoted at a higher rate than men across all levels of seniority, positively impacting the gender balance. In 2018, AstraZeneca was ranked 12th in the FTSE 100 for Women on Boards and seventh for Women on Executive Committees and Direct Reports.

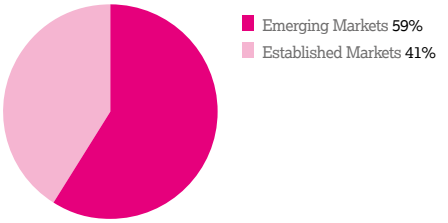
Our Women as Leaders programme aims to encourage more women into senior roles – approximately 600 women had completed the programme by the end of 2018. Of those who provided feedback, 55% have either been promoted, or had their remit expanded, or been identified for future promotions. In addition, we have developed women's networks in most countries, continued to hold women's summits in various locations around the world and continued to support mentoring relationships, for example introducing mentoring by senior women for emerging talent in Operations.

In 2018, 80% of vacancies across the top three levels of our organisation were filled internally, reflecting our long-term commitment to develop high-quality leaders and the rigour of our leadership succession planning. To ensure our senior leadership reflects our diverse geographic footprint, we track the country of origin of senior leaders and reflect this in our diversity targets. In 2018, 19.4% of employees who are either members of the SET, or their direct reports, have a country of origin that is an Emerging Market or Japan (an increase from 5% in 2012 and ahead of our 2018 target of 15%).

Diversity is integrated into our Code of Ethics and associated workforce policy. In addition to the two diversity metrics tracked in the AstraZeneca scorecard (representation of women in senior roles and senior leadership country of origin that is an Emerging Market or Japan), on a bi-annual basis, the SET and Board are provided 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 SET is also provided with a quarterly summary of key workforce metrics, including gender diversity and leadership ethnic diversity. Within the US, we track overall ethnic minority representation, ethnic minority representation in senior roles, and ethnic minority representation in succession plans.

In addition to the Global Standard on Inclusion and Diversity, in 2018 we published new Global Standards on sexual harassment and bullying. Drawing on our commitment to respect and equal opportunity, we aim to build a culture where everyone feels safe to 'speak up'. This is important, not just for those who feel they have seen or experienced unwelcome attention or behaviour, but also to ensure that colleagues recognise the value they bring when they share their different perspectives and ideas. This is integral to making the most of our diversity of thought, because it is the foundation of our ability to innovate. The Standards are being reinforced by specific training and education across the organisation on the importance of speaking up (which includes challenging behaviours that are inconsistent with our Values and Code of Ethics), demonstrating inclusive leadership and responding to allegations of misconduct. We have multiple channels available for reporting. Allegations are taken very seriously and handled in a manner that is sensitive to the confidentiality and security of those making a report and will be subject to global oversight.

Sales and Marketing workforce composition



Generate a passion for people development

We encourage employees to take ownership of their own development and expect leaders to spend time supporting their employees' development. To support this, we have implemented a global platform to increase the visibility and accessibility of job opportunities and received over 22,000 applications from internal candidates through this platform in 2018.

In 2017, we implemented a best-practice cloud-based global learning management system to ensure that opportunities to learn are available to all employees. In 2018, we continued to leverage this technology as part of our ambition to continuously transform the learning culture in AstraZeneca.

Following the successful launch of 'Leading People' in 2017 (a social online learning platform aimed at managers), 'Leading Self' was rolled out across the organisation aimed at employees below manager level. Over 5,400 employees have accessed this innovative, social online learning experience. In 2018, we piloted our 'Leading Business' programme, connecting 100 managers from all areas and regions of AstraZeneca to develop their leadership capability. We continue to see a positive impact of these experiences in engagement and retention measures.

Human rights

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. To that end, we integrate human rights considerations into our processes and practices. We are also committed to ensuring that there is no modern slavery or human trafficking in our supply chains or any part of our business. Our full statement required under section 54 of the UK Modern Slavery Act is available on our website, www.astrazeneca.com.

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 measure human rights by means of a labour review survey every two years in all countries where we have a presence. The review focuses on ILO core themes, including freedom of association and collective bargaining, child labour, discrimination, working hours and wages, including questions on the Living Wage. Where local gaps to ILO minimum standards are identified, such as maternity leave or grievance procedures, we put in place local plans to close those gaps where allowed by relevant national legislation. Our reporting in this area is assured by Bureau Veritas.

For more information about the assurance provided by Bureau Veritas, see page 231.

In 2017, we signed up to the 'Fair Wage' database. These data are being used in our end of 2018 survey to measure performance more independently and to inform future direction in the fair/living wage space.

Managing change

We continue to implement plans to invest in our three strategic R&D centres in the US, UK and Sweden. We encourage and support employees to relocate and have made good progress. For example, of the more than 2,500 employees working in Cambridge, 569 have relocated from other sites in the UK. In addition to the 1,100 employees hired between 2015 and 2017, we hired a further 452 permanent employees in Cambridge in 2018. We are using interim infrastructure in and around Cambridge to house these employees until our new site on the Cambridge Biomedical Campus is ready. For employees who do not accept offers to relocate to Cambridge, we provide career support, outplacement support and competitive severance packages.

For more information on this move, see Cambridge on page 27.

As outlined in the Manufacturing capabilities section on page 34, in January 2019 we made the difficult decision to discontinue operations at our biologics manufacturing facilities at Boulder and Longmont CO, US.

In January 2019, we announced plans to realign R&D and parts of our Commercial business to ensure we can execute on our priorities and strategy. We have established dedicated teams who, guided by a clear set of People Principles, will ensure the transition is executed as quickly as possible, keep our employees regularly informed and treat them fairly, and comply with local legislative and HR policies and practices, including consulting with employee representatives as required.

For more information on our restructuring programme, see the Financial Review from page 74.

Employee relations

We seek to follow a global approach to employee relations guided by global employment principles and standards, local laws and good practice. We 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 2016, 58% (106 countries surveyed) of countries in which AstraZeneca operates recognise and have a relationship with trade unions. Where trade unions do not exist in an area of operation, 99% of countries have established arrangements to engage similarly with their workforce. Our most recent survey commenced in October 2018, with conclusions due at the end of February 2019.

Safety, health and wellbeing

We work to promote a safe, healthy and energising work environment for employees and partners. Our standards apply globally and are stated in our Code of Ethics available on www.astrazeneca.com/sustainability. Due diligence includes establishing and monitoring a set of safety, health and wellbeing targets aimed at supporting our people and keeping AstraZeneca among the sector leaders in performance. Our reporting in this area is in the Sustainability Data Summary available on www.astrazeneca.com/sustainability and is assured by Bureau Veritas.

For more information about the assurance provided by Bureau Veritas, see page 231.

Safety

Vehicle collisions

Year	Collisions per million km	Target
2018	**3.74**	**3.58**
2017†	4.05	3.76
2016†	4.66	4.00
2015 baseline	4.13	

Work-related injuries

Year	Reportable injury rate per million hours worked	Target
2018	**1.31**	**1.50**
2017†	1.48	1.60
2016†	1.57	1.69
2015 baseline†	1.78	

† Data re-stated.

As shown above, we made further progress against our strategic targets in 2018, achieving a 26% reduction in the work-related injury rate and a 9% reduction in vehicle collision rate from the 2015 baseline. In addition, there were no work-related fatalities during 2018. Building on our previous success in establishing a culture of health and wellbeing, we continue to focus on active health promotion. We have programmes to address all four essential health activities – healthy eating and drinking, physical activity, tobacco cessation and mental wellbeing – at 65% of our sites.

In 2018, we carried out several activities and initiatives focused on continuous improvements in key risk areas, including driver safety (our highest risk for significant injury and fatalities), behavioural safety, ergonomics, office safety, fall prevention, workplace pressure management and work-life balance.

Sustainability

We want to be valued and trusted by our stakeholders as a source of great medicines over the long term. That is why 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. This means delivering our business strategy in a way that broadens access to our medicines, minimises the environmental footprint of our products and processes, and ensures that ethics and transparency underpin everything we do.

Sustainability strategy

Our sustainability strategy is aligned with our Purpose and business strategy, allowing us to maximise the benefit for our patients, our business, broader society and the planet. In late 2018, a structured sustainability materiality assessment that engaged external and internal stakeholders reaffirmed our direction and refined the priority areas. We measure our progress through annual and long-term targets. We show performance in our Sustainability Data Summary located on www.astrazeneca.com/sustainability.

Learn more in our 2018 Sustainability Report available on our website, www.astrazeneca.com/sustainability.

1. Broadening access to healthcare

We aim to improve lives by increasing access to health

Priority areas	Information in this Annual Report
> Disease prevention and treatment > Affordability > Investments in health systems > Responsible R&D > The environment's impact on health	> Emerging market healthcare, from page 32 > Broadening access to healthcare, on page 43

2. Furthering ethics and transparency

We commit to furthering ethics and transparency in everything we do

Priority areas	Information in this Annual Report
> Ethical business culture > Inclusion & diversity > Talent & workforce evolution > Workforce wellbeing and safety > Responsible supply chain > Human rights	> Code of Ethics and policy framework, on page 43 > Bioethics and responsible research, from page 44 > Develop a strong and diverse pipeline of leaders, on page 40 > Managing change and Employee relations, on page 41 > Safety, health and wellbeing, on page 41 > Ethical supply chain management, from page 45 > Human rights, on page 41 > Community investment, on page 48

3. Protecting the environment

We strive to reduce environmental impacts on human health and the natural world

Priority areas	Information in this Annual Report
> Greenhouse gas emissions > Waste > Water > Product environmental stewardship > Pharmaceuticals in the environment	> Greenhouse gas, on page 46 > Waste, on page 47 > Water, on page 47 > Product environmental stewardship, on page 47 > Pharmaceuticals in the environment, on page 47

Benchmarking and assurance

Recognition of our work in sustainability

DJSI

MEMBER OF Dow Jones Sustainability Indices In Collaboration with RobecoSAM

> Named in the Dow Jones Sustainability World and Europe Indices
> Attained industry-best scores for: Environmental Reporting, Labour Practice Indicators and Health Outcome Contribution

ATMI

access to medicine index

> Ranked ninth overall in the 2018 Access to Medicine Index
> Recognised for a Best Practice in Pricing and one of nine companies recognised for an Innovative Practice

CDP

CDP DRIVING SUSTAINABLE ECONOMIES

> Water A List – among the top 1.5% of companies participating in CDP's water security programme for our commitment to transparency around environmental risks and demonstration of sustainable water management
> Climate change B List – in recognition of our strategy and actions to reduce emissions and mitigate climate change
> Supplier Engagement leader board – among the top 3% of companies assessed by CDP to be awarded a position on the leader board in recognition of our actions to reduce emissions and lower climate-related risks in the supply chain

ISAE3000 Assured

BUREAU VERITAS

> Bureau Veritas has provided independent external assurance to a limited level in accordance with the International Standard on Assurance Engagements 3000 (ISAE3000), and in accordance with ISAE3410 Assurance Engagements on Greenhouse Gas Statements for the sustainability information contained within this Annual Report and Form 20-F

For more information, see Sustainability: supplementary information on page 231 and the letter of assurance available on www.astrazeneca.com/sustainability.

Sustainability governance

Sustainability governance frames the way we operate. Geneviève Berger, a Non-Executive Director, oversees the implementation of our sustainability matters on behalf of the Board of Directors. Our ambition is to be a leader in sustainability by delivering the strategy from the materiality assessment. Every member of the SET is accountable for a specific sustainability initiative and Katarina Ageborg is responsible for the global strategy.

Our Sustainability Advisory Board (SAB) comprises five SET members and four external sustainability experts. It met twice in 2018 to provide guidance on strategic direction, recommendations for opportunities, and insights and feedback. Throughout the year, we engaged with employees and external stakeholders, including investors, Ministries of Health, healthcare providers, NGOs, patients and suppliers.

1. Broadening access to healthcare

Marketplace from page 11 demonstrates the burden of NCDs, with 41 million deaths annually which disproportionately affects low- and middle-income countries where nearly three quarters of these deaths occur. In Return to Growth from page 29, we review how, as a business focused on medicines for NCDs, we aim to meet the challenges posed in each of our Regions, particularly for those patients in Emerging Markets who may need help to access our medicines and where barriers to healthcare are not always pricing related.

Our activities demonstrate how we are working to improve access to healthcare by making our medicines available and more affordable to people on a commercially and socially sustainable basis. Through partnerships with government and NGOs, we develop health systems' infrastructure by building capacity to help improve access to medical treatment and care.

Disease prevention is the focus of the Young Health Programme (YHP), our award-winning global disease prevention programme.

For more information on YHP, see page 48.

To address local needs, our programmes are typically governed by their respective commercial markets. The process includes setting and measuring performance towards targets. We have internal targets and our annual Sustainability Report lists our external targets and progress. We undergo third-party assurance for these external targets and our reporting in this Annual Report is assured by Bureau Veritas – for more information see page 231.

2. Ethics and transparency

We want to be valued not only for our medicines but also for the way we work. We seek to operate in a transparent and ethical way and expect the same high standards from our suppliers and partners. Whether it is investing in technological alternatives to animals in science for our research or refusing to tolerate bribery or any other form of corruption, we aim to go beyond what is required of us to be an example of how good business is done.

Code of Ethics and policy framework

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 empowers employees to make decisions in the best interests of the Group and the people we serve, now and in the long term, by outlining our commitments in simple terms and focusing on why these commitments matter. The Code also 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 2018, 100% of all active employees completed the annual training on the Code of Ethics.

The Code includes four high-level Global Policies covering Science, Interactions, Workplace and Sustainability. These Global Policies will continue to be complemented by underlying Global Standards and will, over time, replace the current suite of Global Policies which 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.

Ethical sales and marketing

We are committed to employing high ethical standards of sales and marketing practice worldwide, in line with our policy framework. We maintain a robust compliance programme in our efforts to ensure compliance with all applicable laws, regulations and adopted industry codes. As outlined in Global Compliance and Internal Audit Services on page 105, our compliance programme is delivered by dedicated compliance professionals who advise on and monitor adherence to our policy framework.

These professionals also support our line managers locally in ensuring that their staff meet our standards. A network of nominated signatories reviews our promotional materials and activities against applicable requirements. Our Internal Audit Services, in partnership with external audit experts, also conduct compliance audits on selected marketing companies. Our reporting in relation to ethical sales and marketing is assured by Bureau Veritas.

For more information about the assurance provided by Bureau Veritas, see page 231.

Approximately 36,100 employees are engaged in our commercial activities and, in 2018, we identified four confirmed breaches of external sales and marketing regulations or codes (2017: six). There were 2,042 instances, most of them minor, of non-compliance with the Code or supporting requirements in our Commercial Regions, including instances by employees and third parties (2017: 1,431). We removed a total of 169 employees and third parties from their roles as a result of these breaches (a single breach may involve more than one person). We also formally warned 534 others and provided further guidance or coaching on our policies to 1,865 more. The Audit Committee are provided with the breach statistics on a quarterly basis. Further commentary on the most serious breaches is also provided to the Audit Committee.

Anti-bribery/anti-corruption

Anti-bribery/anti-corruption is a key element of our policy framework, with principles and requirements underpinning the Code commitment that we do not tolerate bribery or any other form of corruption. We conveyed our commitment to ethical behaviour in the 2018 annual Code training, reinforced through anti-bribery/anti-corruption training materials delivered and made available to relevant employees and third parties.

Bribery and corruption remains a business risk as we launch new medicines in markets across the globe and enter into partnerships and collaborations. When working with third parties, we are committed to working only with those who embrace high standards of ethical behaviour consistent with our own. Bribery and corruption risk is a focus of our third-party risk management process, as well as our Business Development due diligence procedures. It is also a focus of our monitoring and audit programmes. Global Compliance monitors a range of commercial activities associated with bribery and corruption risk, and the majority of marketing company audits include anti-bribery/anti-corruption work programmes.

100%

100% of all active employees completed training on our Code of Ethics

"Our commitment to working in a transparent and ethical manner is essential to achieving scientific leadership and delivering life-changing medicines."

Transparency reporting

AstraZeneca is committed to the highest standards of conduct in all our operations, including the disclosure of payments to healthcare practitioners (HCPs), healthcare organisations (HCOs) and patient groups, with full transparency where recipients have provided consent and in accordance with all current obligations covering the 43 markets with reporting requirements. In the US, Europe, Australia and Japan our external transparency reporting meets the requirements of the Physician Payments Sunshine Act (Open Payments), European Federation of Pharmaceutical Industries and Associations (EFPIA) Disclosure Code, Medicines Australia (MA) Code of Practice, and the Japanese Pharmaceutical Manufacturers Association (JPMA) Disclosure Code, as well as applicable local and state transparency requirements. Further, we have progressive plans to expand our disclosure activities in another six markets across Canada, Latin America, Asia Pacific, North Africa and the Middle East regions over the next two years. We are progressively heading towards increased disclosure in additional markets globally and, in all locations, we are committed to ensuring payments are justified and reasonable.

Bioethics and responsible research

Our commitment to working in a transparent and ethical manner is essential to achieving scientific leadership and delivering life-changing medicines. 'Bioethics' refers to the range of ethical issues that arise from the study and practice of biological and medical science, and our Bioethics Policy sets out our principles in key subject matter areas. These principles apply to all our research activity, whether conducted by us or by third parties acting on our behalf. The following sections summarise our activities in the main areas, and our Bioethics Policy is available on our website, www.astrazeneca.com/sustainability.

Our Bioethics Advisory Group (BAG) is sponsored by the Chief Medical Officer and exists to oversee the operation of the Bioethics Policy. It acts as a source of bioethical advice to the business, bringing together the subject matter leads for each of the key bioethical areas, supported by other experts and specialists. BAG receives reports on governance and practice from subject matter leads, responds to requests for advice and support from the business, and carries out horizon-scanning activities to identify emerging scientific, technological and regulatory issues. BAG met six times in 2018. Ethical discussions in 2018 included the potential therapeutic use of human stem cells in patients, the implications of continuing advances in precise genome editing technologies, and issues around consent and withdrawal of consent for use of patient samples and data.

Clinical trials

We believe that transparency enhances the understanding of how our medicines work and benefit patients. At www.AstraZenecaClinicalTrials.com, we publish information about our clinical research, as well as the registration and results of our clinical trials – regardless of whether they are favourable – for all products and all phases, including marketed medicines, drugs in development and drugs where development has been discontinued.

In 2018, we conducted a range of clinical trials across regions as shown in the charts on the right. This broad span helps ensure that study participants reflect the diversity of patients for whom our medicines are intended and identifies the patients for whom the medicine may be most beneficial. Our global governance process provides the framework for ensuring a consistent, high-quality approach worldwide. Protecting participants throughout the trial process is a priority and we have strict procedures to help ensure participants are not exposed to unnecessary risks.

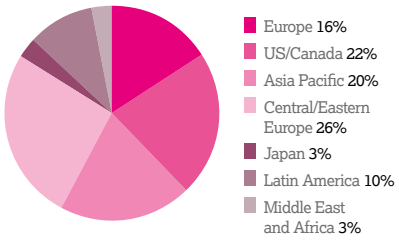
All our clinical studies are designed and finally interpreted in-house. Some are conducted by contract research organisations (CROs) on our behalf and we require these organisations to comply with our global standards.

As of 31 December 2018, we shared anonymised individual patient-level data from 136 studies with 37 research teams and responded to 111 requests from external researchers using our portal, http://astrazenecagroup-dt.pharmacm.com to request our clinical data and reports to support additional research. In 2018, we continued to participate in the industry-wide portal www.trialsummaries.com where we publish Trial Result Summaries in easy-to-understand language and translate these to the local language for all sites where a study is conducted. As of 31 December 2018, we published Trial Result Summaries for 66 AstraZeneca studies.

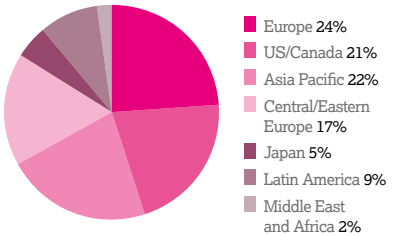
For more information, see our website, www.astrazeneca.com, or our clinical trials website, www.AstraZenecaClinicalTrials.com.

Clinical trials by region

Small molecule studies



Biologics studies



Patient safety

One of our core Values is to put patients first and, by detecting, assessing, understanding and preventing adverse effects or any other drug-related problems not identified during the development process, our pharmacovigilance processes and systems seek to minimise the risks and maximise the benefits of our medicines for patients.

For all our medicines, under development as well as on the market, we have systems in place for identifying and evaluating possible adverse drug effects. Information concerning the safety profile of our medicines is provided to regulators, healthcare professionals and, where appropriate, patients. Each medicine has a dedicated safety team, which includes a responsible global safety physician and one or more pharmacovigilance scientists. Marketing companies have assigned patient safety managers in place.

Our Chief Medical Officer is accountable for the benefit and risk profiles of our products, providing medical oversight and enforcing risk assessment processes that help us make efficient and informed decisions about patient safety. As part of our commitment to patient safety, in 2017, we developed an upgraded safety signal management platform to provide risk oversight for all our products. Following an extensive pilot test phase during 2018, we launched the platform across all marketed products and continue to seek refinements to make it an industry leader in pharmacovigilance. We also began exploring the use of emerging technologies, such as automation support, machine learning and digital communication interfaces. These tools will have the potential to enhance our product safety evaluation, communication and risk mitigation capabilities.

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 and their underlying mechanisms, which helps us develop effective, new and personalised medicines.

When we conduct this important research, we maintain policies and processes to ensure that we comply with the law, meet regulatory concerns and maintain ethical standards. We place an emphasis on informed consent that protects the rights and expectations of donors and families throughout the process of our acquisition, use, storage and disposal of the samples. Protecting the confidentiality of a donor's identity is of the utmost importance, and a key part of our process includes the coding of biological samples and associated data (including genetic data).

In rare circumstances, we may use human fetal tissue (hFT) or human embryonic stem cells (hESC). In these circumstances, an internal review of the scientific validity of the research proposal will be conducted and permission to use the tissue will be granted only when no other scientifically reasonable alternative is available. We also insist our third-party vendors adopt the highest ethical standards and we rigorously assess the ability of tissue suppliers to meet our quality and ethical expectations. We are committed to minimising the use of fetal tissue by exploring technological alternatives.

In 2018, an additional research proposal that includes use of cells derived from hFT was approved, resulting in three projects using hFT having progressed as at 31 December. An additional three projects using hESC were approved in 2018, resulting in nine projects using 13 different hESC lines or derived cells having been approved to date.

Animal research

We are committed to helping the public understand the continuing need for animals in research, and our approach to replacing, reducing and refining our use of animals (the 3Rs).

We share our 3Rs advances externally through presentations at international conferences and workshops, and contribute to the work of organisations and societies supporting the 3Rs around the world. Our Chief Veterinary Officer leads the Council for Science and Animal Welfare (C-SAW), which is the governance and oversight body for the use of animals in research and development, providing assurance to senior leaders on our responsible use of animals. C-SAW drives initiatives on the 3Rs, openness about our use of animals, and promotes a culture of care in the way we conduct our research. For example, C-SAW runs an annual global awards scheme recognising excellence in the 3Rs, achievements in openness about the use of animals and the best examples of a caring research culture. Each year, one of the 3Rs award winners is further selected to receive a CEO Award for the 3Rs. In 2018, this went to a group who achieved a six-fold reduction in the numbers of mice needed for particular studies by the application of novel experimental design. C-SAW also promotes global learning and continuing professional development opportunities for employees working with animals and provides general information and education opportunities both within and outside AstraZeneca.

Animal research use 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 commitment to the 3Rs, our animal use would be much greater. In 2018, animals were used for in-house studies 121,823[1] times (2017: 131,615). In addition, animals were used on our behalf for CRO studies 29,853 times (2017: 28,545). In total, over 97% were rodents or fish.

Technology has not yet advanced to the stage where animal use can be eliminated, and animal studies therefore remain a small, but necessary, part of the process of developing new drugs. We are alert to the issues around the use of animals and are working constantly to ensure our animal studies are properly justified, conducted and reported.

[1] 2018 figure includes some animals used only for breeding.

For more information, see our 2018 Sustainability Report available on our website, www.astrazeneca.com/sustainability.

Ethical supply chain management

Every employee and contractor who sources goods and services on behalf of AstraZeneca is expected to follow responsible business processes, which are embedded into our newly updated Global Standard for the Procurement of Goods and Services. All our procurement professionals receive detailed training on responsible procurement.

Our ethical standards are integral to our procurement and partnering activities and we monitor compliance through assessments and improvement programmes. We work only with those suppliers whose standards of ethical behaviour are consistent with our own. We will not use suppliers who are unable to meet our standards. Our Global Standard Expectation of Third Parties is published on our website, www.astrazeneca.com/sustainability.

To achieve this, we have an established process for third party risk management. This process assesses risk based upon defined criteria. These include risks related to bribery and corruption, data privacy, the environment

12,967

12,967 assessments of suppliers in 2018 to ensure they meet our ethical standards

$19m

$19 million committed to resource efficiency projects at our manufacturing and R&D sites in 2018

"We follow the science to protect the planet by managing our impact on the environment across all our operations."

and wages. Each step of the process provides an additional level of assessment, and we conduct more detailed assessments on those relationships identified as higher risk. Through this risk-mitigation process, we seek to better understand the partner's risk approach and seek to ensure the partner understands and can meet our standards.

We conducted a total of 12,967 assessments in 2018, taking our total number of assessments to 27,257 since we established this process in May 2014. Of the assessments undertaken in 2018, 3,390 were in the Asia Pacific region, 4,035 in Europe and 3,965 in the Americas. The remaining 1,577 assessments relate to global suppliers and those based in the Middle East and Africa.

In 2018, we conducted 45 audits on high-risk suppliers (external manufacturing partners), seeking to ensure that they employ appropriate practices and controls. Eighty six percent of these suppliers met our expectations, with a further 14% implementing improvement plans to address minor instances of non-compliance. Through our due diligence process, we rejected seven suppliers because of reputational concerns due to high anti-bribery/anti-corruption risk.

3. Protecting the environment

We follow the science to protect the planet by managing our impact on the environment across all our operations. Our Code of Ethics is the overarching document for our environmental management system. It applies to all functions and locations and is supported by global standards and procedures that establish mandatory requirements in key risk areas. We monitor and manage performance through comprehensive assurance programmes that include performance reporting and internal auditing. We are on track to deliver our 2016 to 2025 natural resources targets.

Our 2018 targets (against a 2015 baseline) included:

- reducing our operational greenhouse gas (GHG) footprint in line with our approved Science Based Target
- limiting the increase in our energy consumption to no more than 2% to 1,841 GWh
- limiting the increase in our waste generation to less than 7% to 32,811 tonnes
- reducing water use by 7% to 4.03 million m^3.

The table opposite provides data on our global GHG emissions, energy use, waste production and water consumption for 2018. The data coverage includes 100% of our owned and controlled sites globally. Regular review of the data is carried out to ensure accuracy and consistency. This has led to changes in the data for previous years. To support the achievement of our targets, a resource efficiency capital fund has been in place since 2015 to invest in projects at sites. In 2018, $19 million (2017: $19 million) was committed to resource efficiency projects at our manufacturing and R&D sites, and a further $15 million has been committed for 2019.

Greenhouse gas

We are working to reduce our GHG emissions by, among other things, investment in improving energy and fuel efficiency and pursuing lower-carbon alternatives to fossil fuels, utilising a hierarchy approach of avoiding emissions where possible, reducing emissions from necessary activities, and substituting our energy sources for lower carbon alternatives. During 2018, we made progress towards our verified science-based targets for Scope 1 and Scope 2 emissions through increased fuel efficiency of our commercial sales fleet and procurement of electricity from certified renewable sources increasing to represent 69% of total electricity imports. Our total Scope 1 and Scope 2 emissions have been reduced by 31% from our 2015 baseline. We have continued to make progress on our science-based targets for Scope 3 emission sources through continued achievement in switching freighting of goods from air to sea and improved accounting of our Scope 3 footprint that will lead to future efficiency improvements. Including emissions from patient use of our inhaler therapies, our operational GHG footprint totalled 1,769,110 metric tonnes in 2018, a reduction of 0.4% from our 2015 baseline.

For more information on our pressurised metered dose inhaler (pMDI) therapies, see the Product environmental stewardship section opposite.

Energy use

To reduce GHG emissions, we recognise the need to reduce our demand for energy in the first instance, maximise the efficiency of the energy we do use and, where feasible, substitute our energy use with renewable sources. Due to anticipated net increase in activity across our site network in 2018, we aimed to limit increases in total energy consumption to 2% above our 2015 baseline. Over the same period, we completed seven in-depth energy audits to identify new opportunities for energy efficiency that will be implemented over the next three years. In 2018, our energy use was 1,854 GWh, an increase of 3%. We have made further progress on our target to use 100% renewable power by 2025. In 2018, we used certified zero emission power equivalent to 61% of total power consumption, including 3,358 MWh of renewable power generated on our sites.

For more information on GHG emissions reporting, see Sustainability: supplementary information on page 231.

Operational greenhouse gas footprint emissions (tonnes CO_2e)[1]

2018	**1,769,110**
2017	1,705,047
2016	1,683,959
2015	1,776,508

1,769,110 tonnes CO_2e

Energy consumption (MWh)[1]

2018	**1,853,813**
2017	1,745,547
2016	1,785,357
2015	1,805,236

1,853,813 MWh

% total energy from renewables[1]
2018 29%
2017 27%
2016 25%
2015 6%

Waste production (tonnes)

2018	**31,500**
2017	31,063
2016	31,791
2015	30,665

31,500 tonnes

Water use (million m^3)

2018	**4.01**
2017	3.89
2016	4.02
2015	4.34

4.01 million m^3

[1] Regular review of the data is carried out to ensure accuracy and consistency. This has led to changes in the data from previous years. The majority of adjustments made are not material individually, except for business air travel (new data supplier, leading to restated baseline) and product use phase (recalculated using improved life-cycle emissions data). The data quoted in this Annual Report are generated from the revised data.

Waste

Waste management is another key aspect of our commitment to minimise environmental impact. Due to anticipated growing activity across our site network in 2018, we aimed to limit increases in our waste volumes to a 7% increase from our 2015 baseline. In 2018, our total waste was 31,500 metric tonnes, a 3% increase on 2015. As waste generation is linked to production volumes, our waste reduction ambitions are going to be challenged as our business grows. However, we are focusing on processes to boost our operational efficiency and investing in waste reduction projects to help us reach our target to reduce waste generation by 10% by 2025. While waste prevention is an essential goal, we seek to maximise treatment by material recycling and avoiding landfill disposal when prevention is impractical.

Water

We recognise the need to use water responsibly and, where possible, to minimise water use in our facilities. In 2018, we targeted a 7% reduction from our 2015 water use. In 2018, our water footprint was 4.01 million m^3, an 8% reduction. Water reduction and reuse projects throughout our site network have improved the efficiency of water use across our operations. Our major sites and those in water-stressed areas work to Water Conservation Plans to ensure we are managing our water risks and to facilitate sharing of best practice in water stewardship around our site network.

Product environmental stewardship

We are committed to ensuring effective environmental management of our products from pre-launch through to product end-of-life. We work at all stages of a medicine's life-cycle from the design of API production and formulation processes, devices and packaging through distribution, patient use and final disposal.

As part of our progress towards our 2025 environmental targets, our 2018 targets included:

> Safe API discharges for AstraZeneca sites (100%) and globally managed first tier suppliers (>90%). Target met – safe API discharges confirmed.

Our pMDI therapies rely on hydrofluoroalkane (HFA) propellants, which are emitted during use and disposal, and contribute to our Scope 3 GHG footprint. While HFAs have no ozone depletion potential and a third or less of the global warming potential than the chlorofluorocarbons they replaced, they are still potent greenhouse gases. During 2018, we initiated a project spanning all key functions in the business to investigate options available from an environmental, technical, regulatory, medical and commercial viewpoint. The environmental review includes life-cycle assessment (LCA) of current products and potential options, ecotoxicity and fate studies of alternative propellants and an initial pilot study for pMDI take-back and recycling programmes. It is imperative that decisions to address the product use phase GHG footprint do not substitute the climate impact for another environmental impact.

Pharmaceuticals in the environment

We aim to lead our industry in understanding and mitigating the effects of pharmaceuticals in the environment (PIE). An estimated 98% of pharmaceuticals get into the environment as a result of patient use (excretion or improper disposal). While API discharge from production is only a small proportion of the environmental burden, it is the part we as an industry can deal with directly. We manage the manufacturing discharge of our APIs in a responsible manner to ensure that we do not exceed the safe discharge standards set for our own manufacturing sites and those of key suppliers. We review compliance with these safe discharge standards annually. Using a concept called 'ecopharmacovigilance', we review emerging science and literature for new information that might change the way we assess and manage any environmental risks associated with our products through patient use and API production. A thorough assessment of the environmental risks resulting from the patient use of all our APIs has indicated that all our medicines currently pose low or insignificant environmental risk.

We also conduct collaborative research to understand the fate, behaviour and impact of pharmaceuticals on the environment. In 2018, we co-authored 21 peer-reviewed publications to enhance our knowledge of the risks associated with this emerging issue.

As part of our progress towards our 2025 environmental targets, our 2018 targets included:

> management of PIE through our ecopharmacovigilance programme. Target met – programme delivered.

Further information on our efforts in this area, including environmental risk assessment data for our medicines, is available on our website, www.astrazeneca.com/sustainability/environmental-sustainability.

Community investment

Wherever we work in the world, we aim to make a positive impact on our communities. Our Global Standard on Contributions encompasses 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 2018, we gave more than $57 million (2017: $25 million) through our community investment activities to more than 1,000 non-profit organisations in 70 countries. The increase reflects a change in practice with more large multi-year agreements with payments being made in the first year of the agreement. The amount includes more than $17.5 million (2017: $4 million) for product donations that were given in support of public health needs and disaster relief. The increase reflects changes in the volume and mix of product donated. In addition to these community investments, we also donated more than $686 million (2017: $401 million) of medicines in connection with patient assistance programmes around the world, the largest of which is our AZ&Me programme in the US.

For more information about AZ&Me, see page 31.

Our global disaster relief partner is the British Red Cross. In 2018, we entered into a two-year partnership that will support humanitarian aid to people affected by armed conflict in Northern Nigeria. Our global product donation partners are Americares, Direct Relief International and Health Partners International of Canada.

In 2018, we launched the Step Up! Young Health Global Grants Programme. Designed to complement our work in the field of adolescent health and NCD prevention, this programme offered grants of up to $10,000 to non-profit organisations that are innovating to improve the health and wellbeing of young people. A total of $160,375 of funding was committed through this programme in 2018 for 17 projects in 14 countries.

We continue to support *Connections for Cardiovascular Health*℠, a programme of the AstraZeneca HealthCare Foundation that was launched in 2010 to address heart health in the US. In 2018, the AstraZeneca HealthCare Foundation provided $1.16 million in grants to 11 non-profit organisations for programmes that aim to help prevent, better manage and reduce cardiovascular disease.

Making a positive impact on our communities is also about volunteering. We encourage our employees to volunteer and support their efforts with one day's leave for community service. In 2018, our employees volunteered more than 39,000 hours on community projects in countries around the world.

For more information on the Step Up! Young Health Global Grants Programme, visit www.younghealthprogrammeyhp.com.

For more information on the AstraZeneca HealthCare Foundation's *Connections for Cardiovascular Health*℠ programme, visit www.astrazeneca-us.com/foundation.

For more information on the AstraZeneca HealthCare Foundation, see the Glossary on page 240.

Young Health Programme

Non-communicable disease (NCD) prevention among young people continued to be an area of focus as we mark the ninth year of our award-winning Young Health Programme (YHP). Despite the fact that more than two thirds of premature deaths from NCDs can be linked to behaviours that first began in adolescence, young people and their health continues to be an under-recognised, under-served and under-researched component of the global health agenda. In 2018, we reached nearly 335,000 young people with health information on NCDs and risk behaviours and trained more than 5,500 peer educators and healthcare workers. In partnership with local governmental and non-governmental groups, we launched new programmes in Indonesia, Serbia, Turkey and Australia and approved the development of new programmes in Vietnam, Myanmar, Mexico and Panama. This brings the total number of developing and active YHP initiatives to 20.

We supported our partners, NCD Child and Plan International, as they advocated for the inclusion of adolescent health and NCD prevention in the Political Declaration on NCDs and at the United Nation's Third High Level Meeting on NCDs. We invested in new research on adolescent risk behaviours, policy recommendations and health economic analyses to support the argument for additional investment in and attention to NCD prevention among young people. We continued to mentor and support the development of young global health leaders by sending a delegation of 20 young people to the One Young World Summit in The Hague, Netherlands.

YHP was named Community Investment Program of the Year by Ethical Corporation's 2018 Responsible Business Awards.

Further information on YHP can be found on its website, www.younghealthprogrammeyhp.com.

Learn more in our 2018 Sustainability Report on www.astrazeneca.com/sustainability.

Donation programmes

In some countries, such as the US, where many individuals remain without insurance and cannot afford our medications, we offer a free drug patient assistance programme – AZ&Me – for qualifying patients. In other countries with evolving health systems, we partner to address challenges in access with a combination of donated products and financial support to build capacity and support patient needs. In Cambodia, since 2010, our partnership with Americares and the Sihanouk Hospital Centre of Hope (SHCH) has supported the Cambodia Breast Cancer Initiative. The partnership aims to strengthen existing treatment services while expanding in scale to reach additional patients. In 2018, the programme screened 963 new patients; provided information on early detection and screening to more than 14,700 individuals; diagnosed 93 cases of breast cancer and continued to treat 661 patients who were previously diagnosed; and administered more than 24,000 units of free AstraZeneca medicines to post-menopausal breast cancer patients in the SHCH's treatment cohort.

For more information about AZ&Me, see page 31.

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:

- Environmental matters on pages 46-47 and page 231
- Employees from page 38
- Social matters from page 42
- Respect for human rights on page 41
- Anti-corruption and anti-bribery matters from page 43

References to our policies, due diligence processes and information on how we are performing against various measures in these areas, are contained throughout the Strategic Report. Information on the Group's Principal Risks are included in Risk Overview from page 70 and information on the non-financial key performance indicators relevant to our business is included in Key Performance Indicators from page 20. A description of our business model is contained in Business model and life-cycle of a medicine from page 8.

There is a critical unmet need in the treatment of advanced ovarian cancer: only 20% of women will be cured and more than 70% will relapse within three years following their initial therapy. The best opportunity to achieve sustained remission, with potential for a cure, is to treat patients when they are newly diagnosed. However, current treatment options only provide a modest improvement in time to relapse. Once a patient relapses their disease is considered incurable and, for the majority of women, they go on to receive multiple lines of treatment.

By using *Lynparza* maintenance therapy earlier in the treatment pathway, the SOLO-1 trial results show that 60% of newly-diagnosed patients with a BRCA mutation remain progression-free at three years compared to 27% of patients receiving placebo. At 41 months, the median progression-free survival (PFS – see Glossary on page 241) had not been reached for patients treated with *Lynparza*, compared to 13.8 months for patients treated with placebo, indicating that there may be a group of patients who continue to remain progression-free for a long time or, perhaps, are cured.

Since the initial approval of *Lynparza* four years ago, the ovarian cancer and overall PARP inhibitor environment has become increasingly competitive but, with SOLO-1, AstraZeneca and MSD have the potential to transform the standard of care for women with advanced BRCA-mutated ovarian cancer, while reinforcing the importance of testing for BRCA mutations at the time of diagnosis.

Science *can* help find a cure for ovarian cancer

20%
Only 20% of women will be cured of ovarian cancer

>70%
will relapse within three years following their initial therapy

A portfolio of DNA damage response inhibitors that selectively kill cancer cells while minimising the impact on normal cells.

Oncology

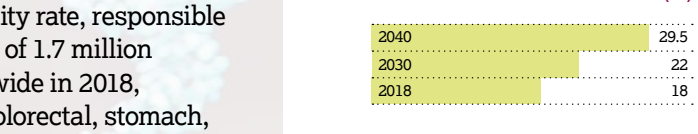
Our ambition is to push the boundaries of science to change the practice of medicine, transform the lives of patients living with cancer, and ultimately eliminate cancer as a cause of death. To do this, we focus on R&D and on our commercial capabilities to deliver a new generation of medicines that have the potential to redefine the treatment of cancer.

Unmet medical need and world market

> Cancer is the second leading cause of death globally.
> Lung cancer has the highest cancer mortality rate, responsible for the deaths of 1.7 million people worldwide in 2018, followed by colorectal, stomach, liver and breast cancer.
> Breast cancer is among the most common types of cancer, affecting 4.6 million people worldwide. Other common cancers include prostate and ovarian cancer.

Part of AstraZeneca's antibody-drug conjugate scientific platform to target specific leukaemia cells.

Estimated annual cancer cases (m)

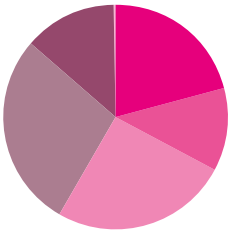


1.7m
Lung cancer was responsible for the deaths of 1.7 million people in 2018.

70%
Approximately 70% of the world's cancer deaths occur in low- and middle-income countries.

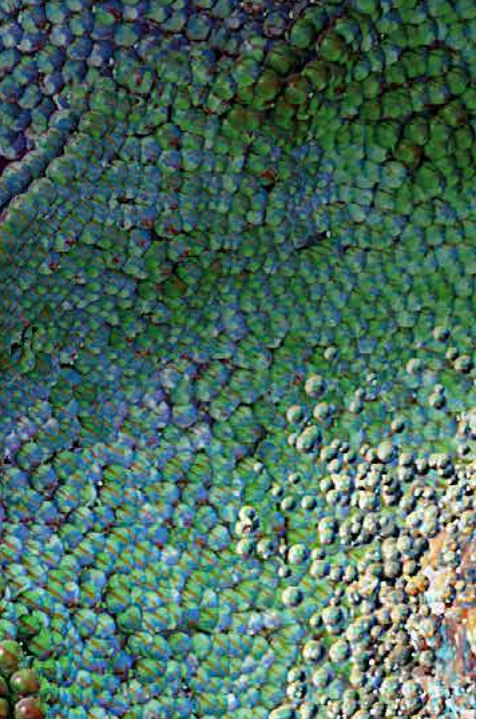
Therapy area world market
(MAT/Q3/18)

$106.6bn
Annual worldwide market value



- Chemotherapy $22.5bn
- Hormonal therapies $12.5bn
- Monoclonal antibodies (mAbs) $27.3bn
- Small molecule targeted agents $30.1bn
- Immune checkpoint inhibitors $14.2bn
- Other oncology therapies $0.1bn

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



Key marketed products and revenues 2018

The continued renewal of our commercial portfolio, the regulatory approvals of new indications for several established brands, and the rapid geographic expansion of our launches drove Oncology performance in 2018.

Oncology revenue

$6,028m

29% of total

2017: $4,024m

2016: $3,383m

Product	Disease area	Revenue	Commentary
Tagrisso (osimertinib)	Lung cancer	↑ $1,860m, up 95% (93% at CER)	Approved in more than 55 countries, including the US, Japan and EU, for 1st line EGFRm advanced non-small cell lung cancer (NSCLC), and more than 80 countries, including the US, Japan, China and the EU, for 2nd line use in patients with EGFRm T790M mutation-positive advanced NSCLC.
Lynparza (olaparib)	Ovarian cancer Breast cancer	↑ $647m, up 118% (116% at CER)	Approved in more than 60 countries for advanced ovarian cancer and approved in the US and Japan for metastatic breast cancer.
Imfinzi (durvalumab)	Lung cancer Bladder cancer	n/m $633m, movement n/m	Approved in more than 40 countries, including the US, EU and Japan, for locally advanced, unresectable, stage 3 NSCLC and in the US, Canada, Brazil, Israel, Australia, Hong Kong, the United Arab Emirates and India for locally advanced or metastatic urothelial carcinoma.
Calquence (acalabrutinib)	Mantle cell lymphoma (MCL)	n/m $62m, movement n/m	Approved in the US, the United Arab Emirates and Brazil for previously treated MCL.
Lumoxiti (moxetumomab pasudotox-tdfk)	Hairy cell leukaemia (HCL)		Approved in the US for ≥3rd line relapsed or refractory HCL. In 2018, the commercialisation rights of *Lumoxiti* were licensed to Innate Pharma for the US and EU.
Legacy			
Iressa (gefitinib)	Lung cancer	↓ $518m, down 2% (4% at CER)	
Faslodex (fulvestrant)	Breast cancer	↑ $1,028m, up 9% (9% at CER)	Approved in combination with CDK4/6 inhibitors.
Zoladex (goserelin acetate implant)	Prostate cancer Breast cancer	↑ $752m, up 2% (2% at CER)	
Arimidex (anastrozole)	Breast cancer	↓ $212m, down 2% (3% at CER)	
Casodex/*Cosudex* (bicalutamide)	Prostate cancer	↓ $201m, down 7% (8% at CER)	
Others		↔ $115m, up 1% (down 1% at CER)	

Full product information from page 217.

Our strategy for Oncology

In 2018, we divided our Oncology business into five franchises that reflect both our commercial priorities and our key scientific platforms:

> *Tagrisso* and tumour drivers and resistance mechanisms
> *Imfinzi* and immuno-oncology
> *Lynparza* and DNA damage response (DDR)
> *Calquence* and haematology
> Mature portfolio

These franchises enable us to best deliver against four strategic priorities we have embraced in order to achieve our ambition of eliminating cancer as a cause of death.

1. Focus research on four scientific platforms: Our broad pipeline of next-generation medicines is aimed at expanding our treatment options for solid tumours and haematological cancers. We are exploring several monotherapy and combination approaches across four scientific platforms:

> **Tumour drivers and resistance:** Developing therapies that target specific molecular mutations to attack cancer cells.
> **Immuno-oncology:** Using the body's immune system to help fight cancer.
> **DNA damage response:** Targeting the DNA repair process to block tumour cells' ability to reproduce.
> **Antibody-drug conjugates:** Arming antibodies with cancer-killing agents for specific tumour targeting.

2. Focus on early stages of disease and relapsed or refractory patients: To move the current cancer treatment paradigm, we recognise we must both identify and treat patients earlier in their disease progression when there is a possibility of cure, and also improve the treatment of relapsed or refractory patients to extend survival and deliver the most transformative outcomes.

3. Lead precision medicine in the most prevalent and deadly tumour types: On our path to eliminating cancer as a cause of death, we have set ourselves the goal of improving five-year survival in tumour types where mortality remains high, such as ovarian and NSCLC. We also continue to concentrate on biomarker-driven indications where the benefits to patient populations are tangible and significant.

4. Leverage our global footprint: To deliver these treatment-changing solutions to as many patients in need as possible, we are building capacity across all geographies. In addition, through our Oncology Business Unit we are increasing focus and improving response time in key markets such as the US, UK, Italy, France, Germany, Spain, Japan and China.

Therapy Area Review
Oncology *continued*

2018 pipeline highlights

Our robust pipeline includes 83 projects in various stages of clinical development, from recently approved products to earlier-stage molecules in clinical trials.

In 2018, we presented new clinical data at major medical congresses and secured multiple regulatory milestones, reflecting our continuing investment in oncology as one of our key growth drivers. Highlights include:

- Important new data from the pivotal Phase III PACIFIC trials in NSCLC, demonstrating a statistically significant benefit in overall survival with *Imfinzi*.
- Results from the Phase III SOLO-1 trial, investigating *Lynparza* in 1st line maintenance therapy for advanced ovarian cancer.
- Results from the Phase III MYSTIC and EAGLE trials exploring *Imfinzi* as monotherapy or in combination with tremelimumab respectively in 1st line setting of metastatic NSCLC and in recurrent or metastatic head and neck squamous cell carcinoma (HNSCC).

Full details are given in the Development Pipeline from page 212 and highlights from the progress our Oncology pipeline made in 2018 against our KPIs are shown below.

Life-cycle phases – R&D

New molecular entity (NME) Phase II starts/progressions

Over 20 clinical trials in Phase II explore combination and monotherapy approaches for tumours where high unmet medical need persists, like head and neck, gastric, breast, lung and ovarian cancers.

Product	Cancer type
AZD2811	Solid tumours
Imfinzi + *Lynparza*	Bladder cancer (BAYOU)
Imfinzi + monalizumab	Solid tumours
Oleclumab + *Imfinzi*	Solid tumours

NME and major life-cycle management (LCM) positive Phase III investment decisions

Life-cycle management is critical to realising the full potential of our medicines and establishing sustainable franchises. In 2018, we started 10 new Phase III trials bringing the total number of ongoing Phase III trials to 29.

Product	Cancer type
Imfinzi + CTx	Muscle invasive bladder cancer (NIAGARA)
Imfinzi + CTx	Neoadjuvant NSCLC (AEGEAN)
Imfinzi + TACE	Locoregional hepatocellular carcinoma (HCC) concurrent (EMERALD-1)
Imfinzi + tremelimumab	1st line limited disease small cell lung cancer (SCLC) (ADRIATIC)
Imfinzi + tremelimumab + CTx	1st line urothelial cancer (NILE)
Lynparza + abiraterone	All-comers 1st line metastatic castration resistant prostate cancer (PROpel)
Tagrisso	EGFRm leptomeningeal cancer (BLOSSOM)

Plus eight projects where investment decisions have been made but clinical trials have yet to start.

NME and major LCM regional submissions

In 2018, positive pivotal trial data from our oncology pipeline fuelled regulatory submissions. We received three Orphan Drug designations for *Lynparza* in pancreatic cancer (POLO) in the US and selumetinib in neurofibromatosis type 1 (SPRINT) in the US and EU, and benefited from three Priority Reviews.

Product	Cancer type	Region
Imfinzi	Stage 3 NSCLC (PACIFIC)	China
Lumoxiti	3rd line HCL (PLAIT)	US
Lynparza	1st line ovarian cancer (SOLO-1)	US, EU, China, Japan
Lynparza	gBRCA metastatic breast cancer (OlympiAD)	EU
Tagrisso	1st line NSCLC (FLAURA)	China

Life-cycle phases – approvals

NME and major LCM regional approvals

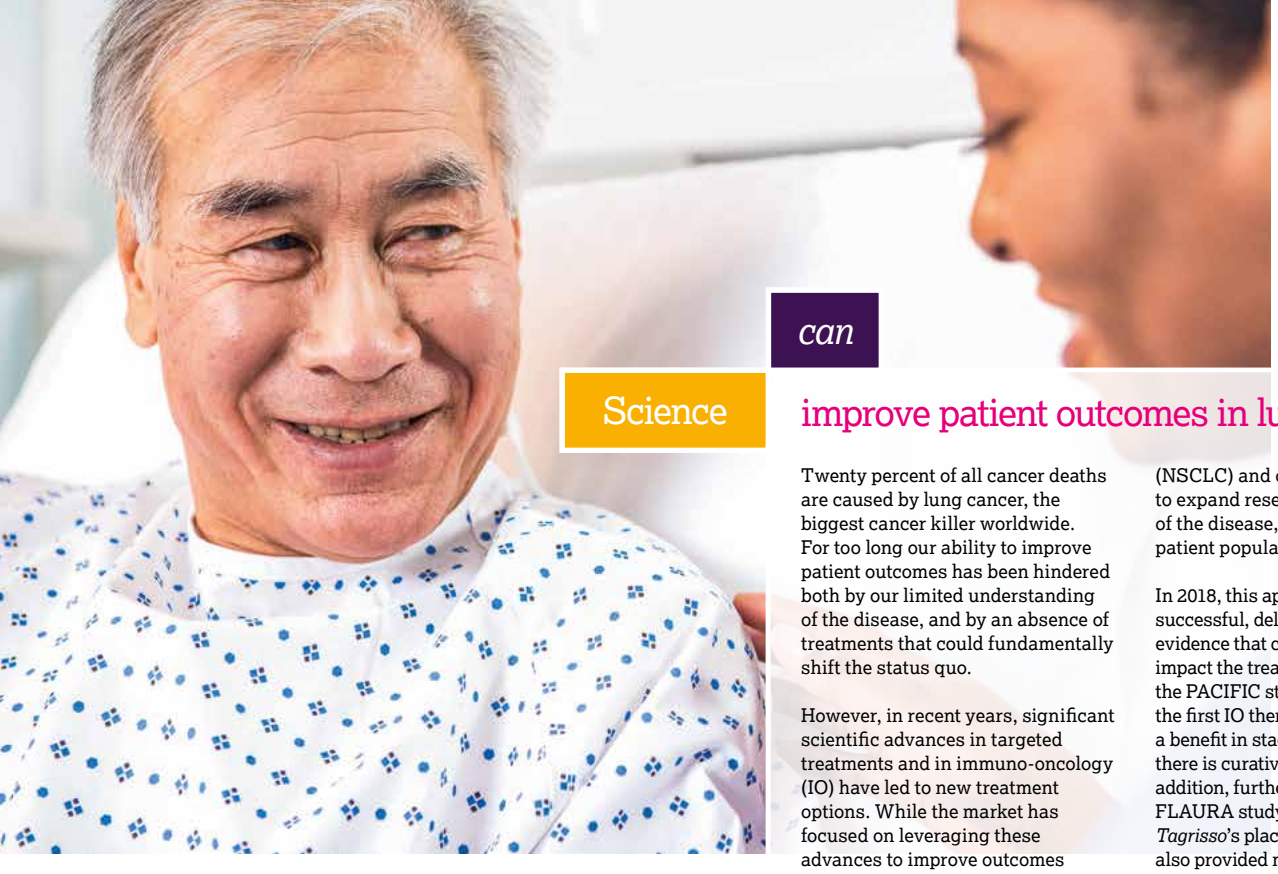
In the US, EU, Japan and China, we secured 13 new regional approvals in 2018, underlining our commitment to providing patients with access to life-changing medicines globally.

Product	Cancer type	Region
Imfinzi	Unresectable stage 3 NSCLC (PACIFIC)	US, Japan, EU
Lumoxiti	3rd line HCL	US
Lynparza	1st line ovarian cancer (SOLO-1)	US
Lynparza	2nd line ovarian cancer (SOLO-2)	Japan, EU, China
Lynparza	gBRCA metastatic breast cancer (OlympiAD)	US, Japan
Tagrisso	1st line NSCLC (FLAURA)	US, EU, Japan

Discontinued projects

Product	Cancer type	Reason
Calquence + vistusertib	BTK + mTor haematalogical tumours	Safety/efficacy
Imfinzi + tremelimumab	PD-L1 + CTLA-4 3rd line NSCLC (ARCTIC)	Safety/efficacy
Imfinzi + tremelimumab	2nd line HNSCC (EAGLE)	Safety/efficacy
Imfinzi + tremelimumab	1st line NSCLC (MYSTIC)	Safety/efficacy
Imfinzi or *Imfinzi* + (tremelimumab or danvatirsen)	Diffuse large B-cell lymphoma (DLBCL)	Safety/efficacy
Imfinzi + MEDI0562	Solid tumours	Safety/efficacy
Imfinzi + MEDI9197	Solid tumours	Safety/efficacy
MEDI-565	CEA BITE GI tumours	Safety/efficacy
MEDI0562	Solid tumours	Safety/efficacy
MEDI1873	Solid tumours	Strategic
MEDI4276	HER2 solid tumours	Safety/efficacy
MEDI9197	Solid tumours	Safety/efficacy
Selumetinib	Differentiated thyroid cancer (ASTRA)	Safety/efficacy
Tremelimumab + MEDI0562	Solid tumours	Safety/efficacy
Vistusertib	mTOR stage 1/2 solid tumours	Safety/efficacy

For more information on the life-cycle of a medicine, see page 9.



Science *can* improve patient outcomes in lung cancer

Twenty percent of all cancer deaths are caused by lung cancer, the biggest cancer killer worldwide. For too long our ability to improve patient outcomes has been hindered both by our limited understanding of the disease, and by an absence of treatments that could fundamentally shift the status quo.

However, in recent years, significant scientific advances in targeted treatments and in immuno-oncology (IO) have led to new treatment options. While the market has focused on leveraging these advances to improve outcomes for late-stage patients, we have leveraged our heritage in EGFRm non-small cell lung cancer (NSCLC) and our broad IO pipeline to expand research into earlier stages of the disease, and to emerging patient populations.

In 2018, this approach proved to be successful, delivering clinical evidence that could significantly impact the treatment of NSCLC. With the PACIFIC study, *Imfinzi* became the first IO therapy to demonstrate a benefit in stage 3 NSCLC where there is curative possibility. In addition, further data from the FLAURA study not only reaffirmed *Tagrisso*'s place in 1st line, but they also provided new insights into optimising treatment for metastatic EGFRm NSCLC, where five-year survival rates remain at less than 15%.

2018 review – strategy in action

Oncology is one of our main therapy areas and has a major role to play in our Return to Growth, with an aim of launching six new oncology medicines between 2014 and 2020.

In 2015 and 2016, we continued to build our oncology business by investing in a robust clinical development programme and by making strategic partnerships and acquisitions, such as acquiring a majority equity stake in Acerta Pharma to establish our footprint in haematology.

In 2017, we created the Oncology Business Unit (OBU) focused on eight key markets, with the aim of accelerating the uptake of our new medicines through strategic focus, quick decision making, and adequate investments.

In 2018, based on the commercial uptake of our new medicines, and the maturity of their late-stage clinical programmes, we organised the OBU into five franchises: *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence* and our mature portfolio.

Tagrisso and tumour drivers and resistance mechanisms

Tagrisso is our best-in-class, highly-selective, irreversible inhibitor of the activating sensitising EGFR mutation (EGFRm) and the resistance mutation T790M.

Our tumour drivers and resistance (TDR) mechanisms platform explores the inhibition of genetic disease drivers as a clinically validated approach to shrink tumours and improve progression-free survival (PFS) and overall survival (OS). Tumours, however, eventually develop resistance to these therapies. Our programmes seek to develop therapies that target resistance mechanisms and the mutations that cause cancer cells to proliferate.

In 2018, *Tagrisso* was approved for 1st line EGFRm advanced NSCLC, based on the positive results from the Phase III FLAURA trial. The approval was granted in the US in April, in the EU in June and in Japan in August.

By December 2018, it was approved in more than 55 countries for 1st line EGFRm advanced NSCLC, and in more than 80 countries for 2nd line use in patients with EGFRm T790M mutation-positive advanced NSCLC.

In October 2018, new data from the FLAURA Phase III trial presented at the European Society for Medical Oncology (ESMO) 2018 Congress provided insights on the resistance mechanisms observed after treatment with 1st line *Tagrisso* in patients with previously untreated EGFRm NSCLC who experienced disease progression during the trial period. As expected, there was no evidence of the acquired EGFR T790M mutation and the most frequently experienced resistance mechanisms – MET (mesenchymal epithelial transition factor) amplification and C797X mutations – were confirmed.

Based on these findings, we announced the initiation of ORCHARD, an open-label, multi-centre, multi-drug Phase II platform trial in patients with advanced NSCLC who have experienced disease progression following 1st line therapy with *Tagrisso*.

During 2018, we also confirmed our commitment to tackling earlier stages of EGFRm NSCLC with the ADAURA and LAURA clinical trials. ADAURA will assess the efficacy and safety of *Tagrisso* in EGFRm stage Ib-3A NSCLC, following complete tumour resection with or without adjuvant chemotherapy, and LAURA will assess the efficacy and safety of *Tagrisso* following chemoradiation in patients with stage 3 unresectable EGFRm NSCLC. Our next generation of TDR projects continued to progress in 2018:

- Savolitinib, a selective inhibitor of c-MET receptor tyrosine kinase, is being investigated in partnership with Chi-Med in combination with *Tagrisso* in EGFR mutated lung cancers which also have amplification of MET, a common resistance mechanism in patients progressing on *Tagrisso*. It is also being explored as monotherapy in NSCLC patients with MET Exon 14 skipping mutations, and in combination with *Imfinzi* in renal cancer.
- Selumetinib, an MEK inhibitor, part of the portfolio agreement with MSD, continued to be investigated in the SPRINT trial for neurofibromatosis type 1. Selumetinib was granted Orphan Drug designation in the US and Europe for this potential indication in 2018. Promising early combination data of novel ERK inhibitor AZD0364 and selumetinib in KRAS-mutated tumours was presented at the American Association for Cancer Research annual meeting in April 2018. However, in the second quarter of 2018, after the ASTRA trial failed to meet its primary endpoint, further Phase III development of selumetinib in thyroid cancer was discontinued.
- Capivasertib (AZD5363) had promising Phase II data presented at the American Society of Clinical Oncology (ASCO) conference in June 2018 showing an OS improvement in combination with paclitaxel in patients with 1st line metastatic triple negative breast cancer. Capivasertib is also in Phase II trials in ER+ breast cancer in combination with *Faslodex* and in prostate cancer in combination with enzalutamide.

Other agents in early development include: AZD9496 and AZD9833, selective oestrogen receptor degraders (SERD) in Phase I development for the treatment of oestrogen receptor positive (ER+) breast cancer; AZD5153, a bromodomain 4 inhibitor in Phase I for solid tumours; and AZD8186, an inhibitor of PI3 kinase β and δ in Phase II for solid tumours.

Imfinzi and immuno-oncology

Imfinzi, a human mAb that binds to PD-L1 and blocks the interaction of PD-L1 with PD-1 and CD80, is the cornerstone of our extensive IO programme. In 2018, it received approval for locally-advanced, unresectable, stage 3 NSCLC in more than 40 countries, including the US, EU and Japan. It also secured approval for locally-advanced or metastatic urothelial carcinoma (bladder cancer) in Canada, Brazil, Israel, Hong Kong, Australia, the United Arab Emirates and India.

Immuno-oncology (IO) is a promising therapeutic approach that harnesses the patient's own immune system to help fight cancer. We aim to become scientific leaders in IO by identifying novel approaches that enhance the immune system's ability to fight cancer, both with IO medicines on their own, and in conjunction with other medicines.

In 2018, our comprehensive IO clinical programme continued to provide insights on the clinical potential of *Imfinzi* in a variety of different clinical settings, both as a monotherapy as well as in combination with chemotherapy and tremelimumab.

Early-stage NSCLC

In May 2018, we announced positive topline OS results for the Phase III PACIFIC trial of *Imfinzi* in patients with unresectable stage 3 NSCLC. Data that show *Imfinzi* reduced the risk of death by nearly one third were subsequently presented on 25 October during the Presidential Symposium of the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer. With the PACIFIC trial results, we are the first company to demonstrate the benefits of treating NSCLC patients with an immuno-therapy where curative intent is the treatment goal, ie before the disease has spread to multiple organs.

Lung cancer is a key area of focus for our IO portfolio and in 2018 we announced our commitment to investigate the full potential of *Imfinzi* in early-stage NSCLC with the Phase III ADJUVANT (BR.31), PACIFIC-2 and PACIFIC-5 trials:

- ADJUVANT will explore the benefits of treatment with *Imfinzi* following complete tumour resection.
- PACIFIC-2 will assess efficacy and safety of *Imfinzi* given concurrently with platinum-based chemotherapy radiation in stage 3 NSCLC patients.
- PACIFIC-5 will assess the efficacy and safety of *Imfinzi* as consolidation therapy in patients with locally-advanced, unresectable NSCLC.

Late-stage NSCLC

In April 2018, we announced the results of the Phase III ARCTIC trial exploring *Imfinzi* and tremelimumab in monotherapy or in combination in 3rd line locally-advanced or metastatic NSCLC. The data, presented on 22 October at the ESMO 2018 Congress, demonstrated that *Imfinzi* monotherapy provided a clinically meaningful reduction of the risk of death compared to chemotherapy in patients with PD-L1 high/positive tumours and that the combination did not significantly improve PFS or OS compared to chemotherapy in patients with PD-L1 low/negative tumours.

In November 2018, the final analysis of the MYSTIC trial showed that for patients with stage 4 (metastatic) NSCLC, whose tumours express PD-L1 on 25% or more of their cancer cells, *Imfinzi* monotherapy and the combination of *Imfinzi* plus tremelimumab did not meet the primary endpoints of improving OS compared to the current standard of care (SoC) chemotherapy. The results presented at the December ESMO-IO Congress showed that *Imfinzi* monotherapy demonstrated meaningful clinical activity in patients whose tumours express PD-L1 on 25% or more of their cancer cells, but this result did not meet statistical significance. The data support further analysis in exploratory subgroups, including blood tumour mutational burden (bTMB) analyses.

We also continued our efforts to explore ways to improve outcomes for patients who have relapsed or are diagnosed with metastatic disease. In this setting, *Imfinzi* is being investigated as a monotherapy and in combination with tremelimumab and/or chemotherapy in the PEARL, NEPTUNE and POSEIDON trials.

Beyond NSCLC

In December 2018, the final data from the EAGLE study showed *Imfinzi* monotherapy and the combination of *Imfinzi* plus tremelimumab did not meet the primary endpoints of improving OS compared to SoC chemotherapy in patients with recurrent or metastatic HNSCC who experienced disease progression following platinum-based chemotherapy. We continue to explore the potential of *Imfinzi* and tremelimumab in HNSCC in the ongoing KESTREL trial, in patients with 1st line recurrent or metastatic disease, with data expected in the first half of 2019. Our extensive IO programme also includes ongoing Phase III trials in small cell lung cancer (SCLC) with CASPIAN, in bladder cancer (POTOMAC, NIAGARA, DANUBE, NILE) and in hepatocellular carcinoma (HIMALAYA).

In addition to these major clinical trials, our IO pipeline, one of the largest in the industry, continued to progress:

- MEDI9447: In June 2018, data from the Phase I study of oleclumab (MEDI9447), targeting ecto-5'-nucleotidase (CD73), in combination with *Imfinzi* in advanced pancreatic cancer and colorectal cancer was presented at the ASCO annual meeting.
- AZD9150: In October 2018, data from the SCORES Phase II study in patients with 2nd line HNSCC showed encouraging tumour response rate for the combination of danvatirsen (AZD9150, STAT3 antisense oligonucleotide) with *Imfinzi*, including biopsy data showing modulation of the tumour microenvironment.
- Monalizumab: In October 2018, we announced a new agreement with Innate Pharma in which we will exercise our existing option to obtain full oncology rights to monalizumab, a first-in-class humanised anti-NKG2A antibody which has demonstrated positive Phase II results in head and neck cancer and presents opportunities in colorectal cancer and haematological malignancies as well. The agreement also provided us with access to Innate Pharma's anti-CD39 mAb, IPH5201, plus four additional IO molecules, increasing the breadth and depth of our IO portfolio.
- AZD4635, an Adenosine 2A receptor (A2AR) inhibitor is being explored as monotherapy and in combination with *Imfinzi* in solid tumours in Phase II trials. In addition, combination trials of AZD4635 with oleclumab (anti-CD73 Ab), and with oleclumab and *Imfinzi* are ongoing with the goal of testing increased adenosine axis blockade, a key immunosuppressive mechanism.
- MEDI0680, an anti-programmed cell death protein 1 (PD1) mAb that blocks interactions with PD1 and its ligands, is being investigated in combination with *Imfinzi* in a Phase II study to treat solid tumours.
- MEDI0457, a DNA vaccine against human papilloma virus (HPV) 16/18 is being investigated in combination with *Imfinzi* in a Phase II study in patients with HPV-associated head and neck tumours.
- Potential new products in Phase I include MEDI5752, a novel bispecific antibody designed to target dual checkpoints on immune cells, and MEDI5083 targeting CD40 receptor. These agents are in Phase I development for a range of solid tumours and have the potential for combination with other molecules in the portfolio, including *Imfinzi*.

Lynparza and DNA damage response

Lynparza is our best-in-class oral poly ADP ribose polymerase (PARP) inhibitor, the flagship of our DDR programme.

Our DNA damage response (DDR) platform exploits mechanisms that selectively damage tumour cell DNA to shrink tumours and improve Progression Free Survival (PFS) and Overall Survival (OS). Our market-leading programmes focus on multiple ways to identify and exploit vulnerabilities to kill the tumour cells, while minimising toxicity to the patient.

In 2018, *Lynparza* became the first and only PARP inhibitor approved beyond ovarian cancer for the treatment of germline BRCA-mutated (gBRCAm) HER2- metastatic breast cancer in the US and Japan. The US approval in January 2018 and the Japan approval in July 2018 were based on the Phase III OlympiAD trial which demonstrated the benefits of *Lynparza* over chemotherapy for patients with gBRCAm HER2- metastatic breast cancer.

2018 has been a significant year for *Lynparza* as it fully benefited from the global strategic oncology collaboration with MSD to co-develop and co-commercialise the product, both as a monotherapy and in combination with other medicines, for multiple cancer types. In addition, new market entries, the tablet formulation (now approved in all major regions) and new indications in advanced breast cancer and for a broad label in platinum-sensitive relapsed ovarian cancer regardless of BRCA status also expanded the medicine's availability to new patients. By December 2018, *Lynparza* had been approved in more than 60 countries.

In October 2018, the SOLO-1 Phase III trial data demonstrated the significant benefit of extending PFS much earlier in the patient journey, bringing the goal of long-term remission and cure in ovarian cancer even closer. The results of SOLO-1, presented as part of the Presidential Symposium at the ESMO 2018 Congress, and published simultaneously in the New England Journal of Medicine, showed that 60% of women with newly diagnosed advanced BRCA-mutated ovarian cancer treated with *Lynparza* for 1st line maintenance therapy remained progression-free at three years compared to 26.9% with placebo following platinum-based chemotherapy. At 41 months of follow-up, the median PFS was not reached in the *Lynparza* arm, while it had been reached at 13.8 months within the placebo arm. In December 2018, just a few weeks after the filing submission in the US, the FDA approved *Lynparza* for 1st line maintenance therapy in patients with BRCAm advanced ovarian cancer.

Our combination approach of *Lynparza* with other small molecules and biologics has significantly expanded in 2018. Cediranib, our orally administered multi-vascular endothelial growth factor receptor (VEGFR) inhibitor, is currently being tested in combination with *Lynparza* in the Phase IIb CONCERTO trial in patients with platinum-resistant recurrent ovarian cancer. Results are expected late in 2019. The DUO programme of *Lynparza* with *Imfinzi* has been extended to new potential indications (bladder cancer, NSCLC, ovarian cancer). Building on the PROfound Phase III trial that explores the efficacy and safety of *Lynparza* versus enzalutamide or abiraterone in subjects with metastatic castration-resistant prostate cancer, we started the Phase III PROpel trial that will assess the combination of *Lynparza* with abiraterone in 1st line metastatic castration-resistant prostate cancer.

In addition, from our extensive DDR portfolio, five other products continued to advance through early development. These include:

- AZD1775, a Wee1 inhibitor in Phase II development for ovarian and other solid tumours in combination with *Lynparza*, in combination with chemotherapy, and as monotherapy.
- AZD6738, an Ataxia Telangiectasia and Rad3 related (ATR) serine/threonine protein kinase inhibitor in Phase II development in combination with *Lynparza* for triple negative breast cancer, gastric cancer and other solid tumours. It is also being investigated in combination with *Calquence* in chronic lymphocytic leukaemia, and in combination with radiation therapy and chemotherapy, as well as a monotherapy.
- AZD2811 an Aurora Kinase inhibitor in development for Phase II in SCLC and acute myeloid leukaemia.
- AZD0156 and AZD1390, ATM inhibitors in Phase I for solid tumours.

Calquence and haematology

Calquence is our irreversible oral Bruton's tyrosine kinase (BTK) inhibitor.

The use of antibody-drug conjugates (ADC) is a clinically validated, highly potent approach that selectively targets cancer cells by combining innovative antibody engineering capabilities with cytotoxic drug molecules, to attack and kill the tumour while minimising toxicity to the patient.

In 2018, *Calquence* experienced encouraging early uptake in the US market following an October 2017 approval for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

In December 2018, at the American Society of Hematology congress, we presented the two-year follow-up results of the ACE-LY-004 Phase II trial showing sustained benefits for patients treated with *Calquence* in relapsed or refractory MCL. In addition, the updated results of the Phase I/II ACE-CL-001 trial, assessing the long-term safety and efficacy of *Calquence* in a cohort of previously untreated patients with chronic lymphocytic leukaemia (CLL), showed high response rates and demonstrated an acceptable safety profile. The median time on study was 33 months, with 91% of patients remaining on treatment with *Calquence* at the time of analysis.

In September 2018, *Lumoxiti* became the first medicine from our ADC scientific platform to get approved, and our fifth new oncology medicine since 2014.

Lumoxiti is a first-in-class anti-CD22 recombinant immunotoxin and the first new treatment option for hairy cell leukaemia (HCL) in over 20 years. It was approved in the US for the treatment of adult patients with relapsed or refractory HCL who have received at least two prior systemic therapies, including treatment with a purine nucleoside analogue.

In October 2018, we announced we will license the US commercial rights of *Lumoxiti* to Innate Pharma. Innate Pharma, with our support, will continue EU development and commercialisation, pending regulatory submission and approval. Innate Pharma will recognise revenues and co-commercialise *Lumoxiti* with us in the US and will take full responsibility by mid-2020. In addition, as part of the Innate Pharma agreement, we acquired monalizumab, a first-in-class, humanised anti-NKG2A antibody with a novel mode of action that is being investigated in several haematological malignancies and solid tumours.

In 2018, we also continued to advance our haematology early-phase clinical programme, with AZD5991, an MCL1 inhibitor, and AZD4753, a CDK9 inhibitor, both being investigated as part of our cell death programme, and ADCs, MEDI7247 and MEDI2228.

Mature portfolio

In 2018, our established oncology brands – *Faslodex*, *Zoladex* and *Iressa* – delivered good sales.

Faslodex continued to benefit from several 2017 1st line label extensions, based on the Phase III FALCON trial, for the treatment of post-menopausal women with oestrogen receptor positive, locally-advanced or metastatic breast cancer, not previously treated with endocrine therapy. In addition, the body of evidence supporting the use of *Faslodex* as a backbone therapy for use in combination in the treatment of advanced breast cancer continued to grow. All major CDK4/6 inhibitors, a new class of medicine for ER+/HER2- breast cancer, now include use with *Faslodex* in their labels.

Zoladex returned to value growth in 2018 following a six-year period of slowly declining sales across Europe and Japan. The growth was based on increased access to medical castration and ovarian suppression, as well as earlier detection and diagnosis in prostate and breast cancers, predominantly in China and the Emerging Markets.

Iressa sales declined slightly following generic entries in select markets and the initial uptake of *Tagrisso* in 1st line EGFRm advanced NSCLC.

Cardiovascular, Renal and Metabolism

Cardiovascular, renal and metabolic (CVRM) diseases combined are killing more than 20 million people each year. Yet, in many cases, each condition is managed in isolation. As science uncovers commonalities between these diseases and their associated complications, we aim to transform how CVRM diseases are understood and treated.

Nucleotide therapies – antiMRNA.

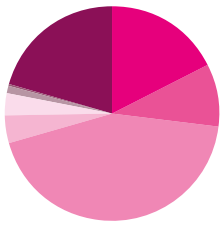
Unmet medical need and world market

20m
Number of deaths from CVRM diseases worldwide every year.

>93%
Proportion of people with type-2 diabetes that have at least one other CV, renal or metabolic condition.

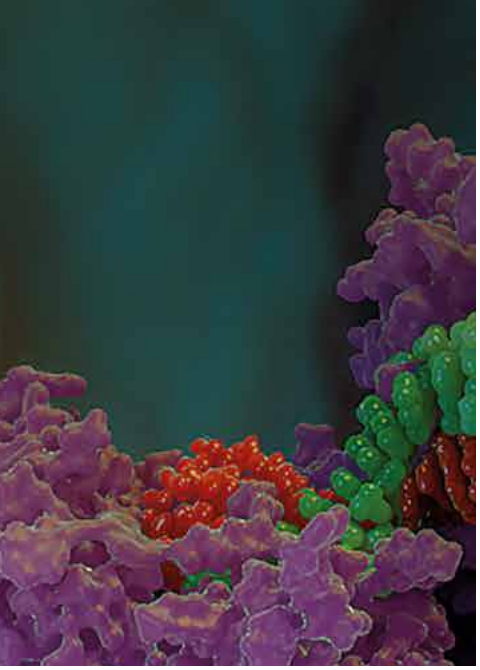
Therapy area world market
(MAT/Q3/18)

$183.8bn
Annual worldwide market value



- High blood pressure **$33.3bn**
- Abnormal levels of blood cholesterol **$17.7bn**
- Diabetes **$82.5bn**
- Thrombosis **$7.7bn**
- CKD **$6.5bn**
- CKD associated anaemia **$2.0bn**
- Hyperkalaemia **$0.3bn**
- Other CV **$38.8bn**

Source: IQVIA.
AstraZeneca focuses on specific segments within this overall therapy area market. CVRM total sales excludes partial double counting of hyperkalaemia and CKD associated anaemia market sales, which results from definitions overlapping with CKD and other CV.



Key marketed products and revenues 2018

CVRM supported AstraZeneca's Return to Growth by achieving blockbuster status for two of its main innovative medicines, *Farxiga* and *Brilinta*. Overall CVRM Product Sales were $6,710 million for 2018, down 8% on 2017 (8% at CER).

CVRM revenue

$6,710m

32% of total

2017: $7,266m

2016: $8,116m

Product	Disease area	Revenue	Commentary
Brilinta/*Brilique* (ticagrelor)	Acute coronary syndromes (ACS) and high-risk patients with history of myocardial infarction (MI)	↑ $1,321m, up 22% (21% at CER)	Approved in more than 100 countries for ACS and more than 60 countries for high-risk patients with history of heart attack; included in major guidelines. *Brilinta* delivered consistent quarter-over-quarter growth in 2018 in all regions.
Farxiga/ *Forxiga* (dapagliflozin)	Type-2 diabetes	↑ $1,391m, up 30% (30% at CER)	Approved in more than 90 countries to improve glycaemic control in adult patients with type-2 diabetes; included in major guidelines. It had a solid performance in 2018, driven by strong volume growth in a highly competitive market.
Onglyza (saxagliptin)	Type-2 diabetes	↓ $543m, down 11% (11% at CER)	Approved in more than 85 countries for the treatment of adults with type-2 diabetes; included in guidelines. *Onglyza* maintained a strong performance in 2018 in Emerging Markets, driven by China, while facing US price pressure.
Bydureon (exenatide XR injectable suspension)	Type-2 diabetes	↑ $584m, up 2% (1% at CER)	Approved in more than 70 countries to improve glycaemic control in adults with type-2 diabetes; included in major guidelines. In 2018, *Bydureon* continued launch progress with *BCise* in a highly dynamic GLP-1 class.
Byetta (exenatide injection)	Type-2 diabetes	↓ $126m, down 28% (28% at CER)	
Symlin (pramlintide acetate)	Diabetes	↓ $34m, down 29% (29% at CER)	
Legacy			
Crestor (rosuvastatin calcium)	Dyslipidaemia Hyper-cholesterolaemia	↓ $1,433m, down 39% (40% at CER)	Financial impact following the 2017 expiries in the US, EU and Japan receded in second half of 2018. Licensed from Shionogi. The extension of the global licence agreement with Shionogi for *Crestor* and the modification of the royalty structure became effective 1 January 2014.
Seloken/ *Toprol-XL* (metoprolol succinate)	Hypertension Heart failure Angina	↑ $712m, up 2% (4% at CER)	Divested rights in Europe to Recordati in May 2017. Divested US rights to Aralez effective 4 October 2016.
Atacand/ *Atacand* HCT/ *Atacand* Plus (candesartan cilexitil)	Hypertension Heart failure	↓ $260m, down 13% (12% at CER)	Divested rights to Cheplapharm in 28 European markets in July 2018. Licensed from Takeda Chemicals Industries Ltd.
Others		↓ $306m, down 11% (12% at CER)	

Our strategy for CVRM

CVRM diseases often coexist and many patients have symptoms or underlying pathologies associated with more than one CVRM disease. We are therefore focusing our efforts on the commonalities between these diseases and their underlying mechanisms to better understand how our portfolio might be used to address multiple risk factors or co-morbidities, and whether combinations of medicines might offer unique patient benefits.

We have a three-pronged science-driven strategy to address this extended CVRM risk:

1. Today, we are delivering life-changing results in the discrete core cardiovascular (CV) disease areas and their complications, with medicines already being used or in late-stage development:
> **Metabolic disease:** *Farxiga*, *Bydureon*, *Onglyza*, *Qtern*
> **Heart failure:** *Farxiga*
> **Renal:** *Lokelma*, roxadustat, *Farxiga*
> **Atherosclerosis:** *Brilinta*, *Epanova*, *Crestor*.

2. For the future, we are investing in science to demonstrate CV and mortality benefits by slowing the underlying progression of CV-related disease and protecting the organs of the CV system.

3. Ultimately, we are looking to do more than slow CV-related disease. We want to modify, or even halt, the natural course of the disease itself and regenerate organs.

Our new approach to care

Our aim is to improve care for CVRM patients by adopting a holistic approach to each patient and finding a seamless way in which to treat their diseases. We want to promote interdisciplinary collaboration among CV, renal and diabetes specialists and primary care physicians in order to change clinical practice and provide complete care for CVRM patients. Our approach is exemplified by:

1. Partnerships: We are actively seeking broader and stronger collaborations with respected academic institutions, research organisations, patient advocacy groups and healthcare companies.

2. Research: By taking risks, we can study compounds and treatments across diseases and combinations. We are seeking not only to understand the development and implications of each condition, but the interactions between two or more conditions, and how deterioration in one could adversely affect the others.

3. Real-world settings: Using data from real-world studies, we are better able to evaluate the connections between CVRM conditions and follow-up on patient outcome measures. For example, recent research collected multi-national real-world evidence (RWE) from more than 300,000 patients across six countries.

Therapy Area Review
Cardiovascular, Renal and Metabolism *continued*

2018 pipeline highlights

We have 29 potential medicines and medicine combinations in our pipeline, including small molecules and biologics, to address cardiac regeneration and individual conditions, such as chronic kidney disease (CKD), acute coronary syndromes (ACS), heart failure (HF) and non-alcoholic steatohepatitis (NASH) as well as in the broader CVRM disease context.

Full details are given in the Development Pipeline from page 212 and highlights from the progress our CVRM pipeline made in 2018 against our KPIs are shown below.

Life-cycle phases – R&D

New molecular entity (NME) Phase II starts/progressions

Our pioneering approach to exploring CV disease and heart regeneration saw advances in three Phase II clinical trials.

Product	Disease
AZD4831	Heart failure
AZD8601	CV disease
MEDI6012	CV disease

NME and major life-cycle management (LCM) positive Phase III investment decisions

We broadened our HF research to include a Phase III trial evaluating the effects of *Farxiga* on reducing CV death or worsening HF in patients with HF and a preserved ejection fraction (HFpEF), alongside functional and systematic studies for patients with both preserved and reduced ejection fraction (HFpEF/HFrEF).

Product	Disease
Farxiga/Forxiga	Heart failure (DELIVER)

Plus one project where investment decision has been made but clinical trial has yet to start.

NME and major LCM regional submissions

Our metabolism portfolio made significant regulatory strides, with five regulatory filings for our oral medicines and combination oral medicines, plus three major market data submissions from our injectables medicines.

Product	Disease	Region
Bydureon	Type-2 diabetes cardiovascular outcomes trial (CVOT) (EXSCEL)	EU, US, China
Bydureon BCise	Type-2 diabetes CVOT (DURATION programme harmonisation)	US
Bydureon BCise	Type-2 diabetes CVOT (EXSCEL)	US
Farxiga/Forxiga	Type-1 diabetes (DEPICT)	EU, Japan, US
Farxiga/Forxiga combination: saxagliptin + dapagliflozin + metformin	Type-2 diabetes	EU, US
Qtern	Dual add-on type-2 diabetes	US

Plus two projects where submissions have been made but have yet to be accepted.

Life-cycle phases – approvals

NME and major LCM regional approvals

We made important progress in advancing new molecules like *Lokelma* and roxadustat to address unmet needs of renal patients, as well as adding clinical evidence on clinically relevant CV outcomes alongside device enhancements of our established medicine, *Bydureon*, in the EU.

Product	Disease	Region
Bydureon	Add-on to insulin (DURATION 7)	US
Bydureon	CVOT (EXSCEL)	EU
Bydureon BCise	Type-2 diabetes weekly auto-injector	EU
Lokelma	Hyperkalaemia	EU, US
Roxadustat[1]	Chronic kidney disease anaemia	China

[1] Development and commercialisation collaboration with FibroGen in China. FibroGen holds the NDA.

Discontinued projects

Product	Disease	Reason
None	–	–

For more information on the life-cycle of a medicine, see page 9.

Science *can* help address the early complications of type-2 diabetes

People with type-2 diabetes have a two to five times greater risk of heart failure plus an increased risk of a heart attack or stroke.

In November 2018, we announced the full results from the DECLARE-TIMI 58 SGLT-2 inhibitor cardiovascular outcomes trial (CVOT) for *Farxiga*. The trial included more than 17,000 patients with type-2 diabetes across 33 countries, more than four years of follow-up and included those with multiple CV risk factors and those with established CV disease. This trial showed that *Farxiga* significantly reduced the risk of hospitalisation for heart failure or CV death by 17%. It also demonstrated a strong safety profile in a medicine class where some physicians have had concerns.

Farxiga has the potential to further transform the management of all patients with type-2 diabetes. We are moving towards doctors being able to choose treatment beyond control of blood-glucose to cardio-renal protection.

Heart failure

- Continues to have a worse survival rate than some cancers following diagnosis with a 50% survival rate after five years.
- Is the most common cause of hospitalisation in patients older than 65.
- Represents a considerable societal and economic burden: 25% of hospitalised patients are readmitted within 30 days and, at six months, readmission rates are almost 50%.

2018 review – strategy in action

We have adopted a unique CVRM strategy which includes investing in rigorous clinical programmes evaluating the use of our medicines in large patient populations in both Established and Emerging Markets. These trials include ambitious global randomised clinical trials (RCTs) that are as close as possible to clinical practice, as well as transformational RWE research.

- **Randomised clinical trials:** More than 60,000 patients are currently participating in our R&D-led CV trials at more than 6,000 sites worldwide. Our focus on diabetes research includes almost 50 clinical trials worldwide, with an enrolment target of 56,000 patients. These RCTs include the DapaCare Programme, OLYMPUS and ROCKIES, and THEMIS.
- **Real-world evidence data:** Our RWE studies include CVD-REAL and PRACTICAL, which both set out to deliver innovative data from large-scale settings.

Cardiovascular disease

Brilinta is an oral antiplatelet treatment for ACS, an umbrella term for sudden chest pain and other symptoms due to ischaemia (insufficient blood supply) to the heart, and for the long-term prevention of CV death, heart attack and stroke for patients with a history of heart attack.

In its ACS indication, *Brilinta* 90mg is approved in more than 100 countries, and is included in major ACS treatment guidelines globally. In its indication for the long-term prevention of CV death, heart attack and stroke for patients with a history of heart attack, since approval in 2016, *Brilinta* 60mg is now approved in over 70 countries.

We presented results of a new analysis of the PLATO trial at the American College of Cardiology meeting in March 2018, showing total mortality was reduced by 51% and CV death was reduced by 48%, when patients with ACS were treated with *Brilinta* within seven days prior to having heart bypass surgery, compared to patients treated with clopidogrel.

At the European Society of Cardiology (ESC) Congress, real-world data further reinforced the need to manage persistent ischaemic risk in patients, especially those with additional risk factors. PRECLUDE-2, an analysis of data from the ongoing SWEDEHEART quality registry involving more than 100,000 patients, found that the majority of post-myocardial infarction (MI) patients who have at least two CV disease risk factors, showed a marked but gradual increase in incidence of CV death, MI or stroke. The CV risk in patients with type-2 diabetes in the ATHENA study involving more than 300,000 patients demonstrated that diabetic patients who also have coronary artery disease, or who have experienced a prior heart attack or a stroke, are at greater risk of future CV death, heart attack and stroke than patients with just diabetes alone.

During the year, the first patient was enrolled into THALES, a new randomised, placebo-controlled Phase III dual antiplatelet therapy trial in stroke. This study forms part of PARTHENON, our largest ever CV outcomes programme involving more than 80,000 patients, within which THEMIS is the next major trial due to read out, studying the benefit of *Brilinta* for the prevention of CV events in patients with type-2 diabetes and coronary artery disease.

We continue to advance our large-scale CV outcomes trial (CVOT) (STRENGTH) to evaluate the safety and efficacy of *Epanova* on CV outcomes in combination with statin therapy for the treatment of patients with mixed dyslipidaemia who are at increased risk of CV disease. STRENGTH is the largest CVOT of any prescription omega-3 and completed enrolment in April 2017, with approximately 13,000 patients. Results are expected in 2020.

We are investigating the role of SGLT-2 inhibition in patients with heart failure as part of our DapaCare programme overleaf.

Crestor is approved in over 115 countries for the treatment of dyslipidaemia and hypercholesterolaemia (elevated cholesterol). The financial impact following the 2017 patent expiries in the US, EU and Japan receded in the second half of 2018. *Crestor* is now subject to generic competition in a number of markets.

In July 2018, we announced an agreement with Cheplapharm for the rights in Europe to *Atacand* (candesartan cilexetil) and *Atacand* Plus (fixed-dose combination of candesartan cilexetil and hydrochlorothiazide). *Atacand* is a prescription medicine for the treatment of heart failure and hypertension.

Therapy Area Review
Cardiovascular, Renal and Metabolism *continued*

Renal diseases

Our ambition is to revolutionise the treatment of chronic kidney disease (CKD). We are investing in therapies across the continuum of CKD care, from disease modification during an early-stage diagnosis to managing life-threatening complications as patients progress to dialysis and end-stage renal disease.

Roxadustat is a first-in-class oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) that could transform the management of anaemia of CKD for patients both on dialysis and not on dialysis. We are collaborating in the development and commercialisation of roxadustat in the US, China and other markets not covered by an agreement between FibroGen and Astellas. In December 2018, we announced with FibroGen the approval of roxadustat by the National Medical Products Administration, marking the first time that a first-in-class medicine was approved first in China. Later in December 2018, we announced that the primary endpoints were met in OLYMPUS and ROCKIES, two AstraZeneca-sponsored trials within the global Phase III programme for roxadustat conducted by AstraZeneca, FibroGen and Astellas. These trials will contribute to a pooled safety analysis, which is anticipated during the first half of 2019 and will inform the US regulatory submission.

We are preparing for a broad launch of *Lokelma*, a best-in-class treatment for hyperkalaemia, in major markets. In March 2018 *Lokelma* was approved by the EMA and in May 2018, *Lokelma* was approved by the FDA. Subsequently, our focus was on ensuring broad availability to patients at launch in the US and Europe in 2019. In October 2018, we presented positive Phase III data from HARMONIZE Global, a *Lokelma* trial whose data will support future registrations in Japan, Russia, Korea and Taiwan.

We are exploring whether the medicines in our portfolio could modify the progression of CKD or offer organ protection as part of our DapaCare programme (see below).

Metabolic diseases

We are focused on redefining how diabetes is treated in unison with CV and renal diseases and the risk factors, harnessing complementary mechanisms of action and focusing on diverse populations with significant co-morbidities, such as CV disease (particularly heart failure), obesity, NASH, as well as diabetic nephropathy and CKD. Our global clinical research programmes seek to advance understanding of the treatment-effects of our diabetes medicines on these co-morbidities across broad patient populations that represent today's clinical practice in order to help more patients achieve treatment goals earlier in their disease.

Our industry-leading DapaCare clinical trial programme will enroll nearly 30,000 patients in RCTs and mechanistic studies exploring new ways to extend the therapeutic value of *Farxiga* to patients with and without type-2 diabetes, many of whom have not seen treatment advances in decades. DapaCare is our answer to the need for comprehensive research and treatment at a time when there is a fundamental shift in how diabetes, CV and renal diseases are managed.

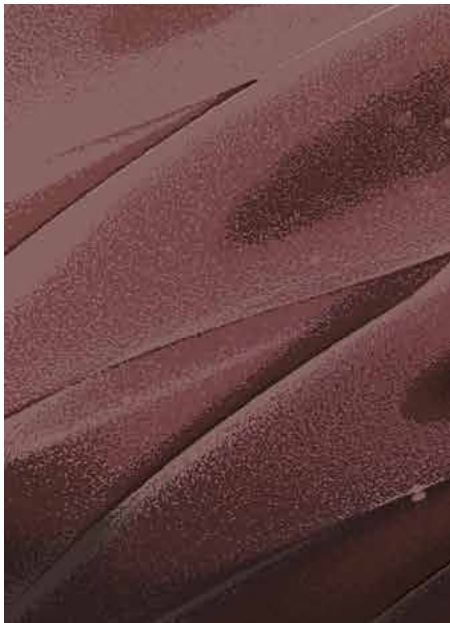
In addition to our leading CVOT, DECLARE (see case study on page 59), and our RWE study, CVD-REAL, we have invested in two pivotal *Farxiga* outcomes trials in HF, evaluating patients with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF), both in patients with and without type-2 diabetes. These, along with several mechanistic studies, make *Farxiga* a potential first-in-class treatment to address a significant unmet need in HF. Further research from the DapaCare programme is investigating renal outcomes and CV mortality in patients with CKD, the natriuretic effect and volume changes in type-2 diabetes with preserved or impaired renal function, and changes in proteinuria in non-diabetes and kidney diseases.

In type-1 diabetes, final results from the DEPICT programme trials were presented and published in 2018, and formed our regulatory submissions currently under review in the EU (EMA), Japan (PMDA) and the US (FDA), for *Farxiga* as an adjunct treatment to insulin for adults with type-1 diabetes. If approved, *Farxiga* may be the first selective SGLT-2 inhibitor with this indication, representing an important advancement for people with type-1 diabetes who have not seen meaningful treatment progression in decades. In February 2019, the Committee for Medicinal Products for Human Use (CHMP) of the EMA issued a positive recommendation from the EMA to use *Farxiga* in adults with type-1 diabetes as an adjunct to insulin in patients with BMI $\geq$ 27 kg/m^2, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy. Regulatory decisions for the type-1 indication are expected in the first half of 2019 in the EU and Japan. The US regulatory decision is expected in the second half of 2019.

Bydureon, our glucagon-like peptide-1 (GLP-1) receptor agonist for type-2 diabetes, has become more convenient and available this year to patients in multiple countries whose blood sugar remains uncontrolled with other treatments, supported by our Phase III trial, EXSCEL, the largest and longest CVOT on the GLP-1 class. Additionally, *Bydureon BCise*, a new formulation in an easy-to-use, once-weekly device that does not require titration, was approved by the EC. With 3Sbio Inc., we also gained approval for *Bydureon* across China, making it the first once-weekly GLP-1 in a nation with an estimated 114 million patients living with diabetes.

We are also advancing promising investigational agents that bring new approaches to metabolic diseases and their complications. In June, the first clinical results from a Phase IIa study conducted on MEDI0382, our oxyntomodulin-like peptide molecule being studied for patients with type-2 diabetes, were presented at the American Diabetes Association and simultaneously published in *The Lancet*, demonstrating the potential to become a first-in-class treatment for type-2 diabetes, NASH and obesity.

We follow the science to new clinical solutions for metabolic diseases and are working with leaders in the global diabetes community to overcome obstacles to optimal care. Led by Primary Care Diabetes Europe, we have partnered to launch Early Action in Primary Care to address clinical inertia and resistance to early use of innovative treatments like SGLT-2s and GLP-1s. In addition, with the research group, Health Economics and Outcomes Research, we will issue a first-of-its-kind predictive analysis on the economic value to health systems across Europe and the US of treating diabetes and CV complications together, with the goal of improving reimbursement policy and patient outcomes.



can

Science

advance our understanding of the repair and regeneration of tissues

For the estimated 26 million people worldwide with heart failure, recent scientific progress in blood vessel and heart muscle regeneration may lead to new ways of treating their disease. Not so long ago, we assumed that heart failure was an almost inevitable consequence of damage to or death of cells in the heart's main pumping chamber, the left ventricle, caused by lack of oxygen due to an impaired blood supply. However, we now know that there may be ways to help regeneration of blood vessels around heart muscle cells that are damaged by a heart attack, by high blood pressure or other cardiovascular problems that occur as people get older.

Our pioneering research is based on:

- Advances in understanding of vascular biology and the biological action of vascular endothelial growth factor A (VEGF-A) in stimulating formation of new blood vessels and helping to repair damaged heart muscle.
- Developments in messenger ribonucleic acid (mRNA) technology to boost production of VEGF-A in areas of the heart (mRNA is an essential part of the process by which genes in the form of DNA are decoded to make proteins).

The vascular and cardiac regeneration initiative brings together the complementary skills and expertise of scientists from AstraZeneca and Moderna. This important collaboration, which began in 2013, is advancing the science of tissue regeneration for cardiovascular and metabolic diseases and in other therapy areas. It is rapidly translating laboratory findings into clinical trials of novel therapeutic modalities, for example patients undergoing coronary artery bypass graft surgery (AZD8601).

26m

26 million people worldwide with heart failure

Stem cell differentiating into heart muscle (cardiac regeneration).

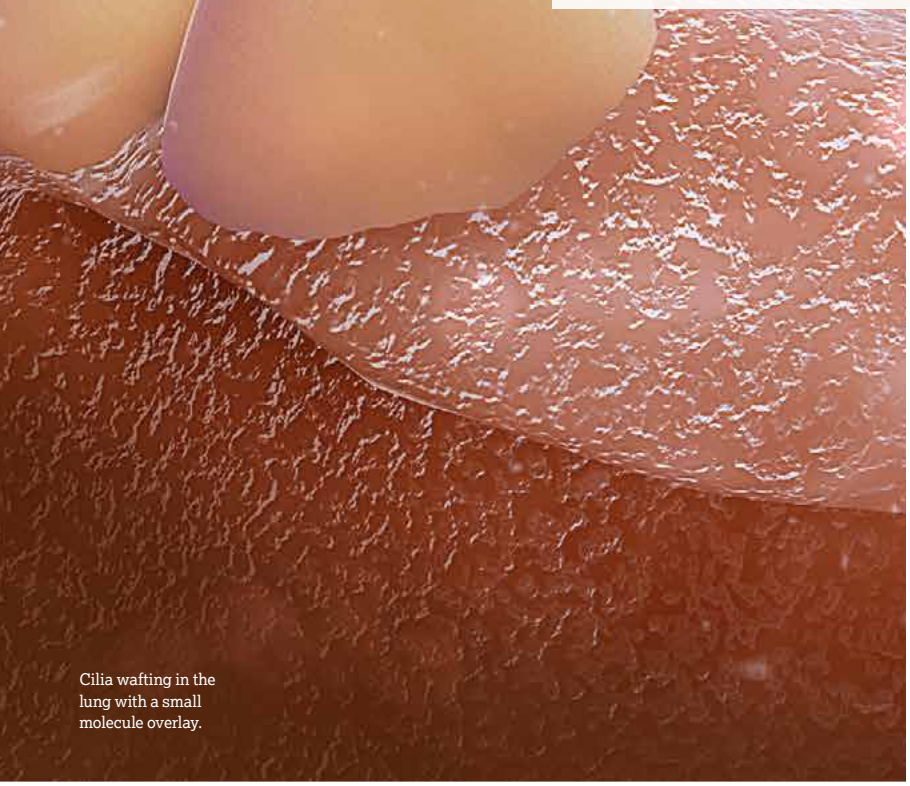
Respiratory

We aim to transform the treatment of asthma and COPD with our growing portfolio of inhaled and biologic medicines. Our research focuses on the underlying causes of respiratory diseases, using new modalities to pursue previously hard-to-reach targets, with the ambition of achieving remission or even cures for patients.

Unmet medical need and world market

Today, more than 700 million people have asthma or chronic obstructive pulmonary disease (COPD). About 250 million of these people are in our 12 largest commercial markets, but more than 175 million of these individuals do not receive maintenance treatment for these chronic diseases. Despite currently available medicines, therapeutic advances are needed to reduce morbidity and mortality.

We estimate that new medicines and Emerging Markets will drive 7% annual growth over the next decade, reaching $47 billion by 2028.



Cilia wafting in the lung with a small molecule overlay.

339m

Some 339 million individuals worldwide have asthma, with prevalence expected to rise. Severe asthma accounts for about 10% of asthma patients but 50% of the physical and socio-economic burden of asthma. Millions of patients underuse their anti-inflammatory maintenance controller treatments (which treat the underlying inflammation of the disease) and are reliant on reliever medications.

384m

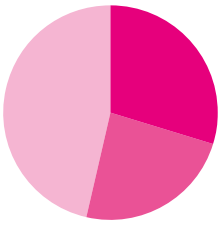
Globally, some 384 million people have COPD, and it is predicted to be the third leading cause of death by 2020. COPD exacerbations represent a significant burden for patients, carers and society. Even one severe exacerbation can significantly reduce lung function and is associated with higher mortality.

Therapy area world market

(MAT/Q3/18)

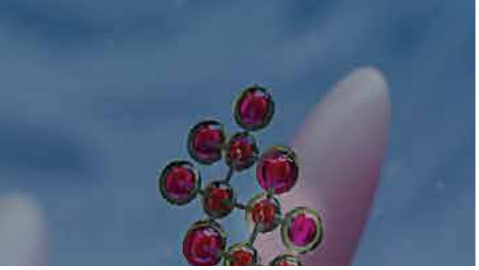
$68.4bn

Annual worldwide market value



- Asthma $20.5bn
- COPD $16.2bn
- Other $31.7bn

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



Key marketed products and revenues 2018

Our Respiratory business returned to growth in 2018, with sales of $4,911 million, up 4% (3% at CER). *Symbicort* held its position as the leading inhaled corticosteroid (ICS)/long-acting beta2-agonist (LABA) in volume sales. *Pulmicort* continued to deliver strong revenue growth, led by Emerging Markets in which China stood out. In biologics, *Fasenra* had strong launches in 35 markets and achieved leadership in new prescriptions in the IL-5 severe asthma class in the US and Japan.

Respiratory revenue

$4,911m

23% of total

2017: $4,706m

2016: $4,753m

Product	Disease area	Revenue	Commentary
Symbicort (budesonide/formoterol)	Asthma COPD	↓ $2,561m, down 9% (10% at CER)	Continued leadership of ICS/LABA class with revenue impacted by expected pricing pressure; AstraZeneca's largest medicine by sales.
Pulmicort (budesonide)	Asthma	↑ $1,286m, up 9% (8% at CER)	Brand growth led by Emerging Markets with leadership in China.
Fasenra (benralizumab)	Severe asthma	n/m $297m, movement n/m	Successful first year launch; leading the IL-5 class in new prescriptions (US and Japan).
Daliresp/Daxas (roflumilast)	COPD	↓ $189m, down 5% (5% at CER)	250mcg tablet approved as a starting dose in the US and Europe.
Tudorza/Eklira (aclidinium)	COPD	↓ $110m, down 27% (29% at CER)	Reflects the flat long-acting muscarinic antagonist (LAMA) market. Sales in the US declined by 62% reflecting the impact of federal purchases.
Duaklir (aclidinium/formoterol)	COPD	↑ $95m, up 20% (14% at CER)	Growth in Europe is in line with expectations.
Bevespi Aerosphere (glycopyrrolate/formoterol)	COPD	↑ $33m, up 106% (106% at CER)	*Bevespi Aerosphere* revenue and growth is in line with expectations based on focused investment in 2018, reflecting low class growth.
Others	Asthma COPD	↑ $340m, up 20% (18% at CER)	Mature portfolio. Divestment of rights to *Alvesco*, *Omnaris* and Zetonna to Covis.

Our strategy for Respiratory

Respiratory is one of our main therapy areas, and our medicines reached more than 18 million patients as maintenance therapy in 2018. We have a strong pipeline with more than 33,000 patients participating in Phase I-IV respiratory clinical trials across the world.

Our ambition is to transform outcomes for patients with respiratory diseases through:

1. Our strength in inhaled combination medicines.
2. A leading biologics portfolio.
3. A robust early pipeline where our goal is to achieve disease modification, early intervention and cure.

In inhaled medicine, our focus is on two key areas of clinical care. In asthma, we are working to prevent attacks by reducing over-reliance on reliever monotherapy and advancing anti-inflammatory reliever therapy, which is now under regulatory review for a licence extension based on the landmark *Symbicort Turbuhaler* SYGMA trials. We continue to invest in *Symbicort* given its value in the treatment of asthma and COPD, also reflected by its continued leadership in the ICS/LABA class. In COPD, we are advancing our next generation inhaled *Aerosphere* portfolio with the ambition of reducing exacerbation rates using our investigational triple therapy, PT010, earlier in the course of the disease than recommended in guidelines today.

In biologics, we aim to transform outcomes among patients with the greatest unmet medical need and relegate chronic oral steroid use to last resort, given its association with adverse events. Our first respiratory biologic, *Fasenra*, is for severe eosinophilic asthma and is being investigated for other eosinophil-driven diseases. Approved in November 2017, *Fasenra* already leads the IL-5 class in new prescriptions in the US and Japan. In the future, tezepelumab, a potential first-in-class anti-thymic stromal lymphopoietin (TSLP) mAb that blocks a key upstream driver of inflammation in asthma, has the potential to become "the broadest biologic for the treatment of persistent uncontrolled asthma seen to date"* if the Phase III programme reflects the positive Phase IIb data, as noted in the *New England Journal of Medicine*.

Our early pipeline continues to grow and includes new drug modalities allowing us to address hard-to-reach targets in the lung that were previously seen as inaccessible, for example: the *Anticalin* protein AZD1402, an inhaled IL4Rα antagonist currently in Phase I development for asthma, in collaboration with Pieris Pharmaceuticals.

Our respiratory market leadership in China positions us well to support improvements in acute treatment using our leading nebulisation portfolio and establishing maintenance inhaled treatment as the standard of care in asthma and COPD. Each day the paediatric nebulisation programme we support treats 300,000 patients, enabling them to receive guideline-recommended acute care for their condition.

* Elisabeth H. Bel. Moving Upstream – Anti-TSLP in Persistent Uncontrolled Asthma. *New England Journal of Medicine*. 2017; 377:10.

Therapy Area Review
Respiratory *continued*

2018 pipeline highlights

The progress of our pipeline in 2018 reflects our commitment to transforming critical areas of care in respiratory.

We advanced *Symbicort Turbuhaler* and PT027 (ICS/SABA combination) as anti-inflammatory reliever therapies in asthma. With PT010, our inhaled triple therapy, we made our first regulatory submissions and published positive Phase III KRONOS data that demonstrated its potential to improve lung function in patients with COPD. KRONOS data also demonstrated the potential to significantly reduce exacerbation risk versus LAMA/LABA in a patient population that was not required to have had an exacerbation in the previous 12 months (a population classified as GOLD B in international guidelines, where triple therapy is currently not recommended). In line with our strategy to transform outcomes with respiratory biologics, *Fasenra* was granted additional regulatory approvals around the world for severe, eosinophilic asthma, while our anti-TSLP biologic, tezepelumab, was granted US FDA Breakthrough Therapy designation (our first for a respiratory medicine) for severe asthma patients without an eosinophilic phenotype, including those who are ineligible for biologic therapies today.

Full details of our pipeline are given in the Development Pipeline from page 212 and highlights from the progress our Respiratory pipeline made against our KPIs in 2018 are shown below.

Life-cycle phases – R&D

New molecular entity (NME) Phase II starts/progressions

Product	Disease
None	–

NME and major life-cycle management (LCM) positive Phase III investment decisions

Our co-development partner, Avillion, achieved first subjects in the PT027 Phase III programme. PT027 is an investigational fixed-dose combination of budesonide (an inhaled corticosteroid) and albuterol (a short-acting beta2-agonist).

Product	Disease
PT027*	Asthma

Plus one project where investment decision has been made.

* Led by partner Avillion.

NME and major LCM regional submissions

Key regulatory acceptances included our first filings for PT010 (triple therapy) in COPD in Japan and China, and *Symbicort* as an anti-inflammatory reliever in mild asthma in the EU.

Product	Disease	Region
Bevespi Aerosphere	COPD	Japan, China
Fasenra	Self administration, autoinjector (GRECO/GREGALE)	EU, US
PT010	COPD	Japan, China
Symbicort	Mild asthma	EU

Life-cycle phases – approvals

NME and major LCM regional approvals

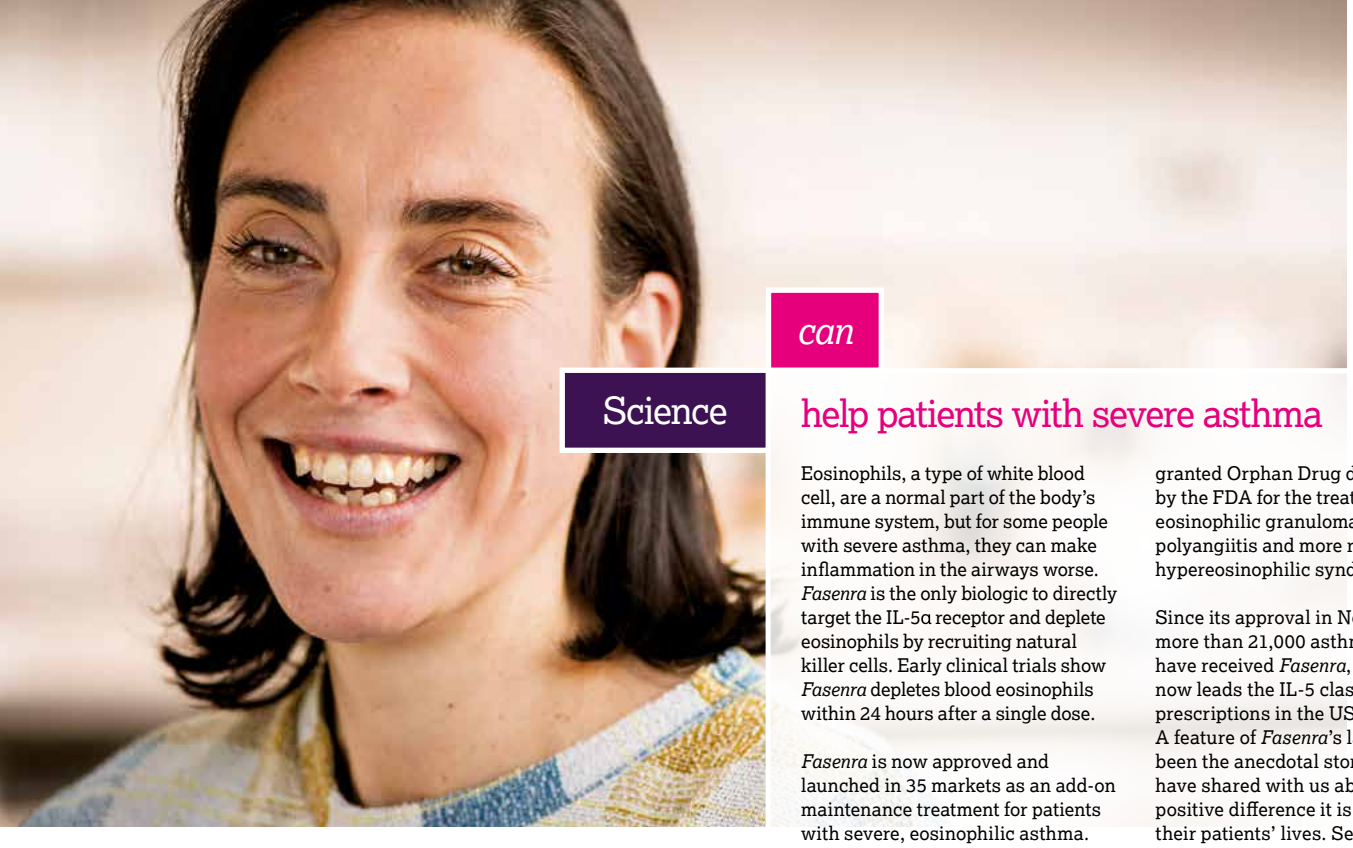
Further regional approvals were seen with *Fasenra* for severe asthma in Japan and severe eosinophilic asthma in the EU – with the product now launched in more than 35 markets and *Bevespi Aerosphere* for COPD in the EU.

Product	Disease	Region
Bevespi	COPD	EU
Fasenra	Severe asthma	EU, Japan

Discontinued projects

Product	Disease	Reason
AZD7594 + abediterol	COPD	Safety/efficacy

For more information on the life-cycle of a medicine, see page 9.



Science *can* help patients with severe asthma

Eosinophils, a type of white blood cell, are a normal part of the body's immune system, but for some people with severe asthma, they can make inflammation in the airways worse. *Fasenra* is the only biologic to directly target the IL-5α receptor and deplete eosinophils by recruiting natural killer cells. Early clinical trials show *Fasenra* depletes blood eosinophils within 24 hours after a single dose.

Fasenra is now approved and launched in 35 markets as an add-on maintenance treatment for patients with severe, eosinophilic asthma. Patients receive *Fasenra* as a fixed-dose subcutaneous injection via a pre-filled syringe every eight weeks after initial loading doses. *Fasenra* has been investigated for self-administration and in an autoinjector device; regulatory submissions were made in 2018 and we anticipate decisions in 2019. In addition, *Fasenra* is being investigated for indications in other eosinophil-driven diseases, including severe nasal polyposis, and has been granted Orphan Drug designation by the FDA for the treatment of eosinophilic granulomatosis with polyangiitis and more recently, hypereosinophilic syndrome.

Since its approval in November 2017, more than 21,000 asthma patients have received *Fasenra*, which now leads the IL-5 class in new prescriptions in the US and Japan. A feature of *Fasenra*'s launch has been the anecdotal stories clinicians have shared with us about the positive difference it is having on their patients' lives. Severe asthma is a debilitating disease, which impacts many aspects of a patient's life and these stories reflect the difference an effective biologic medicine can have for these patients.

The launch success of *Fasenra* also supports our view that biologic treatment rates will significantly increase in the coming years in line with the evolution of treatment in other inflammatory diseases.

2018 review – strategy in action

Strength in inhaled combination medicines

Our strength in inhaled combination medicines was reflected in 2018 with *Symbicort*, which retained its position as the number one ICS/LABA combination globally in volume terms and is a cornerstone of current asthma and COPD care. We continue to invest in *Symbicort*, which remains AstraZeneca's number one medicine in Product Sales in 2018.

Pricing pressure continues to impact *Symbicort* performance but was in line with expectations as prices rebase ahead of anticipated generic entries. This trend continues to be offset by Emerging Market growth, led by demand for acute and maintenance care in China. In March, the NMPA approved *Symbicort Turbuhaler* as a maintenance and reliever therapy, designed for the treatment of asthma in adolescent patients (12-17 years) in China.

In May 2018, positive results from the Phase III SYGMA trials of *Symbicort Turbuhaler* were published in the *New England Journal of Medicine* and presented at the American Thoracic Society International Congress. The trials, which met their primary objectives, evaluated the efficacy of *Symbicort Turbuhaler*, taken only as needed without maintenance therapy, as an anti-inflammatory reliever compared with standard of care medicines for mild asthma. In November, we announced that the Swedish Medical Products Agency had accepted our regulatory submission for the EU to expand the indication for *Symbicort Turbuhaler*, as an anti-inflammatory reliever as needed, in patients with mild asthma. Millions of patients with asthma are reliant on their reliever medications, which improve symptoms but do not treat the inflammation of this disease, and they underuse anti-inflammatory maintenance controller treatments, resulting in preventable exacerbations. In China, the Chinese Journal of General Practitioners guidelines were updated to incorporate the SYGMA data. This update recommended *Symbicort* as a potential treatment for all asthma severities.

We significantly progressed all Phase III trials supporting PT010 – KRONOS, SOPHOS, TELOS and ETHOS. The Phase III KRONOS trial was published in September in *The Lancet Respiratory Medicine*. KRONOS evaluated the efficacy and safety of triple combination therapy, PT010, versus dual combination therapies *Bevespi Aerosphere*, *Symbicort Turbuhaler* and PT009. In the trial, PT010 met six of seven primary endpoints versus dual comparators and PT009 met two non-inferiority endpoints to support the qualification of PT009 as an active comparator. In a key secondary endpoint, PT010 showed a statistically significant 52% reduction in the rate of moderate or severe COPD exacerbations compared with *Bevespi Aerosphere* in a patient population that was not required to have had an exacerbation in the previous 12 months. The adverse events profile was consistent with that observed in previous trials and the incidence of adjudicated pneumonia was low and comparable in all treatment arms.

During the first half of 2018, the Phase III SOPHOS trial read out, which compared two doses of PT009 to PT005. PT009 met its primary endpoint and delivered superior efficacy to PT005 at morning pre-dose through forced expiratory volume (FEV) 1 at Week 24. In September 2018, the TELOS Phase III trial, which investigated the efficacy and safety of PT009 in patients with moderate to very severe COPD, regardless of whether or not they had had an exacerbation in the prior year, showed that PT009 is an effective maintenance treatment for patients with COPD and a suitable comparator for PT010. The data were presented at the European Respiratory Society Congress and were published in the *European Respiratory Journal*. SOPHOS and TELOS were designed to qualify PT009 as an active comparator in the PT010 clinical trial programme.

In July 2018, the ETHOS Phase III trial, which further investigates the efficacy and safety of PT010, completed enrolment of 8,400 patients across 28 countries.

In addition, during the second half of 2018, the regulatory submissions for PT010 were accepted by the Japan MHLW and the China NMPA, based on the KRONOS Phase III trial. In January 2019, PT010 received Priority Review designation from China's NMPA.

Bevespi Aerosphere's progress also continued in 2018 with regulatory approvals in Canada and Australia. In December 2018, the European Commission approved *Bevespi Aerosphere* in a pressurised metered-dose inhaler (pMDI) as a maintenance dual bronchodilator treatment to relieve symptoms in adult patients with COPD. In Japan and China, the regulatory submissions for *Bevespi Aerosphere* were accepted during the third quarter of the year.

In August 2018, we announced top-line results from the AERISTO Phase IIIb trial for *Bevespi Aerosphere* in patients with moderate to very severe COPD. In the trial, *Bevespi Aerosphere* demonstrated non-inferiority to umeclidinium/vilanterol on peak FEV1 but did not demonstrate superiority on peak FEV1 or non-inferiority on trough FEV1. The efficacy and safety of *Bevespi Aerosphere* has been established by the Phase III PINNACLE trial programme involving more than 5,000 patients.

Our medicines partnered with Circassia also made progress. In the second half of 2018, the FDA accepted the *Duaklir* NDA for the maintenance treatment of patients with COPD. We anticipate a Prescription Drug User Fee Act action date in the first half of 2019. In the first half of 2018, on behalf of Circassia, we submitted an sNDA for *Tudorza* to the FDA. The submission was based on the results from the ASCENT trial, which achieved its co-primary endpoints for safety (no increase in cardiovascular risk MACE) and efficacy (COPD exacerbation reduction). It is anticipated that the US label will be updated accordingly in the first half of 2019. In December 2018, Circassia announced plans to acquire the full rights to *Tudorza* in the US.

In addition, a 250mcg tablet for *Daliresp/Daxas* was approved by the FDA in January 2018 and the EMA in April 2018 to be used as a starting-dose treatment for the first four weeks, followed by an increase to the maintenance dosage of 500mcg. *Daxas* is indicated for maintenance treatment of severe COPD associated with chronic bronchitis in adult patients with a history of frequent exacerbations, as an add-on to bronchodilator treatment.

In May 2018, Phase IIa data for AZD8871 were presented in a late-breaking oral presentation at the American Thoracic Society International Congress 2018. AZD8871 is an inhaled long-acting dual muscarinic antagonist/β2 adrenoceptor agonist under development for the treatment of COPD.

Biologic medicines

Our first respiratory biologic, *Fasenra*, continued to receive product approvals in 2018 with launches in more than 35 countries. In January 2018, the EMA approved *Fasenra* as an add-on maintenance treatment in adult patients with severe, inadequately controlled eosinophilic asthma, despite their treatment with high-dose ICS plus LABA. In Japan, *Fasenra* was approved as an add-on treatment for bronchial asthma in patients who continue to experience asthma exacerbations despite treatment with high-dose ICS and other asthma controller(s).

Currently only 10% of eligible patients in our top 12 commercial markets receive a biologic treatment, whereas biologic treatment rates in more mature inflammatory disease markets, such as rheumatoid arthritis and psoriasis, are 30–50% and growing. The main factors that will drive the rate of growth include: availability of effective medicines; improved clinical capabilities and capacity for severe asthma; and administration of biologics and evidence enabling the reduction or discontinuation of maintenance oral corticosteroid use. AstraZeneca is investing to accelerate these drivers 'beyond the medicine' which should support biologics having the kind of impact that they have had in other inflammatory diseases. The opportunity to transform more lives is significant.

In May 2018, we announced top-line results from two Phase III trials, GALATHEA and TERRANOVA, for *Fasenra* in patients with moderate to very severe COPD. The trials did not meet their primary endpoints of a statistically significant reduction of exacerbations. We are reviewing the full data set and do not currently intend to make a regulatory submission in COPD based on these data.

In September 2018, results from the BORA Phase III extension trial evaluating the long-term safety and efficacy of *Fasenra* as an add-on maintenance treatment in patients with severe eosinophilic asthma who had previously completed one of the two pivotal placebo-controlled SIROCCO or CALIMA Phase III trials, were presented in a late-breaking oral presentation at the European Respiratory Society International Congress 2018, and subsequently published in *The Lancet Respiratory Medicine* in November. In BORA, *Fasenra* showed a safety and tolerability profile similar to that observed in the predecessor trials, with no increase in the frequencies of overall or serious adverse events.

Improvements in efficacy measures observed with *Fasenra* in SIROCCO or CALIMA were maintained over the second year of treatment. During the first quarter of 2018, we also commenced a Phase III trial of *Fasenra* for the treatment of nasal polyposis. During the second quarter, we commenced the Phase IIIb PONENTE trial further evaluating *Fasenra*'s potential to eliminate maintenance oral corticosteroid use in patients with severe refractory eosinophilic asthma.

During the third quarter of 2018, the SOLANA Phase IIIb trial did not meet its primary endpoint. SOLANA is a randomised, double-blinded, parallel group, placebo-controlled Phase IIIb trial. The trial is designed to evaluate the onset and maintenance of effect and the safety of *Fasenra* in patients with severe, eosinophilic asthma. We are evaluating the full data set and anticipate the results will be submitted for publication in a medical journal.

In November 2018, the FDA granted Orphan Drug designation for *Fasenra* for the treatment of eosinophilic granulomatosis with polyangiitis. In February 2019, *Fasenra* was also granted Orphan Drug designation for the treatment of hypereosinophilic syndrome.

In the fourth quarter of 2018, we submitted regulatory filings in the US and the EU for the addition of self-administration and an autoinjector device for *Fasenra* in severe asthma. Decisions are anticipated in 2019.

In September 2018, with our partner Amgen, we announced that the FDA had granted Breakthrough Therapy designation for tezepelumab in patients with severe asthma without an eosinophilic phenotype, including those who are ineligible for biologic therapies today. This was the seventh Breakthrough Therapy designation we have received from the FDA since 2014, and the first in respiratory medicine. Tezepelumab is currently in development in the Phase III PATHFINDER clinical trial programme.

Other Disease Areas

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 autoimmunity, infection, neuroscience and gastroenterology, where we follow an opportunity-driven approach and often work through partnerships.

Unmet medical need and world market

The WHO estimates that seasonal influenza may result in 290,000 to 650,000 deaths each year due to respiratory diseases alone.

Key marketed products and revenues 2018

Nexium is continuing to perform strongly in China, while sales for the rest of the world are in line with expectations given pressures from generic competition. Following the renewed recommendation from the Advisory Committee on Immunization Practices of *FluMist* Quadrivalent in the US, *FluMist* returned to the US market in the third quarter.

Revenue from other products

$3,400m

16% of total

2017: $4,156m

2016: $5,067m

Product	Disease area	Revenue	Commentary
Infection			
Fluenz Tetra/ *FluMist* Quadrivalent (live attenuated influenza vaccine)	Influenza	↑ $110m, up 41% (44% at CER)	Approved in the US, EU, Canada, Israel and Hong Kong. *FluMist* returned to the US market in the third quarter of 2018, in time for the 2018-2019 influenza season. Daiichi Sankyo holds rights to *Fluenz* Tetra/ *FluMist* Quadrivalent in Japan.
Synagis (palivizumab)	Respiratory syncytial virus (RSV)	↓ $665m, down 3% (3% at CER)	Divested US rights to Sobi. AbbVie holds rights to *Synagis* outside the US.
Neuroscience			
Movantik/ *Moventig* (naloxegol)	Opioid induced constipation	↓ $109m, down 11% (11% at CER)	Licensed from Nektar Therapeutics. Kyowa Hakko Kirin has held rights in the EU since March 2016. Knight Therapeutics Inc. has held rights in Canada and Israel since December 2016. Co-commercialisation in the US with Daiichi Sankyo.
Seroquel IR/ *Seroquel XR* (quetiapine fumarate)	Schizophrenia Bipolar disease	↓ $361m, down 29% (31% at CER)	Luye Pharma holds rights to *Seroquel* and *Seroquel XR* in the UK, China and other international markets. The rights to *Seroquel* and *Seroquel XR* in Japan are partnered with Astellas.
Vimovo (naproxen and esomeprazole)	Osteoarthritic pain	↓ $70m, down 11% (13% at CER)	Licensed from Pozen and divested worldwide rights (ex-US) to Grünenthal in October 2018. Divested US rights to Horizon Pharma Inc. since November 2013.
Gastroenterology			
Losec/ *Prilosec* (omeprazole)	Proton pump inhibitor to treat acid-related diseases	↔ $272m, flat (down 2% at CER)	
Nexium (esomeprazole)	Proton pump inhibitor to treat acid-related diseases	↓ $1,702m, down 13% (14% at CER)	Divested European rights to Grünenthal in October 2018.

Therapy Area Review
Other Disease Areas
continued

Our strategy for Other Disease Areas and 2018 pipeline highlights

Our approach in these other disease areas looks to maximise revenue through externalisation and on-market products, advance the novel product pipeline with partnerships where appropriate, and preserve a stake in the most promising assets.

Full details of our pipeline are given in the Development Pipeline from page 212 and highlights from the progress of our Other Disease Areas pipeline made in 2018 against our KPIs are shown below.

Life-cycle phases – R&D

New molecular entity (NME) Phase II starts/progressions

Product	Disease
AZD9567	Rheumatoid arthritis
MEDI7352	Painful diabetic neuropathy

NME and major life-cycle management (LCM) positive Phase III investment decisions

Product	Disease
None	–

NME and major LCM regional submissions

Product	Disease	Region
None	–	–

Life-cycle phases – approvals

NME and major LCM regional approvals

An additional regional approval was seen with *Nexium* in Japan, which enables and increases patient access to this medicine.

Product	Disease	Region
*Linzess**	Irritable bowel syndrome with constipation	China
Nexium	Paediatric and sachet gastroesophageal disease (GERD)	Japan

* Approved in January 2019.

Discontinued projects

Product	Disease	Reason
Lanabecestat	BACE early Alzheimer's disease	Safety/efficacy
MEDI9314	IL4R atopic dermatitis	Strategic

For more information on the life-cycle of a medicine, see page 9.

2018 review – strategy in action

Infection

Seasonal influenza is a serious public health problem that causes severe illness and death in high-risk populations. In 2018, the US Advisory Committee on Immunization Practices, under the Centers for Disease Control and Prevention, reinstated its recommendation that *FluMist* Quadrivalent (live attenuated influenza vaccine – LAIV) should be used in the US for the 2018-2019 influenza season. The recommendation followed a presentation of positive results from a US study in children between the ages of 2 to <4 years evaluating the shedding and antibody responses of the H1N1 strain in *FluMist* Quadrivalent. The study demonstrated that the new 2017-2018 H1N1 LAIV post-pandemic strain (A/Slovenia) performed significantly better than the 2015-2016 H1N1 LAIV post-pandemic strain (A/Bolivia), which was previously associated with reduced effectiveness. The antibody response induced with the new H1N1 LAIV strain was comparable to earlier data seen with the highly effective H1N1 LAIV strain included in the vaccine before the 2009 influenza pandemic.

In 2018, Public Health England released provisional vaccine effectiveness (VE) data from the recent 2017-2018 influenza season. VE across all vaccine types was low against the circulating A/H3N2 virus, and all influenza manufacturers are continuing to work with public health authorities to optimise protection against influenza. These latest data also demonstrated *Fluenz* Tetra provided good protection against H1N1 post-pandemic and influenza B strains during the 2017-2018 season, further supporting the improvements made in characterising and selecting H1N1 post-pandemic LAIV strains following our recent investigation into reduced effectiveness.

FluMist Quadrivalent/*Fluenz* Tetra 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. We also have an ongoing agreement with the WHO to donate and supply stock at reduced prices in the event of an influenza pandemic.

MEDI8852, an investigational human mAb for the treatment of patients hospitalised with Type A strain influenza, obtained a grant from the US Department of Defense to conduct a Phase I/IIa study in September 2018. It received Fast Track designation from the FDA in March 2016.

Respiratory syncytial virus (RSV) is a common seasonal virus and the most prevalent cause of lower respiratory tract infections (LRTI) among infants and young children. It is the leading cause of hospitalisations and admissions to paediatric intensive care units and leads to nearly 150,000 deaths globally in children under five years of age, with the majority of deaths occurring in developing countries. 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. *Synagis* is approved in more than 80 countries and we continue to work with our worldwide partner, AbbVie, outside the US, to protect vulnerable infants.

In November 2018, we announced the divestment of *Synagis*' US rights to Sobi. Sobi will commercialise *Synagis* in the US and around 130 AstraZeneca employees will transfer to Sobi as part of the transaction. Sobi also has the right to participate in payments from the US profits and losses for MEDI8897.

MEDI8897, an extended half-life RSV mAb being investigated for the prevention of LRTI caused by RSV in infants and young children, is progressing in collaboration with Sanofi. It is being developed for use among a broad population of late pre-term and healthy full-term infants, so that they may only require one dose during an RSV season. In November 2018, we announced that the primary analysis for the pivotal, Phase IIb trial to evaluate the safety and efficacy of MEDI8897 showed that the trial met its primary endpoint. Following these results, in January 2019, the EMA granted MEDI8897 access to its PRIME (PRIority MEdicines) scheme and in February 2019, the FDA granted Breakthrough Therapy designation for MEDI8897.

Neuroscience

In June 2018, we announced with Lilly, the discontinuation of the Phase III clinical trials of lanabecestat, an oral beta secretase cleaving enzyme (BACE) inhibitor, for the treatment of Alzheimer's disease. The decision was based on recommendations by an independent data monitoring committee, which concluded that both the AMARANTH trial, in early Alzheimer's disease, and the DAYBREAK-ALZ trial, in mild Alzheimer's disease dementia, were not likely to meet their primary endpoints upon completion and therefore should be stopped for futility. As a result of this decision, the related AMARANTH extension trial was also discontinued. High-level results in December 2018 of the AMARANTH and DAYBREAK-ALZ trials confirmed no significant disease slowing was observed in any of the Phase III trials, confirming that the action to discontinue the trials was the correct decision.

We also collaborate with Lilly on MEDI1814, an antibody selective for amyloid-beta 1-42 (Aβ1-42) that is currently in Phase I trials as a potential disease-modifying treatment for Alzheimer's disease.

We are progressing MEDI7352 in painful diabetic neuropathy, which is in Phase II and continue our collaboration with Takeda on MEDI1341 for Parkinson's disease, which is in Phase I.

In May 2018, we announced an agreement with Luye Pharma for the sale and licence of the rights in the UK, China and other international markets to *Seroquel* and *Seroquel XR*. We had previously partnered the rights to *Seroquel* and *Seroquel XR* in Japan and Venezuela under prior agreements. *Seroquel*, used primarily to treat schizophrenia and bipolar disease, has lost its compound patent protection globally. The *Seroquel XR* formulation patents have now also expired in the majority of markets.

Autoimmunity and inflammation

In February 2018, six molecules from our early-stage inflammation and autoimmunity programmes were spun out into an independent biotech company, Viela Bio. The new company will focus on developing medicines for severe autoimmune diseases by targeting the underlying causes of each disease. The molecules include inebilizumab, currently in Phase II trial development for the treatment of neuromyelitis optica spectrum disorder, a rare condition that affects the optic nerve and spinal cord in approximately five in 100,000 people.

We announced in August 2018 that anifrolumab, a developmental mAb that inhibits the activity of all type I interferons (IFN), did not meet the primary endpoint in the TULIP 1 Phase III trial in systemic lupus erythematosus (SLE). A full evaluation of the combined TULIP 1 and TULIP 2 data will be conducted to determine next steps for anifrolumab in SLE. The Phase II trials in lupus nephritis and for a subcutaneous route of administration in SLE remain ongoing, as does the long-term extension trial in SLE.

In April 2016, AstraZeneca licensed its US rights to develop and commercialise *Zurampic* and *Duzallo* to Ironwood. In August 2018, Ironwood notified AstraZeneca of its intent to terminate the licence for convenience. In November 2018, Ironwood notified the FDA that it had discontinued the manufacturing of the products and contemporaneously informed AstraZeneca that it is working on withdrawing the NDAs for these products and terminating the FDA required post-marketing study. This process is expected to take several months.

Gastrointestinal

Use of *Nexium* continued to grow in a limited number of markets such as China and Japan in 2018. This growth is expected to continue following additional approvals in China for high-dose treatment of peptic ulcer bleeding and in Japan for paediatric patients from the age of one, with the innovative *Nexium* sachet formulation. The re-examination periods for adult indications/dosage of *Nexium* capsules and *Nexium* sachets have been extended for two years in Japan, until 30 June 2021. This enables the completion of another clinical trial for long-term treatment in the new paediatric population. *Nexium* is subject to generic competition globally, except for Japan.

In October 2018, we announced that we had entered into an agreement with Grünenthal for the rights to *Nexium* in Europe and *Vimovo* worldwide (excluding the US).

In January 2019, Ironwood announced they had received marketing authorisation from the NMPA in China for *Linzess* for the treatment of patients with irritable bowel syndrome with constipation. We entered into a collaboration in China with Ironwood in 2012.

Our products

While this Therapy Area Review concentrates on our key marketed products, many of our other products are crucial to our business in certain countries in Emerging Markets.

For more information on our potential new products and product life-cycle developments, please see the Therapy Area pipeline tables on pages 52, 58, 64 and 68 and the Development Pipeline table from page 212. For information on Patent Expiries of our Key Marketed Products, see from page 217.

Indications for each product described in this Therapy Area Review may vary among countries. Please see local prescribing information for country-specific indications for any particular product.

For those of our products subject to litigation, information about material legal proceedings can be found in Note 29 to the Financial Statements from page 194.

Details of relevant risks are set out in Risk from page 220.

Risk Overview

We face a diverse range of risks and uncertainties. Those risks which have the potential to have a material impact on our business or results of operations are our Principal Risks.

The Board has carried out a robust assessment of the Principal Risks facing the Group, including those that threaten its business model, future performance, solvency or liquidity. The table overleaf provides insight into the ongoing Principal Risks, outlining why effective management of these risks is important and relevant to the business, how we are managing them and which risks are rising, falling or have remained static during the past 12 months.

Our approach to risk management is designed to encourage clear decision making on which risks we take and how we manage these risks. Fundamental to this process is a sound understanding of every risk's potential strategic, commercial, financial, compliance, legal and reputational implications.

Further information on our key risk management and assurance processes can be found in Risk from pages 220 to 230 which also includes a description of circumstances under which principal and other risks and uncertainties might arise in the course of our business and their potential impact.

Progress in the delivery of Group-wide restructuring initiatives has been sufficient for the Board to determine that the risk 'Delivery of Gains from Productivity Initiatives' (previously listed as a Principal Risk) is no longer a Principal Risk. The Board will, however, continue to monitor strategic initiatives and their impact on employee engagement.

Managing risk

We work to ensure that we have effective risk management processes in place to support the delivery of our strategic priorities. This enables us to meet the expectations of our stakeholders and upholds our Values. We monitor our business activities and external and internal environments for new, emerging and changing risks to ensure that these are managed appropriately. The Board believes that existing processes provide it with adequate information on the risks and uncertainties we face. Details of these risks and the potential impacts on our business are contained on pages 220 to 230.

Risk management embedded in business processes

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

The Board defines the Group's risk appetite, enabling 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. Our risk management approach is aligned to our strategy and business planning processes. We cross-check financial risks and opportunities identified through the business planning process and integrate our findings into the overall risk management reporting. Line managers are accountable for identifying and managing risks and for delivering business objectives in accordance with the Group's risk appetite.

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. Every year, we map these risks to AstraZeneca's risk 'taxonomy'. This process provides a Group-wide assessment for the Board, Audit Committee and SET. 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. Supporting tools are in place to assist risk leaders and managers in managing, monitoring and planning for risk, and we continue to work on developing our risk management standards and guidelines. Global Compliance, Finance and Internal Audit Services support SET by

advising on policy and standard setting, monitoring and auditing, and communication and training, as well as reporting on the adequacy of line management processes as they apply to risk management.

We have a business resilience framework which governs our ability to prevent or quickly adapt to situations while maintaining continuous business operations and safeguarding our people, processes and reputation. Within this we have business continuity plans to address situations in which specific risks have the potential to severely impact our business. These plans include training and crisis simulation activities for business managers.

More information about our Global Compliance function and the Code of Ethics can be found in the Corporate Governance Report from page 91.

Viability statement

In accordance with provision C.2.2 of the 2016 UK Corporate Governance Code, the Board has determined that a three-year period to 31 December 2021 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 downside reflecting some of the Principal Risks detailed on pages 72 to 73.

- **Scenario 1** Principal Risk: demand, pricing, market access and competitive pressures; quality and execution of commercial strategies; secure and protect product IP. Lower than anticipated growth rates, adverse impact of generic competition and greater than anticipated pressure on pricing across multiple products and markets.
- **Scenario 2** Principal Risk: delivery of pipeline and new products. Assumes no launches of new products.
- **Scenario 3** Principal Risk: maintain supply of compliant, quality product. Regulatory observation or other equipment failure results in a 12-month outage at one of our key manufacturing sites.
- **Scenario 4** Principal Risk: achieve strategic plans and meet targets and expectations. Income from divestment of core assets reinvested into core therapy areas and new products reduced by half.
- **Scenario 5** Principal Risk: externally driven demand, pricing, access and competitive pressures. Failure to establish EU-based regulatory testing and release capability for a product leads to inability to supply impacted products into the EU following a 'no deal Brexit' outcome.
- **Scenario 6** Principal Risk: meet regulatory and ethical expectations on commercial practices including bribery and corruption and scientific exchanges. Legal, regulatory non-compliance or cyber incident causes reputational damage in a key market resulting in a significant and ongoing reduction in market share.

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 above, the Group is able to rely on its committed credit facilities, 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.

Brexit

On 23 June 2016, the UK held a referendum on the UK's continuing membership of the EU, the outcome of which was a decision for the UK to leave the EU (Brexit). The progress of current negotiations between the UK Government and the EU and the ratification of the outcome of those negotiations by the UK and EU parliaments will likely determine the future terms of the UK's relationship with the EU, as well as to what extent the UK will be able to continue to benefit from the EU's single market and other arrangements. Until the Brexit negotiation and parliamentary ratification processes are completed, it is difficult to anticipate the potential impact on AstraZeneca's market share, sales, profitability and results of operations. The Group operates from a global footprint and retains flexibility to adapt to changing circumstances. The uncertainty during and after the period of negotiation is also expected to increase volatility and may have an economic impact, particularly in the UK and Eurozone. The Group has responded by engaging proactively with key external stakeholders and establishing a cross-functional internal steering and implementation committee to understand, assess, plan and implement operational actions that may be required. Many of these actions are being implemented based on assumptions rather than defined positions so that the Group is able to mitigate the risks arising from variable external outcomes. The Group has adopted a base case planning assumption of hard Brexit/No deal since the time of the referendum and has taken appropriate actions to date based on those assumptions. Currently, many actions have been implemented or are in process including, but not limited to: engagement with government and regulators; duplication of release testing and procedures for products for the EU27 and the UK markets; transfer of regulatory licences, re-design of packaging and labelling, additional inventory builds and changes to logistics plans and shipping routes; customs and duties set up for introduction or amendment of existing tariffs or processes; associated IT systems reconfigurations; and banking arrangement changes. The Board reviews the potential impact of Brexit regularly as an integral part of its Principal Risks (as outlined overleaf) rather than as a standalone risk. The Board most recently reviewed the Group's Brexit readiness plans at its meeting in December 2018 and continues to assess its impact.

Risk Overview
continued

Principal Risks

Strategy key

- Achieve Scientific Leadership
- Return to Growth
- Be a Great Place to Work
- Achieve Group Financial Targets

Trend key

- Increasing risk
- Decreasing risk
- Unchanged

Risk category and Principal Risks	Context/potential impact	Management actions	Trend versus prior year
Product pipeline and intellectual property			
Delivery of pipeline and new products	The development of any pharmaceutical product candidate is a complex, risky and lengthy process involving significant financial, R&D and other resources. A project may fail or be delayed at any stage of the process due to a number of factors, which could reduce our long-term growth, revenue and profit	> Prioritise and accelerate our pipeline > Strengthen pipeline through acquisitions, licensing and collaborations > Focus on innovative science in three main therapy areas	Unchanged
Meet quality, regulatory and ethical drug approval and disclosure requirements	Our pharmaceutical products and commercialisation processes are subject to extensive regulation. Delays in regulatory reviews and approvals impact patients and market access, and can materially affect our business or financial results	> 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 process, timelines and guidance	Unchanged
Secure and protect product IP	Discovering and developing medicines requires a significant investment of resources. For this to be a viable investment, new medicines must be safeguarded from being copied for a reasonable amount of time. If we are not successful in obtaining, maintaining, defending or enforcing our IP rights, our revenues could be materially adversely affected Third parties may allege infringement of their IP, and may seek injunctions and/or damages, which, if ultimately awarded, could adversely impact our commercial and financial performance	> Active management of IP rights and IP litigation	Unchanged
Commercialisation			
Externally driven demand, pricing, access and competitive pressures	Operating in over 100 countries, we are subject to political, socioeconomic and financial factors both globally and in individual countries. There can be additional pressure from governments and other healthcare payers on medicine prices and sales in response to recessionary pressures, reducing our revenue, profits and cash flow	> Focus on Growth Platforms > Demonstrating value of medicines/health economics > Global footprint > Diversified portfolio	Increasing risk Global economic and political conditions placing downward pressure on healthcare pricing and spending, and therefore on revenue
Quality and execution of commercial strategies	If commercialisation of a product does not succeed as anticipated, or its rate of sales growth is slower than anticipated, there is a risk that we may not be able to fully recoup the costs in launching it	> Focus on Growth Platforms > Accelerate and risk share through business development and strategic collaborations and alliances	Increasing risk The number of new product launches is increasing. Maximising the commercial potential of these new products underpins the success of our strategy and the delivery of our short- and medium-term targets
Supply chain and business execution			
Maintain supply of compliant, quality product	Delays or interruptions in supply can lead to recalls, product shortages, regulatory action, reputational harm and lost sales	> Establishment of new manufacturing facilities, creating capacity and technical capability to support new product launches, particularly biologics > Business continuity and resilience initiatives, disaster and data recovery and emergency response plans > Contingency plans including dual sourcing, multiple suppliers and stock levels > Quality management systems	Unchanged

Risk category and Principal Risks	Context/potential impact	Management actions	Trend versus prior year
Supply chain and business execution *continued*			
Information technology, data security and privacy	Significant disruption to our IT systems, cybersecurity incidents including breaches of data security, or data privacy failure, could harm our reputation and materially affect our financial condition or results of operations. This could lead to regulatory penalties or non-compliance with laws and regulations	> Cybersecurity framework and dashboard > Privacy office oversees compliance with data privacy legislation > Disaster and data recovery plans > Strategies to secure critical systems and processes > Regular cybersecurity and privacy training for employees	Growing multi-faceted cyber threat. Tougher legislative environment governs data protection following introduction of new EU GDPR legislation
Attract, develop, engage and retain talented and capable employees at all levels	Failure to attract and retain highly skilled personnel may weaken our succession plans for critical positions in the medium term. Employee uncertainty as a result of, for example, Brexit or organisational change may result in a lower level of employee engagement which could impact productivity and turnover. Both could adversely affect the achievement of our strategic objectives	> Targeted recruitment and retention strategies deployed > Identification and active support of staff potentially impacted by Brexit > Development of our employees > Evolve our culture > Focus on simplification	
Legal, regulatory and compliance			
Safety and efficacy of marketed products	Patient safety is very important to us and we strive to minimise the risks and maximise the benefits of our medicines. Failure to do this could adversely impact our reputation, our business and the results of operations, and could lead to product liability claims	> 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	The number of new products in our marketed portfolio is growing and is anticipated to increase further as our pipeline develops. Our ability to accurately assess the safety and efficacy of new products is inherently limited due to relatively short periods of product testing and relatively small clinical study patient samples
Defence of product, pricing and practices litigation	Investigations or legal proceedings could be costly, divert management attention or damage our reputation and demand for our products. Unfavourable resolutions could subject us to criminal liability, fines, penalties or other monetary or non-monetary remedies, adversely affecting our financial results	> Combined internal and external counsel management	
Meet regulatory and ethical expectations on commercial practices, including bribery and corruption, and scientific exchanges	Any failure to comply with applicable laws, rules and regulations, including bribery and corruption legislation, may result in civil and/or criminal legal proceedings and/or regulatory sanctions, fines or penalties, impacting financial results	> Strong ethical and compliance culture > Established compliance framework in place including annual Code of Ethics training for all employees > Focus on due diligence and oversight of third-party engagements	Increasing government and regulatory scrutiny and evolving compliance challenges as complexity of business relationships increases
Economic and financial			
Achieve strategic plans and meet targets and expectations	Failure to successfully implement our business strategy may frustrate the achievement of our financial or other targets or expectations. This failure could, in turn, damage our reputation and materially affect our business, financial position or results of operations	> Focus on Growth Platforms and innovative science in three main therapy areas > Strengthen pipeline through acquisitions, licensing and collaborations > Appropriate capital structure and balance sheet > Portfolio-driven decision making process governed by senior executive-led committees	Increasing challenge to balance long- and short-term investments as we navigate a period of loss of exclusivity on key brands while seeking to maximise the commercial potential of new product launches

Financial Review

2018 marked our return to Product Sales growth with strong performance from Growth Platforms and New Medicines more than offsetting the continued impact from patent expiries.

"Product sales grew 4% to $21.0 billion driven by outstanding performance of our Oncology medicines; Emerging Markets sales continued to grow; and New CVRM grew by 12% (CER:12%)."

In 2018, Product Sales grew 4% to $21.0 billion driven by outstanding performance of our Oncology medicines, which grew 50% (CER: 49%), led by *Tagrisso*, *Lynparza* and *Imfinzi*. Emerging Markets sales continued to grow, especially in China, and it is now our largest region by total Product Sales. New CVRM grew 12% (CER:12%) to $4.0 billion with both *Farxiga* and *Brilinta* delivering sales over $1.3 billion annually. Total Revenue was $22.1 billion, a 2% decline led by lower Externalisation Revenue of $1.0 billion, a 55% reduction from 2017. In 2018, $0.8 billion of Externalisation Revenue was received as part of our collaboration with MSD on *Lynparza* and selumetinib.

Reported R&D expenses increased by 3% as a result of higher intangible asset impairment charges. Core R&D expenses declined by 3% with focus on resource prioritisation, productivity improvements and improved development processes all delivering cost reductions whilst maintaining high levels of activity. Reported SG&A expenses declined by 2% (CER: 3%) primarily due to the decrease in fair value of contingent consideration liabilities. Core SG&A expenses increased by 10% (CER: 9%) due to commercial and medical affairs support for New Medicines and to drive growth in China.

Reported other operating income was $2.5 billion in the year and included income from various disposal transactions, including the sale of the rights to *Nexium* in Europe to Grünenthal and the sale of the rights to *Seroquel* and *Seroquel XR* in UK, China and other international region markets to Luye Pharma.

The Reported tax rate of (3)% and Core tax rate of 11% for the year benefitted from a favourable net adjustment of $0.3 billion to deferred tax, reflecting the recently announced reductions to the Dutch and Swedish income tax rate. Additionally, there was a $0.2 billion benefit to the Reported and Core tax rates resulting from a reduction in tax provisions.

Reported operating profit declined by 8% (CER: 7%) to $3.4 billion and Core operating profit decreased by 17% (CER: 17%) to $5.7 billion in the year. Reported EPS was $1.70 and Core EPS was $3.46.

We generated a net cash inflow from operating activities of $2.6 billion in the year and we maintained a strong, investment-grade credit rating. During the year, we issued new bonds totalling $3.0 billion and repaid $1.4 billion of maturing bonds. We ended the year with total gross debt of $19.1 billion, $6.1 billion of cash, investments and derivatives, with net debt of $13.0 billion.

Marc Dunoyer
Chief Financial Officer

The purpose of this Financial Review is to provide a balanced and comprehensive analysis of the financial performance of the business during 2018, the cash flow and liquidity position of the business, the financial position as at the end of the year, and the main business factors and trends which could affect the future financial performance of the business.

Business background and results overview

The business background is covered in the Marketplace section from page 11, the Therapy Area Review from page 50 and describes in detail the developments in 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, such as:

- The risk of competition from generics following loss of patent protection or patent expiry of one of our products, or an 'at risk' launch by a competitor, or the launch of a competitive product in the same class as one of our products, with potential adverse effects on sales volumes and prices. Details of patent expiries for our key marketed products are included in Patent Expiries of Key Marketed Products from page 217.
- The adverse impact on pharmaceutical prices as a result of the macroeconomic and regulatory environment. For instance, in the US, political leadership has continued to consider drug pricing controls and transparency measures at national and local levels. In other parts of the world, governments have continued to implement and expand price control measures, including reference pricing.
- The timings of new product launches, which can be influenced by national regulators, the speed to market relative to competitor products and the risk that such new products do not succeed as anticipated, together with the rate of sales growth and costs following new product launches.
- Currency fluctuations. Our functional and reporting currency is the US dollar, but we have substantial exposures to other currencies, in particular the Chinese renminbi, euro, Japanese yen, pound sterling and Swedish krona.
- Macro factors such as greater demand from an ageing population and increasing requirements of Emerging Markets.
- Supply chain risks including the failure of third parties to supply timely quality products, such as raw materials, and the risk of catastrophic failure of critical internal processes leading to an inability to research, manufacture or supply products to patients.

Further details of the risks faced by the business are given in Risk Overview from page 70 and Risk from page 220.

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.

The most significant features of our financial results in 2018 are:

- Total Revenue down 2% to $22,090 million (CER: 2%). Product Sales were up 4% (CER: 4%) reflecting the performance of New Medicines and the ongoing growth in Emerging Markets.
  - Oncology sales increased by 50% (CER: 49%) with *Tagrisso* up 95% (CER: 93%) to $1,860 million, *Imfinzi* sales reaching $633 million arising primarily in the US and *Lynparza* sales of $647 million representing growth of 118% (CER: 116%), driven by expanded use in the treatment of ovarian cancer and first approval in the treatment of breast cancer.
  - New CVRM sales increased by 12% (CER: 12%) to $4,004 million and included *Farxiga* sales of $1,391 million with growth of 30% (CER: 30%) including a sales increase of 45% (CER: 52%) in Emerging Markets and *Brilinta* sales of $1,321 million representing growth of 22% (CER: 21%).
  - Respiratory was up 4% (CER: 3%) reflecting growth for *Pulmicort* and the success of the 2017 launch of *Fasenra*, offset by a continued fall in US Product Sales of *Symbicort*.
  - Emerging Markets grew by 12% (CER: 13%) to $6,891 million, making it the Group's largest region by Product Sales for the first time. China sales increased by 28% (CER: 25%) to $3,795 million. Oncology sales in China were up 44% (CER: 41%) partly underpinned by the 2017 launch of *Tagrisso*.
- Reported operating profit was down 8% (CER: 7%) to $3,387 million (2017: $3,677 million) driven by declines in Total Revenue and the increase to Reported R&D expenses.
- Core operating profit was also down 17% (CER: 17%) to $5,672 million (2017: $6,855 million). The difference between Core and Reported operating profit is largely driven by the impact of non-core amortisation and impairment of intangibles. The decrease from prior year was driven by a credit to core adjustments from the release of legal provisions.

- Reported operating margin of 15% of Total Revenue was one percentage point down on 2017 (CER: one percentage point). Core operating margin was 26% of Total Revenue (2017: 31%).
- Reported EPS was down 28% (CER: 29%) to $1.70. Core EPS was also down 19% (CER: 19%) to $3.46.
- Dividends paid amounted to $3,484 million (2017: $3,519 million).

Measuring performance

The following measures are referred to in this Financial Review when reporting on our performance both in absolute terms, but more often in comparison to earlier years:

- Reported performance: 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, as reflected in our Group Financial Statements prepared in accordance with IFRSs as adopted by the EU and as issued by the IASB (IFRS).
- Non-GAAP financial measures: Core financial measures, EBITDA, Net debt, Ongoing Externalisation Revenue and Initial Externalisation Revenue are non-GAAP financial measures because they cannot be derived directly from the Group Consolidated Financial Statements. Management believes that these non-GAAP financial measures, when provided in combination with Reported results, will provide investors with helpful supplementary information to better understand the financial performance and position of the Group on a comparable basis from period to period. These non-GAAP financial measures are not a substitute for, or superior to, financial measures prepared in accordance with GAAP.
- Core financial measures are adjusted to exclude certain significant items, such as:
  - amortisation and impairment of intangible assets, including impairment reversals but excluding any charges relating to IT assets
  - charges and provisions related to our global restructuring programmes, which include charges that relate to the impact of our global restructuring programmes on our capitalised manufacturing facilities and IT assets
  - other specified items, principally comprising acquisition-related costs and credits, which include fair value adjustments and the imputed finance charge relating to contingent consideration on business combinations, legal settlements and foreign-exchange gains and losses on certain non-structural intra-group loans. In determining the adjustments to arrive at the Core result, we use a set of established principles relating to the nature and materiality of individual items or groups of items, excluding, for example, events which (i) are outside the normal course of business, (ii) are incurred in a pattern that is unrelated to the trends in the underlying financial performance of our ongoing business, or (iii) are 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 2018 Reconciliation of Reported results to Core results table on the opposite page for a reconciliation of Reported to Core performance, as well as further details of the adjustments.
- EBITDA is defined as 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. Reference should be made to the Reconciliation of Reported Profit Before Tax to EBITDA included on page 78 of this Annual Report.
- Net debt is defined as interest-bearing loans and borrowings net of cash and cash equivalents, other investments and net derivative financial instruments. Reference should be made to the Net debt reconciliation table included on page 82 of this Annual Report.
- Ongoing Externalisation Revenue is defined as Externalisation Revenue excluding Initial Externalisation Revenue (which is defined as Externalisation Revenue that is recognised at the point in time control is transferred). Ongoing Externalisation Revenue comprises, among other items, milestones, profit sharing and royalties. Reference should be made to the Externalisation Revenue table on page 78 of this Annual Report.
- Constant exchange rate (CER) growth rates: These are also non-GAAP measures. These measures remove the effects of currency movements by retranslating the current year's performance at the previous year's average exchange rates and adjusting for other exchange effects, including hedging. A reconciliation of the Reported results adjusted for the impact of currency movements is provided in the 2018 Reported operating profit table on the page opposite.
- Gross and operating margin percentages: These measures set out the progression of key performance margins and illustrate the overall quality of the business.
- Prescription volumes and trends for key products: These measures can represent the real business growth and the progress of individual products better and more immediately than invoiced sales.

We strongly encourage readers of the 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.

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 into the impact of 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.

We believe that disclosing non-GAAP financial and growth measures, in addition to our Reported financial information, enhances 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 financial measures that illustrate clearly, on a year-on-year or period-by-period basis, the impact on our performance caused by factors such as changes in revenues and expenses driven by volume, prices and cost levels relative to such prior years or periods.

Readers of the Annual Report should note that Core results cannot be achieved without incurring the costs that the Core measures exclude such as:

- Amortisation of intangible assets which generally arise from business combinations and individual licence acquisitions. We adjust for these charges because their pattern of recognition is largely uncorrelated with the underlying performance of the business. However, a significant part of our revenues could not be generated without owning the associated acquired intangible assets.
- Charges and provisions related to our global restructuring programmes which can take place over a significant period of time, given the long life-cycle of our business. 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. However, our Core results do reflect the benefits of such restructuring initiatives.

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

As shown in the 2018 Reconciliation of Reported results to Core results table to the right, our reconciliation of Reported financial information to Core financial 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 financial 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 financial measures merely allow investors to differentiate between different kinds of costs and they should not be used in isolation. Readers should also refer to our Reported financial information in the 2018 Reported operating profit table and our reconciliation of Core financial measures to Reported financial information in the Reconciliation of Reported results to Core results table, both to the right, for our discussion of comparative Actual 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.

Results of operations – summary analysis of year ended 31 December 2018

2018 Reported operating profit

	2018			2017	Percentage of Total Revenue		Reported 2018 compared with Reported 2017	
	Reported $m	CER growth $m	Growth due to exchange effects $m	Reported $m	Reported 2018 %	Reported 2017 %	Actual growth %	CER growth[1] %
Product Sales	**21,049**	**733**	**164**	20,152			**4**	**4**
Externalisation Revenue	**1,041**	**(1,274)**	**2**	2,313			**(55)**	**(55)**
Total Revenue	**22,090**	**(541)**	**166**	22,465			**(2)**	**(2)**
Cost of sales	**(4,936)**	**(542)**	**(76)**	(4,318)	**(22.3)**	(19.2)	**14**	**13**
Gross profit	**17,154**	**(1,083)**	**90**	18,147	**77.7**	80.8	**(5)**	**(6)**
Distribution expenses	**(331)**	**(20)**	**(1)**	(310)	**(1.5)**	(1.4)	**7**	**6**
Research and development expenses	**(5,932)**	**(151)**	**(24)**	(5,757)	**(26.9)**	(25.6)	**3**	**3**
Selling, general and administrative expenses	**(10,031)**	**310**	**(108)**	(10,233)	**(45.4)**	(45.5)	**(2)**	**(3)**
Other operating income and expense	**2,527**	**697**	**–**	1,830	**11.4**	8.1	**38**	**38**
Operating profit	**3,387**	**(247)**	**(43)**	3,677	**15.3**	16.4	**(8)**	**(7)**
Net finance expense	**(1,281)**	**(27)**	**141**	(1,395)				
Share of after tax losses of joint ventures and associates	**(113)**	**(58)**	**–**	(55)				
Profit before tax	**1,993**	**(332)**	**98**	2,227			**(10)**	**(14)**
Taxation	**57**	**(574)**	**(10)**	641				
Profit for the period	**2,050**	**(906)**	**88**	2,868				
Basic earnings per share ($)	**1.70**			2.37			**(28)**	**(29)**

[1] As detailed on page 76, CER growth is calculated using prior year actual results adjusted for certain exchange effects including hedging.

2018 Reconciliation of Reported results to Core results

	2018 Reported $m	Restructuring costs $m	Intangible amortisation and impairments $m	Diabetes Alliance[4] $m	Other[3] $m	2018 Core[1] $m	Core 2018 compared with Core 2017[1] Actual growth %	Core 2018 compared with Core 2017[1] CER growth %
Gross profit	**17,154**	**432**	**187**	**–**	**–**	**17,773**	**(4)**	**(4)**
Product Sales gross margin %[2]	***76.6***					***79.5***		
Distribution expenses	**(331)**	**–**	**–**	**–**	**–**	**(331)**	**7**	**6**
Research and development expenses	**(5,932)**	**94**	**572**	**–**	**–**	**(5,266)**	**(3)**	**(3)**
Selling, general and administrative expenses	**(10,031)**	**181**	**1,582**	**(60)**	**(323)**	**(8,651)**	**10**	**9**
Other operating income and expense	**2,527**	**(10)**	**4**	**–**	**(374)**	**2,147**	**10**	**10**
Operating profit	**3,387**	**697**	**2,345**	**(60)**	**(697)**	**5,672**	**(17)**	**(17)**
Operating margin as a % of Total Revenue	***15.3***					***25.7***		
Net finance expense	**(1,281)**	**–**	**–**	**337**	**208**	**(736)**		
Taxation	**57**	**(146)**	**(487)**	**(73)**	**109**	**(540)**		
Basic earnings per share ($)	**1.70**	**0.43**	**1.47**	**0.16**	**(0.30)**	**3.46**	**(19)**	**(19)**

[1] Each of the measures in the Core column in the above table is a non-GAAP measure.
[2] Gross margin as a % of Product Sales reflects gross profit derived from Product Sales, divided by Product Sales.
[3] See page 81 for further details of other adjustments.
[4] Relating to the 2014 acquisition of BMS's share of Global Diabetes Alliance.

Total Revenue

Total Revenue for the year was down 2% (CER: 2%) to $22,090 million, comprising Product Sales of $21,049 million up 4% (CER: 4%) and Externalisation Revenue of $1,041 million, a decrease of 55% (CER: 55%).

By Geography

Product Sales in Emerging Markets continued to increase with growth of 12% (CER: 13%) to $6,891 million in 2018, including growth in China of 28% (CER: 25%) to $3,795 million. Sales of *Tagrisso* in Emerging Markets increased by $212 million in the year to $347 million, an increase of 157% (CER: 159%). US Product Sales were up 11% (CER: 11%) to $6,876 million, reflecting the success of the new Oncology medicines and the strong performance of *Fasenra*. In Europe, Product Sales declined by 6% (CER: 10%) to $4,459 million, reflecting the continued impact from generic competition on *Crestor*. Established Markets sales declined 8% (CER: 9%) to $2,823 million with sales in Japan down 9% (CER: 11%) to $2,004 million largely driven by the decline in *Crestor* sales, which declined by 66% (CER: 67%) to $166 million in the year as the impact of generic competition from 2017 took effect.

By Product

Our largest selling products in 2018 were *Symbicort* ($2,561 million), *Tagrisso* ($1,860 million), *Nexium* ($1,702 million) and *Crestor* ($1,433 million). Global sales of *Symbicort* declined by 9% (CER: 10%) with 13% growth in Emerging Markets (CER: 14%) being more than offset by declines in US and Europe due to the impact of a competitive environment on net pricing. *Tagrisso* sales grew by 95% (CER: 93%) reflecting strong market penetration following 2017 approvals in US and China. *Nexium* sales were down 13% (CER: 14%) reflecting continued lower demand as a result of the loss of exclusivity from 2015, however the decline in sales has been slower than expected. *Crestor* sales declined by 39% (CER: 40%) as the impact of generic competition continued to take effect. There were also continued strong performances in the year from *Farxiga* and *Brilinta*, with *Farxiga* growing by 30% (CER: 30%) and *Brilinta* by 22% (CER: 21%).

Reconciliation of Reported Profit Before Tax to EBITDA

	2018 $m	2017 $m	**Actual growth %**	**CER growth %**
Reported profit before tax	**1,993**	2,227	**(10)**	**(14)**
Net finance expense	**1,281**	1,395	**(8)**	**2**
Share of after tax losses of joint ventures and associates	**113**	55	**104**	**104**
Depreciation, Amortisation and Impairment	**3,753**	3,036	**24**	**24**
EBITDA	**7,140**	6,713	**6**	**7**

Growth Platforms

	2018 Product Sales $m	2017 Product Sales $m	**Actual growth %**	**CER growth %**
Emerging Markets	**6,891**	6,149	**12**	**13**
Respiratory	**4,911**	4,706	**4**	**3**
New CVRM[1]	**4,004**	3,567	**12**	**12**
Japan	**2,004**	2,208	**(9)**	**(11)**
Oncology[2]	**6,028**	4,024	**50**	**49**
Total Growth Platform Product Sales[3]	**18,464**	16,396	**13**	**12**

[1] New Cardiovascular, Renal & Metabolic Diseases, incorporating *Brilinta* and Diabetes.
[2] Oncology comprises total Oncology Product Sales.
[3] Certain Product Sales are included in more than one Growth Platform. Total Growth Platform sales represents the net total sales for all Growth Platforms.

Externalisation Revenue

	2018 $m	2017 $m
Externalisation Revenue – Initial		
Crestor (Almirall)	**61**	–
Lynparza/selumetinib (MSD)	**–**	997
Zoladex (TerSera)	**–**	250
MEDI8897 (Sanofi)	**–**	127
Other	**51**	118
Total Initial Externalisation Revenue	**112**	1,492
Ongoing Externalisation Revenue		
Lynparza/selumetinib (MSD) – option exercised	**400**	250
Lynparza/selumetinib (MSD) – milestone	**390**	–
Zoladex (TerSera) – milestone	**35**	–
Global non-US anaesthetics portfolio (Aspen) – milestone	**–**	150
brodalumab (Valeant) – milestone	**–**	130
AZD3293 (Lilly) – milestone	**–**	50
Royalties	**49**	108
Other	**55**	133
Total Ongoing Externalisation Revenue	**929**	821
Total Externalisation Revenue	**1,041**	2,313

Growth Platforms

In the periods under review, our Growth Platforms included products in our three main therapy areas, and a focus on the Emerging Markets and Japan. Our Growth Platforms grew by 13% (CER: 12%), representing 84% of Total Revenue after removing the effect of certain Product Sales which are included in more than one Growth Platform.

Product Sales in Emerging Markets grew by 12% compared to 2017 (CER: 13%) to $6,891 million partly driven by a strong performance from *Tagrisso* with growth of 157% (CER: 159%). Product Sales in China increased by 28% in 2018 (CER: 25%), representing 55% of Emerging Markets Product Sales in the year.

Product Sales of Respiratory medicines increased by 4% (CER: 3%), with the impact of pricing pressure in the US for *Symbicort* being more than offset by a strong performance by Respiratory in Emerging Markets and higher demand for *Pulmicort* in China.

New CVRM grew by 12% (CER: 12%) with revenue of $4,004 million (2017: $3,567 million). Within New CVRM, sales of *Brilinta* in the year were $1,321 million, an increase of 22% (CER: 21%). *Brilinta* sales in the US were up 16% to $588 million, as it remained the branded oral anti-platelet market leader.

Our Diabetes Product Sales were 8% higher than in 2017, driven primarily by growth of 30% on *Farxiga* (CER: 30%) with global sales of $1,391 million as it continued to be our largest-selling Diabetes medicine and SGLT-2 class growth was supported by growing evidence around cardiovascular benefits, including data from the CVD-REAL study that was published in March 2017.

Japan Product Sales declined by 9% (CER: 11%) with growth on *Tagrisso* and *Forxiga*, outweighed by the impact of the entry of generic competition to *Crestor* in 2017.

Product Sales of Oncology medicines increased to $6,028 million in 2018 (2017: $4,024 million), $1,860 million of which came from *Tagrisso* (2017: $955 million), which continues to be our leading medicine for the treatment of lung cancer and received regulatory approval in more than 55 countries by the end of 2018.

Externalisation Revenue

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

- In November 2018, AstraZeneca entered into an agreement with Swedish Orphan Biovitrum AB (Sobi) to sell the US rights to *Synagis*. Under the agreement Sobi will also have the right to participate in AstraZeneca's share of US profits and losses related to MEDI8897. The deal was completed on 23 January 2019 and AstraZeneca received an upfront consideration of $1.6 billion, including cash of $966 million and ordinary shares in Sobi with an initial market value of $600 million. This income was recorded in 2019. AstraZeneca will also receive up to $470 million in sales-related payments for *Synagis*, $175 million following the submission of the Biologics License Application (BLA) for MEDI8897, potential net payments of $110 million for other MEDI8897 profit-related milestones and $60 million in non-contingent payments for MEDI8897 during the period from 2019 to 2021.
- In December 2017, AstraZeneca entered into an agreement effective January 2018 with Almirall, under which Almirall is granted an exclusive and perpetual licence to distribute and undertake certain manufacturing activities related to *Crestor* and *Provisacor* in Spain. Almirall made an upfront payment of €51 million on completion of the deal and will pay additional sales-related milestones of up to €55 million plus a royalty for ten years.
- 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. Under the collaboration, the companies will develop and commercialise *Lynparza* jointly, both as monotherapy and in combination with other potential medicines. AstraZeneca and MSD will also jointly develop and commercialise AstraZeneca's selumetinib, an oral, potent, selective inhibitor of MEK, part of the mitogen-activated protein kinase (MAPK) pathway, currently being developed for multiple indications including thyroid cancer. Independently, AstraZeneca and MSD will develop and commercialise *Lynparza* in combination with their respective PD-L1 and PD-1 medicines, *Imfinzi* and *Keytruda*. Under the terms of the agreement, the two companies will share the development and commercialisation costs for *Lynparza* and selumetinib monotherapy and non-PD-L1/PD-1 combination therapy opportunities. Gross profits from *Lynparza* and selumetinib Product Sales generated through monotherapies or combination therapies will be shared equally. MSD will fund all development and commercialisation costs of *Keytruda* in combination with *Lynparza* or selumetinib. AstraZeneca will fund all development and commercialisation costs of *Imfinzi* in combination with *Lynparza* or selumetinib. AstraZeneca will continue to manufacture *Lynparza* and selumetinib. 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 Externalisation Revenue on deal completion in 2017, with the remaining $0.6 billion deferred to the balance sheet. AstraZeneca will book all Product Sales of *Lynparza* and selumetinib; gross profits due to MSD under the collaboration will be recorded under Cost of Sales.
- In November 2017, MSD exercised the first licence option resulting in Externalisation Revenue of $250 million.
- In January 2018, the FDA expanded the approved use of *Lynparza* to include the treatment of patients with certain types of breast cancer. The approval triggered a $70 million milestone payment from MSD to AstraZeneca.
- In June 2018, net sales of *Lynparza* reached $250 million cumulative sales threshold, triggering a sales-related milestone of $100 million to fall due to AstraZeneca.
- In November 2018, MSD exercised the second licence option resulting in Externalisation Revenue of $400 million. In addition to the exercise of this option, net sales of *Lynparza* reached the $500 million cumulative sales threshold, triggering a sales-related milestone of $150 million to fall due to AstraZeneca.
- In December 2018, AstraZeneca was notified of an FDA approval of *Lynparza*, which triggered the SOLO-1 $70 million milestone payment to AstraZeneca.
- In March 2017, AstraZeneca announced an agreement to develop and commercialise MEDI8897 jointly with Sanofi. Under the terms of the global agreement, Sanofi made an upfront payment of €120 million and will pay up to €495 million upon achievement of certain development and sales-related milestones. All costs and profits are shared equally. The US element of this collaboration is the subject of a participation agreement with Sobi, entered into in November 2018 and effective 23 January 2019.

- 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 through milestones totalling up to $70 million, as well as recurring quarterly sales-based payments at mid-teen percent 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. In December 2018, TerSera paid a sales-related milestone of $35 million to AstraZeneca.
- In October 2016, the Group announced an agreement with Aralez for the rights to the branded and authorised generic (marketed by Par Pharmaceuticals) for *Toprol-XL* (metoprolol succinate) in the US. Aralez paid $175 million upon completion of the transaction. Aralez will also pay up to $48 million in milestone and sales-related payments, as well as mid-teen percentage royalties on Product Sales. AstraZeneca continues to manufacture and supply *Toprol-XL* and the authorised generic medicine to Aralez. In May 2018, Aralez announced a change in strategic direction and the closure of their US commercial operations and this was followed shortly afterwards by an announcement that they had formally moved in bankruptcy proceedings. A provision of $14 million has been recorded for overdue receivables.
- In June 2016, AstraZeneca announced that it had entered into a commercialisation agreement with Aspen for rights to its global anaesthetics portfolio outside the US. The agreement covers seven established medicines – *Diprivan*, *EMLA* and five local anaesthetics (*Xylocaine*, *Marcaine*, *Naropin*, *Carbocaine* and *Citanest*). Under the terms of the agreement, Aspen acquired the commercialisation rights for an upfront consideration of $520 million. In July 2017, Aspen achieved the first Product Sales related payment milestone triggering a payment to AstraZeneca of $150 million. In September 2017, AstraZeneca announced that it had entered into an agreement with Aspen, under which Aspen acquired the residual rights to the seven established anaesthetics medicines. This new agreement completed in October 2017 and income under this arrangement is now recorded in Other operating income and expense, in line with our definition of Externalisation Revenue in the Accounting Policy note on page 155.
- In February 2016, the Group entered into a licensing agreement with CMS for the commercialisation rights in China to *Plendil* (felodipine). Under the terms of the agreement, CMS paid AstraZeneca $310 million for the licence ($155 million in 2016 and a further $155 million in 2017).
- In September 2015, AstraZeneca announced that the Group had entered into a collaboration agreement with Valeant under which AstraZeneca granted an exclusive licence to Valeant to develop and commercialise brodalumab, except in Japan and certain other Asian countries. Valeant assumed all development costs associated with the regulatory approval for brodalumab. Under the terms of the agreement, Valeant made an upfront payment to AstraZeneca of $100 million in 2015. The agreement also included pre-launch milestones of up to $170 million and further sales-related milestone payments of up to $175 million. After approval, profits would be shared between Valeant and AstraZeneca. In February 2017, the FDA approved brodalumab injection for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy and have failed to respond or lost response to other systemic therapies, triggering a milestone payment of $130 million to AstraZeneca.

As detailed in Risk from page 220, 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 reaction to the product candidate or indications of other safety concerns). The potential future milestones quoted above are subject to these risks.

Gross margin, operating margin and earnings per share

Reported gross profit declined by 5% (CER: 6%) to $17,154 million. Core gross profit declined by 4% (CER: 4%) to $17,773 million. The declines primarily reflected the lower level of Externalisation Revenue and an adverse impact from an increase in the Cost of Sales. The difference between Reported and Core Gross Margin arose predominantly on the $0.3 billion restructuring costs associated with the impairment of site-related assets and inventory from the US Biologics site closures in Longmont and Boulder, CO.

Reported R&D expenses in the year increased by 3% (CER: 3%) to $5,932 million as a result of increased intangible asset amortisation and impairment. Intangible asset impairment charges of $539 million were recorded following analysis of relevant clinical trial data. Core R&D expenses declined by 3% to $5,266 million reflecting the continued focus on resource prioritisation and productivity improvements.

Reported SG&A expenses decreased by 2% (CER: 3%) to $10,031 million primarily due to the revaluation of contingent consideration liabilities arising on business combinations. Core SG&A expenses increased by 10% (CER: 9%) to $8,651 million reflecting investment in the launch of new medicines.

Reported Other operating income and expense in the year was up 38% (CER: 38%) at $2,527 million which includes $695 million from the sale of the rights to *Nexium* in Europe to Grünenthal, $527 million on the sale of the rights to *Seroquel* and *Seroquel XR* in UK, China and other international region markets to Luye Pharma, $210 million from the sale of rights to *Atacand* in Europe to Cheplapharm, milestone receipts of $172 million from the disposal of the anaesthetics portfolio outside the US to Aspen, and $139 million from the sale of global rights to *Alvesco*, *Omnaris* and *Zetonna* to Covis. As these elements of our income arose from product divestments, where we no longer retain significant ongoing economic interest, in accordance with our Externalisation Revenue definition in the Accounting Policy note on page 155 and the requirements of IFRS 15 'Revenue from Contracts with Customers', proceeds from these divestments are recorded as other operating income.

Reported operating profit declined by 8% (CER: 7%) to $3,387 million in the year. The Reported operating margin declined by one percentage point (CER: one percentage point) to 15% of Total Revenue. The decrease was primarily driven by declines in Total Revenue and Reported gross margin as well as the aforementioned increase in Reported R&D expenses. Core operating profit declined by 17% (CER: 17%) in the year to $5,672 million. The Core operating profit margin decreased by five percentage points to 26% of Total Revenue.

Reported net finance expense decreased by 8% (CER: increased 2%) in the year to $1,281 million (2017: $1,395 million) reflecting the effect of higher Net debt and an adverse movement in the fair value of bonds and derivative instruments and offset by lower levels of discount unwind on Acerta Pharma liabilities. Core net finance expense increased by 13% (CER: 11%) in the year to $736 million.

Reported profit before tax declined by 10% (CER: 14%) in the year to $1,993 million (2017: $2,227 million), reflecting the lower level of Externalisation Revenue, lower Reported gross margin and the increase in Reported R&D expenses. Pre-tax adjustments to arrive at Core profit before tax amounted to $2,830 million in 2018 (2017: $3,923 million), comprising $2,285 million adjustments to operating profit (2017: $3,178 million) and $545 million to net finance expense (2017: $745 million). EBITDA increased by 6% (CER: 7%) to $7,140 million.

Excluded from Core results were:

- Restructuring expenses totalling $697 million (2017: $807 million) were largely driven by $252 million fixed asset impairment and $75 million inventory write off resulting from the announcement of the US Biologics site closures in Longmont and Boulder, CO.
- Amortisation totalling $1,663 million (2017: $1,319 million) relating to intangible assets, except those related to IT and to our acquisition of BMS's share of our Global Diabetes Alliance (which are separately detailed below). Further information on our intangible assets is contained in Note 9 to the Financial Statements from page 169.
- Intangible impairment charges of $683 million (2017: $488 million) excluding those related to IT. Further details relating to intangible asset impairments are included in Note 9 to the Financial Statements from page 169.
- Costs associated with our acquisition of BMS's share of our Global Diabetes Alliance in February 2014 amounting to $277 million (2017: $954 million) and included a fair value credit of $482 million, amortisation charges of $422 million and discount unwinds in Sweden and US of $337 million.
- Other charges which includes net legal provisions amounted to a credit of $489 million (2017: $355 million) and was primarily driven by a $352 million settlement of legal action in Canada in relation to patent infringement of *Losec/Prilosec*, recognised in other income. Further details of legal proceedings in which we are currently involved are contained within Note 29 to the Financial Statements from page 194.
- Also included in other charges are a $208 million discount unwind charge (2017: $305 million) and a $126 million credit (2017: $309 million) for net fair value adjustments relating to contingent consideration and the Acerta Pharma put option arising on our other business combinations as detailed in Note 19 to the Financial Statements from page 177.
- Additionally in 2017 a one-off adjustment of $617 million reflecting adjustments to deferred tax in line with the reduction to the US federal tax rate.

Reported EPS of $1.70 in the year represented a decline of 28% (CER: 29%). The performance was driven by a decline in Externalisation Revenue and increased Cost of Sales, partly offset by an increase in other operating income and expense. Core EPS in the year declined by 19% (CER: 19%) to $3.46.

The Reported tax rate of (3)% and the Core tax rate in the year of 11% benefited from a favourable adjustment of $297 million to deferred taxes, reflecting the recently-announced reductions in Dutch and Swedish corporate income tax rates and a $188 million benefit from reductions of tax provisions. Excluding these benefits, both the Reported and Core tax rates would have been 21%. The income tax paid for the year was $537 million (27% of Reported profit before tax). This was $594 million higher than the tax charge for the year as a result of certain items with no cash impact including $297 million deferred tax credit reflecting the reduction in Dutch and Swedish income tax rates, $509 million of other deferred tax credits, $188 million provision releases relating to the expiry of the statute of limitations and on the conclusion of tax authority review, other net increases in provisions for tax contingencies, partially offset by refunds following a previously disclosed agreement of inter-government transfer pricing arrangements and other cash tax timing differences. 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. The taxes we pay and collect represent a significant contribution to the countries and societies in which we operate.

Total comprehensive income decreased by $2,516 million from the prior year, resulting in a net income of $991 million for 2018. The decrease in other comprehensive income included foreign exchange losses arising on designating borrowings in net investment hedges of $520 million (2017: gains of $505 million), foreign exchange losses arising on consolidation of $449 million (2017: gains of $536 million) and net losses on equity investments measured at fair value through other comprehensive income of $171 million (2017: $nil), offset by a gain on fair value movements on cash flow hedges transferred to profit and loss of $111 million (2017: $315 million).

Restructuring

Since 2007, we have undertaken significant efforts to restructure and reshape our business to improve our long-term competitiveness. The first phases of this restructuring, involving the integration of MedImmune, efficiencies within the R&D function and a reduction in SG&A costs, were completed in 2011. The targeted commercial restructuring announced in 2015 has also been successfully completed with a total cost of $151 million.

In 2016, we announced plans to advance our strategy through sharper focus by streamlining operations, primarily in Commercial and Manufacturing, to redeploy investment to key therapy areas, particularly Oncology. Restructuring costs associated with this programme were initially forecast to be $1.5 billion by the end of 2017 and generate net annualised benefits of $1.1 billion by 2018. The total cost estimate is now $1.3 billion to be incurred by the end of 2019, with benefits expected to be $1.1 billion in 2019. In addition to the 2016 plan, there are two further active programmes. The first is the continuation of the Phase 3 restructuring that was announced in 2012, superseded by Phase 4 in 2013 and subsequently expanded in 2014. This initiative consists of centralisation of our global R&D footprint into three strategic centres, transformation of the IT organisation, closure of a number of manufacturing facilities and other activities to simplify and streamline the organisation. At the time of the announcement, the Phase 4 programme was estimated to incur $3.2 billion of costs and deliver $1.1 billion of annualised benefits by 2016. By the end of 2018, the Phase 4 programme had incurred costs of $3.5 billion, creating headroom for investment in our pipeline and launch capability. The Phase 4 programme is now expected to complete in 2021, with total programme costs estimated to be $3.7 billion and annualised benefits of $1.2 billion.

The second step was initiated in 2016 and relates to multi-year transformation programmes within our G&A functions (principally Finance and HR) with anticipated costs by the end of 2018 of $270 million. We expect these transformation programmes to deliver annualised benefits of $100 million by the end of 2019. By the end of 2018, these programmes had incurred costs of $304 million with total expected costs rising to $376 million.

The aggregate restructuring charge incurred in 2018 across all our restructuring programmes was $697 million (2017: $807 million), including the US Biologics site closures at Longmont and Boulder, CO, and other acquired assets. 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 readiness preparations and planning

Following the UK referendum outcome in June 2016 for the UK to leave the EU, the UK Government and European Commission have been negotiating the terms on which the UK would leave the EU and the framework for the future relationship. While a draft Withdrawal Agreement has been agreed between the UK government and the EU, at this time it remains unclear whether this will be ratified by the UK parliament in its current form, amended or if the UK will leave the EU without a deal. In the absence of a ratified agreement, it is unclear what trading relationships the UK will have with the EU and other significant trading partners after 29 March 2019 given the range of political and legal options. Until the Brexit negotiation process is completed, it is difficult to anticipate the potential impact on our market share, sales, profitability, cashflows and results of operations.

In response to this situation, the Group has taken the decision to implement appropriate actions to mitigate where possible the potential risk of disruption to the supply of medicines (including potential new medicines currently undergoing clinical trials) including, but not limited to, duplication of release testing and procedures for products based in the EU27 and the UK, transfer of regulatory licences, customs and duties set up for introduction or amendment of existing tariffs or processes and associated IT systems reconfiguration. In addition, the Group has engaged with its major suppliers to assess their readiness and continues to work with them to mitigate the risk of disruption to supply chains.

The costs associated with this and certain other actions directly related to Brexit will be charged as restructuring with the majority of such costs expected to be cash costs. The current estimate of these costs is around $40 million. However, until the Brexit process is concluded by the UK and EU parliaments and the impacts of transition to any new arrangement between them are known with clarity, it is difficult to anticipate the overall potential impact on the Group's operations and hence the final expected costs to be incurred.

Cash flow and liquidity – for the year ended 31 December 2018

Summary cash flows

	2018 $m	2017 $m	2016 $m
Net debt brought forward at 1 January	**(12,679)**	(10,657)	(7,762)
Profit before tax	**1,993**	2,227	3,552
Sum of changes in interest, depreciation, amortisation, impairment, and share of after tax losses on joint ventures and associates	**5,147**	4,486	3,707
Movement in working capital and short-term provisions	**(639)**	(50)	926
Tax paid	**(537)**	(454)	(412)
Interest paid	**(676)**	(698)	(677)
Gains on disposal of intangible assets	**(1,885)**	(1,518)	(1,301)
Fair value movements on contingent consideration arising from business combinations	**(495)**	109	(1,158)
Non-cash and other movements	**(290)**	(524)	(492)
Net cash inflow from operating activities	**2,618**	3,578	4,145
Disposal/(purchase) of intangibles (net)	**2,010**	1,082	559
Non-contingent payments on business combinations	**–**	(1,450)	(2,564)
Payment of contingent consideration from business combinations	**(349)**	(434)	(293)
Other capital expenditure (net)	**(1,218)**	(1,319)	(1,405)
Investments	**443**	(2,121)	(3,703)
Dividends	**(3,484)**	(3,519)	(3,561)
Share proceeds	**34**	43	47
Distributions	**(3,450)**	(3,476)	(3,514)
Other movements	**65**	(3)	177
Net debt carried forward at 31 December	**(13,003)**	(12,679)	(10,657)

Net debt reconciliation

	2018 $m	2017 $m	2016 $m
Cash and cash equivalents	**4,831**	3,324	5,018
Other investments[1,2]	**895**	1,300	898
Cash and investments	**5,726**	4,624	5,916
Overdraft and short-term borrowings	**(755)**	(845)	(451)
Finance leases	**–**	(5)	(93)
Current instalments of loans	**(999)**	(1,397)	(1,769)
Loans due after one year	**(17,359)**	(15,560)	(14,495)
Loans and borrowings	**(19,113)**	(17,807)	(16,808)
Net derivative financial instruments	**384**	504	235
Net debt	**(13,003)**	(12,679)	(10,657)

[1] Other investments in 2018 include $46 million (2017: $70 million) of non-current Treasury investments.
[2] Other investments include non-current investments, which are included within the balance of $833 million (2017: $933 million) in the Statement of Financial Position on page 150. 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 $1,838 million (2017: $1,823 million) shown in non-current other payables.

Bonds issued in 2018 and 2017

	Repayment dates	Face value of bond $m	Net book value of bond at 31 December $m
Bonds issued in 2018:			
3.5% USD bond	2023	850	**845**
Floating rate USD notes	2023	400	**400**
4% USD bond	2029	1,000	**992**
4.375% USD bond	2048	750	**736**
Total 2018		3,000	**2,973**
Bonds issued in 2017:			
2.375% USD bond	2022	1,000	**994**
Floating rate USD notes	2022	250	**250**
3.125% USD bond	2027	750	**743**
Total 2017		2,000	**1,987**

Cash flow and liquidity

Net cash generated from operating activities was $2,618 million in the year ended 31 December 2018, compared with $3,578 million in 2017. The 2018 operating cash inflows reflected the increase in the movement of working capital and short-term provisions impacted by the reduction of provisions relating to legal settlements, as well as launch support for new medicines.

Net investment cash inflows were $443 million (2017: outflow of $2,121 million).

Investment cash outflows for 2018 include $349 million (2017: $434 million) of payments against contingent consideration arising on business combinations and $328 million (2017: $294 million) for the purchase of other intangible assets. 2017 investment cash outflows included a $1,450 million payment to the shareholders of Acerta Pharma, a contractual obligation triggered by the first regulatory approval for *Calquence*, following on from our majority investment in Acerta Pharma in 2016.

Investment cash inflows include $2,338 million (2017: $1,376 million) from the sale of intangible assets, including $700 million on sale of *Nexium* rights in Europe to Grünenthal, $482 million relating to the 2017 sale of our remaining anaesthetic portfolio to Aspen, $354 million on the sale of *Alvesco*, *Omnaris* and *Zetonna* rights outside the US to Covis Pharma, $275 million from the sale of UK, China and other international regions rights to *Seroquel XR* and *Seroquel* IR to Luye Pharma and $205 million from the sale of European rights to *Atacand* to Cheplapharm. The comparative period in 2017 included $300 million from the disposal of EU rights for *Seloken*, $200 million from the divestment of *Zomig* rights outside Japan, $200 million relating to the sale of our remaining anaesthetic portfolio to Aspen and $175 million regarding the *Zavicefta* divestment to Pfizer.

Net cash distributions to shareholders were $3,450 million (2017: $3,476 million), including dividends of $3,484 million (2017: $3,519 million). Proceeds from the issue of shares on the exercise of share options amounted to $34 million (2017: $43 million).

In August 2018, we issued $3.0 billion of bonds in the US dollar debt capital markets with maturities of five, ten and 30 years and repaid a $1.0 billion 1.75% bond and a $0.4 billion floating rate bond, both of which matured in November 2018.

At 31 December 2018, outstanding gross debt (interest-bearing loans and borrowings) was $19,113 million (2017: $17,807 million). Of the gross debt outstanding at 31 December 2018, $1,754 million is due within one year (2017: $2,247 million). Net debt at 31 December 2018 was $13,003 million, compared to $12,679 million at the beginning of the year, as a result of the cash flows as described above. At 31 December 2018, cash, cash equivalents and liquid investments totalled $4.8 billion and undrawn committed cash facilities totalled $4.1 billion.

Financial position – 31 December 2018

All data in this section is on a Reported basis.

Summary statement of financial position

	2018 $m	Movement $m	2017 $m	Movement $m	2016 $m
Property, plant and equipment	**7,421**	**(194)**	7,615	767	6,848
Goodwill and intangible assets	**33,666**	**(4,347)**	38,013	(1,231)	39,244
Assets held for sale	**982**	**982**	–	–	–
Inventories	**2,890**	**(145)**	3,035	701	2,334
Trade and other receivables	**6,089**	**233**	5,856	382	5,474
Trade and other payables	**(19,611)**	**(130)**	(19,481)	493	(19,974)
Provisions	**(891)**	**577**	(1,468)	(50)	(1,418)
Net income tax payable	**(957)**	**(131)**	(826)	128	(954)
Net deferred tax liabilities	**(907)**	**899**	(1,806)	1,048	(2,854)
Retirement benefit obligations	**(2,511)**	**72**	(2,583)	(397)	(2,186)
Non-current other investments (excluding Treasury investments of $46m in 2018 (2017: $70m))	**787**	**(76)**	863	150	713
Investment in associates and joint ventures	**89**	**(14)**	103	4	99
Net debt	**(13,003)**	**(324)**	(12,679)	(2,022)	(10,657)
Net assets	**14,044**	**(2,598)**	16,642	(27)	16,669

Property, plant and equipment

In 2018, Property, plant and equipment decreased by $194 million to $7,421 million. Additions of $1,034 million (2017: $1,311 million) were offset by depreciation of $614 million (2017: $624 million), impairments of $291 million (2017: $78 million), exchange adjustments of $301 million (2017: $352 million) and disposals and other movements of $22 million (2017: $194 million).

Business combinations

In 2016, we acquired a majority equity stake in Acerta Pharma. No business acquisitions were made in 2018 or 2017. Further details of our business combinations are contained in Note 26 to the Financial Statements from page 186.

Goodwill and intangible assets

Our goodwill of $11,707 million (2017: $11,825 million) principally arose on the acquisition of MedImmune in 2007, the restructuring of our US joint venture with MSD in 1998 and the acquisition of BMS's share of the Global Diabetes Alliance.

Intangible assets amounted to $21,959 million at 31 December 2018 (2017: $26,188 million). The decrease was mainly driven by amortisation in the year of $2,165 million (2017: $1,829 million) and the reclassification of assets held for sale of $982 million in respect of *Synagis*. Intangible asset additions were $513 million in 2018 (2017: $441 million). Impairment charges in the year amounted to $683 million (2017: $491 million) including impairments on MEDI0680 and *Eklira*. Disposals of intangible assets totalled $339 million in the year (2017: $307 million).

Further details of our additions to intangible assets, and impairments recorded, are included in Note 9 to the Financial Statements from page 169.

Receivables, payables and provisions

Trade and other receivables decreased by $233 million with trade receivables increasing by $193 million to $2,995 million principally as a result of higher invoiced sales in the US.

Trade and other payables increased by $130 million in 2018 to $19,611 million. The increase was due to higher rebates in the US and China, partially offset by a deferred income release on the *Lynparza* and selumetinib collaboration.

The decrease in provisions of $577 million in 2018 included a $456 million reduction on legal provisions and a $132 million reduction to severance provisions. Further details of the charges made against provisions are contained in Notes 20 and 29 to the Financial Statements on page 178 and from page 194, respectively.

Contingent consideration

The majority of our business acquisitions have included elements of consideration that are contingent on future development and/or sales milestones, with both the Diabetes and Respiratory acquisitions in 2014 also including royalty payments linked to future revenues. The acquisitions of ZS Pharma in 2015 and Acerta Pharma in 2016 had no contingent consideration element and there were no relevant acquisitions in 2017 and 2018.

Our agreement with BMS provides for $0.6 billion in milestones and various sales-related royalty payments up until 2025. Our transaction with Almirall includes further payments of up to $0.6 billion for future development, launch, and various other sales-related milestone payments, and sales-related royalty payments as detailed in Note 19 to the Financial Statements from page 177.

All these future payments are treated as contingent consideration liabilities, and are fair valued using decision-tree analyses, with key assumptions, including the probability of success, the potential for delays and the expected levels of future revenues. The fair value is updated at each reporting date to reflect our latest estimate of the probabilities of these key assumptions. Given the long-term nature of the liabilities, the fair value calculation includes the discounting of future potential payments to their present value using discount rates appropriate to the period over which payments are likely to be made. Over time, as the target date of a consideration payment approaches, the discount in absolute terms of such future potential payment to its present value decreases. Therefore, in each period we take a corresponding charge reflecting the passage of time. We refer to this charge as 'discount unwind'. The calculation of the fair value is considered to be a key estimate.

Both the discount unwind and any movements of the fair value of the underlying future payments can result in significant income statement movements. As detailed in the Results of operations section above, these movements are treated as non-Core items in our income statement analysis. In 2018, we recorded an interest charge of $416 million on the discount unwind on contingent consideration arising on our business combinations, and a net fair value decrease on contingent consideration of $495 million (which resulted in a credit to our income statement for the same amount) driven, principally, by revised forecasts for revenues for our Diabetes franchise. At 31 December 2018, our contingent consideration liability was $5,106 million (2017: $5,534 million) with the movements of the balance detailed in the table to the right.

Tax payable and receivable

Net income tax payable has increased by $131 million (2017: decrease of $128 million) to $957 million, principally due to the receipt of cash in the year following a previously disclosed agreement of inter-government transfer pricing arrangements and other cash tax timing differences, offset by tax provision releases following expiry of statute of limitations and on conclusion of tax authority review. The tax receivable balance of $207 million (2017: $524 million) principally relates to cash tax timing differences.

Net deferred tax liabilities decreased by $899 million (2017: $1,048 million) in the year mainly reflecting adjustments to deferred tax arising from the Dutch and Swedish income tax rate reductions and deferred tax associated with movements in intangible assets. The decrease in net deferred tax liabilities in 2017 reflected adjustments to deferred taxes in line with the reduction to the US federal income tax rate from 35% to 21% and recognition of previously unrecognised deferred tax assets. Additional information on the movement in deferred tax balances is contained in Note 4 to the Financial Statements from page 163.

Retirement benefit obligations

In terms of the Group's major defined benefit plans, approximately 91% of our total retirement defined benefit obligations (or around 80% of net obligations) are concentrated in the UK, the US and Sweden. The UK and US are now largely legacy arrangements as they have been closed to new entrants since 2000. In line with local regulations the collectively bargained Swedish plan is still open to employees born before 1979.

Net retirement benefit obligations decreased by $72 million in 2018 (2017: increase of $397 million) to $2,511 million. Net re-measurement adjustments of $46 million arose principally from higher discount rate assumptions in the UK and US driven by rises in long-term bond yields which lowered the present value of the liabilities, offset by lower than expected investment performance and lower discount rate assumptions in Sweden, where bond yields have fallen. A positive $124 million impact of exchange rate movements also arose in the year as the US dollar strengthened against pound sterling and Swedish krona, reducing liability obligations in US dollar terms. Employer contributions to the pension schemes of $174 million also contributed to the reduction in the net retirement benefit obligation. Benefits paid amounted to $620 million (2017: $581 million).

In the UK, a High Court judgement issued on 26 October 2018 relating to Guaranteed Minimum Pensions (GMPs) is expected to create a precedent for other UK defined benefit pension schemes and therefore is expected to increase the liabilities of the UK Pension Fund. The ruling requires the equalisation of member benefits to address

Contingent consideration arising on business combinations

	2018			2017		
	Acquisition of BMS's share of Diabetes Alliance $m	**Other business combinations $m**	**Total 2018 $m**	Acquisition of BMS's share of Diabetes Alliance $m	Other business combinations $m	Total 2017 $m
At 1 January	**4,477**	**1,057**	**5,534**	4,240	1,217	5,457
Settlements	**(349)**	**–**	**(349)**	(284)	(150)	(434)
Fair value adjustments	**(482)**	**(13)**	**(495)**	208	(99)	109
Discount unwind	**337**	**79**	**416**	313	89	402
At 31 December	**3,983**	**1,123**	**5,106**	4,477	1,057	5,534

Payments due by period

	Less than 1 year $m	**1-3 years $m**	**3-5 years $m**	**Over 5 years $m**	**Total 2018 $m**	Total 2017 $m
Bank loans and other borrowings[1]	**2,403**	**4,233**	**3,882**	**17,405**	**27,923**	25,879
Finance leases	**–**	**–**	**–**	**–**	**–**	5
Operating leases	**188**	**261**	**99**	**136**	**684**	614[2]
Contracted capital expenditure	**625**	**–**	**–**	**–**	**625**	570
Total	**3,216**	**4,494**	**3,981**	**17,541**	**29,232**	27,068

[1] Bank loans and other borrowings include interest charges payable in the period, as detailed in Note 27 to the Financial Statements on page 188.

[2] The Group has revised the presentation of operating leases from 2017 to include operating leases that have been identified during the transition to IFRS 16 as having previously been omitted from this disclosure. This resulted in an increase in 2017 from $523 million to $614 million.

gender inequality in instances where GMP benefits are currently unequal. The estimated impact based on the broad profile of the UK Pension Fund results in a past service cost of £17 million ($23 million) and has been recognised in the income statement for 2018.

The Group has undertaken several initiatives to reduce our net defined benefit pension obligation exposure and manage the associated long-term financial risks. As well as paying cash contributions when required, in the UK, a freeze on pensionable pay has been in effect from 30 June 2010. In the US, both the qualified and non-qualified US pension plans were closed to future accrual in December 2017. Furthermore, liability management exercises have been carried out in the UK, including a Pension Increase Exchange exercise in 2016/2017 along with improvements to the 'at retirement' process to better support members in their retirement decisions.

Further details of our accounting for post-retirement benefit plans are included in Note 21 to the Financial Statements from page 178.

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 153.

We also have taxation contingencies. These are described in the Taxation section in the Critical accounting policies and estimates section on page 90 and in Note 29 to the Financial Statements from page 194.

Off-balance sheet transactions and commitments

We have no off-balance sheet arrangements and our derivative activities are non-speculative. The table on page 84 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 29 to the Financial Statements on page 194. As detailed in Note 29, payments to our collaboration 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, therefore, 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 over 260 major or strategically important business development transactions over the past three years, one of which was accounted for as business acquisitions under IFRS 3 'Business Combinations', being the majority investment in Acerta Pharma in 2016.

In addition to the business development transactions detailed under Externalisation Revenue from page 79 of this Financial Review, the following significant collaborations remain in the development phase:

- In April 2015, we entered into two oncology agreements with Innate Pharma: firstly, a licence which provides us with exclusive global rights to co-develop and commercialise IPH2201 in combination with *Imfinzi* and, secondly, an option to license exclusive global rights to co-develop and commercialise IPH2201 in monotherapy and other combinations in certain treatment areas. Under the terms of the combination licence, we assumed exclusive global rights to research, develop and commercialise IPH2201 in combination with *Imfinzi*. We jointly fund Phase II studies with Innate Pharma and we lead the execution of these studies. Under the terms of the agreements, we made an initial payment to Innate Pharma of $250 million, which included the consideration for exclusive global rights to co-develop and commercialise IPH2201 in combination with *Imfinzi*, as well as access to IPH2201 in monotherapy and other combinations in certain treatment areas. The agreement includes a Phase III initiation milestone of $100 million, as well as additional regulatory and sales-related milestones. We record all sales and will pay Innate Pharma double digit royalties on net sales. The arrangement includes the right for Innate Pharma to co-promote in Europe for a 50% profit share 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 million to acquire a 9.8% stake in Innate Pharma. The $100 million option fee and $50 million have been capitalised as intangible assets, along with the premium paid over market price for the investment in Innate Pharma. The payment for future programmes will be expensed as research and development 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 July 2013, we entered into a strategic collaboration with FibroGen to develop and commercialise roxadustat (FG-4592), a first-in-class oral compound in late-stage development for the treatment of anaemia associated with chronic kidney disease and end-stage renal disease (ESRD). This broad collaboration focuses on the US, China and all major markets excluding Japan, Europe, the CIS, the Middle East and South Africa, which are covered by an existing agreement between FibroGen and Astellas. Under the arrangement, we 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. We will be responsible for the US commercialisation of roxadustat, with FibroGen undertaking specified promotional activities in the ESRD segment in this market. The companies will also co-commercialise roxadustat in China where FibroGen will be responsible for clinical trials, regulatory matters, manufacturing and medical affairs, and we will oversee promotional activities and commercial distribution.
- In March 2013, we signed an exclusive agreement with Moderna to discover, develop and commercialise pioneering medicines based on *messenger RNA Therapeutics* for the treatment of serious cardiovascular, metabolic and renal diseases, as well as cancer. Under the terms of the agreement, we made an upfront payment of $240 million. We will have exclusive access to select any target of our choice in cardiometabolic and renal diseases, as well as selected targets in oncology, over a period of up to five years for subsequent development of *messenger RNA Therapeutics*. In addition, Moderna is entitled to an additional $180 million for the achievement of three technical milestones. Through this agreement, we have the option to select up to 40 drug products for clinical development and Moderna will be entitled to development and commercial milestone payments as well as royalties on drug sales. We will lead the pre-clinical, clinical development and commercialisation of therapeutics resulting from the agreement and Moderna will be responsible for designing and manufacturing the *messenger RNA Therapeutics* against selected targets. We are currently progressing 19 projects across CVRM and Oncology. Utilising both companies' expertise, significant progress has also been made with the technology platform, with the focus on formulation, safety, and drug metabolism and pharmacokinetics.

We determine the above 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. Because 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 2018 was 1,267 million (2017: 1,266 million). 0.8 million Ordinary Shares were issued upon share option exercises for a total of $34 million. Shareholders' equity decreased by $2,492 million to $12,468 million at the year end. Non-controlling interests were $1,576 million (2017: $1,682 million), with the decrease in the year as a result of the losses attributable to shareholders of the non-controlling interest in Acerta Pharma.

Dividend and share repurchases

The Board has recommended a second interim dividend of $1.90 (146.8 pence, 17.46 SEK) to be paid on 27 March 2019. This brings the full-year dividend to $2.80 (215.2 pence, 25.38 SEK). Against Core earnings per share the Group had a dividend cover ratio of 1.2:1 in 2018 (2017: 1.5:1).

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.

Dividends for 2018

	$	Pence	SEK	Payment date
First interim dividend	0.90	68.4	7.92	10 September 2018
Second interim dividend	1.90	146.8	17.46	27 March 2019
Total	**2.80**	**215.2**	**25.38**	

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. Subject to the filing of these Financial Statements with the UK Companies House, the distributable reserves of the parent company as at 31 December 2018 amounts to $13,443 million (2017: $16,715 million), details are included in the Consolidated Statement of Changes in Equity on page 151. The distributable reserves are sufficient to pay dividends for a number of years, as, when required, the parent company can receive dividends from its subsidiaries to increase distributable reserves.

Future prospects

As outlined earlier in this Annual Report, our strategy is focused on innovation, returning to growth and building a sustainable, durable and more profitable business.

In support of this, we made certain choices around our three strategic priorities:

- Our immediate priorities are to continue to drive Product Sales of our on-market medicines through investment in our Growth Platforms and our portfolio of legacy medicines outside of the Growth Platforms. The Growth Platforms include products in our three main therapy areas, and a focus on the Emerging Markets and Japan. We are also pursuing business development and investment in R&D. We have already accelerated a number of projects and progressed them into Phase III development.
- Our late-stage pipeline is progressing ahead of plans. Our science-driven, collaborative culture is driving increased R&D productivity.
- Our long-term aspiration, in line with our strategic ambition, is to achieve scientific leadership and sustainable growth.

Full Year 2019: additional commentary

In 2019, the sum of Externalisation Revenue and Core other operating income and expense is anticipated to decline versus 2018. Core operating expenses are expected to increase by a low single-digit percentage. Specific support for medicine launches and China sales delivered compelling results in 2018 and elements of that support will continue. The Group will retain flexibility in its investment approach. Core operating profit is anticipated to increase, ahead of Product Sales, by a mid-teens percentage compared with 2018. Without the impact of the reduction in initial income from externalisation and divestment transactions completed in 2018 and 2019, Core operating profit in 2019 is expected to increase at a significantly higher rate, reflecting strong expected growth of the Group's underlying business. Capital expenditure is expected to be broadly stable and restructuring expenses are targeted to reduce compared with 2018. A Core tax rate of 18% to 22% is expected for 2019.

These targets represent management's current estimates and are subject to change. Please see the Cautionary statement regarding forward-looking statements on page 244.

Financial risk management

Financial risk management policies

Insurance

Our risk management processes are described in Risk Overview from page 70. These processes enable us to identify risks that can be partly or entirely mitigated through the use of insurance. We negotiate the best available premium rates with insurance providers on the basis of our extensive risk management procedures. We focus our insurance resources on the most critical areas, or where there is a legal requirement, and where we can get best value for money. We purchase an external multi-line insurance programme to mitigate against significant financial loss arising from business risks including liability, business interruption, property damage, and directors' and officers' liability. In order to contain insurance costs, as of February 2006, we adjusted our product liability coverage profile, accepting uninsured exposure above $100 million.

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 rate, foreign currency and credit. We have a centralised treasury function to manage these risks in accordance with Board-approved policies. Specifically, liquidity risk is managed through maintaining access

to a number of sources of funding to meet anticipated funding requirements, including committed bank facilities, cash resources and use of debt factoring.

Interest rate risk is managed through maintaining a debt portfolio that is weighted towards fixed rates of interest. Accordingly, our net interest charge is not significantly affected by movements in floating rates of interest. We monitor the impact of currency on a portfolio basis (to recognise correlation effect), and may hedge to protect against significant adverse impacts on cash flow over the short to medium term. We hedge the currency exposure that arises between the booking and settlement dates on non-local currency purchases and sales by subsidiaries and the external dividend. Significant intra-group loans that give rise to foreign exchange movements are also hedged.

Credit risk is managed through setting and monitoring credit limits appropriate for the assessed risk of the counterparty.

The Group utilises factoring arrangements for selected trade receivables. These factoring arrangements qualify for full derecognition of the associated trade receivables under IFRS 9 'Financial Instruments'.

Our capital and risk management objectives and policies are described in further detail in Note 27 to the Financial Statements from page 187 and in Risk Overview from page 70. Sensitivity analysis of the Group's exposure to exchange rate and interest rate movements is also detailed in Note 27 to the Financial Statements from page 189.

Critical accounting policies and estimates

Our Financial Statements are prepared in accordance with IFRS as adopted by the EU (adopted IFRS) and as issued by the IASB, and the accounting policies employed are set out in the Group Accounting Policies section in the Financial Statements from page 153. 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:

- revenue recognition
- research and development (including impairment reviews of associated intangible assets)
- business combinations and goodwill (and contingent consideration arising from business combinations)
- litigation and environmental liabilities
- employee benefits
- taxation.

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 and product returns, 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 payment are also deducted 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 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 overleaf.

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, such estimates involve judgements on aggregate future sales levels, segment mix and the customers' contractual performance.

Overall adjustments between gross and net US Product Sales amounted to $9,662 million in 2018 (2017: $8,468 million) with the increase driven by an overall increase in our US Product Sales and changes in product mix.

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 154.

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 recalls, 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.

Gross to net Product Sales

US pharmaceuticals

	2018 $m	2017 $m	2016 $m
Gross Product Sales	**16,538**	14,637	19,640
Chargebacks	**(2,224)**	(2,299)	(3,449)
Regulatory – Medicaid and state programmes	**(1,304)**	(1,462)	(1,903)
Contractual – Managed-care and Medicare	**(4,600)**	(3,598)	(5,219)
Cash and other discounts	**(286)**	(30)	(358)
Customer returns	**(119)**	(37)	(130)
US Branded Pharmaceutical Fee	**(140)**	3	(145)
Other	**(989)**	(1,045)	(1,071)
Net Product Sales	**6,876**	6,169	7,365

Movement in provisions

US pharmaceuticals

	Brought forward at 1 January 2018 $m	Provision for current year $m	Adjustment in respect of prior years $m	Returns and payments $m	Carried forward at 31 December 2018 $m
Chargebacks	**206**	**2,220**	**4**	**(2,159)**	**271**
Regulatory – Medicaid and state programmes	**749**	**1,482**	**(178)**	**(1,161)**	**892**
Contractual – Managed-care and Medicare	**1,267**	**4,685**	**(85)**	**(4,325)**	**1,542**
Cash and other discounts	**4**	**286**	**–**	**(286)**	**4**
Customer returns	**386**	**119**	**–**	**(144)**	**361**
US Branded Pharmaceutical Fee	**63**	**99**	**41**	**(151)**	**52**
Other	**151**	**989**	**–**	**(996)**	**144**
Total	**2,826**	**9,880**	**(218)**	**(9,222)**	**3,266**

	Brought forward at 1 January 2017 $m	Provision for current year $m	Adjustment in respect of prior years $m	Returns and payments $m	Carried forward at 31 December 2017 $m
Chargebacks	562	2,432	(133)	(2,655)	206
Regulatory – Medicaid and state programmes	807	1,568	(106)	(1,520)	749
Contractual – Managed-care and Medicare	1,443	3,815	(217)	(3,774)	1,267
Cash and other discounts	6	29	1	(32)	4
Customer returns	473	36	1	(124)	386
US Branded Pharmaceutical Fee	260	105	(108)	(194)	63
Other	161	1,030	15	(1,055)	151
Total	3,712	9,015	(547)	(9,354)	2,826

	Brought forward at 1 January 2016 $m	Provision for current year $m	Adjustment in respect of prior years $m	Returns and payments $m	Carried forward at 31 December 2016 $m
Chargebacks	324	3,470	(21)	(3,211)	562
Regulatory – Medicaid and state programmes	777	1,976	(73)	(1,873)	807
Contractual – Managed-care and Medicare	2,206	5,517	(298)	(5,982)	1,443
Cash and other discounts	44	358	–	(396)	6
Customer returns	467	130	–	(124)	473
US Branded Pharmaceutical Fee	264	195	(50)	(149)	260
Other	186	1,071	–	(1,096)	161
Total	4,268	12,717	(442)	(12,831)	3,712

For products facing generic competition, we may lose the ability to estimate the levels of returns from wholesalers with the same degree of precision that we can for products still subject to patent protection. This is because we may have limited or no insight into a number of areas: the actual timing of the generic launch (for example, a generic manufacturer may or may not have produced adequate pre-launch inventory); the pricing and marketing strategy of the competitor; the take-up of the generic; and (in cases where a generic manufacturer has approval to launch only one dose size in a market of several dose sizes) the likely level of switching from one dose to another. Under our accounting policy, revenue is recognised only when the amount of the revenue is considered highly probable not to reverse. Our approach in meeting this condition for products facing generic competition will vary from product to product depending on the specific circumstances.

The adjustment in respect of prior years increased 2018 net US pharmaceuticals revenue by 3.2% (2017: 8.9%; 2016: 6.0%). However, taking into account the adjustments affecting both the current and the prior year, 2017 revenue would have been reduced by 4.5% and 2016 revenue would have been increased by 1.4%, by adjustments between years.

We have distribution service agreements with major wholesaler buyers which serve to reduce the speculative purchasing behaviour of the wholesalers and reduce short-term fluctuations in the level of inventory they hold. We do not offer any incentives to encourage wholesaler speculative buying and attempt, where possible, to restrict shipments to underlying demand when such speculation occurs.

Component revenue accounting

A consequence of charging all internal R&D expenditure to the income statement in the year in which it is incurred (which is normal practice in the pharmaceutical industry) is that we own valuable intangible assets which are not recorded on the Statement of Financial Position. We also own acquired intangible assets which are included on the Statement of Financial Position. As detailed on page 8, our business model means that, from time to time, we sell such assets and generate income. Sales of product lines are often accompanied by an agreement on our part to continue manufacturing the relevant product for a reasonable period (often about two years) while the purchaser constructs its own manufacturing facilities. Details of the Externalisation Revenue accounting and the key judgements involved are described within our Externalisation Revenue accounting policy on page 155.

Research and development (including impairment reviews of associated intangible assets)

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 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 key estimates which are highly sensitive and depend upon key assumptions as detailed in Note 9 to the Financial Statements from page 169. Sales forecasts and specific allocated costs (which have both been subject to appropriate senior management sign-off) are risk-adjusted and discounted using appropriate rates based on our post-tax weighted average cost of capital. Our weighted average cost of capital reflects factors such as our capital structure and our costs of debt and equity.

The accounting for our intangible assets is fully explained in Note 9 to the Financial Statements from page 169, including details of the estimates and assumptions we make in impairment testing of intangible assets.

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'.

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. Further details of our recent business acquisitions are included in Note 26 to the Financial Statements from page 186.

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 profit. 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 19 to the Financial Statements from page 177.

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 above, 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 8 to the Financial Statements on page 168. 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 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. In addition, our recent business combinations, as detailed in Note 26 to the Financial Statements from page 186, have added significant product, marketing and distribution intangible rights to our intangible asset portfolio. We are satisfied that the carrying values of our intangible assets as at 31 December 2018 are fully justified by estimated future cash flows. The accounting for our intangible assets is fully explained in Note 9 to the Financial Statements from page 169, 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 29 to the Financial Statements from page 194.

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 (more than 50% assessed probability) and we are able to make a reasonable estimate of the loss, we indicate the loss absorbed or the amount of the provision accrued.

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 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 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.

Employee benefits

In relation to the Group's defined benefit pension and healthcare arrangements, we apply IAS 19 'Employee Benefits' and recognise 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 the values, these are considered to be key estimates.

Investment decisions in respect of defined benefit schemes are based on underlying actuarial and economic circumstances with the intention of ensuring that the schemes have sufficient assets to meet liabilities as they fall due, rather than meeting accounting requirements. The local fiduciary bodies which govern the investment of pension fund assets will invest across a broad range of asset classes and employ specialist investment managers with different investment styles. This will ensure that the investment strategy is diversified across a broad range of return drivers. In addition, local fiduciary bodies will also seek to hedge liability risks (interest rate and inflation risk where applicable) inherent in the measurement of the liabilities and therefore reduce volatility in the funding level, where this is practical and cost effective to do so. The Group plays an active role in providing input and support into these decisions.

In assessing the discount rate applied to the obligations, we have used rates on AA corporate bonds with durations corresponding to the maturities of those obligations, except in Sweden where we have used rates on mortgage bonds as the market in high quality corporate bonds is insufficiently deep. In all cases, the pension costs recorded in the Financial Statements are assessed in accordance with the advice of independent qualified actuaries but require the exercise of significant judgement in relation to assumptions for long-term mortality, price inflation, and future salary and pension increases.

Further details of the estimates and assumptions we make in calculating post-retirement benefit plans are included in Note 21 to the Financial Statements from page 178.

Taxation

Accruals for tax contingencies require management to make judgements and estimates of exposures in relation to tax audit issues. Tax benefits are not recognised unless the tax positions will probably be sustained based upon management's interpretation of applicable laws and regulations and the likelihood of settlement. Once considered probable of not being sustained, management reviews each material tax benefit to assess whether a provision should be taken against full recognition of the benefit on the basis of potential settlement through negotiation and/or litigation. Accruals for tax contingencies are measured using the single best estimate of likely outcome approach.

We face a number of audits in jurisdictions around the world and, in some cases, are in dispute with the tax authorities. The issues under discussion are often complex and can require many years to resolve.

Further details of the estimates and assumptions we make in determining our recorded liability for transfer pricing contingencies and other tax contingencies are included in the Tax section of Note 29 to the Financial Statements from page 194.

Sarbanes-Oxley Act Section 404

As a consequence of our NYSE 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 (eg 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.

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
- Chairman's Statement
- Chief Executive Officer's Review
- Business model and life-cycle of a medicine
- Marketplace
- Strategy
- Key Performance Indicators
- Business Review
- Therapy Area Review
- Risk Overview
- Financial Review

and has been approved and signed on behalf of the Board.

A C N Kemp
Company Secretary
14 February 2019

Corporate Governance

Chairman's Introduction

In this Governance Report, we report on how we ensured that the principles of good governance applied to everything we did throughout the year.

"I too set great store by ensuring the Board did the right thing as we oversaw implementation of our strategy of returning to sustainable growth."

Changes to our Governance reporting
This year, we have made a number of changes to the structure of our reporting around Governance to make the information more accessible.

The Corporate Governance Report now contains the following sections:

- Board of Directors and SET: which shows the members of the Board, Board Committees and SET as at 14 February 2019, from page 94.
- Activities of the Board: which describes the key activities of the Board during 2018, including the Board effectiveness review conducted in 2018, from page 98.
- Connecting with our stakeholders: which sets out how the Group has engaged with its key stakeholders during 2018, from page 100.
- Compliance with the UK Corporate Governance Code: which describes how we have complied with the UK Corporate Governance Code published in 2016, from page 102.
- Other Governance information: a separate section contains other governance-related disclosures, including those required as a result of our listing on the NYSE, as well as Directors' Report disclosures, from page 105.
- Committee Reports: from our four Board Committees, from page 107.

The strategy on which we embarked in 2013, and to which we have been committed in the years since, bore fruit in 2018 as we returned to Product Sales growth. Good governance has underpinned our success and will continue to do so.

Sound governance and sustainable growth

Following the science and putting patients first are two of the AstraZeneca Values. Employees' commitment to and embodiment of those Values has been an essential element in the transformation of the organisation that saw us return to Product Sales growth. Doing the right thing is another value espoused by our employees and, as your Chairman, I too set great store by ensuring the Board did the right thing as we oversaw implementation of our strategy of returning to sustainable growth.

In this Governance Report, we report on how we ensured that the principles of good governance applied to everything we did throughout the year and, where we found challenges, how we addressed them. We do so mindful of the enhanced requirements of the UK Corporate Governance Code which we will be reporting on in our next Annual Report. The panel to the left indicates the enhancements we have made to the Annual Report in respect of 2018.

A strong Board

Good governance requires a strong board which we are fortunate to have at AstraZeneca.

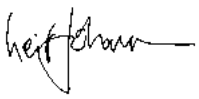
On 1 January 2019, we welcomed Professor Tony Mok to the Board. Tony is a leading clinical oncologist and world-renowned expert in precision medicine for lung cancer. He will make a significant contribution to AstraZeneca's science-led transformation.

At the end of 2018, we said farewell to Shriti Vadera who had served on the Board for eight years. She was an exceptional colleague during a period of pipeline renewal. Her diligence, focus and constant commitment to our success will be missed. On behalf of all her Board colleagues, I thank her for her service and wish her every success in the future.

Transparent leadership

I am grateful to all the members of the Board for their individual contributions to what was an eventful and successful year. I am particularly grateful to those members of the Board who bear the added responsibility of chairing its Committees. As previously announced, Rudy Markham will be stepping down from the Board at the end of the Annual General Meeting in April 2019. As a result, Graham Chipchase became our senior independent Non-Executive Director on 1 January 2019, in addition to his role chairing the Remuneration Committee, and Philip Broadley will become Chairman of the Audit Committee. Nazneen Rahman became Chairman of the Science Committee in July 2018.

This year, for the first time, and to enhance our reporting transparency, each of the Committee Chairmen is providing their own report on their activities during 2018 which you can read in this Annual Report. My thanks to them all.



Leif Johansson
Chairman

Corporate Governance Overview

Delivery

How our governance supports the delivery of our strategy

All Directors are collectively responsible for the success of the Group. The Non-Executive Directors exercise independent, objective judgement in respect of Board decisions, and scrutinise and challenge management. They also have various responsibilities concerning the integrity of financial information, internal controls and risk management.

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. 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 Board conducts an annual review of the Group's overall strategy. The CEO, CFO and Senior Executive Team (SET) take the lead in developing our strategy, which is then reviewed, constructively challenged and approved by the Board.

Governance structure

The Board has delegated some of its powers to the CEO and operates with the assistance of four Committees:

Board
Corporate Governance Report on page 98

- **Audit Committee** – Report from page 110
- **Remuneration Committee** – Report from page 120
- **Nomination and Governance Committee** – Report from page 108
- **Science Committee** – Report from page 107

In addition to the SET, we have two senior level governance bodies:

Senior Executive Team (SET)
Details of our SET on page 96

- **Early Stage Product Committees** – Page 96
- **Late Stage Product Committee** – Page 96

Following the organisational changes announced in January 2019, the future and structure of these governance bodies will be reviewed in the first quarter of 2019. For more information, see page 96.

Attendance in 2018

Board Committee membership and meeting attendance in 2018

● Board or Committee Chairman

Name	Board	Audit	Remuneration	Nomination and Governance	Science
Geneviève Berger	13(13)				2(2)
Philip Broadley	13(13)	6(6)	1(1)		
Graham Chipchase	13(13)		● 6(6)	5(5)	
Deborah DiSanzo	13(13)	2(2)			
Marc Dunoyer	13(13)				
Leif Johansson	● 13(13)		5(6)	● 5(5)	
Rudy Markham	12(13)	● 6(6)	5(6)	5(5)	
Sheri McCoy	13(13)	6(6)	2(2)		
Nazneen Rahman	13(13)			3(3)	● 2(2)
Pascal Soriot	13(13)				
Shriti Vadera – *retired 31 December 2018*	13(13)	3(3)	6(6)		
Marcus Wallenberg	11(13)				2(2)

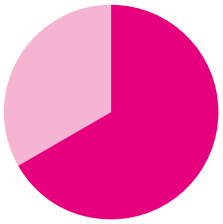
Note: number in brackets denotes number of meetings during the year that Board members were entitled to attend.

For more information, see Changes to the composition of the Board and its Committees for the year ended 31 December 2018 on page 94

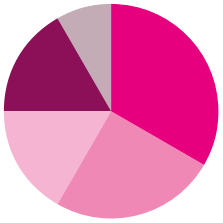
Board of Directors
as at 14 February 2019

Board composition
as at 14 February 2019

Gender split of Directors



Directors' nationalities



Length of tenure of Non-Executive Directors

<3 years
5
Philip Broadley
Deborah DiSanzo
Sheri McCoy
Tony Mok
Nazneen Rahman

3-6 years
0

6-9 years
3
Leif Johansson
Geneviève Berger
Graham Chipchase

>9 years
2
Rudy Markham
Marcus Wallenberg

Committee Membership Key

- Committee Chairman
- (A) Audit
- (R) Remuneration
- (NG) Nomination and Governance
- (S) Science

* Date of first appointment or election to the Board.

Leif Johansson (NG) (R)
Non-Executive Chairman of the Board (April 2012*)

Skills and experience: From 1997 to 2011, Leif was Chief Executive Officer of AB Volvo. Prior to that, he served at AB Electrolux, latterly as Chief Executive Officer from 1994 to 1997. He was a Non-Executive Director of BMS from 1998 to September 2011, serving on the Board's Audit Committee, and Compensation and Management Development Committee. Leif was Chairman of global telecommunications company, LM Ericsson, from 2011 to 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. He has been a member of the Royal Swedish Academy of Engineering Sciences since 1994 (Chairman 2012 to 2017). Leif is also a member of the European Round Table of Industrialists (Chairman 2009 to 2014) and a Member of the Council of Advisors, Boao Forum for Asia.

Pascal Soriot
Executive Director and CEO (October 2012*)

Skills and experience: Pascal brings a passion for science and medicine as well as significant experience in established and emerging markets, strength of strategic thinking, a successful track record of managing change and executing strategy, and the ability to lead a diverse organisation. He served as Chief Operating Officer of Roche's pharmaceuticals division from 2010 to September 2012 and, prior to that, Chief Executive Officer of Genentech, a biologics business, where he led its successful merger with Roche. Pascal joined the pharmaceutical industry in 1986 and has worked in senior management roles in numerous 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.

Marc Dunoyer
Executive Director and CFO (November 2013*)

Skills and experience: Marc's career in pharmaceuticals, which has included periods with Roussel Uclaf, Hoechst Marion Roussel and GSK, has given him extensive industry experience, including finance and accounting; corporate strategy and planning; research and development; sales and marketing; business reorganisation; and business development. Marc is a qualified accountant and joined AstraZeneca in 2013, serving as Executive Vice-President, Global Product and Portfolio Strategy (GPPS) from June to October 2013. Prior to that, he served as Global Head of Rare Diseases at GSK and (concurrently) Chairman, GSK Japan. He holds an MBA from HEC, Paris and a Bachelor of Law degree from Paris University.

Other appointments: Marc was appointed to the Board of Orchard Therapeutics in June 2018.

Graham Chipchase (R) (NG)
Senior independent Non-Executive Director (April 2012*)

Skills and experience: Graham is Chief Executive Officer and a Director of Brambles Limited, the global supply-chain logistics company listed on the Australian Securities Exchange. Brambles operates in over 60 countries, primarily through the CHEP and IFCO brands. Graham served as Chief Executive Officer of global consumer packaging company Rexam PLC from 2010 to 2016 after serving at Rexam as Group Director, Plastic Packaging and Group Finance Director. Previously, he was Finance Director of Aerospace Services at the global engineering group GKN PLC from 2001 to 2003. After starting his career with Coopers & Lybrand Deloitte, he held various finance roles in the industrial gases company The BOC Group PLC (now part of The Linde Group). He is a Fellow of the Institute of Chartered Accountants in England and Wales and holds an MA (Hons) in chemistry from Oriel College, Oxford.

Other appointments: Chief Executive Officer of Brambles Limited.

Changes to the composition of the Board and its Committees for the year ended 31 December 2018

Philip Broadley
Became a member of the Remuneration Committee on 1 December 2018.

Nazneen Rahman
Became a member of the Nomination and Governance Committee and appointed as Chairman of the Science Committee on 1 July 2018.

Sheri McCoy
Became a member of the Remuneration Committee on 1 July 2018.

Deborah DiSanzo
Became a member of the Audit Committee on 1 November 2018.

Shriti Vadera
Stepped down as a member of the Audit Committee on 30 June 2018 and retired from the Board and as a member of the Remuneration Committee on 31 December 2018 after eight years of service.

Graham Chipchase
Became senior independent Non-Executive Director on 1 January 2019.

Geneviève Berger S

Non-Executive Director
(April 2012*)

Skills and experience: Geneviève was Chief Science Officer at Unilever PLC & NV, and a member of the Unilever Leadership Executive from 2008 to April 2014. She holds three doctorates – in physics, human biology and medicine – and was appointed Professor of Medicine at Université Pierre & Marie Curie, Paris in 1995. Her previous positions include Professor and Hospital Practitioner at Hôpital de la Pitié-Salpêtrière in Paris; Director General at the Centre National de la Recherche Scientifique; Chairman of the Health Advisory Board of the EU Commission; and Non-Executive Director of Smith & Nephew plc. Geneviève oversees sustainability matters on behalf of the Board.

Other appointments: In May 2015, Geneviève was appointed as a Director of Air Liquide SA for a term of four years. She is currently Chief Research Officer at Firmenich SA, Geneva, Switzerland.

Philip Broadley A R

Non-Executive Director
(April 2017*)

Skills and experience: Philip has significant financial and international business experience, having previously been Group Finance Director of Prudential plc for eight years and Old Mutual plc for six years. He started his career at Arthur Andersen where he was a partner for seven years. He is a past Chairman of the 100 Group of Finance Directors in the UK. 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.

Other appointments: Philip chairs the Audit Committees of Legal & General Group plc and Stallergenes Greer plc. He is a member of the Oxford University Audit Committee. He is Treasurer of the London Library and Chairman of the Board of Governors of Eastbourne College.

Deborah DiSanzo A

Non-Executive Director
(December 2017*)

Skills and experience: Deborah is a Harvard University Advanced Leadership Fellow. Prior to this, she served as General Manager for IBM Watson Health, the IBM business unit founded to advance AI in health. Deborah has a distinguished career working at the intersection of healthcare and technology. Prior to IBM, she was CEO of Philips Healthcare, having previously held executive roles at Agilent and Hewlett-Packard. Deborah has been honoured by multiple organisations as a top health influencer including *Health Data Management*, who named her as one of the top 20 people to watch in healthcare IT, and *Modern Healthcare*, who list her as a Top 25 Women in Healthcare. She is the recipient of *Xconomy's* X of the Year Award as a Tech and Health Connector. Babson College recognised Deborah's impact in the world as one of the institutions leading entrepreneurial alumni leaders. Deborah earned an MBA from Babson College and a BS from Merrimack College.

Other appointments: Deborah is a Harvard University Advanced Leadership Fellow.

Rudy Markham A R NG

Non-Executive Director
(September 2008*)

Skills and experience: Rudy has significant international business and financial experience, having formerly held various senior commercial and financial positions with Unilever, culminating in his appointment as its Chief Financial Officer. He has also served as a Non-Executive Director of the UK Financial Reporting Council from 2007 to 2012, as Chairman and a Non-Executive Director of Moorfields Eye Hospital NHS Foundation Trust, and as a Non-Executive Director of Legal & General Group plc.

Other appointments: Rudy is a non-executive member of the Board of United Parcel Services Inc. He is also Vice Chairman of the Supervisory Board of Corbion NV (formerly CSM NV), a Fellow of the Chartered Institute of Management Accountants and a Fellow of the Association of Corporate Treasurers.

Appointed post year-end

Sheri McCoy A R

Non-Executive Director
(October 2017*)

Skills and experience: Sheri is retired Chief Executive Officer of Avon Products, Inc. Prior to joining Avon in 2012, Sheri 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 that represented more than 60% of the company's revenues. Sheri joined Johnson & Johnson as a scientist in research and development and subsequently managed businesses in every major product sector, including consumer, prescription medicines and medical devices, 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 Master's degree in chemical engineering from Princeton University and an MBA from Rutgers University, both in New Jersey, US.

Other appointments: Sheri serves on the boards of Stryker, Kimberly-Clark and Novocure. She is also an industrial adviser for EQT partners where she chairs Certara, the private company, and is a trustee for Stonehill College, Easton, Massachusetts.

Nazneen Rahman S NG

Non-Executive Director
(June 2017*)

Skills and experience: Nazneen has significant scientific, medical and data analysis experience. Her research integrates these to identify and clinically implement human disease genes. She has a strong focus on cancer predisposition genes, in which she is an internationally-recognised expert. She was Head of the Division of Genetics and Epidemiology at the Institute of Cancer Research (ICR), London and Head of Cancer Genetics at the Royal Marsden NHS Foundation Trust for 10 years to 2018. Nazneen was also the founder and Director of the TGLclinical Genetic Testing Laboratory, which used new sequencing technologies to deliver fast, affordable, cancer gene testing to the NHS. Nazneen qualified in medicine from Oxford University in 1991, gained her Certificate of Completion of Specialist Training in medical genetics in 2001 and completed a PhD in molecular genetics in 1999. She has a strong commitment to open science and science communication and has garnered numerous awards, including a CBE in the 2016 Queen's birthday honours in recognition of her contribution to medical sciences.

Marcus Wallenberg S

Non-Executive Director
(April 1999*)

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, Temasek Holdings Limited, and the Knut and Alice Wallenberg Foundation.

Tony Mok S

Non-Executive Director
(January 2019*)

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, with his main focus on biomarker and molecular targeted therapy in lung cancer. He has led and co-led multiple international Phase III trials, including as the principal investigator and first author on the landmark *Iressa* Pan-Asia Study, which confirmed the application of precision medicine for advanced lung cancer. He has also contributed to the development of clinical research infrastructure in China and Asia. Tony is currently the Treasurer of the International Association for the Study of Lung Cancer, having previously served as President, and is on the Board of Directors of the American Society of Clinical Oncology. His work has been recognised by numerous awards including the ESMO Lifetime Achievement Award in 2018.

Other appointments: Tony is a Non-Executive Director of Hutchison China MediTech Limited and a co-founder and the Chairman of Sanomics Limited.

Senior Executive Team (SET)
as at 14 February 2019

Pascal Soriot
CEO

See page 94.

Marc Dunoyer
CFO

See page 94.

In addition to the SET, we have two senior level governance bodies accountable for making key decisions regarding our portfolio and pipeline. Following the organisational changes announced in January 2019, we are creating two therapy area-focused R&D units, one for BioPharmaceuticals (CVRM and Respiratory) and one for Oncology. Consequently, the future structure and nature of these governance bodies will be reviewed in the first quarter of 2019.

Early Stage Product Committees (ESPCs)

The ESPCs are senior level, cross-functional governance bodies with accountability for oversight of our early-stage small molecule and biologics portfolio to Proof of Concept stage.

The ESPCs seek to deliver a flow of products to GMD for Phase III development through to launch. The ESPCs also seek to maximise the value of our internal and external R&D investments through robust, transparent and well-informed decision making that drives business performance and accountability.

Specifically, the ESPCs have responsibility for the following:

- approving early-stage investment decisions
- prioritising the respective portfolios
- licensing activity for products in Phase I and earlier
- delivering internal and external opportunities
- reviewing allocation of R&D resources.

Late Stage Product Committee (LSPC)

The LSPC is also a senior level governance body, accountable for the quality of the portfolio post-Phase III investment decision. Jointly chaired by the EVPs of GMD and GPPS, members include, as appropriate, members of the SET, including the CEO and CFO, and members of the GMD and GPPS leadership teams.

The LSPC seeks to maximise the value of our investments in the late-stage portfolio, also ensuring well-informed and robust decision making. Specific accountabilities include:

- approval of the criteria supporting Proof of Concept
- decision to invest in Phase III development based on agreement of commercial opportunity and our plans to develop the medicine
- evaluation of the outcome of the development programme and decision to proceed to regulatory filing
- decision to invest in life-cycle management activities for the late-stage assets
- decision to invest in late-stage business development opportunities.

Other SET members during the year were:

Bahija Jallal
During 2018, Bahija Jallal was Executive Vice-President, MedImmune. Bahija left AstraZeneca in January 2019.

Mark Mallon
During 2018, Mark Mallon was Executive Vice-President, Global Product and Portfolio Strategy, Global Medical Affairs and Global Corporate Affairs. Mark left AstraZeneca in January 2019.

Katarina Ageborg
Executive Vice-President, Sustainability and Chief Compliance Officer

Katarina was appointed Executive Vice-President, Sustainability in 2017 and has been a member of SET since 2011. She has overall responsibility for the delivery, design and implementation of the Company's sustainability programme, covering three priority areas: access to healthcare; environmental protection; and ethics and transparency. She leads the Global Sustainability function, including teams focusing on Compliance, and Safety, Health and Environment. Katarina was also appointed President of AstraZeneca AB (Sweden) in 2018, and her role is focused on strengthening corporate reputation and relations by actively representing the company in the Swedish business and academic community. Prior to her current roles, Katarina led the Global Intellectual Property function from 2008 to 2011, during which time she streamlined the organisation and launched a new patent filing strategy before taking the role as Chief Compliance Officer. Katarina holds a Master of Law Degree from Uppsala University School of Law in Sweden and ran her own law firm before joining AstraZeneca in 1998.

Sean Bohen
Executive Vice-President, Global Medicines Development and Chief Medical Officer

Sean has been Executive Vice-President, GMD since September 2015 and leads our global late-stage development organisation for both small molecules and biologics, driving a medicines pipeline which features novel and groundbreaking science focusing on three main therapy areas – Oncology, Cardiovascular, Renal & Metabolic diseases and Respiratory disease. He is also the Company's Chief Medical Officer and is responsible for patient safety across the entire AstraZeneca and MedImmune portfolio. He joined AstraZeneca from Genentech, where he held several senior leadership roles across various therapy areas and within early and late development. Before this, Sean was a Clinical Instructor in Oncology at Stanford University School of Medicine, a research associate at the Howard Hughes Medical Institute and a postdoctoral fellow at the National Cancer Institute. He is a graduate of the University of Wisconsin-Madison and later earned his doctorate in biochemistry and his medical degree at the University of California, San Francisco.

Pam Cheng
Executive Vice-President, Operations & Information Technology

Pam joined AstraZeneca in June 2015 after having spent 18 years with Merck/MSD in Global Manufacturing and Supply Chain and Commercial roles. Pam was the Head of Global Supply Chain Management & Logistics for Merck from 2006 to 2011 and led the transformation of Merck supply chains across the global supply network. More recently, Pam was President of MSD China, responsible for MSD's entire business in China. Prior to joining Merck, Pam held various engineering and project management positions at Universal Oil Products, Union Carbide Corporation and GAF Chemicals. Pam holds Bachelor's and Master's degrees in chemical engineering from Stevens Institute of Technology in New Jersey and an MBA in marketing from Pace University in New York. In addition to her role at AstraZeneca, Pam serves as a non-executive Director of the Codexis Inc. Board (CDXS). Pam also serves as an Advisor to the International Society of Pharmaceutical Engineering (ISPE) Board of Directors.

Fiona Cicconi
Executive Vice-President, Human Resources

Fiona joined AstraZeneca in September 2014 as Executive Vice-President, Human Resources and is responsible for the overall design and delivery of the Company's people strategy, impacting over 60,000 employees in more than 100 countries. She started her career at General Electric, where she held various human resources roles within the oil and gas business, which included experience in major global acquisitions and driving change. Subsequently, Fiona spent a number of years at Cisco, overseeing human resources in seven countries in Europe and latterly handling employee relations in Europe, Middle East and Africa, before joining Roche in 2006. There, she was most recently responsible for global human resources for Pharma Technical Operations, where her primary focus was to identify and develop a sustainable supply of leadership and talent from within the organisation.

Ruud Dobber

Executive Vice-President, BioPharmaceuticals Business

Ruud was appointed Executive Vice-President, BioPharmaceuticals Business in January 2019 and is responsible for product strategy and commercial delivery for CVRM and Respiratory. Prior to this, Ruud held the role of Executive Vice-President, North America and was responsible for driving growth and maximising the contribution of the commercial operations in North America. Ruud joined Zeneca in 1997 and has held various senior commercial and leadership roles including Executive Vice-President, Europe. Ruud was also responsible for the development of our late-stage, small molecule antibiotic pipeline as well as its global commercialisation and was Regional Vice-President for European, Middle East and African region, Regional Vice-President for the Asia Pacific region and Interim Executive Vice-President, GPPS. Ruud was a member of the Board and Executive Committee of the European Federation of Pharmaceutical Industries and Associations and was previously Chairman of the Asia division of Pharmaceutical Research and Manufacturers of America. Ruud holds a doctorate in immunology from the University of Leiden, Netherlands and began his career as a research scientist in immunology and ageing.

David Fredrickson

Executive Vice-President, Oncology Business

Dave was appointed Executive Vice-President, Global Head Oncology Business in October 2017 and is responsible for driving growth and maximising the commercial performance of the global oncology and haematology portfolio. In addition, he plays a critical leadership role in setting the Oncology portfolio and product strategy for the organisation. Previously, Dave served as President of AstraZeneca K.K. in Japan, and Vice-President, Specialty Care in the US, spanning oncology, infectious disease, and neuroscience medicines. Dave joined AstraZeneca from Roche/Genentech in 2014, where he was Business Unit Manager, Oncology in Spain and held growing commercial responsibilities in strategy, marketing and sales in the US. He also served for nine years at the Monitor Group, LLC (now Monitor Deloitte Group, LLC), a global strategy consultancy. He has served as Vice Chairman of the European Federation of Pharmaceutical Industries and Associations (EFPIA) Japan and was a member of the Board of the Japan Pharmaceutical Manufacturers Association (JPMA). He is a graduate of Georgetown University (DC) in Government.

Menelas Pangalos

Executive Vice-President, Research & Development BioPharmaceuticals

Mene Pangalos was appointed as Executive Vice-President, R&D BioPharmaceuticals in January 2019 and is responsible for R&D from discovery through to late-stage development for CVRM and Respiratory. Prior to this, he served as Executive Vice-President of AstraZeneca's IMED Biotech Unit and Global Business Development. Since joining AstraZeneca in 2010, Mene has led a transformation of our R&D productivity and has championed an open approach to working with academic and other external partners. Mene previously held senior R&D roles at Pfizer, Wyeth and GSK. Mene holds an Honorary PhD from Glasgow University and is a Fellow of the Academy of Medical Sciences, the Royal Society of Biology and Clare Hall, University of Cambridge. He sits on the Medical Research Council, co-chairs the Life Sciences Council Expert Group on Innovation, Clinical Research and Data and is a member of the Life Sciences Industrial Strategy Implementation Board and National Genomics Board. He is also a Board member of the British Pharmaceutical Group and Cambridge University's Judge Business School.

Jeff Pott

General Counsel

Jeff was appointed General Counsel in January 2009 and has overall responsibility for all aspects of AstraZeneca's Legal and IP function. He joined AstraZeneca in 1995 and has worked in various litigation roles, where he has had responsibility for IP, anti-trust and product liability litigation. Before joining AstraZeneca, he spent five years at the US legal firm Drinker Biddle and Reath LLP, where he specialised in pharmaceutical product liability litigation and anti-trust advice and litigation. He received his bachelor's degree in political science from Wheaton College and his Juris Doctor Degree from Villanova University School of Law.

Appointed post year-end

Iskra Reic

Executive Vice-President, Europe

Iskra was appointed Executive Vice-President, Europe in April 2017 and is responsible for our BioPharmaceutical sales, marketing and commercial operations across our businesses in 30 European countries. Iskra trained as a Doctor of dental surgery at the Medical University of Zagreb, Croatia. She joined AstraZeneca in 2001 and has held a variety of in-market, regional sales and marketing and general management roles, including in Europe as Head of Commercial Operations for Croatia and Head of Specialty Care Central & Eastern Europe and Middle East & Africa. In 2012, she joined AstraZeneca Russia as Marketing & Strategy Director. She was appointed General Manager Russia in 2014 and, under her leadership, AstraZeneca achieved a leading share in its three main therapy areas and became a top-six prescription medicine pharmaceutical company. Iskra's responsibilities were expanded in 2016 to cover both Russia and the Eurasia Area. Iskra was appointed Area Vice President of Russia and Eurasia area in 2016, where she drove strong performance from a 1,500-strong team in a complex and dynamic region. Iskra has an International Executive MBA from the IEDC-Bled School of Management, Slovenia.

Leon Wang

Executive Vice-President, International and China President

Leon Wang is Executive Vice-President, International and China President. He is responsible for the overall strategy and for driving sustainable growth across the region. Leon joined AstraZeneca China in March 2013 and was promoted to President of AstraZeneca China in 2014. Under Leon's leadership, China has become AstraZeneca's second largest market worldwide, and AstraZeneca has become the second largest and the fastest growing multinational pharmaceutical company in China. In January 2017, Leon was promoted to Executive Vice-President, Asia Pacific Region. Prior to joining AstraZeneca, Leon held positions of increasing responsibility in marketing and business leadership at Roche, where he was a Business Unit Vice-President. In addition, Leon holds several positions in local trade associations and other prominent organisations in China. Leon holds an EMBA from China Europe International Business School, and a Bachelor of Arts from Shanghai International Studies University.

José Baselga

Executive Vice-President, Research & Development Oncology

José joined AstraZeneca in January 2019 as Executive Vice-President, R&D Oncology and is responsible for the oncology portfolio from discovery through to late-stage development. He was formerly Physician-in-Chief at Memorial Sloan Kettering Cancer Center, which became the leader in early-phase clincial trials for cancer therapies and diagnostic genetic sequencing under his leadership. In addition, he was Professor of Medicine at Weill Cornell Medical College and President of the American Association for Cancer Research (AACR). José is an international thought leader on innovation in cancer care and clinical research. His work has led to the approval of life-saving cancer therapies and the creation of several biopharmaceutical companies. José is an elected member of the National Academy of Medicine, the American Society of Clinical Investigation, the Association of American Physicians, and an elected Fellow of the AACR Academy. He is a past President of the European Society for Medical Oncology and recently received their Lifetime Achievement Award. He serves on the Board of Directors of the American Society of Clinical Oncology and AACR.

Corporate Governance Report
Activities of the Board

All Directors are collectively responsible for the success of the Group.

Principal matters considered by the Board in 2018

The principal matters considered by the Board during 2018 and the link to the Group's strategic priorities are set out in the table. As part of the business of each Board meeting, the CEO typically submits a progress report, giving details of business performance and progress against the goals the Board has approved. To ensure that the Board has good visibility of the key operating decisions of the business, members of the SET attend Board meetings regularly and Board members meet other senior executives throughout the year. The Board also receives accounting and other management information about our resources, and presentations from internal and external speakers on legal, governance and regulatory developments.

For more information on the role of the Board and the Non-Executive Directors, see Compliance with the UK Corporate Governance Code from page 102.

Key

- Achieve Scientific Leadership
- Return to Growth
- Be a Great Place to Work
- Achieve Group Financial Targets

Area of focus		Strategic priority
Strategic matters	> The Group's overall strategy, including its long-range plan, annual budget and strategic options	
	> The Group's capital structure, including financing needs, credit rating and capital strategy	
	> Requests for approval of business development transactions of a size requiring Board approval	
	> Dividend decisions	
Operational matters	> Executive management reports, including business performance reports, R&D pipeline updates, the results of key clinical trials, a review of Operations (global manufacturing and supply chain network) and a review of Oncology pricing	
	> Quarterly results announcements	
	> Progress with construction of the Group's new strategic R&D centre and global corporate headquarters at Cambridge Biomedical Campus in the UK	
Stakeholders	> Investor perceptions	
	> Employee gender data	
	> Sustainability matters	
	> Approval of a Board Inclusion and Diversity Policy	
	> Visits to R&D and Commercial sites in the US and a review of the Group's US business	
	> Participation in employee 'town hall' meetings and informal meetings with groups of 'high-potential' employees	
Governance, assurance and risk management	> Reports from Board Committees	
	> Routine succession planning for SET and Board-level roles	
	> Risks arising from Brexit and mitigation plans	
	> Cybersecurity risk and mitigation plans	
	> Year-end governance and assurance reports	
	> The Group's viability and risk appetite statements	
	> The annual review of the performance of the Board, its Committees and individual Directors	
	> Private discussions between Non-Executive Directors only	

Board performance evaluation

2018 Overview

During the year, the Board conducted the annual evaluation of its own performance and that of its Committees and individual Directors. The 2018 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. Linstock has no other commercial relationship with the Company. 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 2018 and was also used by the Chairman as the basis for individual conversations with each Board member prior to the full Board discussion.

The outcomes of the evaluation are set out in the table.

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 2020.

"The Board operates effectively and in a manner that encourages open and frank discussion."

2018 Outcomes

Main areas covered:	Main conclusions and recommendations:
> Board composition and dynamics > Stakeholder oversight > Board meeting management and support > Board Committees > Board oversight > Risk management and internal control > Succession planning and human resource management > Priorities for 2019	> The Board operates effectively and in a manner that encourages open and frank discussion. > The Board identified certain areas that could be improved, including its understanding of our competitors' strategies and performance, careful management of the late stages of the recruitment process for new Non-Executive Directors and developing and refining the role of the Science Committee to ensure it meets the needs of the Board. > The Board should continue to develop a deep understanding of digital technology and its application in the pharmaceutical industry. > The reviews of the Board's Committees did not raise any significant problems and concluded that the Committees are operating effectively. > In respect of the 2018 annual performance evaluation, it was concluded that each Director continues to perform effectively and to demonstrate commitment to his or her role.

Chairman evaluation

Process	Overall conclusion
The 2018 evaluation also included a review of the performance of the Chairman by the other Directors, led by the senior independent Non-Executive Director and absent the Chairman.	No significant issues needed to be addressed. The Chairman's leadership of the Board continued to be regarded as excellent. His management of Board meetings was commended. He created an environment where different views could be freely expressed and enabled all Directors to contribute to discussion and decision-making. He had a good, open and transparent relationship with executive management. His generous time commitment supporting management in other parts of the business was praised. His interactions with employees of the Company at all levels in various parts of the world were excellent. He continued to be very active representing the Company in relation to external stakeholders. The senior independent Non-Executive Director provided feedback to the Chairman after the review of his performance, including minor suggestions for ways in which he might enhance the way the Board operated.

Actions against prior year recommendations

2017 evaluation	2018 actions taken
Provide further opportunities to visit and learn from different AstraZeneca teams and sites to help build a balanced understanding of the business.	In September 2018, the Board made a two-day visit to MedImmune in Gaithersburg, MD, US, our main US hub site, US R&D centre and MedImmune HQ, and to the HQ of our North American commercial business in Wilmington, DE, US. Numerous interactions with employees at all levels took place. The April 2018 Science Committee meeting was held at our R&D site in Gaithersburg, US. In addition, certain Audit Committee members visited our business in China during the year and individual Non-Executive Directors visited our business in Brazil, our South San Francisco site and our sites in Cambridge, UK and Gothenburg, Sweden.
Ensure succession planning activities for business critical roles are undertaken proactively with opportunities for all Board members to input.	Each year, the CEO and the EVP, Human Resources make a presentation to the Board about SET-level succession planning and seek the Board's views and input. Board members have the opportunity during the year to meet potential succession candidates for senior, business critical roles when they make presentations to the Board or, more informally, at dinners or 'high-potential' employee meetings. In addition, the CEO keeps the Board updated about specific SET-level succession plans, seeking Directors' views and input. In a number of cases, the Chairman of the Board and other Non-Executive Directors have met potential candidates and provided feedback ahead of an appointment being made.

Employee engagement: central to AstraZeneca's progress

In 2018, all employees were invited to help shape the next phase of AstraZeneca's strategic journey through a Group-wide strategy crowdsourcing event. The two-week event focused on key themes, including the changing world, future technology, next wave of science and patient-centricity, and generated 56,000 ideas and comments from employees.

In line with the Group's commitment to inclusion, technology was used to enable employees to participate in any language and this supported participation from 70 countries. Technology was also used to help to analyse and prioritise the inputs.

The ideas and comments submitted by employees helped inform recommendations that were made to the AstraZeneca Board as part of the Group's annual strategy review process. The inputs and ideas were also discussed by the Chairman and CEO during engagement events, including an all-employee webcast held across the Group's internal social media platform in December.

56,000

56,000 ideas and comments from employees

Corporate Governance Report
Connecting with our stakeholders

In striving to achieve our Purpose to push the boundaries of science and deliver life-saving medicines, our business touches the lives of many people. We exist in a complex and evolving regulatory and scientific environment and we have a number of key stakeholder groups.

Connecting with our stakeholders

The Board is supportive of the upcoming reporting requirements surrounding stakeholder engagement, against which we will report when they come into effect in 2019.

When making decisions, we take the course of action that we consider best leads to the success of the Company over the long term, and this includes considering the broad range of stakeholders that interact with, and are impacted by, our business.

For more information about our Code of Ethics, see page 43.

Our Values and Code of Ethics empower employees to make the best decisions in the interest of the Group and our stakeholders, and help to ensure that these considerations are made not only at Board level, but throughout our organisation.

The following table summarises our key stakeholders, as well as the engagement that has been undertaken across the business during 2018.

A full list of our stakeholders can be found in our 2018 Sustainability Report at www.astrazeneca.com/sustainability.

	Shareholders, Investors & Analysts	Patients	Employees
Overview Significance of the stakeholder to the business	The Board is accountable to shareholders, and, in accordance with section 172 of the Companies Act 2006, must act in a way that is likely to promote the success of the Company for the benefit of its members as a whole. AstraZeneca aims to ensure that a good dialogue with shareholders, investors and analysts is maintained, and that their issues and concerns are understood and considered.	To achieve our Purpose we need to engage with and understand the needs of patients.	Our 64,600 employees make AstraZeneca what it is. We are committed to ensuring that AstraZeneca is a Great Place to Work for our employees and we rely on their commitment to uphold the Values, deliver the strategic priorities and deliver the changes necessary to sustain and improve short- and long-term performance.
Issues and factors Issues and factors which are most important to the stakeholder group	> Understanding the strategy and operations of the Group > Financial performance and commercial success, including return to sales growth > Successful development of the pipeline > Understanding the exposure to macro-economic risk > Opportunity for dialogue with management on key matters, eg performance and executive remuneration > Sustainability and the environmental and ethical impact of the Group	> Support throughout the entire patient journey – through diagnosis, treatment and wellness > Safety and efficacy of medicines > Access to an uninterrupted supply of medicines	> Understanding the Group performance and the factors that impact this > Engagement with, and the opportunity to put questions and ideas to, senior leaders > Collaboration across the Group and the opportunity to learn and share
Engagement Examples of engagement in 2018	> Annual General Meeting in May 2018 > Board Directors met investors, analysts and investor bodies > Quarterly results conference calls for analysts and investors > Investor Relations Team and senior management met regularly with investors, including office visits, industry and broker conferences, roadshows and group meetings > Comprehensive investor perception study, the results of which were presented to the Board > Hosted an Emerging Markets call in Shanghai with a focus on China	> Engaged patients in our development and clinical trial programmes to ensure a more patient-informed medicine > Collaboration with patient advocacy groups and establishment of patient advisory boards > Established patient support and patient affordability programmes > Organisation of Patient Engagement Day in the US	> CEO and SET provided quarterly performance reports to employees > Group-wide strategy crowdsourcing event generated 56,000 ideas and comments in two weeks > All employees invited to participate in Pulse survey > Board and SET conducted site visits, and in-person and webcast town hall/Q&A sessions with employees > Senior Leadership engagement via Trades Union and Employee Representative forums
Outcomes Any actions which resulted	> The Investor Relations Team has been recognised for best practice by the Investor Relations Society > Following discussions with investors, there has been an increased focus on sustainability matters within our quarterly results announcements	> Patient insight has been integrated into the development of innovative digital technologies (iPREDICT) and clinical trials (study design and protocol simulation) > Initiated a Group-wide initiative on patient-centricity and patient-centric business models > Increased number of programmes deployed to support patients throughout the patient journey	> Ideas generated from the crowdsourcing event reviewed and incorporated into annual strategy recommendations to the Board > Unit action plans developed in response to Pulse survey results

Payers	Government – general business environment	Communities	Suppliers
Across the world, patient access to innovative medicines increasingly depends on public funding. HTA agencies, national and regional healthcare insurance funds and government bodies appraise the clinical and economic value of our medicines following successful regulatory approval. Delays in approval by such bodies could negatively impact market access. It is important that AstraZeneca fosters relations with payer organisations and anticipates relevant trends to respond effectively to payers' requirements.	Government policy determines the business environments in which we operate. This can be through direct policies (eg tax and fiscal policy) and indirect policies that can create a supportive environment for our operations (eg public science and infrastructure investments). Governments may also be responsible for creating and enforcing regulations which govern our licence to operate.	We rely on, and aim to make a positive impact on, the local communities and environment in which we operate, as well as the communities which our medicines reach. Increasingly, communities expect us to support the issues and initiatives that intersect with our area of commercial focus and expertise. Communities have a direct influence on the health and wellbeing of patients, caregivers and families.	In 2018, we spent approximately $13 billion with suppliers on goods or services that are critical to the effective operation of our entire value chain; from discovery to development, manufacturing and supply of our medicines to patients. Many of our business-critical operations (including certain R&D processes, IT systems, HR, finance, tax and accounting services) are managed with the support of our suppliers.
> Access to innovative medicines in a timely, fair and sustainable manner > Predictability and containment of reimbursement expenditure for pharmaceuticals > Breakthrough therapies and the cost impact on public budgets > Transparency and accountability of payer organisations > Management of pricing and generating savings in established/mature product markets	> Investment environment > Research funding and scientific collaborations > Medicines pricing and reimbursement > Trade policy > Regulatory frameworks > Price reporting > Safety and efficacy of drugs > Patient access	> The impact of the our activities and plans on the local area and the environment > Raising awareness of healthcare > Promotion of science-based education and careers > Investment in local infrastructure and capacity building initiatives > Support for programmes, platforms and policy that make healthcare accessible and protects patients	> Understanding of AstraZeneca's strategy and how the supplier can best navigate the organisation to help create innovative and new opportunities > Ability to resolve potential problems and issues in their relationship with AstraZeneca > Creating a trusting environment between the supplier and AstraZeneca > That AstraZeneca acts ethically, fairly and transparently
> Engaged with HTA agencies over the need to reform evaluation criteria in clinical trials > Contributed to the public debate around pricing of innovative medicines and assisted in facilitating a greater understanding of the clinical and economic value of such medicines to society	> Meetings and forum discussions with governments and policy makers to increase understanding of supporting investment in life sciences, regulation of the pharmaceutical industry and improving access to new medicines > In the UK, we engaged extensively on Brexit, to ensure regulatory and policy frameworks support patients' needs and our operations > In the US, we engaged in discussions on evolving the current reimbursement system > Hosted site visits for international and local politicians, including tours of our manufacturing and R&D facilities	> Young Health Programme with its focus on disease prevention and youth reached nearly 335,000 young people > AstraZeneca HealthCare Foundation provided $1.16 million in grants to 11 non-profit organisations for programmes to prevent and reduce CV disease > Donated more than $686 million of medicines in connection with patient assistance programmes around the world > Donations to support more than 1,000 non-profit organisations in 70 countries for a total of $57 million in 2018 > Engaged in capacity building projects such as Healthy Lung Asia, Phakamisa and Healthy Heart Africa	> Engaged with suppliers via summits and meetings with senior management, which allows discussion and partnership between suppliers and AstraZeneca > Enabling small and diverse suppliers in the US access to business opportunities through our participation in outreach events, collaborations, and memberships with various industry groups and diversity councils > Third parties and suppliers are provided access to azethics.com, which allows them to raise concerns in confidence
	> In the UK, we launched a high-level expert group on Innovation, Research and Data co-chaired with Ministers to advise on how to improve the UK research and clinical trials environment	> Expansion of disease prevention programming in connection with government and NGO partnerships in Asia and Latin America > Export of Healthy Lung Asia initiative to Latin America and the Middle East > Increased investment in public-private partnerships as a mechanism to address global and local health issues	> Supplier forums have helped our supply base gain a better understanding of both AstraZeneca's strategy and how we can work with suppliers to create a closer connection between our medicines and the patients we aim to help > In the US we received several external industry recognitions and awards for supporting diverse suppliers

Corporate Governance Report
Compliance with the UK Corporate Governance Code

Corporate governance

We have prepared this Annual Report with reference to the UK Corporate Governance Code published by the UK Financial Reporting Council (FRC) in April 2016.

Our statement of compliance (together with the Corporate Governance Report and other sections of this Annual Report) describes how we apply the main principles of good governance in the UK Corporate Governance Code. We have complied throughout the accounting period with the provisions of the UK Corporate Governance Code, which is available on the FRC's website, www.frc.org.uk.

This statement of compliance should be read in conjunction with the wider Corporate Governance Report from page 98, Nomination and Governance Committee Report from page 108, the Audit Committee Report from page 110 and the Directors' Remuneration Report from page 120.

Leadership

A.1 The role of the Board

The Board discharges its responsibilities as set out in the Corporate Governance Overview on page 93 through a programme of meetings that includes regular reviews of financial performance and critical business issues, review and approval of the Group's strategy and long-range plan, and the formal annual strategy review day.

The Board held 13 meetings in 2018, including its usual annual strategy review. Six took place in London, UK; one was held at AstraZeneca's facilities in the US; and six were held as teleconference or videoconference calls. The Board is currently scheduled to meet six times in 2019 and will meet at such other times as may be required to conduct business.

The Board maintains and periodically reviews 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. The matters that have not been expressly reserved to the Board are delegated by the Board to its Committees or the CEO.

As shown in the Corporate Governance Overview, there are four principal Board Committees. The membership and work of these Committees is described on the following pages. In addition, there may from time to time be constituted *ad hoc* Board Committees for specific projects or tasks. In these cases, the scope and responsibilities of the Committee are documented. The Board provides adequate resources to enable each Committee to undertake its duties.

The membership of the Board as at 14 February 2019 and information about individual Directors is contained in Board of Directors on pages 94 and 95.

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.

A.2 Division of responsibility, A.3 The Chairman

The roles of Chairman and CEO are separate. Leif Johansson, our Non-Executive Chairman, is responsible for leadership of the Board. The CEO, Pascal Soriot is responsible to the Board for the management, development and performance of our business for those matters for which he has been delegated authority from the Board. Although the CEO retains full responsibility for the authority delegated to him by the Board, he has established, and chairs, the SET, which is the vehicle through which he exercises that authority in respect of our business. The roles of the Board, Board Committees, Chairman and CEO are documented, as are the Board's reserved powers and delegated authorities.

Leif Johansson was considered by the Board to be independent upon his appointment as Chairman. In accordance with the April 2016 UK Corporate Governance Code, the test of independence is not appropriate in relation to the Chairman after his appointment.

A.4 Non-Executive Directors

In anticipation of his retirement from the Board at the end of the 2019 AGM, Rudy Markham stepped down from the role of senior independent Non-Executive Director on 31 December 2018, having held the role since April 2015. Graham Chipchase, who joined the Board as a Non-Executive Director in April 2012, was appointed senior independent Non-Executive Director with effect from 1 January 2019. The role of the senior independent Non-Executive Director is to serve as a sounding board for the Chairman 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 Chairman or Executive Directors has failed to resolve, or for which such contact is inappropriate.

As part of the business of each Board meeting, the CEO typically submits a progress report, giving details of business performance and progress against the goals the Board has approved. To ensure that the Board has good visibility of the key operating decisions of the business, members of the SET attend Board meetings regularly and Board members meet other senior executives throughout the year. The Board also receives accounting and other management information about our resources, and presentations from internal and external speakers on legal, governance and regulatory developments. At the end of Board meetings, the Non-Executive Directors meet without the Executive Directors present to review and discuss any matters that have arisen during the meeting and/or such other matters as may appear to the Non-Executive Directors to be relevant in properly discharging their duty to act independently.

Effectiveness

B.1 The composition of the Board	The Board comprises of 10 Non-Executive Directors, including the Chairman, and two Executive Directors – the CEO, Pascal Soriot, and the CFO, Marc Dunoyer. Its responsibilities are set out in the Corporate Governance Overview on page 93. During 2018, the Board considered the independence of each Non-Executive Director for the purposes of the UK Corporate Governance Code and the corporate governance listing standards of the NYSE (Listing Standards). Except for Marcus Wallenberg, the Board considers that all the Non-Executive Directors are independent. The Board noted that, as of September 2017, Rudy Markham had served on the Board for nine years but determined that he remains independent in character and judgement, as evidenced by the way in which he discharges his duties as a Board and Board Committee member.	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 4.07% interest in the issued share capital of the Company as at 14 February 2019. For these reasons, 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. In April 2010, he was appointed as a member of the Science Committee, reflecting his interest in innovation and R&D, knowledge of the history of the Company and its scientific heritage and culture, and his broad experience of other industries and businesses in which innovation and R&D are important determinants of success.
B.2 Appointments to the Board, succession planning and diversity	The Nomination and Governance Committee and, where appropriate, the full Board, regularly review the composition of the Board and the status of succession to both senior executive management and Board-level positions. Directors have regular contact with, and access to, succession candidates for senior executive management positions. For more information on the Board's succession planning, see the Nomination and Governance Committee Report on page 108 and the actions against prior year recommendations in the Board performance evaluation on page 99.	During 2018, a Board Inclusion and Diversity Policy was approved, which can be found on the Company's website, www.astrazeneca.com. For more information on the Board's approach to Inclusion and Diversity, see the Nomination and Governance Committee Report on page 108.
B.3 Commitment	Our expectation is that Non-Executive Directors should be prepared to commit 15 days a year, as an absolute minimum, to the Group's business. In practice, Board members' time commitment exceeds this minimum expectation when all the work that they undertake for the Group is considered, particularly in the case of the Chairman of the Board and the Chairs of the Board Committees. As well as their work in relation to formal Board and Board Committee meetings, the Non-Executive Directors also commit time throughout the year to meetings and telephone calls with various levels of executive management, visits to AstraZeneca's sites throughout the world and, for new Non-Executive Directors, induction sessions and site visits.	On occasions when a Director is unavoidably absent from a Board or Board Committee meeting, for example where a meeting clashes with their other commitments, they still receive and review the papers for the meeting and typically provide verbal or written input ahead of the meeting, usually through the Chairman of the Board or the Chair of the relevant Board Committee, so that their views are made known and considered at the meeting. Given the nature of the business to be conducted, some Board meetings are convened at short notice, which can make it difficult for some Directors to attend due to prior commitments.
B.4 Development	The Nomination and Governance Committee Report from page 108 provides information about the appointment process for new Directors. Newly appointed 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.	As part of each Director's individual discussion with the Chairman, 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.
B.5 Information and support	The Company Secretary is responsible to the Chairman 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.	
B.6 Evaluation	During the year, the Board conducted the annual evaluation of its own performance and that of its Committees and individual Directors. The 2018 evaluation was carried out internally, although Lintstock Ltd, a London-based corporate advisory firm that provides objective and independent counsel to leading European companies, provided support.	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 2020. For details and the conclusions of the Board performance evaluation, see page 99.
B.7 Re-election	In accordance with Article 66 of the Articles, all Directors retire at each AGM and may offer themselves for re-election by shareholders. Accordingly, all the Directors will retire at the AGM in April 2019. The Notice of AGM will give details of those Directors seeking election or re-election.	

Corporate Governance Report
Compliance with the UK Corporate Governance Code *continued*

Accountability

C.1 Financial and business reporting	The Board considers this Annual Report, taken as a whole, to be fair, balanced and understandable, and provides the necessary information for shareholders to assess AstraZeneca's position and performance, business model and strategy.	The Board as a whole takes a keen interest in the Company's financial and business reporting including, in particular, reviewing the Company's quarterly financial results announcements and through its oversight of the Company's Disclosure Committee. For more information about the Disclosure Committee, see Other Governance information on page 105.
C.2 Risk management and internal control	The Board has overall responsibility for our system of internal controls and risk management policies and has an ongoing responsibility for reviewing their effectiveness. During 2018, the Directors continued to review the effectiveness of our system of controls, risk management and high-level internal control processes. These reviews included an assessment of internal controls and, in particular, financial, operational and compliance controls, and risk management and their effectiveness, supported by management assurance of the maintenance of controls reports from Internal Audit Services, as well as the external auditor on matters identified in the course of its statutory audit work. The system of controls is designed to manage rather than eliminate the risk of failure to achieve business objectives and can only provide reasonable (not necessarily absolute) assurance of effective operation and compliance with laws and regulations.	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 and describe our principal risks and uncertainties, see the Risk Overview from page 70 and Risk from page 220.
C.3 Audit Committee and Auditors	The Audit Committee spends a significant amount of its time considering the landscape of enduring risks, specific and current risks, and emerging risks.	For information on the role and work of the Audit Committee, see the Audit Committee Report from page 110.

Remuneration

D.1 The level and components of remuneration, D.2 Procedure	Information about our approach to remuneration and the role and work of the Remuneration Committee, is set out in the Directors' Remuneration Report from page 120. Our Remuneration Policy is available on our website at www.astrazeneca.com.	Subject to specific Board approval in each case, Executive Directors and other 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.

Relations with shareholders

E.1 Dialogue with shareholders	The Board aims to ensure that a good dialogue with our shareholders is maintained and that their issues and concerns are understood and considered. In our quarterly, half-yearly and annual financial and business reporting to shareholders and other interested parties, we aim to present a balanced and understandable assessment of our strategy, financial position and prospects. We make information about the Group available to shareholders through a range of media, including our corporate website, www.astrazeneca.com, which contains a wide range of data of interest to institutional and private investors. We consider our website to be an important means of communication with our shareholders.	Our Investor Relations Team acts as the main point of contact for investors throughout the year. We have frequent discussions with current and potential shareholders on a range of issues, including in response to individual *ad hoc* requests from shareholders and analysts. We also hold meetings to seek shareholders' views. Board members are kept informed of any issues, and receive regular reports and presentations from executive management and our brokers to assist them to develop an understanding of our major shareholders' views about the Group. From time to time, we conduct perception studies with institutional shareholders and a limited number of analysts to ensure that we are communicating clearly with them and that a high-quality dialogue is being maintained. The results of these studies are reported to, and discussed by, the full Board. As discussed above, the senior independent Non-Executive Director, Graham Chipchase, is available to shareholders if they have concerns that contact through the normal channels of Chairman, CEO and/or CFO has failed to resolve, or in relation to which such contact is inappropriate.
E.2 Constructive use of the AGM	All shareholders, including private investors, have an opportunity at the AGM to put questions to members of the Board about our operation and performance. Formal notification of the AGM is sent to shareholders at least one month in advance. All Board members ordinarily attend the AGM to answer questions raised by shareholders. In line with the UK Corporate Governance Code, details of proxy voting by shareholders, including votes withheld, are given at the AGM and are posted on our website following the AGM.	The Company's 2018 AGM was held in London on 18 May 2018. The Company's 2019 AGM will be held on 26 April 2019. The meeting place will be in London, UK. A Notice of AGM will be sent to all registered holders of Ordinary Shares and, where requested, to the beneficial holders of shares.

Corporate Governance Report
Other Governance information

US corporate governance requirements

Our ADSs are traded on the NYSE and, accordingly, we are subject to the reporting and other requirements of the SEC applicable to foreign private issuers. Section 404 of the Sarbanes-Oxley Act requires companies to include in their annual report on Form 20-F filed with the SEC, a report by management stating its responsibility for establishing internal control over financial reporting and to assess annually the effectiveness of such internal control. We have complied with those provisions of the Sarbanes-Oxley Act applicable to foreign private issuers.

The Board continues to believe that the Group has a sound corporate governance framework, good processes for the accurate and timely reporting of its financial position and results of operations, and an effective and robust system of internal controls. We have established a Disclosure Committee, further details of which can be found in the Disclosure Committee section below.

The Directors' assessment of the effectiveness of internal control over financial reporting is set out in the Directors' Annual Report on Internal Controls over Financial Reporting on page 143.

We are required to disclose any significant ways in which our corporate governance practices differ from those followed by US companies under the Listing Standards of the NYSE. In addition, we must comply fully with the provisions of the Listing Standards relating to the composition, responsibilities and operation of audit committees, applicable to foreign private issuers. These provisions incorporate the rules concerning audit committees implemented by the SEC under the Sarbanes-Oxley Act. We have reviewed the corporate governance practices required to be followed by US companies under the Listing Standards and our corporate governance practices are generally consistent with those standards.

Business organisation

Disclosure Committee

Our disclosure policy provides a framework for the handling and disclosure of inside information and other information of interest to shareholders and the investment community. It also defines the role of the Disclosure Committee. The members of the Disclosure Committee in 2018 were: the CFO, who chaired the Disclosure Committee; the EVP, GMD (who is also the Company's Chief Medical Officer); the EVP, GPPS, Global Medical Affairs and Global Corporate Affairs; the General Counsel; the Vice-President, Corporate Affairs; the Head of Investor Relations; and the Vice-President Finance, Group Controller. Other senior executives attend its meetings on an agenda-driven basis. The Deputy Company Secretary acted as secretary to the Disclosure Committee. The Disclosure Committee meets regularly to assist and inform the decisions of the CEO concerning inside information and its disclosure. Periodically, it reviews our disclosure controls and procedures and its own operation as part of work carried out to enable management and the Board to assure themselves that appropriate processes are operating for both our planned disclosures, such as our quarterly results announcements and scheduled investor relations events, and our unplanned disclosures in response to unforeseen events or circumstances.

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.

Global Compliance and Internal Audit Services (IA)

The role of the Global Compliance function is to help the Group achieve its strategic priorities by doing business the right way, with integrity and high ethical standards. Global Compliance continues to focus on ensuring the delivery of an aligned approach to compliance that addresses key risk areas across the business, including risks relating to external parties and anti-bribery/anti-corruption. Our priorities include improving compliance behaviours through effective training and communication; monitoring compliance with our Code of Ethics and supporting requirements; providing assurance that we are conducting appropriate risk assessments and due diligence on third parties whom we engage for services; and ensuring that employees and external parties can raise any concerns. Global Compliance and IA work with various specialist compliance functions throughout our organisation to co-ordinate compliance activities.

We take all alleged compliance breaches and concerns extremely seriously, and investigate them and report the outcome of such investigations to the Audit Committee, as appropriate. Internal investigations are undertaken by staff from our Global Compliance, Human Resources and/or Legal functions. When necessary, external advisers are engaged to conduct and/or advise on investigations.

Serious compliance breaches are raised with the Audit Committee. Where a significant breach has occurred, management, in consultation with our Legal function, will consider whether the Group needs to disclose and/or report the findings to a regulatory or governmental authority.

Global Compliance provides direct assurance to the Audit Committee on matters concerning compliance issues, including an analysis of compliance breaches. Complementing this, IA carries out a range of audits that include compliance-related audits and reviews of the assurance activities of other Group assurance functions. The results from these activities are reported to the Audit Committee.

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.

Internal control objectives considered by IA include:

- consistency of operations or programmes with established objectives and goals and effective performance
- effectiveness and efficiency of operations and employment of resources
- compliance with significant policies, plans, procedures, laws and regulations
- reliability and integrity of management and financial information processes, including the means to identify, measure, classify, and report such information
- 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.

Code of Ethics

Our Code of Ethics (the Code), which is available on our website, www.astrazeneca.com, applies to all Executive and Non-Executive Directors, officers, employees and temporary staff, in all companies within our Group worldwide. A Finance Code complements the Code and applies to the CFO, the Group's principal accounting officers (including key Finance staff in major overseas subsidiaries) and all Finance function employees. 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.

The Code is at the core of our compliance programme. It has been translated into approximately 40 languages and outlines how our commitments to ethics, honesty, integrity and responsibility are to be realised through consistent actions across all areas of the business.

Compliance with the Code is mandatory and every employee receives annual training on it which they are required to complete. The Code is designed to support employee understanding and adherence by outlining our commitments in simple terms and focusing on why these commitments matter. The Code is comprised of our Company Values, expected behaviours and Global Policies, and is further supported by requirements at the global, local and business-unit level, to provide clear guidance and direction to employees in carrying out their daily work. The Code is also reviewed periodically and updated to take account of changing legal and regulatory obligations.

The Code recommends that employees report possible violations to their line managers or to their local Human Resources, Legal, or Compliance partners. The Code also contains information on how to report possible violations through our helpline, which includes the AZethics telephone lines, the AZethics website, and the Global Compliance email and postal addresses. The externally-operated website is available in 38 languages to facilitate reporting. While telephone lines are listed for 123 countries, local carriers may impose in-country dialling restrictions, potentially resulting in disruptions to connectivity. AstraZeneca is updating the AZethics webpages in all languages to provide enhanced dialling information and to prompt the use of online reporting should telephone connectivity be limited. The helpline is available to both employees and to external parties to report any concerns or make enquiries. 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 self-reporting, which 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 2018 Code training. In addition, in 2018, 428 reports of alleged compliance breaches or other ethical concerns were made through the helpline, including reports made by any anonymous route that could be considered whistleblowing; in 2017 there were 359 reports.

Other Matters

Corporate governance statement under the UK Disclosure Guidance and Transparency Rules (DTR)

The disclosures that fulfil the requirements of a corporate governance statement under the DTR can be found in this section and in other parts of this Annual Report as listed below, each of which is incorporated into this section by reference:

- major shareholdings
- Articles.

Shareholder Information from page 232.

Corporate Governance Report
Other Governance information
continued

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 201.

Branches and countries in which the Group conducts business
In accordance with the Companies Act 2006, we disclose below our subsidiary companies that have representative or scientific branches/offices outside the UK:

- AstraZeneca UK Limited: Algeria (scientific office), Angola, Chile, Costa Rica, Croatia, Cuba, Dubai (branch office), Georgia, Ghana (scientific office), Jordan, Kazakhstan, Lebanon, Romania, Russia, Saudi Arabia (scientific office), Serbia, Slovenia (branch office), Syria, Ukraine and Yemen (scientific office)
- AstraZeneca AB: Egypt (scientific office) and Slovakia (branch office)
- AstraZeneca Singapore Pte Limited: Vietnam
- Astra Export & Trading AB: United Arab Emirates (branch office).

Distributions to shareholders – dividends for 2018
Details of our distribution policy are set out in the Financial Review from page 74 and Notes 23 and 24 to the Financial Statements from page 185.

The Company's dividend for 2018 of $2.80 (215.2 pence, SEK 25.38) per Ordinary Share amounts to, in aggregate, a total dividend payment to shareholders of $3,548 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.

A shareholders' resolution was passed at the 2018 AGM authorising the Company to purchase its own shares. The Company did not purchase any of its own shares in 2018. On 31 December 2018, the Company did not hold any shares in treasury.

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 both the Strategic Report (in the Therapy Area Review from page 50) and the Directors' Report. Information on patent expiry dates for key marketed products is included in Patent Expiries of Key Marketed Products from page 217. Our approach to product development and our development pipeline are also covered in detail with additional information by therapy area in the Strategic Report.

The financial position of the Group, its cash flows, liquidity position and borrowing facilities are described in the Financial Review from page 74. In addition, Note 27 to the Financial Statements from page 187 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 16 and 18 to the Financial Statements from page 174.

Having assessed the principal risks and other matters considered in connection with the viability statement on page 71, the Directors consider it appropriate to adopt the going concern basis of accounting in preparing the Annual Report and Financial Statements.

Changes in share capital
Changes in the Company's Ordinary Share capital during 2018, including details of the allotment of new shares under the Company's share plans, are given in Note 23 to the Financial Statements on page 185.

Directors' shareholdings
A shareholders' resolution was passed at the 2018 AGM which updated the Articles and removed the requirement for a Director to become the beneficial owner, within two months of the date of their appointment, of Ordinary Shares in the Company with an aggregate nominal value of $125, which currently represents at least 500 Ordinary Shares. The requirement was removed because such qualification shareholdings are no longer common practice and the cost of obtaining such shares could hinder the recruitment of new Directors.

Full details of each Director's interests in shares of the Company are set out in Directors' shareholdings on pages 137 and 138, along with information about the shareholding expectations of the Remuneration Committee (in respect of Executive Directors and SET members) and the Board (in respect of Non-Executive Directors).

Political donations
Neither the Company nor its subsidiaries made any EU political donations or incurred any EU political expenditure in 2018 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 2019 AGM, similar to that passed at the 2018 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 2018, the Group's US legal entities made contributions amounting in aggregate to $1,156,800 (2017: $1,282,250) 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 27 from page 187, include further information on our use of financial instruments.

External auditor
A resolution will be proposed at the AGM on 26 April 2019 for the re-appointment of PricewaterhouseCoopers LLP (PwC) as auditor of the Company. During 2018, PwC undertook various non-audit services. More information about this work and the audit and non-audit fees that we have paid are set out in Note 31 to the Financial Statements on page 200. The external auditor is not engaged by AstraZeneca to carry out any non-audit work in respect of which it might, in the future, be required to express an audit opinion. As explained more fully in the Audit Committee Report from page 110, the Audit Committee has established pre-approval policies and procedures for audit and non-audit work permitted to be carried out by the external auditor and has carefully monitored the objectivity and independence of the external auditor throughout 2018.

Electronic communications with shareholders
The Company has been authorised by shareholders to place shareholder communications (such as the Notice of AGM and this Annual Report) on the corporate website in lieu of sending paper copies to shareholders (unless specifically requested). While recognising and respecting that some shareholders may have different preferences about how they receive information from us, we will continue to promote the benefits of electronic communication given the advantages that this has over traditional paper-based communications, both in terms of the configurability and accessibility of the information provided and the consequent cost savings and reduction in environmental impact.

Insurance and indemnities
The Company maintained Directors' and Officers' Liability Insurance cover throughout 2018. 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.

Directors' Report
The Directors' Report, which has been prepared in accordance with the requirements of the Companies Act 2006, comprises the following sections:

- Chairman's Statement
- Chief Executive Officer's Review
- Business Review
- Therapy Area Review
- Financial Review: Financial risk management
- Corporate Governance: including the Corporate Governance Report, Science Committee Report, Nomination and Governance Committee Report, and Audit Committee Report
- Directors' Responsibility Statement
- Development Pipeline
- Sustainability: supplementary information
- Shareholder Information

and has been approved by the Board and signed on its behalf.

On behalf of the Board
A C N Kemp
Company Secretary
14 February 2019

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."

Our focus during 2018
> AI, automation, digital technologies and analytics
> *In vivo* biologics; personalised immunotherapy; and biologics device differentiation
> Achieve Scientific Leadership targets
> Scientific competitive intelligence

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, 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 decision-making processes for R&D projects and programmes
> the quality of our scientists and 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 may also consider, from time-to-time, 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.

Membership of the Committee

During 2018, the members of the Science Committee, all of whom have a knowledge of, or an interest in, life sciences, were Nazneen Rahman, who was appointed permanent Chair to the Committee in July 2018, Geneviève Berger and Marcus Wallenberg. As usual, the EVP, GMD; the EVP, IMED; and the EVP, MedImmune participated in meetings of the Science Committee as co-opted members in 2018. The Vice-President, IMED Operations acts as secretary to the Science Committee.

Activities during 2018

The Science Committee met twice in person in 2018, in London, UK and Cambridge, UK.

Key areas of focus for the Science Committee in 2018 included:

> **Artificial Intelligence, automation, digital technologies and advanced analytics:** how knowledge graphs, augmented drug design, AI-led chemical synthesis and advanced image analytics will contribute to patient stratification, prediction of disease progression and therapeutic benefit.
> **The future of *in vivo* biologics:** moving beyond monoclonal antibodies to overcome the challenges inherent in traditional protein therapeutics with DNA, RNA, cell and virus based therapies.
> **Personalised immuno-therapy:** how we are developing the next generation of antibody-drug conjugates, cell therapies, and cancer vaccines with the aim of reducing toxicity and increasing the survival of patients.
> **Biologics device differentiation:** how the current market and technology landscape is influencing our product portfolio and development strategies.
> **Achieve Scientific Leadership targets:** the scientific and patient centric rationale for inclusion of new 2018 opportunities in our corporate scorecard.
> **Scientific competitive intelligence:** how analysis of the external environment enables informed decision making along the product life-cycle.

Yours sincerely,

Nazneen Rahman
Chairman of the Science Committee

The Science Committee's terms of reference are available on our website, www.astrazeneca.com.

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."

Our focus during 2018
> Succession planning for the Board
> Developments in Corporate Governance
> Inclusion and Diversity

Role of the Committee

The Nomination and Governance Committee's role is to recommend to the Board any new Board appointments and to consider, more broadly, succession plans at Board level. It 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 the Company's overall business and strategic needs, both now and in the future. The matrix is set out and further discussed opposite. 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.

The Nomination and Governance Committee considers both planned and unplanned (unanticipated) succession scenarios and met five times in 2018, splitting the majority of its time between succession planning for Non-Executive Directors and continued routine succession planning for the roles of Chairman, CEO and CFO, in each case with the assistance of the search firms MWM Consulting and Korn Ferry (including the appointment of Tony Mok). Korn Ferry periodically undertakes executive search assignments for the Company.

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.

Membership of the Committee

During 2018, the members of the Nomination and Governance Committee were Leif Johansson (Chairman of the Committee), Rudy Markham, Graham Chipchase and Nazneen Rahman (following her appointment to the Committee in July 2018). Each member is a Non-Executive Director and considered independent by the Board. The Company Secretary acts as secretary to the Nomination and Governance Committee.

The attendance record of the Nomination and Governance Committee's members is set out on page 93. Typically, the Chairman of the Committee extends an invitation to any Board member to attend Committee meetings if they wish and several Directors take advantage of this and participate in the Nomination and Governance Committee's meetings.

The Nomination and Governance Committee's terms of reference are available on our website, www.astrazeneca.com.

Inclusion and Diversity

Diversity is integrated across our new 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

Non-Executive Directors' experience, as at 1 January 2019

	Business					Geographic			Industry-specific				
Name	Commercial	Financial	Managerial	Sales & Marketing	Tech & Digital	US	Europe	Asia	Science	Regulatory	Pre-AZ Pharma	Biologics	Medical Doctor/ Physician
Leif Johansson	●		●		●		●	●			●		
Geneviève Berger	●		●				●		●				●
Philip Broadley	●	●	●			●	●						
Graham Chipchase	●	●	●			●	●	●					
Deborah DiSanzo	●		●	●	●	●			●		●		
Rudy Markham	●	●	●	●			●	●					
Sheri McCoy	●		●	●		●			●		●		
Tony Mok	●					●		●	●			●	●
Nazneen Rahman					●		●		●			●	●
Marcus Wallenberg	●	●	●				●	●			●		

and measures (including trends around gender diversity, leadership ethnic diversity and age profile).

More specifically, the Board views gender, nationality and cultural diversity among Board members as important considerations when reviewing its composition. The Board recognises, in particular, the importance of gender diversity.

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 skills matrix used by the Board and Committee is shown above. The biographies of Board members set out on pages 94 and 95 give more information about current Directors in this respect.

The Board adopted an Inclusion and Diversity policy (the Policy) in December 2018, 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. Whilst 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 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. The Board's approach to inclusion and diversity continues to yield successful results. Currently, 40% of the Company's Non-Executive Directors are women and women make up 33% of the full Board. This meets the Policy's aim of 33% female representation on the Board, the same target as set out in the report from Lord Davies published in October 2015.

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 Employees from page 38.

Yours sincerely,

Leif Johansson
Chairman

Audit Committee Report

"The integrity of AstraZeneca's financial reporting is underpinned by effective internal controls, appropriate accounting practices and policies, and the exercise of good judgement."

In this Report we describe the work of the Audit Committee (the Committee) and the significant issues it considered in 2018. Our priorities were to receive assurance over the soundness of our financial reporting and internal controls, risk identification and management, compliance with the Code of Ethics and relevant legislation, cybersecurity and information governance, and business resilience.

Financial reporting

The integrity of AstraZeneca's financial reporting is underpinned by effective internal controls, appropriate accounting practices and policies, and the exercise of good judgement. The Committee reviewed, at least quarterly, the Group's significant accounting matters including contingent liabilities, revenue recognition and deferred tax and, where appropriate, challenged management's decisions before approving the accounting treatment applied. During 2018, the Committee reviewed the Group's significant restructuring programmes initiated from 2013 onwards, including accounting for restructuring charges, and control over capital expenditure and their projection for completion. The Committee continued to monitor the inclusion of Externalisation Revenue in AstraZeneca's Statement of Comprehensive Income. For more information on Externalisation Revenue, please refer to the Financial Review from page 79. The Committee also looked closely at intangible asset impairment reviews, legal provisions and other related charges, to ensure that items are appropriately accounted for in 'Reported' and 'Core' results.

PwC were reappointed as the Company's external auditor by its shareholders at the Company's AGM held in May 2018, serving for the second successive year. The Committee continued to oversee 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.

Risk identification and management

During the year, in addition to its regular reviews of the Group's approach to risk management, the operation of its risk reporting framework and risk mitigation, the Committee considered an audit evaluating the adequacy and effectiveness of the Global Risk Management Framework, noting strengths and opportunities to enhance the framework through targeted improvements. The Committee invited Nazneen Rahman, the Chairman of the Company's Science Committee, to attend one of its meetings to deepen its understanding of the clinical compliance risks facing the Group and to review the compliance regime for good clinical and laboratory practice. The Committee also encouraged the Group's Internal Audit Services Function (IA) to engage with the Science Committee to support its plans for 'second line defence' in the Group's science functions. The Committee intends to further strengthen its links with the Science Committee in 2019.

When identifying risks, we consider the total landscape of enduring risks which are long-standing and business-as-usual in nature. We then consider more specific and current risks – key active risks – which are challenging our business presently. Finally, in order that we scan the horizon and identify risks which may challenge us in the future, we also consider emerging risks. These deliberations provided the framework for the Committee's activities in 2018 and provided the context for the

Our focus during 2018

- Financial reporting, internal controls, and the quality and effectiveness of the external audit
- Cybersecurity, data analytics, GDPR and information governance
- Compliance matters, including fostering a 'speaking up' culture
- Risk management, including the identification, mitigation, monitoring and reporting of risks and lines of management accountability
- Business continuity planning and resilience

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 which assume that the significant risks modelled in the planning process will crystallise and against which management take mitigating actions. The Committee considered in detail the authenticity of each scenario including seeking additional analysis from management as to the indirect/unintended consequences of its proposed mitigating actions, including, for example, assessing the likely response of a broader range of stakeholders. The Committee also assessed the feasibility of the proposed mitigations to the revised scenarios being effected.

For more information on the Viability statement, please refer to the Risk Overview from page 71.

The Committee's consideration of risk management was supported by 'deep dive' reviews of key activities, including:

- cyber defence capability and the continuous enhancements to safeguard critical applications, information assets and business continuity/resilience
- actions to comply with the EU GDPR obligations, which came into force in May 2018
- the post-acquisition integration of ZS Pharma and management of *Lokelma*
- IA's use of data analytics in marketing company audits, and IA's interaction with the Global Business Services function
- the evolution of the Group's Global Business Services organisation, its key achievements, challenges and its management of risks.

In addition to these deep dive reviews, the Committee periodically assured itself of the appropriateness of the Group's planning for Brexit.

Further information on the deep dive reviews can be found in the Business updates section on page 114.

As discussed overleaf, in accordance with its focus on risks arising in key markets and internal controls, the Committee also visited the Group's sites in Shanghai and Wuxi, China, and I visited our site in Wilmington, US, during the year.

For further information on the Group's Principal Risks see the Risk Overview from page 70.

Compliance with the Code of Ethics

The Committee's priorities continue to include overseeing compliance with AstraZeneca's Code of Ethics, high ethical standards, and operating within the law in all countries where we conduct business or have interactions. The Code of Ethics is written in simple and accessible language to empower decision making that reflects AstraZeneca's Values, expected behaviours and key policy principles. During the year the Committee engaged with HR to support the publication of new Global Standards of behaviour to counter the risk of sexual harassment and bullying. AstraZeneca is committed to ensuring that its people feel respected through promoting a culture of inclusion and diversity and fostering a working environment in which its employees feel able and safe to 'speak up'. The Committee also monitored and reviewed 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.

Further information on our Code of Ethics is set out from page 105.

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. In March 2018, Marc Dunoyer (CFO) and I visited AstraZeneca's US commercial business to meet with the finance teams and the lead US external audit partner to discuss continuous improvement of our financial management and internal controls systems and the efficiency of the external audit. In September, we met again with the teams to discuss progress made and noted the further strengthening of the US finance team, both in number and professional skills, through external hires. In October, during the Committee's visit to Shanghai and Wuxi, China, Committee members met with many employees and key stakeholders. Through this engagement the Committee members gained invaluable insight into the opportunities and challenges, and current and emerging risks associated with our activities in China.

Philip Broadley, who will become Chairman of the Audit Committee in March 2019, during the Committee's visit to China.

Committee site visit to Shanghai and Wuxi, China

In October, members of the Audit Committee visited the Group's sites in Shanghai and Wuxi, China. China is AstraZeneca's second-largest national market, with absolute growth that has out-performed other multinational pharmaceutical companies for several years. We have approximately 13,000 employees in China. The Committee enjoyed several meetings with our local management to discuss the opportunities, challenges and risks being managed by senior leaders across a range of activities including R&D, commercialisation, manufacturing, supply and distribution. The Committee also undertook a tour of AstraZeneca's Wuxi manufacturing plant and held an informal 'questions and answers' session with a wide group of employees based in Shanghai. The Committee met physicians and patients at a large hospital in Wuxi and visited the China Commercial Innovation Centre (an open strategic platform designed to promote innovative healthcare practices in China) as well as Dizal Pharmaceutical, a recently formed joint venture with the Chinese SDIC Fund Management Company (an innovative biopharmaceutical enterprise), which demonstrated how innovation and its interconnectivity with smart healthcare has the potential to transform China's healthcare industry.

Further information on the Committee's visit to China can be found above. The Committee also met informally with employees from the Finance, Investor Relations, Corporate Affairs, IA, HR and Global Business Services teams.

During 2018, I participated in the UK Competition and Markets Authority's statutory audit market study, which has the objective of considering whether that market is operating as well as it should. I also participated in the Department for Culture, Media and Sport's annual FTSE 350 Cyber Security Health Survey.

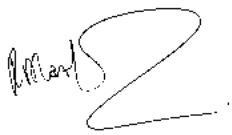
Changes to the membership of the Committee

Shriti Vadera stepped down from the Committee in June 2018, and I thank her for her invaluable insight and significant contribution since she joined the Committee in 2011. We welcomed Deborah DiSanzo as a member of the Committee in November 2018. While Deborah has only served for a short period of time, her long career working at the intersection of healthcare and technology has been shown to be of particular benefit to the Committee as it continues to increase its focus on cybersecurity, the use of 'big data' and privacy matters.

Finally, in light of the fact that I will formally step down from the Board at the conclusion of the Company's AGM in April 2019, the Company announced that Philip Broadley has been chosen by the Board to succeed me as Chairman of the Committee. Philip, who joined the Board and Committee in April 2017, is well-attuned to the working of the Committee and, with his significant international business and financial experience having served as Finance Director at large financial institutions, the Board believes he is well placed to lead the Committee in the coming years.

We hope that you find this information helpful in understanding the work of the Committee. Our dialogue with our shareholders and other stakeholders is valued greatly and we welcome your feedback on this Audit Committee Report.

Yours sincerely,



Rudy Markham
Chairman of the Audit Committee

Principal activities focused on by the Committee in 2018

During 2018 and in January 2019, the Committee considered and discussed the following items:

Financial reporting

- Key elements of the Financial Statements and the estimates and judgements contained in the Group's financial disclosures. Accounting matters considered included the areas described in the Financial Review under 'Critical accounting policies and estimates' (with a focus on accounting issues relevant to revenue recognition, litigation and taxation matters, goodwill and intangible asset impairment) from page 87.
- Monitoring the accounting for Externalisation Revenue in the Group's Consolidated Statement of Comprehensive Income arising from externalisation activities, including the collaboration agreement with Innate Pharma announced in October and the divestment of the US rights of *Synagis* to Sobi which closed in January 2019.
- Robust testing of the appropriateness of management's and the external auditor's analysis and conclusions on judgemental accounting matters.
- The completeness and accuracy of the Group's financial performance against its internal and external key performance indicators.
- 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 in the Financial Statements on page 154.
- The preparation of the Directors' viability statement and the adequacy of the analysis supporting the assurance provided by that statement.
- The adoption, impact and presentation of new financial standards including IFRS 9 'Financial Instruments' and IFRS 15 'Revenue from Contracts with Customers' in the Group's 2018 Financial Statements; and impact assessments for IFRS 16 'Leases' and IFRIC 23 'Uncertainty over Income Tax Treatments' which are effective from 1 January 2019.
- The external auditor's reports on its audit of the Group Financial Statements, and 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.
- 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.

For more information see Sarbanes-Oxley Act Section 404 in the Financial Review on page 90.

Risk and Compliance

- The Group's principal, enduring and emerging risks, including the Group's risk management approach, risk reporting framework and risk mitigation. The Committee also considered how the risk management process was embedded in the Group and assured itself that management's accountability for risks was clear and functioning. More information about the Principal Risks faced by the Group is set out in the Risk Overview section from page 70.
- Quarterly reports from the General Counsel on the status of significant litigation matters and governmental investigations.
- Quarterly reports of work carried out by IA and Finance including the status of follow-up actions with management.
- 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.
- Quarterly reports from Global Compliance regarding key compliance incidents (both substantiated and unsubstantiated), trends arising and the dispersion of incidents across the Group's business functions and management hierarchy including any corrective actions taken so that the Committee could assess the effectiveness of controls, and monitor and ensure the timeliness of remediation.
- 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.
- Progress in remediation of previously identified shortcomings at AstraZeneca's Chennai, India, site relating to Health & Safety, strength of leadership and cultural integration.
- The state of readiness and effectiveness of the Group's business continuity testing and resilience framework at its Global Technology Centres in Chennai, India, and Guadalajara, Mexico.
- 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.

External audit

- Monitoring the effectiveness and quality of the external audit process through: examination and testing of the coverage provided by the external auditor's audit plan, and their performance against it; management's feedback on the conduct of the audit; and considering the level of, and extent to which, the auditors challenged management's assumptions.
- Reviewing quarterly reports from the external auditor over key audit and accounting matters, and business processes, internal controls and IT systems.
- 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 from page 118.

Further information about the audit and non-audit fees for 2018 is disclosed in Note 31 to the Financial Statements on page 200.

Principal activities focused on by the Committee in 2018 *continued*

Performance assessment	> An effectiveness review of IA by considering its performance against the internal audit plan and key activities. The Committee noted how IA had continued to deliver value to the business and acted as a trusted adviser to the Committee during the year. 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, strengthened its thematic reporting to the business, and adapted the audit plan to respond to new or arising risks. The Committee encouraged IA to consider the alignment of its global presence to business risks in the longer term and to more keenly focus on ensuring the timely remediation of findings by the business.	> The Committee conducted the annual evaluation of its own performance, with each Committee member responding to a web-based questionnaire prepared by an external third party. The effectiveness review of the Committee was assessed as high, with the Committee's reporting to the Board commended in particular, and it was thought that the Committee continued to effectively challenge management and support the Compliance function. It was felt that the Committee's interactions with the Science Committee could be further strengthened, and the importance of ensuring an effective transition and handover of the chairmanship of the Committee was highlighted.
Business updates	> Regular updates from the IS/IT team on matters including: the alignment of critical systems and information assets to the Group's cyber defence capability; enhancing segregated networks; and, in particular, the Group's framework for identifying, mitigating and remediating cyber-risk and data breach exposure arising from its use of third-party vendors, including potential legal and regulatory (GDPR) liability, and IS/IT's ability to escalate any associated concerns through the management chain. > Updates from HR on the actions taken in response to the #metoo movement and the publication of Global Standards on sexual harassment and bullying. > An overview of the Group's preparation for GDPR and the progress made since its implementation.	> Assessing the performance of, and progress made by, the Group's Global Business Services function, including its four key towers, namely: Global Commercial Operations; Global Assurance and Reporting Services; Global Finance Services; and Digital. > Assessing the Group's ability to identify patterns of non-compliant behaviour through IA's use of data analytics to develop marketing company audits, and considering how IA can provide more impactful insights to the business. > Considering the risks arising from the Group's third-party distributor relationships in emerging markets and from its strategy for market penetration in China through lower-tier cities, and its management of them. > Considering the circumstances leading to the FDA's 2017 Complete Response Letters for *Lokelma* and the accountabilities for the related remediation actions through a review of the post-acquisition integration of ZS Pharma and the key learnings.

Significant financial reporting issues considered by the Committee in 2018

Reporting issue	Rationale	Committee response	Committee conclusion/ actions taken	Further information
Revenue recognition	The US is our largest single market and sales accounted for 33% of our Product Sales in 2018. Revenue recognition, particularly in the US, is impacted by rebates, chargebacks, returns, other revenue accruals and cash discounts.	The Committee pays particular attention to management's estimates of these items, its analysis of any unusual movements and their impact on revenue recognition informed by commentary from the external auditor.	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 was satisfied with the progress made by management to increase its accuracy in forecasting for managed market rebates and excise fees and, in particular, by managing a year-on-year decline in the level of related accounting true-ups.	Financial Review from page 74 and Note 1 to the Financial Statements on page 160.
Valuation of intangible assets	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 outlines the carrying value of the Group's intangible assets and, in respect of those intangible assets that are identified as at risk of impairment, 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 Committee considered the annual impairment reviews of the Group's intangible assets, including MEDI0680 (a PD-1 monoclonal antibody asset acquired through the acquisition of Amplimmune in 2013), *Eklira/Tudorza*, *Movantik/Moventig*, *Byetta*, *Lokelma* and verinurad. The development programme for MEDI0680 was discontinued and the asset fully impaired due to recent trial data indicating a lower standard of care than a launched competitor. Partial impairments were taken on *Eklira/ Tudorza* as a result of reduced sales forecasts, and on *Movantik/Moventig* following a further review of the market opportunity in the OIC indication, respectively. The *Byetta* review considered the low headroom following the impairment taken in the prior year and sensitivity arising from anticipated generic entry in the US. The Committee also reviewed and agreed with management's conclusions that no impairments were required for verinurad or *Lokelma* and that a reversal of the impairment taken in 2017 for *FluMist* was not appropriate at this stage due to continued uncertainty in relation to *FluMist* sales in the US.	The Committee assures 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 by reviewing 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.	Financial Review from page 74 and Note 9 to the Financial Statements from page 169.

Significant financial reporting issues considered by the Committee in 2018 *continued*

Reporting issue	Rationale	Committee response	Committee conclusion/ actions taken	Further information
Litigation and contingent liabilities	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 about, 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 2018, the more significant included: the favourable settlement of long-standing *Losec* patent infringement and damages actions in Canada and the settlement of *Seroquel* and *Crestor* cases with the State of Texas in the US. The Group continues to defend the allegations arising from the *Nexium* and *Prilosec* product liability litigation in the US, and to manage patent validity challenges to *Calquence* and *Imfinzi* in the US and *Brilinta* in China. The Committee was assured that the Group was effectively managing its litigation risks including seeking appropriate remedies and continuing to vigorously defend its IP rights.	Note 29 to the Financial Statements from page 194.
Tax accounting	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 (VAT). 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.	The Committee was satisfied with the Group's practices in regard to tax liabilities, including, most notably, the accounting impact of the reduction in tax rates in the Netherlands and Sweden as a result of tax reform, which resulted in a reduction of deferred tax balances of $297 million in 2018.	AstraZeneca's 'Approach to Taxation', which was published in December 2018, and covers its approach to governance, risk management and compliance, tax planning, dealing with tax authorities and the level of tax risk the Company is prepared to accept, can be found on our website, www.astrazeneca.com. Note 4 to the Financial Statements from page 163.

Significant financial reporting issues considered by the Committee in 2018 *continued*

Reporting issue	Rationale	Committee response	Committee conclusion/ actions taken	Further information
Retirement benefits	Pension accounting is an important area of focus recognising the level of pension fund deficit and its sensitivity to small changes in interest rates.	The Committee monitors, on a quarterly basis, the Group's funding position for its principal defined benefit pension obligations in Sweden, the UK and the US, including the key actuarial and interest rate assumptions used to determine the value of the Group's liabilities and pension scheme funding requirements. The Committee also reviews, annually, the Group's global funding objective and principles.	The Committee considered the impact of the outcome of the Guaranteed Minimum Pension trial and the resulting increase in the UK liability during 2018. The Committee was assured by the Group's tailored 'journey plans' for the UK and Swedish funds which target full funding over the longer term, on a self-sufficiency funding basis and which aim to close the existing funding gap via a balanced mix of investment returns on existing assets, company contributions, and by hedging the risks inherent in the liability valuation. The Committee was satisfied that the Group's pension fund deficits were appropriately managed during the year.	Financial Review from page 74 and Note 21 to the Financial Statements on page 178.

The role of the Committee and how we have complied

Committee membership and attendance
All Committee members are Non-Executive Directors and considered by the Board to be independent under the UK Corporate Governance Code. The Committee's members are Rudy Markham (Committee Chairman), Philip Broadley, Sheri McCoy and Deborah DiSanzo. Shriti Vadera stepped down as a member of the Audit Committee with effect from 30 June 2018.

In December 2018, the Board determined that, for the purposes of the UK Corporate Governance Code, at least one member of the Committee had recent and relevant financial experience, and Rudy Markham and Philip Broadley were determined to be financial experts for the purposes of the Sarbanes-Oxley Act. The Board also determined that the members of the Committee as a whole had competence relevant to the sector in which the Company operates, as Rudy Markham has served as a Non-Executive Director of the Company for approximately 10 years, Sheri McCoy has had a 30-year career in the pharmaceutical industry, Deborah DiSanzo has healthcare sector experience from her role at IBM Watson Health and Philip Broadley has served as a Non-Executive Director of the Company since April 2017. The Board of Directors' biographies on pages 94 and 95 contain details of each Committee member's skills and experience.

The Committee held six meetings in 2018 and the Committee members' attendance is set out in the table on page 93.

Role and operation of the Committee
The Committee's terms of reference are available on our website, www.astrazeneca.com.

The Committee regularly reports to the Board on how it discharges its main responsibilities, which include the following standing items:

- monitoring the integrity of the Company's financial reporting and formal announcements relating to its financial performance, and reviewing significant financial reporting judgements contained within them
- ensuring the Company's Annual Report and Accounts present a fair, balanced and understandable assessment of the Company's position and prospects by carrying out a formal review of the documentation and receiving a year-end report from management on the internal controls, governance, compliance, assurance and risk management activities that support the assessment
- reviewing the effectiveness of the Company's internal financial controls, internal non-financial controls, risk management systems (including whistleblowing procedures) and compliance with laws and the AstraZeneca Code of Ethics
- monitoring and reviewing the role, resources and effectiveness of the Group's IA function, its Compliance function, the external audit process and overseeing the Group's relationship with its external auditor
- monitoring and reviewing the external auditor's independence and objectivity
- ensuring the provision of non-audit services by the external auditor are appropriate and in accordance with the policy approved by the Committee
- making recommendations to the Board for seeking shareholder approval relating to the appointment, reappointment and removal of the external auditor, and to approve the remuneration and terms of engagement of the external auditor
- monitoring the Company's response to any external enquiries and investigations regarding matters within the Committee's area of responsibility.

Following each Committee meeting, the Committee Chairman informs the Board of the principal matters the Committee considered and of any significant concerns it has or that have been reported by the external auditor, the Vice-President, IA or the Chief Compliance Officer. The Committee identifies matters that require action or improvement and makes recommendations on the steps to be taken. The Committee's meeting minutes are circulated to the Board.

The Committee's work is supported by valuable insight gained from its interactions with other Board Committees, senior executives, managers and external experts. The Committee meetings are routinely attended by: the CFO; the General Counsel; the Vice-President Global Sustainability and Deputy Chief Compliance Officer; the Vice-President, IA; the Vice-President Finance, Group Controller; and the Company's external auditor. The CEO attends on an agenda-driven basis.

In addition, the Committee and separately the Committee Chairman meet privately with: the CFO; the Vice-President Global Sustainability and the Deputy Chief Compliance Officer; the General Counsel; the Vice-President, IA; and the Company's external auditor on an individual basis to ensure the effective flow of material information between the Committee and management.

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 2018.

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 further aid their review, 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 UK Corporate Governance Code, which is set out on page 104.

Internal controls

The Committee receives a report of the matters considered by the Disclosure Committee during each quarter. At the January 2019 meeting, the CFO presented to the Committee the conclusions of the CEO and the CFO following the evaluation of the effectiveness of our disclosure controls and procedures required by Item 15(a) of Form 20-F at 31 December 2018. 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.

There was no change in our internal control over financial reporting that occurred during the period covered by this Annual Report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

For further information on the Company's internal controls, please refer to the Accountability section in the Corporate Governance Report on page 104.

External auditor

Following a competitive tender carried out in 2015, PwC were appointed as the Company's external auditor for the financial year ending 31 December 2017. In May 2018, PwC were reappointed as the Company's auditor for the financial year ending 31 December 2018. Richard Hughes is the lead audit partner at PwC.

Non-audit services and safeguards

The Committee maintains a policy (the Audit and Non-Audit Services Pre-Approval Policy) for the pre-approval of all audit services and permitted non-audit services undertaken by the external auditor, the principal purpose of which is to ensure that the independence of the external auditor is not impaired. The policy covers three categories of work: audit services; audit-related services; and tax services, the latter of which is significantly restricted such that no tax services are pre-approved under the policy. The policy defines the type of work that falls within each of these categories and the non-audit services that the external auditor is prohibited from performing under the rules of the SEC and other relevant UK and US professional and regulatory requirements.

The pre-approval procedures permit certain audit and audit-related services to be performed by the external auditor during the year, 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 Vice-President Finance, Group Controller.

The 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 to be able 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 related to acquisitions and disposals, financial statement audits of employee benefit plans, and review of internal controls. 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 non-audit services in determining whether to pre-approve such services.

The CFO (supported by the Vice-President 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 Chairman 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 non-audit services other than the pre-approved audit and audit-related services are approved by the Audit Committee on a case-by-case basis. In 2018, PwC provided non-audit services including an interim review of the results of the Group for the six months ended 30 June 2018, and audit-related assurance services in respect of the Group's US debt issuance.

Audit/non-audit services

- Statutory audit fees
- Assurance services
- Taxation services
- Other corporate projects

Fees for non-audit services amounted to 7% of the fees paid to PwC for audit, audit-related and other services in 2018 (2017: 4%).

PwC were considered better placed than any alternative audit firm 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 Non-Audit Services Pre-Approval Policy or were presented to Committee members for pre-approval.

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 200.

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 effectiveness considering the views of senior management within the finance function and regular Committee attendees principally against four key factors, namely: judgement; mind-set & culture; skills, character & knowledge; and quality control. Following the effective transition of the Group's external auditor in 2017, the Committee felt that a number of improvements had been made during 2018 including an overall improvement in planning for receipt and assessment of audit deliverables and in communications between management and the external auditor, alongside greater oversight of the US. Accordingly, the Committee concluded that the PwC audit was effective for the financial year commencing 1 January 2018.

In January 2019, the Committee recommended to the Board the reappointment of PwC as the Company's auditor for the financial year ending 31 December 2019. Accordingly, a resolution to reappoint PwC as auditors will be put to shareholders at the Company's AGM in April 2019.

Directors' Remuneration Report

The Remuneration Committee has taken care to ensure that our remuneration arrangements remain aligned to our strategy and to respond to shareholders' feedback.

"The Committee is confident our Remuneration Policy has helped to support our strategy, which we believe will deliver long-term sustainable value for shareholders."

As Chairman of the Remuneration Committee (the Committee), I am pleased to present AstraZeneca's Directors' Remuneration Report for the year ended 31 December 2018.

Our performance made 2018 a defining year for AstraZeneca. Over the last six years we have focused on rebuilding our pipeline, driving our Growth Platforms and delivering important New Medicines to patients. In 2018, AstraZeneca turned the corner and returned to Product Sales growth, driven by a new generation of medicines. Our strong pipeline and financial progress is reflected in our strong total shareholder return performance this year.

The Committee is confident that our Remuneration Policy has helped to support our strategy to deliver long-term sustainable value to our shareholders. We continue to tie remuneration outcomes to the acceleration of innovative science and our Growth Platforms, as well as other important financial metrics. Annual bonus and Performance Share Plan (PSP) measures are closely aligned with our KPIs set out from page 20 of this Annual Report.

While our Policy was approved by 96% of shareholders at the 2017 AGM, the advisory vote on our Remuneration Report at the 2018 AGM received a much lower level of support than we hoped to achieve. We are committed to understanding and addressing our shareholders' concerns and have sought feedback from our largest investors, as well as from proxy voting advisory bodies.

The primary concern we heard related to annual bonus outturns, with some investors questioning whether bonus targets were sufficiently stretching. We were asked for more information about how we set and assess performance targets, as well as more detail on the targets themselves. There was also a request to simplify our incentive structures, which some investors perceive to be complex given the number of metrics used.

We have carefully considered the feedback received, in addition to the UK Corporate Governance Code changes and new reporting regulations that are effective from 1 January 2019, and have made a number of changes to reflect our commitment to best practice. The changes are highlighted on page 123.

2018 performance highlights and remuneration outcomes

2018 performance

Our 2018 scorecard focused on our strategic priorities, Achieving Scientific Leadership, Return to Growth and Achieving Group Financial Targets. During 2018, the commitment of our employees enabled the Company to deliver a number of important medicines for serious illnesses such as *Lynparza*, which has the potential to change medical practice for ovarian cancer patients, and *Tagrisso*, which may set a new standard of care for lung cancer patients. We hope that these achievements will help bring significant improvement to patients and their families. More detail on these medicines and other therapy area achievements can be found from page 50. Highlights of our 2018 performance are summarised below.

Achieve Scientific Leadership

Through our continued focus on innovative science, at the end of 2018 we had eight NMEs in Phase III/Pivotal Phase II or under regulatory review, covering 15 indications.

Our Remuneration Policy can be viewed on our website, www.astrazeneca.com/remunerationpolicy2017.

We also made 28 regulatory submissions in major markets and received 23 approvals for our medicines – record numbers for AstraZeneca. These successes are the product of our high-quality science and product development.

Our commitment to innovative science inevitably risks disappointment as well as the success we strive for. In 2018 we did not have the success we hoped for during Phase III trial results for six projects, including the Phase III MYSTIC trial evaluating *Imfinzi* and *Imfinzi* plus tremelimumab as a 1st line treatment for patients with metastatic (stage 4) non-small cell lung cancer (NSCLC). These setbacks were far outweighed by our successes.

Return to Growth and financial performance

In 2018, we generated less Externalisation Revenue following the high level seen in 2017 as we focused on supporting reinvestment in R&D and new product launches. This impacted Total Revenue, which declined by 2% in the year to $22,090 million.

However, our success in delivering New Medicines to patients is reflected in strong commercial performance. Product Sales in 2018 increased by 4% to $21,049 million, with our New Medicines delivering $2.8 billion in incremental sales at CER and growth of 81%, and the sustained strength of Emerging Markets, up by 12% (13% at CER). Product Sales in China increased by 28% (25% at CER) in the year.

As anticipated at the start of the year, 2018 saw a decline in Core profits due to: the ongoing impact of loss of exclusivity on our legacy products; lower levels of Externalisation Revenue; and increased investment in selling and marketing for our New Medicines and for key markets, such as China, to support their longer-term success. Our Core EPS performance was in line with our expectations as we execute our return to growth strategy, and in 2019 we anticipate an increase in Product Sales to underpin improved Core profitability.

Our cash flow performance was enhanced by the disposal of intangible assets during the year, resulting in strong performance against our scorecard target.

2018 remuneration outcomes

The targets used to assess annual bonus performance for our executives align with our Group scorecard. We set stretching targets after careful consideration of the anticipated challenges and opportunities faced by the business, including the continuing impact of the loss of exclusivity of some of our key medicines. We are mindful of consensus and external guidance in determining the appropriate level of stretch.

Principal activities focused on by the Committee during 2018

Responding to investor feedback and changes to the UK Corporate Governance Code	> Consultation with shareholders and shareholder representative bodies on remuneration following the low vote in favour of the Directors' Remuneration Report at the AGM in May 2018 > Determining and agreeing changes to respond to investor concerns > Review of changes to the UK Corporate Governance Code and new reporting regulations
Annual bonus	> Approval of the 2017 Group scorecard outcome and determination of Executive Directors' annual bonus awards for 2017 > Review of bonuses granted to executives below SET level > Approval of Group scorecard targets used to assess 2018 annual bonus performance
Share plans	> Approval of 2015 PSP and 2014 AZIP performance outcomes > Approval of LTI grants > Approval of performance measures to be attached to PSP awards granted in 2018 > Review of projected outcomes for outstanding PSP and AZIP awards
Other matters	> Review of an in-depth report setting out pay policies and practices for employees across the wider Group > Approval of compensation arrangements for Executive Directors and SET members for 2018 > Review of AstraZeneca's compensation strategy > Consideration of AstraZeneca's UK gender pay gap data > Review of CEO pay ratios vs lower quartile, median and upper quartile UK workers > Discussion of remuneration trends and shareholder views > Review of the Committee's performance, including comments arising from the annual Board evaluation > Review of the Committee's terms of reference > Review of remuneration consultants, and appointment of Willis Towers Watson as adviser

The Group scorecard used to assess annual bonus performance for 2018 was based 70% on financial measures. The progression of our science through clinical trials to regulatory approval is a fundamental measure of performance and represented 30% of the measures.

Formulaic assessment of the Group scorecard resulted in an outcome of 190% of target bonus (95% of maximum). We recognised that the formulaic outcome for 2018 had been influenced by a number of significant one-off events, both positive and negative, which were unforeseeable at the start of the year when targets were set. A significant example being unanticipated reductions in corporate income tax rates that positively impacted Core EPS.

Our strategic performance and pipeline progress has been strong, and shareholders have benefited from strong total shareholder return performance over 2018. After careful consideration of business performance, overall the Committee judged that the formulaic Group scorecard outcome should be adjusted downwards to reflect the financial outturns and the impact of unforeseen one-off events during the year. Therefore the final 2018 bonus outcome for each Executive Director was reduced to 82.5% of maximum. The range of factors taken into account in our assessment is described in more detail from page 129. One third of each Executive Director's bonus will be deferred into AstraZeneca shares to ensure further alignment with shareholders.

Long-term incentives

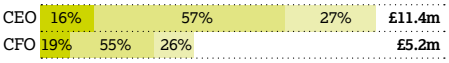
The three-year performance period for PSP awards granted to Executive Directors in 2016 ended on 31 December 2018. Performance against the targets attached to those awards will result in the awards vesting at 79% of maximum, as shown from page 133. This is in part driven by our strong TSR performance. TSR increased by 59% over the performance period, ranking second (upper quartile) in our comparator group of pharmaceutical peers.

Although Executive Directors no longer receive awards under the AstraZeneca Investment Plan (AZIP) as the final award was granted in 2016, outstanding awards remain. The two performance tests (progressive dividend and 1.5 times dividend cover) attached to AZIP awards granted in 2015 were met in three of the four years in the performance period ended 31 December 2018. The Committee considered concerns raised by some shareholders about a change to the operation of the AZIP performance measures, proposed in 2017. These were balanced against concerns raised by other shareholders about the potential for the AZIP, in its previous form, to incentivise a focus on short-term performance. Taking into account the differing shareholder views, the Committee determined that the performance measures should be applied as proposed in 2017, which will result in 75% of this AZIP award vesting. The shares are subject to a further four-year holding period.

The resultant single total figures of remuneration for Mr Soriot and Mr Dunoyer are set out on page 126. As can be seen from the chart on the following page, the majority of each figure consists of variable pay, which is dependent on performance of the business and shareholder experience, and a significant proportion of the value is attributable to share price growth and dividends.

Directors' Remuneration Report *continued*

2018 single total figure of remuneration



- Fixed remuneration
- Variable remuneration
- Value attributable to share price appreciation and dividends

Remuneration in 2019

We are satisfied that our executive remuneration arrangements continue to be well aligned with the delivery of the Company's strategy and the creation of long-term value for shareholders. Incentive opportunities under the annual bonus and PSP will not be changed for 2019. However, the Committee has made a number of changes to performance measures following investor feedback, for simplicity.

The Achieve Scientific Leadership metrics will be replaced with two new Accelerate Innovative Science indices, measuring progression of medicines through clinical trials and on to regulatory approval. This approach simplifies our remuneration structure, by reducing the total number of science metrics, whilst continuing to incentivise performance across the breadth of the pipeline.

For the annual bonus, the weighting of the cash flow metric within the Group scorecard has been increased from 10% to 20%. Therefore, financial measures now account for 80% of the scorecard and science measures account for 20%. This change in weightings reflects the importance of cash flow generation for the phase our business has now entered, as we aim to sustain investment in our pipeline while meeting our capital allocation priorities.

The Committee has reviewed significant analysis (including business plans, reports from the Science Committee and consensus forecasts) to satisfy itself that the 2019 targets require the achievement of appropriately stretching performance. We have disclosed the Accelerate Innovative Science targets for PSP awards to be granted in 2019 at the start of the performance period, as shown on page 135. It should be noted that our science targets will necessarily vary year-on-year, given the influence of external regulatory changes and timing of pipeline progression. Financial targets are set in line with our business strategy and are tested to ensure stretch. For more information on our target setting approach, see pages 128 and 135.

A key principle of our remuneration philosophy is aligning the focus of our executives and our employees collectively to drive Group performance towards the achievement of the same goals. In 2019, the Committee will continue its practice of reviewing in-depth analysis of pay policy and practices for employees across the wider Company to ensure that remuneration decisions are made in the context of pay practices for our workforce.

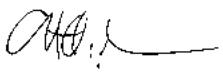
The Committee also remains mindful of the tension between the UK executive pay environment and the highly competitive global pharmaceutical market. We aim to find the right balance to incentivise, reward and retain highly talented individuals appropriately. Mr Soriot and Mr Dunoyer will each receive a salary increase of 3%, effective from 1 January 2019. This is in line with the average increase awarded to the wider UK employee population. No changes will be made to the fee structure for Non-Executive Directors in place during 2019.

Next steps

I hope that you find this Remuneration Report clear in explaining the implementation of our Remuneration Policy during 2018, and the meaningful and thorough response we have made to address investor feedback following the 2018 AGM. We are focused on adhering to best practice in our governance of executive remuneration and will continue to evolve our approach in line with the expectations of our shareholders. We trust that we have provided the information you need to be able to support the resolution to be put to shareholders on this Remuneration Report at the Company's AGM in April 2019.

Our ongoing dialogue with shareholders and other stakeholders is valued greatly and, as always, we welcome your feedback on this Directors' Remuneration Report.

Yours faithfully



Graham Chipchase
Chairman of the Remuneration Committee
14 February 2019

Our response to shareholder feedback

We have engaged extensively with our shareholders to understand the reasons why some shareholders did not support our Annual Reports on Remuneration when voting at the 2017 and 2018 AGMs.

Over the last two years we have made substantial changes to respond to shareholder feedback, including:

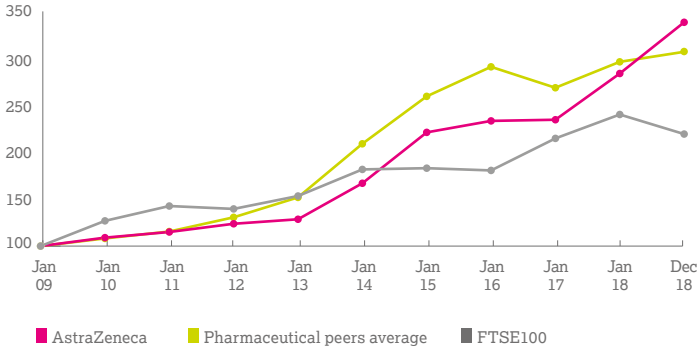
Structure of the bonus for Executive Directors	For 2018, each performance metric was assessed on a standalone basis, so that overperformance against one metric could not compensate for lower performance against another. The payout range for each metric is capped in line with each Executive Director's maximum bonus opportunity. For more information, see page 129.
Simplification	For 2018, the number of bonus metrics was reduced. For 2019, we have further simplified science metrics for the bonus and PSP. For more information, see pages 132 and 135.
Earlier disclosure	We committed to disclosing bonus performance and targets immediately following the end of the performance year, as seen in the 2018 Group scorecard disclosure. For PSP awards to be granted in 2019, we have disclosed science targets at the start of the performance period. For more information, see pages 129 and 135.
More clarity on the target setting process	In discussions, some shareholders asked for more information about how the Committee sets targets and assesses performance. We have included that additional information in this Remuneration Report, to provide clarity and insight for all shareholders and help demonstrate the robustness of our processes. For more information, see page 128.
CEO pay ratio	We have disclosed the CEO pay ratio for the first time, ahead of the new reporting requirement taking effect. For more information, see page 139.
Shareholding guidelines and post-employment shareholding requirements	This year Executive Directors' positions against their shareholding guidelines have been calculated according to the Investment Association's recommended approach. A post-employment shareholding requirement has been introduced, requiring Executive Directors to hold 100% of their shareholding guideline for two years after leaving office. This aims to maintain alignment with shareholders after an Executive Director leaves office. For more information, see page 137.
Pension	We are capping pension contributions for newly-appointed Executive Directors at a level in line with the wider workforce.
Information to shareholders	We have made changes to the format and content of this Remuneration Report, to try and make the information it contains as clear as possible to the reader.

Remuneration at a glance

"In 2018, AstraZeneca turned the corner and returned to Product Sales growth, driven by a new generation of medicines."

How we have performed

Total Shareholder Return



12 months*
+24%

2016-18*
+59%

* 12 month TSR and 36 month TSR have been calculated using three-month calendar averages, from 1 October to 31 December, prior to the start and at the end of the relevant periods.

Delivery against strategy – 2018 Group scorecard performance

Achieve Scientific Leadership

- 9 — NME Phase II starts. Target: 9
- 19 — NME and major LCM positive Phase III investment decisions. Target: 11
- 24* — NME and major LCM regional submissions. Target: 15

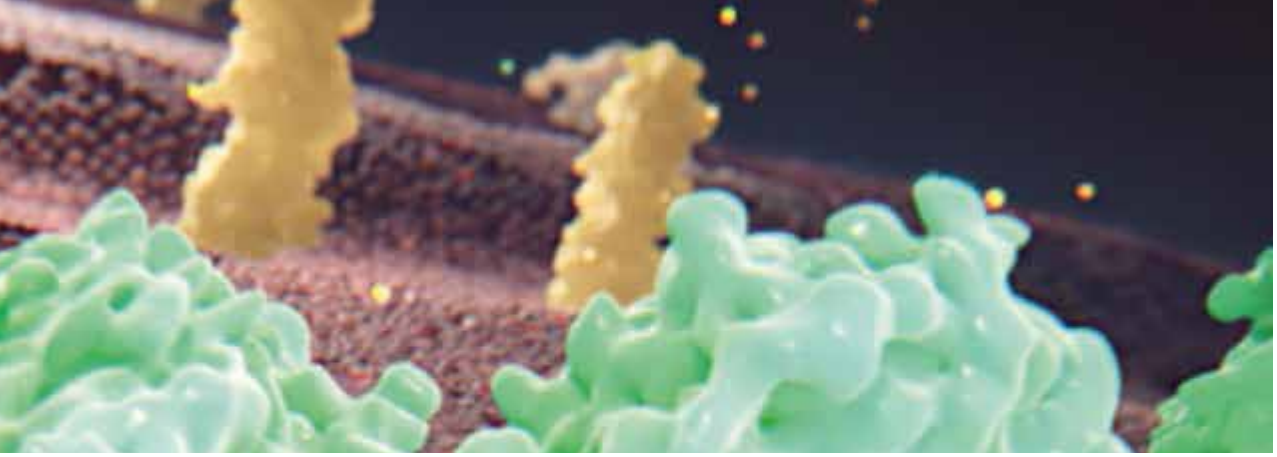
Return to Growth

- $17,116m* — Product Sales from Growth Platforms. Target: $16,381m
- 23 — NME and major LCM regional approvals. Target: 18

Achieve Group Financial Targets

- $3.9bn* — Cash flow. Target: $3.2bn
- $3.60* — Core EPS. Target: $3.40
- $21.1bn* — Total Product Sales. Target: $20.5bn

* For reconciliation with KPIs disclosed from page 20 of this Annual Report and a description of performance measures, see page 130.



What our Executive Directors earned

Executive Directors' remuneration for 2018

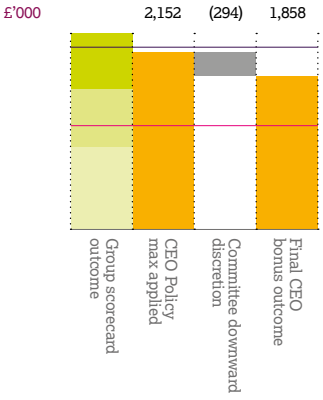
£'000	Fixed remuneration	Annual bonus	Long-term incentive (PSP – Granted 2016)	Long-term incentive (AZIP – Granted 2015)	Single total figure	Change from 2017
Pascal Soriot (CEO)	**1,747**	**1,858** 82.5% of max	**6,780** 79% of max	**888** 75% of max	**11,356**	**+9%**
Marc Dunoyer (CFO)	**995**	**919** 82.5% of max	**2,828** 79% of max	**389** 75% of max	**5,190**	**+5%**
	Base salary, taxable benefits and pension allowance.	One third of annual bonus is deferred into shares, to be held for three years.	PSP award is subject to a further two-year holding period before release.	AZIP award is subject to a further four-year holding period before release. The AZIP is a legacy plan under which no further awards are granted.	Includes Other items, see page 126.	

2018 annual bonus: pages 127 to 132.

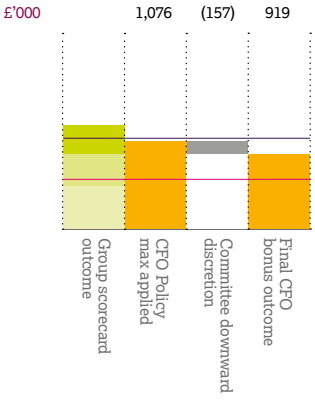
2016 PSP and 2015 AZIP: pages 133 to 134.

2018 annual bonus outcomes

Pascal Soriot



Marc Dunoyer



Key:

- Achieve Scientific Leadership
- Return to Growth
- Achieve Group Financial Targets
- Maximum
- Target

Looking ahead

Executive Directors' remuneration for 2019

	Fixed remuneration	Annual bonus	Long-term incentive
Pascal Soriot (CEO)	Salary: £1,288,530 Benefits fund Pension: 30% salary	Max: 180% salary Target: 100% salary	PSP Max: 500% salary
Marc Dunoyer (CFO)	Salary: £765,290 Benefits fund Pension: 24% salary	Max: 150% salary Target: 90% salary	PSP Max: 400% salary
Change from 2018	Salary increase of 3%. Benefits and pension in line with 2018	No change to target or max. 2019 Group scorecard measures on page 132	No change to max face value. 2019 PSP performance measures on page 135

Annual Report on Remuneration

Key:

Audited

Audited information
Content contained within the Audited panel indicates that all the information within has been subject to audit.

Planned implementation for 2019
Content contained within a grey box indicates planned implementation for 2019.

Executive Directors' remuneration

This section of the Remuneration Report sets out the Executive Directors' remuneration for the year ended 31 December 2018 alongside the remuneration that will be paid to Executive Directors during 2019.

Audited

Executive Directors' single total figure of remuneration for 2018

The single total figure table sets out all elements of remuneration receivable by the Executive Directors in respect of the year ended 31 December 2018, alongside comparator figures from the prior year.

		Fixed			Variable (performance related)			
£'000		Base salary	Taxable benefits	Pension	Annual bonus	Long-term incentives	Other	Total
Pascal Soriot	**2018**	**1,251**	**121**	**375**	**1,858**	**7,669**	**82**	**11,356**
	2017	1,220	122	366	1,916	6,712	93	10,429
Marc Dunoyer	**2018**	**743**	**74**	**178**	**919**	**3,217**	**59**	**5,190**
	2017	725	88	174	1,025	2,916	16	4,944

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. The Annual bonus section is set out on pages 127 to 132 and the Long-term incentives section on pages 133 to 135. Information about the Executive Directors' remuneration arrangements for the coming year, ending 31 December 2019, is highlighted in grey boxes.

Fixed remuneration

Audited

Base salary

When awarding salary increases, the Committee considers, among other factors, the salary increases applied across the UK employee population. Increases in the Executive Directors' salaries for 2018 and 2019 were in line with the UK workforce.

	2018		2019	
£'000	Increase from 2017	Base salary	Increase from 2018	Base salary
Pascal Soriot	2.5%	1,251	3%	1,289
Marc Dunoyer	2.5%	743	3%	765

Audited

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. In 2018, the Executive Directors selected benefits including healthcare insurance, death-in-service provision and advice in relation to tax, and took their remaining allowances in cash.

	2018			2019
£'000	Taken in benefits	Taken as cash	Total taxable benefits	Taxable benefits
Pascal Soriot	15	106	121	in line with 2018
Marc Dunoyer	18	56	74	in line with 2018

Fixed remuneration *continued*

Audited

Pension

The Executive Directors receive a pension allowance calculated as a percentage of base salary. During 2018, both Executive Directors took their pension allowance as a cash alternative to participation in a defined contribution pension scheme. Neither Executive Director has a prospective entitlement to a defined benefit pension by reason of qualifying service.

	2018			2019
£'000	Pensionable salary	Pension allowance	Cash in lieu of pension	Pension allowance
Pascal Soriot	1,251	30% salary	375	30% salary
Marc Dunoyer	743	24% salary	178	24% salary

Other remuneration

Audited

Other items in the nature of remuneration

Deferred shares granted to the Executive Directors under the Deferred Bonus Plan (DBP) in respect of the withheld proportion of their annual bonuses awarded for performance during the year ended 31 December 2014, were released during 2018, on completion of the three-year deferral period. The dividend equivalents accrued on the deferred shares during the deferral period and paid to the Executive Directors at the time of release are included in the Other column.

On 1 December 2018, Marc Dunoyer's option under the all-employee SAYE scheme matured. Details of Mr Dunoyer's SAYE option are set out on page 138. The market price on 3 December 2018, the first trading day following maturity, was 6152 pence which equated to a gain of 2845 pence per option; this amount is included in the Other column.

£'000	Dividend equivalents received on DBP awards released in year	Gain on SAYE options maturing in year	Total Other items in the nature of remuneration
Pascal Soriot	82	–	82
Marc Dunoyer	43	15	59

Annual bonus

Audited

2018 Annual bonus

Annual bonuses earned in respect of performance during 2018 are included in the single total figure table and detailed information on the Committee's approach to target setting and assessment of performance is set out on the following pages.

Under the Deferred Bonus Plan (DBP) one third of each Executive Director's pre-tax bonus is 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 in respect of performance during 2018				
	Bonus potential as % of salary		Bonus payable in cash	Bonus deferred into shares	Total bonus awarded
£'000	Target	Maximum			
Pascal Soriot	100%	180%	1,239	619	1,858 82.5% max
Marc Dunoyer	90%	150%	613	306	919 82.5% max

Annual Report on Remuneration *continued*

Annual bonus *continued*

Our approach to setting targets and assessing performance to determine bonus outturns is thorough, involving the following key stages.

Stage 1 – Group scorecard target setting	Science metrics: At the beginning of each year a cohort of scientific opportunities is specified, on which the Science targets will be based. These opportunities represent potential achievements at each stage of the pipeline, from 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. The Science Committee reviews the stretch of proposed targets taking into account factors such as past performance, the external regulatory environment and internal resourcing and efficiencies. The targets for realisation of these opportunities are ambitious and based on our high success rate to date.	Financial metrics: The Return to Growth measure and Achieve Group Financial Targets metrics align directly with the business's Long Range Plan (LRP), which sets out the financial framework for delivering our strategy and ambitious milestones over the short-, medium- and long-term. The LRP process includes detailed business reviews during which business plans and efficiencies of each unit are reviewed and challenged, leading to a final LRP for the Board to review, challenge and approve. The Committee sets targets based on the Board-approved LRP. As part of the target setting process it also considers consensus expectations and external guidance, as well as anticipated challenges and opportunities. This range of data is used by the Committee to ensure the stretching nature of performance targets can be robustly tested.
Stage 2 – Committee review and approval of targets	Initial targets are proposed by management, which the Committee thoroughly reviews and challenges before the final targets are agreed and approved. Targets are reviewed in draft form in December, with final target setting and approval in January, once the prior year's final results are available to inform the Committee's decisions. For each target, the Committee is provided with considerable supporting material. For example, 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.	For Return to Growth, the Committee considers year-on-year projections at brand/product level and growth rates over a five-year period. Committee members participate in the full Board discussions on the strategy, LRP and budget which form the basis for the targets. For the other financial measures, the Committee considers: how the proposed target aligns with the LRP and budget; prior years' outcomes (in absolute terms and against target); how the ambition has changed from the prior LRP 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. Payout probability analysis conducted by the Committee's independent adviser is considered, to assess the stretch of financial targets.
Stage 3 – Tracking throughout the performance period	The Committee reviews the projected Group scorecard outcome against target at least three times throughout the performance year to monitor progress against targets. This allows ongoing scrutiny, highlighting any	significant events which may impact the scorecard outcome as they arise. It also provides valuable insight for the Committee on how stretching the targets are which informs the target-setting process for the following year.
Stage 4 – Group scorecard assessment	Following year end, performance against each metric is assessed. The Group scorecard outcome is calculated from the combined weighted metric outcomes. Each performance measure is assessed on a standalone basis for each Executive Director, so that underperformance against one measure cannot be compensated for by overperformance against another.	The Science Committee independently considers science achievements to ensure these represent a fair and balanced outcome which reflects genuine achievements and pipeline progression, and then informs the Committee. Apart from cash flow, which is set at actual rates of exchange, the 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. However, the Committee is provided with information to allow it to conduct year-on-year analyses.
Stage 5 – Determination of Executive Directors' bonuses	Once the formulaic Group scorecard outcome has been calculated, the Committee will consider the outcome in the context of overall business performance and the experience of shareholders to determine whether the outcome is fair. The Committee will consider, for example, TSR performance over the period, the Executive Director's personal impact on the delivery of KPIs and pipeline performance beyond the scorecard targets, recognising that the ongoing development of a sustainable pipeline is critical to future and long-term growth. Organisational achievements will also be considered, such as inclusion and diversity targets, and the realisation of technology-based milestones.	Our Group scorecard closely aligns to the delivery of the strategy and many of the Executive Directors' objectives reinforce aspects of the scorecard. Each year there are important individual deliverables beyond the scorecard metrics which the Committee takes into account when determining individual bonuses. Having considered the Group scorecard outcome, overall business performance, the experience of shareholders and individual performance, the Committee will exercise its judgement carefully to determine a final bonus outcome for each Executive Director which is considered fair and appropriate for the year's performance and is in the best interests of shareholders.

2018 Group scorecard assessment

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Performance against the 2018 Group scorecard is set out below. As highlighted in the following table, a majority of our performance measures are based on group KPIs (as indicated by ☐), which directly relate to strategy. A reconciliation between measures used for the bonus assessment and the KPIs set out from page 20 can be found on page 130.

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. 100% of target bonus will payout for on-target performance. For employees, 200% of target bonus will payout for the maximum level of performance, however in line with our Remuneration Policy maximum bonus payouts for the CEO and CFO are capped at 180% and 150% of salary respectively (equivalent to 180% and 167% of target bonus respectively). 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. As shown in the table below, this has resulted in a lower scorecard outcome for the CEO and CFO than the rest of the eligible employee population. Performance below the specified threshold level for a metric will result in 0% payout for that metric. The Committee adjusted the formulaic Group scorecard outcome for 2018 that is shown below, as described on page 131.

2018 Group scorecard performance measures and metrics	Weighting	Threshold for payout	Target	Maximum	Outcome[1]	Formulaic outcomes (% of target) Group scorecard	CEO	CFO	Performance
Achieve Scientific Leadership									
☐ NME Phase II starts	6%	4	9	13	9	6%	6%	6%	
☐ NME and major life-cycle management positive Phase III investment decisions	8%	6	11	16	19	16%	14.4%	13.4%	Our Achieve Scientific Leadership performance is described on pages 25 to 28.
☐ NME and major life-cycle management regional submissions	8%	10	15	19	24	16%	14.4%	13.4%	
☐ NME and major life-cycle management regional approvals	8%	12	18	23	23	16%	14.4%	13.4%	
Subtotal	30%					54%	49%	46%	
Return to Growth									
☐ Product Sales from Growth Platforms ($m)	30%	15,562	16,381	17,201	17,116	57%	52%	48%	Our Return to Growth performance is described on pages 29 to 37.
Subtotal	30%					57%	52%	48%	
Achieve Group Financial Targets									
☐ Cash flow ($bn)	10%	2.9	3.2	3.8	3.9	20%	18%	17%	
☐ Core EPS ($)	20%	3.30	3.40	3.50	3.60	40%	36%	33%	Our Achieve Group Financial Targets performance is described on pages 74 to 90.
☐ Total Product Sales ($bn)	10%	19.9	20.5	21.2	21.1	20%	18%	16%	
Subtotal	40%					80%	72%	66%	
Total[2]	100%					190%	172%	161%	

Note: bar charts are indicative, scales do not start from zero.

[1] Reconciliation with KPI outcomes disclosed from page 20 of this Annual Report and a description of performance measures is shown on the following page.

[2] Due to rounding, the total formulaic outcome differs from the arithmetic total of the individual metric outcomes discussed above.

Annual bonus *continued*

During 2018, AstraZeneca made 28 NME and major life-cycle management regional submissions. However, four of these were discounted when assessing Group scorecard performance. If we do not have Phase III data for a particular submission opportunity when we set the submissions target at the start of the year, only the first regional submission is counted, even though multiple submissions may occur later in the year.

The Return to Growth target is 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 Return to Growth scorecard measure excludes certain medicines that are included in Growth Platform Product Sales reported elsewhere in this Annual Report, due to differences in definitions. The difference for 2018 primarily arose as the scorecard measure included only new medicines within the Oncology Growth Platform. The Cash flow measure is evaluated by reference to net cash flow from operating activities less capital expenditure adding back proceeds from disposal of intangible assets and is set and evaluated at the actual exchange rate. The Core EPS and Total Product Sales measures are evaluated by reference to budget exchange rates, again so that any beneficial or adverse movements in currency, which are outside the Company's control, do not impact reward outcomes. The financial metrics reconcile with other disclosures in this Annual Report as follows:

	Group scorecard outcome	KPI disclosed on pages 20-23	Exchange rate impact	Product Sales excluded	Capital expenditure	Proceeds from disposal of intangible assets
Product Sales from Growth Platforms	$17,116m	$18,464m	($59m)	$1,407m		
Cash flow	$3.9bn	$2.6bn			($1.0bn)	$2.3bn
Core EPS	$3.60	$3.46	($0.14)			
Total Product Sales	$21.1bn	$21.0bn	($0.1bn)			

Overall individual and business performance assessment

Individual assessment

During 2018, the Executive Directors' individual performance was assessed in the following key areas which align with the Company's objectives:

Pascal Soriot

Focus on innovative science	Under Pascal Soriot's leadership, AstraZeneca has turned the corner and returned to Product Sales growth, made possible by Mr Soriot's determined focus on the innovative science and investment necessary to deliver a new generation of medicines for patients, with a rebuilt and sustainable pipeline. Mr Soriot's exceptional leadership was also evident throughout 2018 to benefit AstraZeneca's shareholders, employees and other important stakeholders. For example, he represented AstraZeneca and the innovative biopharmaceutical industry in meetings with world leaders and senior politicians in key markets such as China, Russia, France and Germany, as well as the UK.
Demonstrating leadership to support developments within UK and global life sciences industry	Following from his Chairmanship of the UK Brexit Industry Group in 2017, Mr Soriot co-chaired the Life Sciences Council (LSC) with the UK Secretary of State for Business, Energy and Industrial Strategy and the UK Secretary of State for Health. The LSC, accountable for the strategic direction of life science policy in the UK, developed detailed strategies to develop the UK life sciences industry, as well as prepare for alternative Brexit scenarios. Mr Soriot has been influential in supporting industrial developments globally, including attending the CEO Council with the Chinese President Xi Jinping in June, the China Development Forum Fall Summit, and the WuXi World IOT (Internet of Things) congress in September 2018 as a keynote speaker.
Embedding a culture focused on integrity and sustainability	Through Mr Soriot's leadership in 2018, AstraZeneca continued to be recognised as a global leader in this important area. For example, AstraZeneca was ranked third in the Dow Jones Sustainability Index and was ranked third among all UK companies and 34th overall in the Global 100 Index (a ranking of the world's most sustainable companies across all sectors), placing AstraZeneca in the top 2% of companies for sustainability performance.
Making AstraZeneca a great place to work – achieve demonstrable advances in inclusion, diversity and employee engagement	During 2018, our internal KPIs were exceeded with 19.4% of leaders coming from Emerging Markets, an improvement from 13.5% in 2017. We also saw an increase in the percentage of senior roles held by women and were pleased that AstraZeneca was included in the 2018 Hampton-Alexander Review (7th for women in executive committee roles and their direct reports) and as the only major pharmaceutical company listed in Bloomberg's Gender-Equality Index. Employee engagement is high with internal surveys showing 94% of respondents understand AstraZeneca's future direction and strategic priorities and 83% would recommend AstraZeneca as a great place to work (compared with the Global Pharmaceutical norms of 87% and 80% respectively).

Annual bonus *continued*

Marc Dunoyer

Return to Growth	Mr Dunoyer has sharpened the Company's focus on driving cash flow and was instrumental in the outperformance achieved. He has also focused the Company on making productivity improvements as it moves into the next phase of its strategy which, over time, should result in margin improvements. While maintaining the global organisation's focus on delivering AstraZeneca's 2018 financial objectives, under Mr Dunoyer's stewardship, Global Finance Services were rolled out to our top 12 markets providing standardised and centrally managed efficient financial services. This has driven productivity and created value through robotics and innovation. He has also successfully executed a functional transformation rebalancing finance resources to Regional Delivery Centres in Kuala Lumpur, Malaysia, Warsaw, Poland, and San Jose, Costa Rica, improving efficiency and reducing cost.
Develop Global Business Services function to achieve cost savings	In addition to his responsibilities as CFO, Mr Dunoyer leads the Company's Global Business Services (GBS) Function. GBS is a key enabler of our strategic performance, leveraging digital technology, data analytics and artificial intelligence to create capacity, to simplify and improve processes, and to provide greater automation and smart analytics. Under Mr Dunoyer's leadership, savings of $53 million were realised in 2018 through initiatives such as the expansion of our Global Content Centre, providing local AstraZeneca commercial markets standard product and promotional materials, eliminating inefficiencies and duplication.
Achieve Scientific Leadership – Japan	Mr Dunoyer's additional responsibilities include leading AstraZeneca in Japan, which delivered a strong performance in 2018 exceeding its performance target overall. Seven successful launches in Japan in 2018, including for *Fasenra*, *Lynparza*, *Tagrisso* and *Imfinzi* were significant contributions. An example of the excellent performance delivered under Mr Dunoyer's leadership is the fact that two thirds of patients new to biologic treatments had been treated with *Fasenra* within five months of its approval.
Embedding a culture focused on integrity and sustainability	Mr Dunoyer is the Champion for our Young Health Programme (YHP) which the Board was proud to see named Community Investment Program of the Year by the 2018 Ethical Corporation Responsible Business awards. YHP reflects our commitment to building a sustainable future: it's an investment in young people and an investment in health by empowering young people with knowledge and skills to make healthy choices and take control of their future. In September 2018, Mr Dunoyer visited our YHP site in Kenya to provide some direct support on the ground. By mid-September, the YHP in Kenya had trained 40 peer educators and 54 community-based health workers and volunteers and was working with 47 primary and secondary schools to operationalise school health clubs. It has also trained 129 community leaders on non-communicable disease risk behaviours, Adolescent Sexual and Reproductive Health and gender equality.

Business assessment

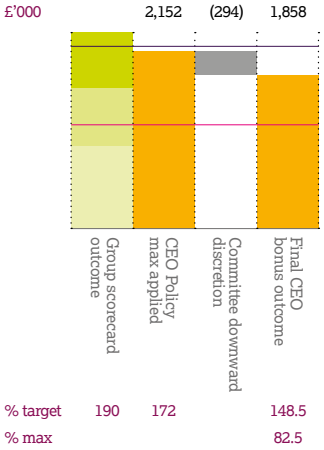
The Committee then reviewed the formulaic Group scorecard outcome for 2018 in the context of business performance and shareholder experience over the year. A number of significant events and one-off items, both positive and negative, that were unforeseen when targets were set were considered. These included: unanticipated reductions in corporate income tax rates (that positively impacted Core EPS); a one-off cash inflow following the resolution of long-running litigation; and a decision of the European Medicines Agency limiting the approval of *Imfinzi* in Europe to a narrower lung cancer patient population than other regulators.

Final determination of Executive Directors' bonuses

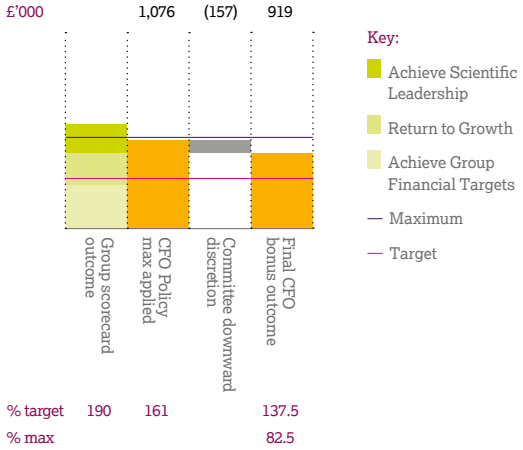
Having taken into account the Executive Directors' personal leadership and achievements during the year and considered the Group scorecard outcome in the context of overall business performance and shareholder experience, the Committee determined that it would be fair and reasonable to make a downwards adjustment to the Group scorecard outcome of 190% of target (95% of scorecard maximum).

The final bonus outcomes were set at 148.5% of target (82.5% of maximum) for Mr Soriot and 137.5% of target (82.5% of maximum) for Mr Dunoyer.

Pascal Soriot



Marc Dunoyer



Annual bonus *continued*

Deferred Bonus Plan

One third of each Executive Directors' pre-tax annual bonus is deferred into shares under the Deferred Bonus Plan (DBP). 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. DBP awards in respect of the deferred portions of bonuses earned in respect of performance during 2018 are expected to be granted in March 2019. Details of the DBP awards granted during 2018, in respect of bonuses earned in respect of performance during 2017, are shown below.

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				2018 Grant	2019 Grant
	Ordinary Shares granted	Grant date	Grant price (pence per share)[1]	Face value £'000	2018 Bonus deferred £'000
Pascal Soriot	13,157	23 March 2018	4853	639	619
Marc Dunoyer	7,037	23 March 2018	4853	342	306

[1] The grant price is the average share price over the three dealing days preceding grant.

2019 Annual bonus performance measures and operation

The Group scorecard measures and weightings for 2019 differ from the 2018 Group scorecard as follows:

> Two new Accelerate Innovative Science indices replace Achieve Scientific Leadership metrics, measuring regulatory milestones (submissions and approvals) and milestones in clinical trials, reflecting late- and early-stage science progression. Moving to dual indices simplifies our remuneration structure, by reducing the number of metrics.

> The weighting of the Cash flow metric within the Group scorecard has been increased from 10% to 20%, with financial measures now accounting for 80% of the scorecard. This change in weightings reflects the importance of cash flow generation for the phase our business has now entered, as we aim to sustain investment in our pipeline while meeting our capital allocation priorities. The Cash flow metric remains as net cash flow from operating activities less capital expenditure adding back proceeds from disposal of intangible assets.

> The Return to Growth measure will now be known as 'Deliver Growth and Therapy Area Leadership' reflecting the next phase of strategy; the underlying measure has not changed.

2019 Group scorecard performance measures and metrics

	Measure weighting	Underlying metrics (if applicable)	Metric weighting	2019 target	
Accelerate Innovative Science	20%	Pipeline progression events	10%	C	N
		Regulatory events	10%	C	N
Deliver Growth and Therapy Area Leadership	30%	Product Sales from Growth Platforms	30%	C	↑
Achieve Group Financial Targets	50%	Cash flow	20%	C	↑
		Core EPS	20%	C	↑
		Total Product Sales	10%	C	↑

Key: ↑ Target increased vs 2018 target; ↓ Target decreased vs 2018 target; ⇔ Target constant; N New measure; C Commercially sensitive

We intend to disclose the 2019 Group scorecard outcome, and details of the performance hurdles and targets, in the 2019 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 performance will be assessed by reference to individual objectives in line with the Company's objectives for the year.

Retrospective disclosure of 2017 performance hurdles

The threshold, target and maximum hurdles for the Return to Growth part of the 2017 Group scorecard were not disclosed in the 2017 Remuneration Report, as they were deemed to be commercially sensitive. The information is now disclosed below. Performance has been evaluated by reference to budget exchange rates.

2017 Group scorecard performance measures and metrics not previously disclosed	Weighting	Threshold	Target	Maximum	Outcome
Return to Growth ($m)					
New CVMD (including *Brilinta*)	6% per measure	3,649	3,841	4,033	3,563
Respiratory		4,588	4,671	4,904	4,609
New Oncology		1,142	1,202	1,262	1,330
Emerging Markets		5,488	5,777	6,066	5,870
Japan		2,215	2,331	2,448	2,335

Long-term incentives

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Long-term incentives included in single total figure: 2016 PSP and 2015 AZIP

The Executive Directors' 2018 single total figures of remuneration include the values of Performance Share Plan (PSP) awards and AstraZeneca Investment Plan (AZIP) awards with performance periods ended 31 December 2018. These shares will not be released and the dividend equivalents will not be paid out 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 2018 (5980.11 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.

Long-term incentive awards with performance periods ended 31 December 2018

				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	Total £'000	Long-term incentives total £'000
Pascal Soriot	2016 PSP	129,713	79%	4,020	2,108	652	6,780	7,669
	2015 AZIP	17,460	75%	624	160	105	888	
Marc Dunoyer	2016 PSP	54,101	79%	1,677	879	272	2,828	3,217
	2015 AZIP	7,646	75%	273	70	46	389	

[1] Calculated using the grant price of 3923 pence for 2016 PSP awards and the grant price of 4762 pence for 2015 AZIP awards.
[2] Calculated using the difference between the grant price and the average closing share price over the three-month period ended 31 December 2018.

The 2016 PSP awards granted on 24 March 2016 are due to vest and be released on 24 March 2021 on completion of a further two-year holding period. Performance over the period from 1 January 2016 to 31 December 2018 will result in 79% of the award vesting, based on the following assessment of performance.

The Aggregate revenue of Growth Platforms target is 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 Adjusted cumulative cash flow measure is evaluated by reference to net cash flow before distributions and other adjustments required by the performance conditions.

The TSR peer group against which performance has been assessed for the 2016 PSP was set at the time of grant and comprised AbbVie, BMS, GSK, Johnson & Johnson, Lilly, MSD, Novartis, Pfizer, Roche Holding and Sanofi-Aventis. AstraZeneca ranked second within the peer group, in the upper quartile. The Committee determined 87.5% of the TSR part of the award should vest, having calculated the outcome on a straight-line basis.

For more information about the TSR performance of the Company, see page 140.

2016 PSP performance measures and metrics	Weighting	Threshold (20% vesting)	Maximum (100% vesting)	Outcome	Payout
Achieve Scientific Leadership					
NME approvals	5%	5	9	10	100%
Major life-cycle management approvals	5%	5	11	14	100%
Phase III/registration NME volume	5%	9	13	11	75%
Prospective peak-year sales from approvals from NME and life-cycle management approvals	5%	6	10	11	100%
Phase II starts	5%	15	22	31	100%
Subtotal[1]	25%				95%
Aggregate revenue of Growth Platforms ($bn)	25%	17.0	20.0	17.5	42%
Adjusted cumulative cash flow ($bn)	25%	9.0	13.5	12.8	93%
Total shareholder return	25%	Median	UQ[2]	2nd	87.5%
Total[1]	100%				79%

Note: bar charts are indicative, scales do not start from zero.
[1] The subtotal and total reflect the weightings of the individual metrics.
[2] UQ = Upper Quartile.

Long-term incentives *continued*

Audited

The AZIP is a legacy plan. The last award under this plan was granted in 2016.

The 2015 AZIP awards granted on 27 March 2015 are due to vest and be released on 1 January 2023 on completion of a further four-year holding period. In 2016, the Committee replaced the original cliff vesting approach for outstanding AZIP awards with a sliding scale, whereby 25% of an award will lapse in respect of any year in the performance period in which either of the performance targets are not achieved.

Performance over the period from 1 January 2015 to 31 December 2018 will result in 75% of the 2015 AZIP vesting, as the dividend cover target was not met in the fourth year of the performance period.

2015 AZIP performance measures	2015	2016	2017	2018
Annual dividend per share at or above $2.80	$2.80	$2.80	$2.80	$2.80
Dividend cover of 1.5 calculated on the basis of Core EPS	1.52	1.54	1.53	1.24

PSP and AZIP award values included in the 2017 single total figure of remuneration have been recalculated using the average closing share price over the three-month period ended 31 December 2018 (5890.11 pence). In the 2017 Remuneration Report these figures were calculated using the average closing share price over the three-month period ended 31 December 2017 (4999.4 pence).

PSP awards granted during 2018

During 2018 conditional awards of shares were granted to Mr Soriot and Mr Dunoyer with face values equivalent to 500% of base salary and 400% of base salary respectively under the PSP. Face value is calculated using the grant price, being the average closing share price over the three dealing days preceding grant.

Performance will be assessed over the period from 1 January 2018 to 31 December 2020 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	128,889	23 March 2018	4853	6,255	31 December 2020	23 March 2023
Marc Dunoyer	61,240	23 March 2018	4853	2,972	31 December 2020	23 March 2023

The 2018, PSP performance measures focused on scientific, commercial and financial performance over the three-year performance period. The five equally weighted performance measures attached to the 2018 PSP awards are detailed below. 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)

TSR performance is assessed against a predetermined peer group of global pharmaceutical companies. The rank which the Company's TSR achieves over the performance period will determine how many shares will vest under this measure. More information about TSR performance, including the peer group, is set out on page 140.

TSR ranking of the Company	% of award that vests
Median	20% (threshold for payout)
Between median and upper quartile	*Pro rata*
Upper quartile	100%

EBITDA

Vesting under this measure is based on the achievement of threshold performance against a target of cumulative Reported EBITDA excluding non-cash movements on fair value of contingent consideration on business combinations and gains on disposals of intangible assets. The level of award vesting under this measure is based on a scale between a threshold target and an upper target.

EBITDA	% of award that vests
$13.0bn	20% (threshold for payout)
Between $13.0bn and $16.0bn	*Pro rata*
$16.0bn	75%
Between $16.0bn and $18.5bn	*Pro rata*
$18.5bn	100%

Long-term incentives *continued*

Audited

Cash flow

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
$8.0bn	20% (threshold for payout)
Between $8.0bn and $9.5bn	*Pro rata*
$9.5bn	75%
Between $9.5bn and $12.0bn	*Pro rata*
$12.0bn and above	100%

Return to Growth

Given the proportion of AstraZeneca's revenue that is now represented by our Growth Platforms, disclosing the threshold and maximum hurdles for the Return to Growth measure could be construed to constitute financial guidance, which is not the Company's intention. The Return to Growth measure is thus considered to be commercially sensitive and will be disclosed following the end of the performance period. This measure is evaluated by reference to budget exchange rates.

Achieve Scientific Leadership

The Achieve Scientific Leadership measure includes three equally weighted metrics: NME approvals, major life-cycle management approvals and Phase III registration. These metrics are an indicator of the Company's longer-term strategic priorities and are thus considered commercially sensitive; the metrics will be disclosed following the end of the performance period.

PSP performance measures for 2019 grant

The 2019 PSP measures differ from the 2018 PSP measures as follows:

> Two new Accelerate Innovative Science indices measuring regulatory events and NME Phase III/registrational volume replace the Achieve Scientific Leadership metrics. Moving to dual indices simplifies our remuneration structure by reducing the number of metrics and allows disclosure of targets at the beginning of the performance period.
> The Return to Growth measure will now be known as 'Deliver Growth and Therapy Area Leadership' reflecting the next phase of strategy; the underlying measure, Product Sales from Growth Platforms, has not changed.

PSP performance measure	Measure weighting	Underlying metrics (if applicable)	Metric weighting	Threshold (20% vesting)	Maximum (100% vesting)
Accelerate Innovative Science	20%	NME Phase III/registrational volume	8%	5	10
		Regulatory events	12%	10	19
Deliver Growth and Therapy Area Leadership	20%			Commercially sensitive until end of performance period	
Cash flow	20%			$10bn	$14bn
EBITDA	20%			$17.5bn	$22.5bn
Relative TSR	20%			Median	Upper quartile

Given the proportion of AstraZeneca's revenue that is now represented by our Growth Platforms, disclosing the threshold and maximum hurdles for the Deliver Growth and Therapy Area Leadership measure could be construed to constitute financial guidance, which is not the Company's intention. The Deliver Growth and Therapy Area Leadership measure is thus considered to be commercially sensitive and will be disclosed following the end of the performance period.

The Deliver Growth and Therapy Area Leadership and EBITDA measures are 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 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 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 140.

As described on page 128 in relation to annual bonus targets, the Committee similarly 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 Long Range Plan. While the adjustments to Reported EBITDA, described above, mean that the PSP hurdles are not directly comparable with market consensus, the Committee will take consensus into account when determining the appropriate level of stretch.

Annual Report on Remuneration *continued*

Non-Executive Directors' remuneration

Non-Executive Directors' single total figure of remuneration for 2018

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The single total figure table sets out all elements of remuneration receivable by the Non-Executive Directors in respect of the year ended 31 December 2018, alongside comparative figures for the prior year.

	2018 Fees £'000	2017 Fees £'000	**2018 Other £'000**	2017 Other £'000	**2018 Total £'000**	2017 Total £'000
Leif Johansson	**625**	575	**65**	39	**690**	614
Geneviève Berger	**110**	87	**–**	–	**110**	87
Philip Broadley – *elected 27 April 2017*	**108**	64	**–**	–	**108**	64
Graham Chipchase	**128**	115	**–**	–	**128**	115
Deborah DiSanzo – *appointed 1 December 2017*	**73**	25	**–**	–	**73**	25
Rudy Markham	**178**	165	**–**	–	**178**	165
Sheri McCoy – *appointed 1 October 2017*	**96**	43	**–**	–	**96**	43
Nazneen Rahman – *appointed 1 June 2017*	**110**	61	**–**	–	**110**	61
Shriti Vadera	**113**	110	**–**	–	**113**	110
Marcus Wallenberg	**103**	87	**–**	–	**103**	87
Former Non-Executive Directors						
Bruce Burlington – *retired 31 August 2017*	**–**	78	**–**	–	**–**	78
Ann Cairns – *retired 24 April 2017*	**–**	31	**–**	–	**–**	31
Total	**1,644**	1,441	**65**	39	**1,709**	1,480

The Chairman's single total figure includes office costs (invoiced in Swedish krona) of £65,000 for 2018 and £39,000 for 2017.

Payments to former Directors

During 2018, no payments were made to former Directors.

Payments for loss of office

During 2018, no payments were made to Directors for loss of office.

Non-Executive Directors' fee structure

The Non-Executive Directors' fee structure that applied during 2018 is set out below, alongside the structure that will be in place during 2019. No changes have been made to fees for 2019. Further information on the Non-Executive Directors' fee structure can be found within the Remuneration Policy, available at www.astrazeneca.com/remunerationpolicy2017.

Non-Executive Director fees	2018 £'000	2019 £'000
Chairman's fee[1]	625	625
Basic Non-Executive Director's fee	88	88
Senior independent Non-Executive Director	30	30
Member of the Audit Committee	20	20
Member of the Remuneration Committee	15	15
Chairman of the Audit Committee or the Remuneration Committee[2]	25	25
Member of the Science Committee	15	15
Chairman of the Science Committee[2]	15	15
Non-Executive Director responsible for overseeing sustainability matters on behalf of the Board	7.5	7.5

[1] The Chairman does not receive any additional fees for chairing, or being a member of, a committee.
[2] This fee is in addition to the fee for membership of the relevant committee.

Executive Directors' external appointments

Marc Dunoyer was appointed a non-executive director of Orchard Therapeutics on 7 June 2018. During 2018 Mr Dunoyer received a gross fee of £12,000 from Orchard Therapeutics, which he retained in full.

Directors' shareholdings

Minimum shareholding requirements

Audited

The CEO is required to build a shareholding and hold shares amounting to 300% of base salary and the CFO is required to hold shares amounting to 200% of base salary, each within five years of their dates of appointment. 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 AZIP shares in holding periods, on a net of tax basis.

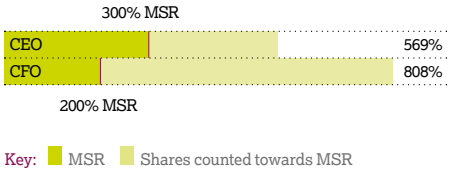
On this basis, as at 31 December 2018 Mr Soriot and Mr Dunoyer held shares worth 569% and 808% of base salary respectively and had fulfilled their minimum shareholding requirements.

The Committee has introduced a further post-employment shareholding requirement for 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.

Position against minimum shareholding requirement (MSR) as a percentage of base salary

	Held beneficially	Shares subject to deferral and holding periods	Shares subject to performance conditions	Value of shares counted towards MSR as a % of base salary[1]
Pascal Soriot	12,498	229,782	422,689	569%
Marc Dunoyer	132,243	72,309	191,422	808%

[1] Value of shares held beneficially and shares subject to deferral and holding periods, calculated net of a theoretical 50% tax rate, as at 31 December 2018.



Key: MSR Shares counted towards MSR

As mentioned in the 2017 Remuneration Report, in the period between his appointment on 1 October 2012 and 31 December 2017, Mr Soriot acquired 250,100 Ordinary Shares using his own resources and received 263,099 Ordinary Shares on the vesting of awards granted under the Company's share plans. Over that period Mr Soriot has gifted 512,699 beneficially owned Ordinary Shares to family members for nil consideration. The family members to whom the shares have been gifted do not constitute connected persons for the purposes of this disclosure, so are not included within Mr Soriot's beneficial shareholding figure in the above table. A detailed breakdown of the Executive Directors' interests under Company share plans is set out on page 138.

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 2018) or, in the case of the Chairman, approximately equivalent to his basic annual fee (£625,000 during 2018). All Non-Executive Directors who had served for a period of three years or more as at 31 December 2018 held sufficient shares to fulfil this expectation.

Directors' interests as at 31 December 2018

The following table shows the beneficial interests of the Directors (including the interests of their connected persons) in Ordinary Shares as at 31 December 2018.

Executive Directors	**Beneficial interest in Ordinary Shares at 31 December 2018**	Beneficial interest in Ordinary Shares at 31 December 2017
Pascal Soriot	**12,498**	500
Marc Dunoyer	**132,243**	127,931
Non-Executive Directors		
Leif Johansson	**39,009**	39,009
Geneviève Berger	**2,090**	2,090
Philip Broadley	**5,215**	4,800
Graham Chipchase	**3,000**	3,100
Deborah DiSanzo	**500**	500
Rudy Markham	**2,452**	2,452
Sheri McCoy	**500**	500
Nazneen Rahman	**500**	500
Shriti Vadera	**10,000**	10,000
Marcus Wallenberg	**63,646**	63,646

Directors' shareholdings *continued*

Audited

Executive Directors' share plan interests

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 2018	Grant price (pence)	Shares granted in year	Shares released in year	Shares lapsed in year	Shares outstanding at 31 December 2018: Shares subject to performance	Shares outstanding at 31 December 2018: Shares in holding period	Performance period end	Vesting and release date
DBP	27/03/2015	13,482	4762	–	13,482	–	**n/a**	**–**	n/a	27/03/2018[1]
	24/03/2016	17,352	3923	–	–	–	**n/a**	**17,352**	n/a	24/03/2019
	24/03/2017	7,968	4880	–	–	–	**n/a**	**7,968**	n/a	24/03/2020
	23/03/2018	–	4853	13,157	–	–	**n/a**	**13,157**	n/a	23/03/2021[2]
PSP	27/03/2015	104,764	4762	–	–	24,096	**–**	**80,668**	31/12/2017	27/03/2020[3]
	24/03/2016	129,713	3923	–	–	–	**129,713**	**–**	31/12/2018	24/03/2021
	24/03/2017	125,009	4880	–	–	–	**125,009**	**–**	31/12/2019	24/03/2022
	23/03/2018	–	4853	128,889	–	–	**128,889**	**–**	31/12/2020	23/03/2023[4]
AZIP	11/06/2013	89,960	3297	–	–	–	**–**	**89,960**	31/12/2016	01/01/2021
	28/03/2014	20,677	3904	–	–	–	**–**	**20,677**	31/12/2017	01/01/2022[5]
	27/03/2015	17,460	4762	–	–	–	**17,460**	**–**	31/12/2018	01/01/2023
	24/03/2016	21,618	3923	–	–	–	**21,618**	**–**	31/12/2019	01/01/2024
Total		**548,003**		**142,046**	**13,482**	**24,096**	**422,689**	**229,782**		

Marc Dunoyer

Share scheme interests	Grant date	Shares outstanding at 1 January 2018	Grant price (pence)	Shares granted in year	Shares released in year	Shares lapsed in year	Shares outstanding at 31 December 2018: Shares subject to performance	Shares outstanding at 31 December 2018: Shares in holding period	Performance period end	Vesting and release date
DBP	27/03/2015	7,111	4762	–	7,111	–	**n/a**	**–**	n/a	27/03/2018[1]
	24/03/2016	8,798	3923	–	–	–	**n/a**	**8,798**	n/a	24/03/2019
	24/03/2017	4,262	4880	–	–	–	**n/a**	**4,262**	n/a	24/03/2020
	23/03/2018	–	4853	7,037	–	–	**n/a**	**7,037**	n/a	23/03/2021[2]
PSP	27/03/2015	45,880	4762	–	–	10,553	**–**	**35,327**	31/12/2017	27/03/2020[3]
	24/03/2016	54,101	3923	–	–	–	**54,101**	**–**	31/12/2018	24/03/2021
	24/03/2017	59,439	4880	–	–	–	**59,439**	**–**	31/12/2019	24/03/2022
	23/03/2018	–	4853	61,240	–	–	**61,240**	**–**	31/12/2020	23/03/2023[4]
AZIP	01/08/2013	8,176	3302	–	–	–	**–**	**8,176**	31/12/2016	01/01/2021
	28/03/2014	8,709	3904	–	–	–	**–**	**8,709**	31/12/2017	01/01/2022[5]
	27/03/2015	7,646	4762	–	–	–	**7,646**	**–**	31/12/2018	01/01/2023
	24/03/2016	9,016	3923	–	–	–	**9,016**	**–**	31/12/2019	01/01/2024
Total		**213,138**		**68,277**	**7,111**	**10,553**	**191,442**	**72,309**		

Interests over share options	Grant date	Options outstanding at 1 January 2018	Exercise price (pence)	Options granted in year	Options matured in year	Options exercised in year	Options outstanding at 31 December 2018: Unexercisable	Options outstanding at 31 December 2018: Available to exercise	Maturity date (first date exercisable)	Last date exercisable
SAYE	28/09/2015	544	3307	–	544	544	**–**	**–**	01/12/2018	31/05/2019[6]
Total		**544**		**–**	**544**	**544**	**–**	**–**		

[1] Market price on release date was 4866 pence.
[2] Award granted following deferral of one third of the annual bonus paid in respect of performance during 2017, further detail on page 132.
[3] 77% of the shares entered the holding period, following assessment of performance over the period to 31 December 2017. The remaining shares lapsed.
[4] Details of PSP awards granted during 2018 are shown on page 134.
[5] 100% of the shares entered the holding period, following assessment of performance over the period to 31 December 2017.
[6] Option was exercised on 3 December 2018. The market price on the date of exercise was 6152 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 2018 and 14 February 2019, there was no change in the interests in Ordinary Shares shown in the tables on pages 137 to 138.

Remuneration in the wider context

When making decisions about executive remuneration and setting the Directors' Remuneration Policy, the Committee takes into account the arrangements in place for AstraZeneca's wider workforce. The Committee undertakes a detailed review of global workforce remuneration data annually. It also considers data on pay trends and practices, such as gender pay gap information, and this year for the first time, the CEO to worker pay ratio.

The approach to determining the compensation of employees globally follows the same principles as for our executives. We offer competitive pay and career opportunities, which attract the best talent; we believe in recognising strong individual performance, and we differentiate reward accordingly. When determining compensation, managers consider how the employee's pay compares to the local market alongside other factors, such as the individual's experience and sustained performance. Bonus budgets are based on the Group scorecard outcome and managers will determine final employee bonuses based on individual performance. Around 25% of the global workforce are eligible for LTI awards.

Being a great place to work is a key pillar of our strategy, and at the heart of our efforts to foster the talents of our people. Pay is just one factor that helps us to attract, retain and develop a talented and diverse workforce. We encourage employees to take ownership of their own development, with the support of leaders throughout the business. Initiatives such as our Women as Leaders programme, which aims to encourage more women into senior roles; tailored online learning platforms for managers and employees covering topics such as unconscious bias; and employee networks, such as our LGBT+ network, help us to fulfil our commitment to fostering an inclusive and diverse workplace. Employee surveys show that 83% of our employees would recommend AstraZeneca as a great place to work; more information about this important part of our strategy is set out on pages 38 to 49.

Change in CEO remuneration compared to other employees

In the table below, changes to the CEO's salary, taxable benefits and annual bonus are compared to a group of employees over the same period (2017 to 2018). The comparator group includes employees in the UK, US and Sweden who represent approximately 25% 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. We have used a consistent employee comparator group, so the same individuals appear in both the 2017 and 2018 figures, allowing a meaningful comparison of salary increases.

	Percentage change for CEO against 2017	Average percentage change for employees against 2017
Salary	2.5%	4.6%
Taxable benefits	(0.4)%	4.6%
Annual bonus	(3.0)%	13.3%

CEO and employee pay ratios

The table below sets out the ratios of the CEO single total figure of remuneration 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), which were published during 2018 and will first apply to AstraZeneca's financial year beginning 1 January 2019. These pay ratios form part of the information that is provided to the Committee on broader employee pay policies and practices to inform remuneration decisions for the Executive Directors.

Year	Method	25th percentile pay ratio	50th percentile pay ratio	75th percentile pay ratio
2018	Option A	230:1	160:1	103:1

Pay data (£'000)	Base salary	Total pay
CEO remuneration	1,251	11,356
UK employees 25th percentile	36	49
UK employees 50th percentile	50	71
UK employees 75th percentile	70	110

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 have chosen Option A which is a calculation based on all UK employees on a full-time equivalent basis. The ratios are based on total pay which includes base salary, benefits, bonus and long-term incentives. The CEO pay is as shown in the single total figure of remuneration table, on page 126. For UK employees, quartile data has been determined as at 31 December 2018, with calculations based on actual pay data for January to November 2018. Estimates have been used for December 2018 pay, annual bonus outcomes and dividend equivalents.

As explained earlier in this Report, the majority of the CEO total pay for the year is driven by performance-related elements, notably the long-term incentive element and share price growth during the period. The ratios may therefore vary significantly year-on-year depending on bonus and PSP outcomes and share price movements. The ratio of CEO pay excluding LTI versus median UK employee pay is 51:1.

Annual Report on Remuneration *continued*

Remuneration in the wider context *continued*

Audited

Relative importance of spend on pay

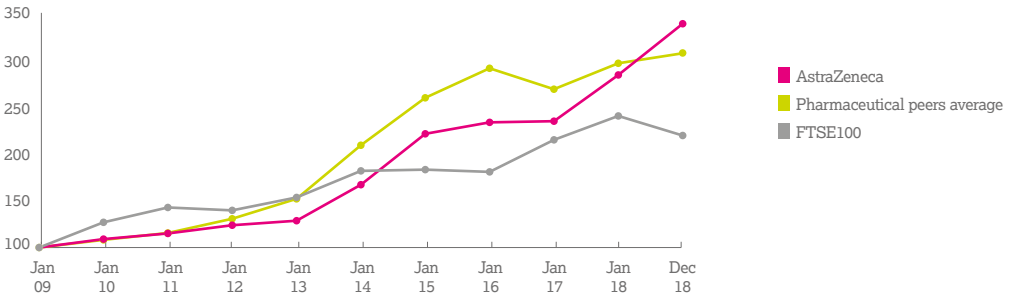
The table below shows the remuneration paid to all employees in the Group, including the Executive Directors, and expenditure on shareholder distributions through dividends. The figures have been calculated in accordance with the Group Accounting Policies and drawn from either the Company's Consolidated Statement of Comprehensive Income on page 149, or its Consolidated Statement of Cash Flows on page 152. Further information on the Group's Accounting Policies can be found from page 153.

	2018 $m	2017 $m	Difference in spend between years $m	Difference in spend between years %
Total employee remuneration	**6,970**	6,486	484	7.5
Distributions to shareholders: dividends paid	**3,484**	3,519	(35)	(1.0)

Total shareholder return (TSR)

The graph below compares the TSR performance of the Company over the past ten years with the TSR of the FTSE100 Index. This graph is re-based to 100 at the start of the relevant period. As a constituent of the FTSE100, this index represents an appropriate reference point for the Company. We have also included a 'Pharmaceutical peers average', which reflects the TSR of our current comparator group and provides shareholders with additional context. This comparator group was adopted in 2017 and is used to assess relative TSR performance for PSP awards granted from 2017 onwards. It consists of AbbVie, Amgen, Astellas, BMS, Celgene, Daiichi Sankyo, Lilly, Gilead, GSK, Johnson & Johnson, MSD, Novo Nordisk, Novartis, Pfizer, Roche, Sanofi, Shire and Takeda. CEO remuneration over the same ten year period is shown after the TSR graph.

TSR over a ten-year period



CEO total remuneration table

Year	CEO	CEO single total figure of remuneration £'000	Annual bonus payout against maximum opportunity %	LTI vesting rates against maximum opportunity %
2018	Pascal Soriot	11,356[1]	83	79
2017	Pascal Soriot	10,429[2]	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]	68	–
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
2011	David Brennan	7,863	74	62
2010	David Brennan	9,690	90	100
2009	David Brennan	5,767	100	62

[1] The 2018 single total figure of remuneration table is shown on page 126.
[2] This figure has been revised using the average closing share price over the three-month period to 31 December 2018, as explained on page 134.
[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.

Governance

Committee membership

During 2018, the Committee members were Graham Chipchase (Chairman of the Committee), Leif Johansson, Rudy Markham, Shriti Vadera, Sheri McCoy (appointed as a Committee member on 1 July 2018) and Philip Broadley (appointed as a Committee member on 1 December 2018). Shriti Vadera retired as a Director of AstraZeneca on 31 December 2018. The Deputy Company Secretary acts as secretary to the Committee. The Committee met six times in 2018 and members' attendance records are set out on page 93. 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 EVP, GMD; the EVP, Human Resources; the SVP, Reward and Diversity; the Senior Director Compensation; the Company Secretary; the Deputy Company Secretary and the Non-Executive Directors forming the Science Committee. The Committee's independent adviser attended all Committee meetings.

Terms of reference

A copy of the Committee's terms of reference is available on our website, www.astrazeneca.com. The Committee conducted a review of its terms of reference during 2018 and recommended certain changes to reflect the revised UK Corporate Governance Code which is effective for the Company from 1 January 2019. The Board approved the recommendation.

Independent adviser to the Committee

During 2018, the Committee carried out a tender process to select an independent adviser. The process involved submission of written proposals followed by shortlisted candidates being interviewed by both Committee members and members of the Company's management. The Committee selected and appointed Willis Towers Watson (WTW) as its independent adviser with effect from September 2018. WTW's service to the Committee was provided on a time-spend basis at a cost to the Company of £56,000, excluding VAT. During 2018, 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. The Committee reviewed the potential for conflicts of interest and judged that there were no conflicts.

Prior to WTW's appointment, the role of independent adviser was held by Deloitte LLP (Deloitte). Deloitte had been reappointed by the Committee as its independent adviser following a tender process in 2013. Deloitte's service to the Committee during 2018 was provided on a time-and-materials basis at a cost of £89,300, excluding VAT. During 2018, Deloitte also provided taxation and legal advice and other non-audit advisory and assurance services to the Group. The Committee reviewed the potential for conflicts of interest and judged that there were no conflicts. Both WTW and Deloitte are members 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 and Deloitte adhere to the code.

Shareholder voting at the AGM

At the Company's AGM on 18 May 2018, shareholders voted in favour of a resolution to approve the Annual Report on Remuneration for the year ended 31 December 2017. The Directors' Remuneration Policy was approved by shareholders at the Company's AGM on 27 April 2017. The Committee has engaged with shareholders to understand the reasons behind the low vote in favour of the Annual Report on Remuneration at the 2018 AGM and taken a number of actions to address this. This is discussed in the letter from the Chairman of the Committee from page 120.

Resolution	Votes for	% for	Votes against	% against	Total votes cast	% of Issued Share Capital voted	Withheld votes
Ordinary Resolution to approve the Directors' Remuneration Policy (2017 AGM)	877,620,302	96.08	35,804,933	3.92	913,425,235	72.17	15,539,511
Ordinary Resolution to approve the Annual Report on Remuneration for the year ended 31 December 2017 (2018 AGM)	616,320,491	65.08	330,706,327	34.92	947,026,818	74.77	30,798,857

Directors' service contracts and letters of appointment

The notice periods and unexpired terms of Executive Directors' service contracts at 31 December 2018 are shown in the table below. AstraZeneca or the Executive Director may terminate the service contract on 12 months' notice.

Executive Director	Date of service contract	Unexpired term at 31 December 2018	Notice period
Pascal Soriot	15 December 2016	12 months	12 months
Marc Dunoyer	6 December 2016	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 Company is mindful of the director independence provisions of the UK Corporate Governance Code and, in this regard, a Non-Executive Director's overall tenure will not normally exceed nine years. The Chairman of the Company 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 (the Regulations) and meets the relevant requirements of the Financial Conduct Authority's Listing Rules. As required by the Regulations, a resolution to approve the Annual Report on Remuneration will be proposed at the AGM on 26 April 2019.

On behalf of the Board

A C N Kemp
Company Secretary
14 February 2019

Financial Statements

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 Group and Parent Company Financial Statements for each financial year. Under that law they are required to prepare the Group Financial Statements in accordance with IFRSs as issued by the IASB and adopted by the EU, and applicable law, and have elected to prepare the Parent Company Financial Statements in accordance with UK Accounting Standards, including FRS 101 'Reduced Disclosure Framework' and applicable law.

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 IFRSs as adopted by the EU
- 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 14 February 2019

Pascal Soriot
Director

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.

The Directors assessed the effectiveness of AstraZeneca's internal control over financial reporting as at 31 December 2018 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, the Directors believe that, as at 31 December 2018, the internal control over financial reporting is effective based on those criteria.

PricewaterhouseCoopers LLP, an independent registered public accounting firm, has audited the effectiveness of internal control over financial reporting as at 31 December 2018 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 2018 and of the Group's profit and cash flows for the year then ended;
- the Group Financial Statements have been properly prepared in accordance with International Financial Reporting Standards (IFRSs) as adopted by the European Union;
- 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 and, as regards the Group Financial Statements, Article 4 of the IAS Regulation.

We have audited the Financial Statements included within the Annual Report and Form 20-F Information 2018 (the "Annual Report"), which comprise: the Consolidated Statement of Financial Position as at 31 December 2018, the Consolidated Statement of Comprehensive Income for the year ended 31 December 2018, the Consolidated Statement of Cash Flows for the year ended 31 December 2018, the Consolidated Statement of Changes in Equity for the year ended 31 December 2018, the Group Accounting Policies and notes to the Group Financial Statements, the Company Balance Sheet as at 31 December 2018, the Company Statement of Changes in Equity for the year ended 31 December 2018, the Company Accounting Policies and notes to the Company Financial Statements.

Our opinion is consistent with our reporting to the Audit Committee.

Separate opinion in relation to IFRSs as issued by the IASB.

As explained in the Group Accounting Policies, the Group, in addition to applying IFRSs as adopted by the European Union, has also applied IFRSs as issued by the International Accounting Standards Board (IASB).

In our opinion, the Group Financial Statements have been properly prepared in accordance 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 to the Group or the Parent Company.

Other than those disclosed in Note 31 to the Financial Statements, we have provided no non-audit services to the Group or the Parent Company in the period from 1 January 2018 to 31 December 2018.

Our audit approach

Overview

Materiality

- Overall Group materiality: $130m (2017: $160m), based on 5% of profit before tax, after adding back (i) intangible asset impairment charges and (ii) fair value movements and the discount unwind on contingent consideration, as disclosed in Notes 9 and 19 respectively.
- Overall Parent Company materiality: $100m (2017: $75m), based on 1% of net assets.

Audit scope

- We identified eleven 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, UK, Sweden, China, Japan, France, Germany, Russia and Brazil as well as the Parent Company and AstraZeneca Treasury Limited.
- We also identified a further six 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 balances related to revenue, research and development expense or property, plant and equipment, as appropriate.
- Audit procedures were performed centrally over certain shared service functions for transaction processing, IT and in relation to various Group functions, including taxation, pensions, goodwill, intangible assets and other investments, and litigation matters, as well as the consolidation.
- Taken together, the above procedures accounted for 85% of the Group's revenue and 70% of the Group's absolute profit before tax.

Key audit matters

- Recognition and measurement of accruals for rebates and returns in the US
- Assessment of the recoverability of the carrying value of intangible assets (product, marketing and distribution rights)
- Accounting for externalisation and collaboration arrangements – in-license and out-licensing arrangements and other types of complex development and collaboration agreements
- Recognition and measurement of litigation and contingent liabilities
- Recognition and measurement of uncertain tax provisions

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.

Capability of the audit in detecting irregularities, including fraud

Based on our understanding of the Group and the industry in which it operates, we identified that the principal risks of non-compliance with laws and regulations related to patent protection, product safety, competition law and environmental matters (see Note 29), and we considered the extent to which non-compliance might have a material effect on the Group Financial Statements. We also considered those laws and regulations that have a direct impact on the financial statements such as the Companies Act 2006 and tax legislation. 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 posting inappropriate journal entries to manipulate financial results and management bias in accounting estimates. The Group engagement team shared this risk assessment with the component auditors referred to in the scoping section of our report below, 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:

- Discussions with management, internal audit, the Deputy Chief Compliance Officer and the Group's legal counsel, including consideration of known or suspected instances of non-compliance with laws and regulations and fraud;
- Evaluation and testing of the operating effectiveness of management's controls designed to prevent and detect irregularities;
- Assessment of matters reported on the Group's whistleblowing helpline and results of management's investigation of such matters;

- Challenging assumptions made by management in their significant accounting estimates in particular in relation to estimation of rebate and return accruals, impairment of intangible assets, and the recognition and measurement of litigation and contingent liabilities and uncertain tax provisions (see related key audit matters below);
- Identifying and testing journal entries, in particular any journal entries posted with unusual account combinations, journals posted by senior management, journals posted and reviewed by the same individual and consolidation journals.

There are inherent limitations in the audit procedures described above and the further removed non-compliance with laws and regulations is from the events and transactions reflected in the financial statements, the less likely we would become aware of it. 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.

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.

Key audit matter	How our audit addressed the key audit matter
Recognition and measurement of accruals for rebates and returns in the US Refer to page 115 (Audit Committee Report), page 154 (Accounting Policies) and Note 19 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 and provide a right of return for certain products, of which the most significant are Medicare Part D, Managed Care and Medicaid. These arrangements lead to material deductions to gross sales in arriving at revenue to recognise the obligations for the Group to provide customers with rebates, discounts, allowances and the right of return, for which unsettled amounts are accrued. The directors have determined an accrual of $4,043m to be necessary at 31 December 2018. Rebate, discount, allowance and return arrangements are complex and establishing an appropriate accrual requires significant estimation on the part of management. Changes in estimates can have a significant financial impact.	We evaluated the design and tested the operating effectiveness of controls over the recognition and measurement of rebates and returns. We determined that we could rely on these controls for the purposes of our audit. We obtained management's calculations for accruals under applicable schemes and assessed the assumptions used by reference to the Group's stated commercial policies, the terms of the applicable contracts, third party data related to patient enrolment in US government funded benefit schemes and historical levels of product returns. We compared the assumptions to contracted prices, historical rebates, discounts, allowances and returns levels (where relevant) and to current payment trends. We also considered the historical accuracy of the Group's estimates in previous years and the effect of any adjustments to prior year's accruals in the current year's results. We formed an independent expectation of the largest elements of the accrual at 31 December 2018 using third party data (where relevant) and compared this expectation to the actual accrual recognised by the Group. Based on the procedures performed, we did not identify any material misstatements in the accruals.
Assessment of the recoverability of the carrying value of intangible assets (product, marketing and distribution rights) Refer to page 115 (Audit Committee Report), page 155 (Accounting Policies) and Note 9 in the Group Financial Statements. The Group has product, marketing and distribution rights and other intangible assets totalling $21,720m, out of a total intangible asset value of $21,959m at 31 December 2018. The carrying values of intangible assets are contingent on future cash flows and there is a risk that the assets will be impaired if cash flows are not in line with expectations. The projections in management's impairment models contain a number of significant estimates including peak year and erosion sales curves, probability of technical and regulatory success factors and discount rates. Changes in these assumptions could lead to an impairment to the carrying value of intangible assets. Our work on intangible assets focussed on assets that were in development (and not being amortised) and launched assets which were individually significant, had lower levels of headroom or where there have been concerns over the recoverability of the carrying value of specific assets in previous periods.	We evaluated the design and tested the operating effectiveness of controls in assessing the carrying value of intangible assets. We determined that we could rely on these controls for the purposes of our audit. For those assets tested we obtained the Group's impairment analyses and: - we tested the accuracy of the impairment models and agreed the cash flow forecasts used in the impairment models to the Board approved Long Range Plan; - we tested the reasonableness of key assumptions including revenue and profit growth or decline, the expected loss of drug exclusivity and the impact of the expiry of patents including comparing certain assumptions to industry and economic forecasts; - for higher risk assets we performed sensitivity analysis focusing on what we consider to be reasonably possible changes in key assumptions; and - we assessed the historical accuracy of forecasts to assess management's forecasting ability. We utilised our in-house valuation experts to assess the valuation techniques used, to independently corroborate the discount rate used by management by reference to market data and to assist with the evaluation of other key assumptions for higher risk assets (primarily probability of technical and regulatory success factors). As a result of our work, we determined that the net impairment charge of $683m recorded for intangible assets was appropriate. We reviewed the disclosures in Note 9 of the Group Financial Statements, including sensitivity analysis based on reasonably possible downsides. We are satisfied that these disclosures are appropriate.

Key audit matter	How our audit addressed the key audit matter
Accounting for externalisation and collaboration arrangements – in-license and out-licensing arrangements and other types of complex development and collaboration agreements. Refer to page 115 (Audit Committee Report), page 155 (Accounting Policies) and Note 1 in the Group Financial Statements. The Group routinely enters into development and commercialisation arrangements and collaborations with other pharmaceutical companies. These include in-license and out-licensing arrangements and other types of complex agreements. In 2018, the Group recognised externalisation revenue of $1,041m. The nature of these arrangements mean that the accounting for externalisation revenue is often inherently complex and judgemental, unusual by definition and presents a higher level of risk.	We evaluated the design and tested the operating effectiveness of controls in place over significant contracts and collaboration agreements. We determined that we could rely on these controls for the purposes of our audit. For each material externalisation revenue transaction we reviewed the underlying contract and management's accounting analysis to understand both the formal terms of the agreement and its commercial substance. We assessed whether components of the transaction were at fair value and whether the rights transferred under the arrangement qualified for revenue recognition having regard to the remaining performance obligations under the arrangement. Where there were ongoing performance obligations we assessed whether an appropriate proportion of revenue had been deferred, including an appropriate margin for the work yet to be performed. Where there was a related intangible asset we assessed whether an appropriate amount of that intangible asset had been derecognised on transfer of the relevant rights. Based on the procedures performed, we consider management's judgements reasonable and did not identify any material misstatements.
Recognition and measurement of litigation and contingent liabilities Refer to page 116 (Audit Committee Report), page 158 (Accounting Policies) and Notes 20 and 29 in the Group Financial Statements. The pharmaceuticals industry is heavily regulated which increases inherent litigation risk. The Group is engaged in a number of legal actions, including patent litigation, product liability, anti-trust and related litigation. At 31 December 2018, the Group held provisions of $198m in respect of legal claims. These provisions are based on judgements and reflect accounting estimates made by management in determining the likelihood and magnitude of an unfavourable outcome on the claims. Accordingly, unexpected adverse outcomes could significantly impact the Group's reported profit and balance sheet position.	We evaluated the design and tested the operating effectiveness of controls in respect of the recognition and measurement of litigation matters. We determined that we could rely on these controls for the purposes of our audit. We read the summary of litigation matters provided by management and held discussions with the Group's legal counsel. We requested and obtained legal letters from certain of the Group's external legal advisors with respect to the matters included in the summary. Where appropriate we examined correspondence connected with the cases. We considered management's judgements on the level of provisioning to be reasonable. We also evaluated the appropriateness of the disclosures in Note 20 and Note 29 which we considered appropriate.
Recognition and measurement of uncertain tax provisions Refer to page 116 (Audit Committee Report), page 156 (Accounting Policies) and Note 29 in the Group Financial Statements. The Group operates in a complex multinational tax environment and is subject to a range of tax risks during the normal course of business including transaction related tax matters and transfer pricing arrangements. Where the amount of tax payable is uncertain, the Group establishes provisions based on management's judgement and estimates of the probable amount of the future liability. At 31 December 2018, the Group has recorded provisions of $942m in respect of uncertain tax positions.	We evaluated the design and tested the operating effectiveness of controls in respect of the recognition and measurement of uncertain tax provisions. We determined that we could rely on these controls for the purposes of our audit. With the assistance of our local and international tax specialists, we evaluated management's judgements and estimates of tax exposures and contingencies in order to assess the adequacy of the Group's tax provisions. In understanding and evaluating management's judgements, we considered the status of recent and current tax authority audits and enquiries, judgemental positions taken in tax returns and current year estimates and developments in the tax environment. Where appropriate, we also read documentation to understand the positions reached. We noted that the assumptions and judgements that are required to formulate the provisions 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 reviewed the disclosures in Note 29 of the Group Financial Statements. We are satisfied that these disclosures are appropriate.

We determined that there were no key audit matters applicable to the Parent Company to communicate in our report.

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 eleven reporting components which required a full scope audit for Group reporting. These are the principal operating units in the US, UK, Sweden, China, Japan, France, Germany, Russia and Brazil as well as the Parent Company and AstraZeneca Treasury Limited. We identified these eleven reporting components as those that, in our view, required an audit of their complete financial information, due to their size or risk characteristics.

We also identified a further six reporting components which had one or more individual financial statement line item balances that were considered significant to the Group's Financial Statements. For these components our work solely focussed on balances related to revenue (Canada, a further reporting component in China, Italy, and Spain), research and development expense (further reporting components in the UK and the US) or property, plant and equipment (further reporting component in the US).

Audit procedures were performed centrally over certain shared service functions for transaction processing, IT and in relation to various Group functions, including taxation, pensions, goodwill, intangible assets and other investments, and litigation matters, as well as the consolidation.

Taken together, the above procedures accounted for 85% of the Group's revenue and 70% of the Group's absolute profit before tax.

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:

	Group Financial Statements	Parent Company Financial Statements
Overall materiality	$130m (2017: $160m)	$100m (2017: $75m)
How we determined it	5% of profit before tax, after adding back intangible asset impairment charges, fair value movements and discount unwind on contingent consideration as disclosed in Notes 9 and 19 respectively.	1% of net assets
Rationale for benchmark applied	The reported profit of the Group can fluctuate due to intangible asset impairment charges and fair value and discount unwind movements on contingent consideration. 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 in AstraZeneca PLC (being investment holding) 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 $10m and $105m.

We agreed with the Audit Committee that we would report to them misstatements identified during our audit above $7m for both the Group Financial Statements and the Parent Company Financial Statements (2017: $7m) as well as misstatements below those amounts that, in our view, warranted reporting for qualitative reasons.

Going concern

In accordance with ISAs (UK) we report as follows:

Reporting obligation	Outcome
We are required to report if we have anything material to add or draw attention to in respect of the directors' statement in the Financial Statements about whether the directors considered it appropriate to adopt the going concern basis of accounting in preparing the Financial Statements and the directors' identification of any material uncertainties to the Group's and the Parent Company's ability to continue as a going concern over a period of at least twelve months from the date of approval of the Financial Statements.	We have nothing material to add or to draw attention to. As not all future events or conditions can be predicted, this statement is not a guarantee as to the Group's and the Parent Company's ability to continue as a going concern. For example, the terms on which the United Kingdom may withdraw from the European Union, which is currently due to occur on 29 March 2019, are not clear, and it is difficult to evaluate all of the potential implications.
We are required to report if the directors' statement relating to Going Concern in accordance with Listing Rule 9.8.6R(3) is materially inconsistent with our knowledge obtained in the audit.	We have nothing to 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. 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 the responsibilities described above and our work undertaken in the course of the audit, the Companies Act 2006 (CA06), ISAs (UK) and the Listing Rules of the Financial Conduct Authority (FCA) require us also to report certain opinions and matters as described below (required by ISAs (UK) unless otherwise stated).

Independent Auditors' Report to the Members of AstraZeneca PLC *continued*

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 2018 is consistent with the financial statements and has been prepared in accordance with applicable legal requirements (CA06).

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 (CA06).

The directors' assessment of the prospects of the Group and of the principal risks that would threaten the solvency or liquidity of the Group

We have nothing material to add or draw attention to regarding:

- The directors' confirmation on page 70 of the Annual Report that they have carried out a robust assessment of the principal risks facing the Group, including those that would threaten its business model, future performance, solvency or liquidity.
- The disclosures in the Annual Report that describe those risks and explain how they are being managed or mitigated.
- The directors' explanation on page 71 of the Annual Report as to how they have assessed the prospects of the Group, over what period they have done so and why they consider that period to be appropriate, and their statement as to whether they have a reasonable expectation that the Group will be able to continue in operation and meet its liabilities as they fall due over the period of their assessment, including any related disclosures drawing attention to any necessary qualifications or assumptions.

We have nothing to report having performed a review of the directors' statement that they have carried out a robust assessment of the principal risks facing the Group and statement in relation to the longer-term viability of the Group. Our review was substantially less in scope than an audit and only consisted of making inquiries and considering the directors' process supporting their statements; checking that the statements are in alignment with the relevant provisions of the UK Corporate Governance Code (the "Code"); and considering whether the statements are consistent with the knowledge and understanding of the Group and Parent Company and their environment obtained in the course of the audit (Listing Rules).

Other Code Provisions

We have nothing to report in respect of our responsibility to report when:

- The statement given by the directors, on page 143, that they consider the Annual Report taken as a whole to be fair, balanced and understandable, and provides the information necessary for the members to assess the Group's and Parent Company's position and performance, business model and strategy is materially inconsistent with our knowledge of the Group and Parent Company obtained in the course of performing our audit.
- The section of the Annual Report on pages 113 to 119 describing the work of the Audit Committee does not appropriately address matters communicated by us to the Audit Committee.
- The directors' statement relating to the Parent 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.

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 (CA06).

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 pursuant to DTR 4 set out on page 143, 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.

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 Parent 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 received 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 shareholders 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 2 years, covering the years ended 31 December 2017 and 31 December 2018.

Richard Hughes (Senior Statutory Auditor)
for and on behalf of
PricewaterhouseCoopers LLP
Chartered Accountants and Statutory Auditors
London
14 February 2019

Consolidated Statement of Comprehensive Income
for the year ended 31 December

	Notes	2018 $m	2017 $m	2016 $m
Product Sales	1	**21,049**	20,152	21,319
Externalisation Revenue	1	**1,041**	2,313	1,683
Total Revenue		**22,090**	22,465	23,002
Cost of sales		**(4,936)**	(4,318)	(4,126)
Gross profit		**17,154**	18,147	18,876
Distribution costs		**(331)**	(310)	(326)
Research and development expense	2	**(5,932)**	(5,757)	(5,890)
Selling, general and administrative costs	2	**(10,031)**	(10,233)	(9,413)
Other operating income and expense	2	**2,527**	1,830	1,655
Operating profit		**3,387**	3,677	4,902
Finance income	3	**138**	113	67
Finance expense	3	**(1,419)**	(1,508)	(1,384)
Share of after tax losses in associates and joint ventures	10	**(113)**	(55)	(33)
Profit before tax		**1,993**	2,227	3,552
Taxation	4	**57**	641	(146)
Profit for the period		**2,050**	2,868	3,406
Other comprehensive income:				
Items that will not be reclassified to profit or loss:				
Remeasurement of the defined benefit pension liability	21	**(46)**	(242)	(575)
Net losses on equity investments measured at fair value through other comprehensive income		**(171)**	–	–
Fair value movements related to own credit risk on bonds designated as fair value through profit and loss		**8**	(9)	–
Tax on items that will not be reclassified to profit or loss	4	**56**	16	136
		(153)	(235)	(439)
Items that may be reclassified subsequently to profit or loss:				
Foreign exchange arising on consolidation	22	**(450)**	536	(1,050)
Foreign exchange arising on designating borrowings in net investment hedges	22	**(520)**	505	(591)
Fair value movements on cash flow hedges		**(37)**	311	(115)
Fair value movements on cash flow hedges transferred to profit and loss		**111**	(315)	195
Fair value movements on derivatives designated in net investment hedges	22	**(8)**	(48)	(4)
Costs of hedging		**(54)**	–	–
Amortisation of loss on cash flow hedge		**1**	1	1
Net available for sale (losses)/gains taken to equity		**–**	(83)	139
Tax on items that may be reclassified subsequently to profit or loss	4	**51**	(33)	86
		(906)	874	(1,339)
Other comprehensive (loss)/income for the period, net of tax		**(1,059)**	639	(1,778)
Total comprehensive income for the period		**991**	3,507	1,628
Profit attributable to:				
Owners of the Parent		**2,155**	3,001	3,499
Non-controlling interests	25	**(105)**	(133)	(93)
Total comprehensive income attributable to:				
Owners of the Parent		**1,097**	3,640	1,722
Non-controlling interests	25	**(106)**	(133)	(94)
Basic earnings per $0.25 Ordinary Share	5	**$1.70**	$2.37	$2.77
Diluted earnings per $0.25 Ordinary Share	5	**$1.70**	$2.37	$2.76
Weighted average number of Ordinary Shares in issue (millions)	5	**1,267**	1,266	1,265
Diluted weighted average number of Ordinary Shares in issue (millions)	5	**1,267**	1,267	1,266
Dividends declared and paid in the period	24	**3,539**	3,543	3,540

All activities were in respect of continuing operations.

$m means millions of US dollars.

Consolidated Statement of Financial Position
at 31 December

	Notes	2018 $m	2017 $m	2016 $m
Assets				
Non-current assets				
Property, plant and equipment	7	**7,421**	7,615	6,848
Goodwill	8	**11,707**	11,825	11,658
Intangible assets	9	**21,959**	26,188	27,586
Investments in associates and joint ventures	10	**89**	103	99
Other investments	11	**833**	933	727
Derivative financial instruments	12	**157**	504	343
Other receivables	13	**515**	847	901
Deferred tax assets	4	**2,379**	2,189	1,102
		45,060	50,204	49,264
Current assets				
Inventories	14	**2,890**	3,035	2,334
Trade and other receivables	15	**5,574**	5,009	4,573
Other investments	11	**849**	1,230	884
Derivative financial instruments	12	**258**	28	27
Income tax receivable		**207**	524	426
Cash and cash equivalents	16	**4,831**	3,324	5,018
Assets held for sale	17	**982**	–	–
		15,591	13,150	13,262
Total assets		**60,651**	63,354	62,526
Liabilities				
Current liabilities				
Interest-bearing loans and borrowings	18	**(1,754)**	(2,247)	(2,307)
Trade and other payables	19	**(12,841)**	(11,641)	(10,486)
Derivative financial instruments	12	**(27)**	(24)	(18)
Provisions	20	**(506)**	(1,121)	(1,065)
Income tax payable		**(1,164)**	(1,350)	(1,380)
		(16,292)	(16,383)	(15,256)
Non-current liabilities				
Interest-bearing loans and borrowings	18	**(17,359)**	(15,560)	(14,501)
Derivative financial instruments	12	**(4)**	(4)	(117)
Deferred tax liabilities	4	**(3,286)**	(3,995)	(3,956)
Retirement benefit obligations	21	**(2,511)**	(2,583)	(2,186)
Provisions	20	**(385)**	(347)	(353)
Other payables	19	**(6,770)**	(7,840)	(9,488)
		(30,315)	(30,329)	(30,601)
Total liabilities		**(46,607)**	(46,712)	(45,857)
Net assets		**14,044**	16,642	16,669
Equity				
Capital and reserves attributable to equity holders of the Company				
Share capital	23	**317**	317	316
Share premium account		**4,427**	4,393	4,351
Capital redemption reserve		**153**	153	153
Merger reserve		**448**	448	448
Other reserves	22	**1,440**	1,428	1,446
Retained earnings	22	**5,683**	8,221	8,140
		12,468	14,960	14,854
Non-controlling interests	25	**1,576**	1,682	1,815
Total equity		**14,044**	16,642	16,669

The Financial Statements from pages 149 to 204 were approved by the Board and were signed on its behalf by

Pascal Soriot
Director

Marc Dunoyer
Director

14 February 2019

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 2016	316	4,304	153	448	1,435	11,834	18,490	19	18,509
Profit for the period	–	–	–	–	–	3,499	3,499	(93)	3,406
Other comprehensive loss	–	–	–	–	–	(1,777)	(1,777)	(1)	(1,778)
Transfer to other reserves[1]	–	–	–	–	11	(11)	–	–	–
Transactions with owners									
Dividends	–	–	–	–	–	(3,540)	(3,540)	–	(3,540)
Dividends paid by subsidiary to non-controlling interest	–	–	–	–	–	–	–	(13)	(13)
Acerta Pharma put option (Note 25)	–	–	–	–	–	(1,825)	(1,825)	–	(1,825)
Changes in non-controlling interest (Note 25)	–	–	–	–	–	–	–	1,903	1,903
Issue of Ordinary Shares	–	47	–	–	–	–	47	–	47
Share-based payments charge for the period (Note 28)	–	–	–	–	–	241	241	–	241
Settlement of share plan awards	–	–	–	–	–	(281)	(281)	–	(281)
Net movement	–	47	–	–	11	(3,694)	(3,636)	1,796	(1,840)
At 31 December 2016	316	4,351	153	448	1,446	8,140	14,854	1,815	16,669
Profit for the period	–	–	–	–	–	3,001	3,001	(133)	2,868
Other comprehensive income	–	–	–	–	–	639	639	–	639
Transfer to other reserves[1]	–	–	–	–	(18)	18	–	–	–
Transactions with owners									
Dividends	–	–	–	–	–	(3,543)	(3,543)	–	(3,543)
Issue of Ordinary Shares	1	42	–	–	–	–	43	–	43
Share-based payments charge for the period (Note 28)	–	–	–	–	–	220	220	–	220
Settlement of share plan awards	–	–	–	–	–	(254)	(254)	–	(254)
Net movement	1	42	–	–	(18)	81	106	(133)	(27)
At 31 December 2017	317	4,393	153	448	1,428	8,221	14,960	1,682	16,642
Adoption of new accounting standards[2]	–	–	–	–	–	(91)	(91)	–	(91)
Profit for the period	–	–	–	–	–	2,155	2,155	(105)	2,050
Other comprehensive loss[3]	–	–	–	–	–	(1,058)	(1,058)	(1)	(1,059)
Transfer to other reserves[1]	–	–	–	–	12	(12)	–	–	–
Transactions with owners									
Dividends	–	–	–	–	–	(3,539)	(3,539)	–	(3,539)
Issue of Ordinary Shares	–	34	–	–	–	–	34	–	34
Share-based payments charge for the period (Note 28)	–	–	–	–	–	219	219	–	219
Settlement of share plan awards	–	–	–	–	–	(212)	(212)	–	(212)
Net movement	–	34	–	–	12	(2,538)	(2,492)	(106)	(2,598)
At 31 December 2018	317	4,427	153	448	1,440	5,683	12,468	1,576	14,044

[1] Amounts charged or credited to other reserves relate to exchange adjustments arising on goodwill.
[2] The Group adopted IFRS 15 'Revenue from Contracts with Customers' from 1 January 2018. See page 153.
[3] Included within Other comprehensive loss of $1,059m is a charge of $54m relating to Costs of hedging.

Consolidated Statement of Cash Flows
for the year ended 31 December

	Notes	2018 $m	2017 $m	2016 $m
Cash flows from operating activities				
Profit before tax		**1,993**	2,227	3,552
Finance income and expense	3	**1,281**	1,395	1,317
Share of after tax losses of associates and joint ventures	10	**113**	55	33
Depreciation, amortisation and impairment		**3,753**	3,036	2,357
(Increase)/decrease in trade and other receivables		**(523)**	83	1,610
Increase in inventories		**(13)**	(548)	(343)
(Decrease)/increase in trade and other payables and provisions		**(103)**	415	(341)
Gains on disposal of intangible assets	2	**(1,885)**	(1,518)	(1,301)
Fair value movements on contingent consideration arising from business combinations	19	**(495)**	109	(1,158)
Non-cash and other movements	16	**(290)**	(524)	(492)
Cash generated from operations		**3,831**	4,730	5,234
Interest paid		**(676)**	(698)	(677)
Tax paid		**(537)**	(454)	(412)
Net cash inflow from operating activities		**2,618**	3,578	4,145
Cash flows from investing activities				
Non-contingent payments on business combinations		**–**	(1,450)	(2,564)
Payment of contingent consideration from business combinations	19	**(349)**	(434)	(293)
Purchase of property, plant and equipment		**(1,043)**	(1,326)	(1,446)
Disposal of property, plant and equipment		**12**	83	82
Purchase of intangible assets		**(328)**	(294)	(868)
Disposal of intangible assets		**2,338**	1,376	1,427
Purchase of non-current asset investments		**(102)**	(96)	(230)
Disposal of non-current asset investments		**24**	70	3
Movement in short-term investments and fixed deposits		**405**	(345)	(166)
Payments to joint ventures	10	**(187)**	(76)	(41)
Interest received		**193**	164	140
Payments made by subsidiaries to non-controlling interests		**–**	–	(13)
Net cash inflow/(outflow) from investing activities		**963**	(2,328)	(3,969)
Net cash inflow before financing activities		**3,581**	1,250	176
Cash flows from financing activities				
Proceeds from issue of share capital		**34**	43	47
Issue of loans		**2,971**	1,988	2,491
Repayment of loans		**(1,400)**	(1,750)	–
Dividends paid		**(3,484)**	(3,519)	(3,561)
Hedge contracts relating to dividend payments		**(67)**	(20)	18
Repayment of obligations under finance leases		**–**	(14)	(16)
Movement in short-term borrowings		**(98)**	336	(303)
Net cash outflow from financing activities		**(2,044)**	(2,936)	(1,324)
Net increase/(decrease) in Cash and cash equivalents in the period		**1,537**	(1,686)	(1,148)
Cash and cash equivalents at the beginning of the period		**3,172**	4,924	6,051
Exchange rate effects		**(38)**	(66)	21
Cash and cash equivalents at the end of the period	16	**4,671**	3,172	4,924

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 the Companies Act 2006 and International Financial Reporting Standards (IFRSs) as adopted by the EU (adopted IFRSs) in response to the IAS regulation (EC 1606/2002). The Consolidated Financial Statements also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB).

The adoption of IFRS 9 'Financial Instruments' from 1 January 2018 has resulted in changes to the Group's accounting policies. IFRS 9 replaced the provisions of IAS 39 that relate to the recognition, classification and measurement of financial assets and financial liabilities, derecognition of financial instruments, impairment of financial assets and hedge accounting. In accordance with the transitional provisions in IFRS 9, comparative figures have not been restated and the Group has identified that there was no material impact on the Group's Retained earnings as at 1 January 2018.

(i) Classification and measurement

On the date of initial application, 1 January 2018, the Group's management has assessed which business models apply to the financial assets and financial liabilities held by the Group and has classified its financial instruments into the appropriate IFRS 9 categories. The main effects resulting from this reclassification are as follows:

	Measurement category		Carrying amounts		
	Original (IAS 39)	New (IFRS 9)	Original $m	New $m	Difference $m
Non-current financial assets					
Other investments					
Equity securities[1]	Available for sale	FVOCI	933	933	–
Derivative financial instruments	Held for trading	FVPL	504	504	–
Other receivables	Amortised cost	Amortised cost	489	489	–
Current financial assets					
Trade and other receivables					
Trade receivables – not subject to factoring	Amortised cost	Amortised cost	2,475	2,475	–
Trade receivables – subject to factoring[2]	Amortised cost	FVOCI	327	327	–
Other receivables	Amortised cost	Amortised cost	949	949	–
Other investments					
Equity securities and bonds[3]	Available for sale	FVPL	1,150	1,150	–
Fixed Deposits	Amortised cost	Amortised cost	80	80	–
Derivative financial instruments	Held for trading	FVPL	28	28	–
Cash and cash equivalents					
Cash at bank and in hand	Amortised cost	Amortised cost	784	784	–
Short-term deposits excluding money market funds	Amortised cost	Amortised cost	1,391	1,391	–
Money market funds[4]	Amortised cost	FVPL	1,149	1,149	–
Current financial liabilities					
Derivative financial instruments	Held for trading	FVPL	(24)	(24)	–
Non-current financial liabilities					
Derivative financial instruments	Held for trading	FVPL	(4)	(4)	–

[1] Equity securities investments reclassified from available to sale to assets at fair value through Other comprehensive income. These are strategic investments held directly in other pharmaceutical and biotech companies.
[2] Trade receivables that are subject to debt factoring arrangements were held at amortised cost under IAS 39. Under IFRS 9 these receivables are held under the 'hold to collect and sell' business model at fair value through other comprehensive income, however their carrying value and their fair value are considered to be materially the same.
[3] Equity security investments reclassified from available to sale to assets at fair value through profit or loss. These are primarily short-term assets invested as part of our cash management strategy to maximise gains on our liquid resources.
[4] Money market funds – the Group is invested in constant net asset value funds where liquidity is offered with same day access for subscription and redemption. Because they fail the 'solely payments of principal and interest' test criteria under IFRS 9 they are measured at fair value through profit or loss, although the fair value is materially the same as amortised cost.

(ii) Derivatives and hedging activities

The Group's risk management strategies and hedge documentation are aligned with the requirements of IFRS 9. All hedge relationships designated under IAS 39 are treated as continuing hedges under IFRS 9 and there was no impact from the adoption of IFRS 9 on prior periods.

(iii) Impairment of financial assets

The Group has financial assets that are subject to the new IFRS 9 expected credit loss model and the Group was required to revise its impairment methodology under IFRS 9 for these assets. The identified impairment change at 1 January 2018 was immaterial and the impact of the change in impairment methodology on the Group's Retained earnings was assessed as nil.

From 1 January 2018, the Group assesses on a forward looking basis the expected credit losses associated with its debt instruments carried at amortised cost and fair value through Other comprehensive income. In the prior year, the impairment of trade receivables was assessed based on the incurred loss model. The Group established an allowance for impairment that represented its estimate of incurred losses where it was deemed that a receivable may not have been recoverable. When the debt was deemed irrecoverable the allowance account was written off against the underlying receivable.

The Group has adopted IFRS 15 'Revenue from Contracts with Customers' which replaces existing accounting standards. It provides enhanced detail on the principle of recognising revenue to reflect the transfer of goods and services to customers at a value which the Group expects to be entitled to receive. The standard also updates revenue disclosure requirements.

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

The previous accounting for externalisation transactions under IAS 18 includes an analysis of the performance obligations under the arrangement and upfront revenue recognition requires the transfer of substantive rights, for example a licence to use the intellectual

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

The Group has retrospectively applied the standard from 1 January 2018 recognising the cumulative effect of initially applying the standard as an increase to contract liabilities, which are a component of Trade and other payables of $133m to defer Externalisation Revenue previously recognised, an increase to Prepayments and accrued income, which are a component of Trade and other receivables of $20m to recognise Externalisation Revenue previously not recognised, a total related tax adjustment of $22m and a corresponding net adjustment to the opening balance of Retained earnings of $91m. There is no restatement to prior periods as permitted in the transition rules for IFRS 15. The impact of initial application in the year to 31 December 2018 as compared with the year to 31 December 2017 is the recognition of additional Externalisation Revenue of $27m in the year to 31 December 2018.

In addition to the above standard amendments and new adoptions, effective from 1 January 2018, the Group has changed its presentation of Trade and other payables resulting in the following:

(1) Liabilities for product returns, discounts and other product sales adjustments are shown together with liabilities for rebates and chargebacks;
(2) Clinical trial accruals and the Acerta Pharma put option liability are shown separately;
(3) Other trade-related accruals are shown within Other accruals.

The revised presentation has no impact on the total of Trade and other payables, the Group's Statement of Financial Position, the Statement of Cash Flows or the Statement of Comprehensive Income.

After applying the requirements of IFRS 15 for revenue contract related liabilities, and following an internal review of the presentation of liabilities, the Group considers that further disaggregation of the balances in Trade and other Payables would improve the clarity and understanding of those balances.

The Group has revised the comparative presentation of Trade and other payables in Note 19 for the changes related to: (1) liabilities for product returns, discounts and other product sales adjustments; and (2) clinical trial accruals and the Acerta Pharma put option. The Group has assessed the change related to (3) other trade-related accruals as not material for revision under IAS 8 'Accounting Policies, Changes in Accounting Estimates and Errors' and therefore the comparative presentation of Trade and other payables in Note 19 has not been revised for this presentational change.

During the year, the Group has adopted the amendments to IFRS 2 'Classification and Measurement of Share-based Payment Transactions' and the interpretation within IFRIC 22 'Foreign Currency Transactions and Advance Consideration'. The adoptions have not had a significant impact on the Group's Statement of Comprehensive Income, Statement of Financial Position and Statement of Cash Flows.

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.

Basis for preparation of Financial Statements on a going concern basis

The Group has considerable financial resources available. As at 31 December 2018, the Group has $7.1bn in financial resources (cash balances of $4.8bn and undrawn committed bank facilities of $4.1bn, of which $3.4bn is available until April 2022, $0.5bn is available until December 2020 (extendable to December 2021) and $0.2bn is available until December 2019 (extendable to December 2020), with only $1.8bn of debt due within one year). The Group's revenues are largely derived from sales of products which are covered by patents which provide a relatively high level of resilience and predictability to cash inflows, although our revenue is expected to continue to be significantly impacted by the expiry of patents over the medium term. In addition, government price interventions in response to budgetary constraints are expected to continue to adversely affect revenues in many of our mature markets. However, we anticipate new revenue streams from both recently launched medicines and products in development, and the Group has a wide diversity of customers and suppliers across different geographic areas. Consequently, the Directors believe that, overall, the Group is well placed to manage its business risks successfully. 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.

Judgements include matters such as the determination of operating segments while estimates focus on areas such as carrying values, estimated useful lives of Intangible assets, potential obligations and Contingent consideration.

The accounting policy descriptions set out the areas where judgements and estimates need exercising, the most significant of which are revenue recognition, research and development (including impairment reviews of associated Intangible assets), business combinations and Goodwill (and Contingent consideration arising from business combinations), litigation and environmental liabilities, employee benefits and taxation. Financial risk management policies are detailed in Note 27.

AstraZeneca's management considers the following to be the most important accounting policies in the context of the Group's operations.

Revenue

Revenues comprise Product Sales and Externalisation Revenue.

Product Sales are revenues arising from contracts with customers. Externalisation Revenue arises from other contracts. However, the recognition and measurement principles of IFRS 15 are applied as set out below.

Revenues exclude 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 key 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.

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 returns 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.

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.

Externalisation Revenue

Externalisation Revenue includes income from collaborative arrangements on the Group's products where the Group has sold certain rights associated with those products, but retains a significant ongoing economic interest, through for example the ongoing supply of finished goods or participation in profit share arrangements.

These arrangements may include development arrangements, commercialisation arrangements and collaborations. Income may take the form of upfront fees, milestones, profit sharing and royalties.

The licences we grant are typically rights to use intellectual property which do not change during the period of the licence. Those licences are generally unique and therefore, 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 sale 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 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 highly probable. The determination of highly probable represents a key judgement.

Where Externalisation Revenue is recorded and there is a related Intangible asset, 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 sold.

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 partner profit shares arising from collaborations, and foreign exchange gains and losses arising from business trading activities.

Research and development

Research expenditure is recognised in profit in the year in which it is incurred.

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 recognised in profit 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 2018, no amounts have met 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 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. The determination of the useful economic life is considered a key judgement.

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 9.

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 profit.

Business combinations and goodwill

On the acquisition of a business, fair values are attributed to the identifiable assets and liabilities. Attributing fair values is a key judgement. 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 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 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.

Group Accounting Policies
continued

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 key estimate. 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.

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'. 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 key 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.

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 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 sustained based upon management's interpretation of applicable laws and regulations and the likelihood of settlement.

Once considered probable of not being sustained, management reviews each material tax benefit to assess whether a provision should be taken against full recognition of the benefit on the basis of potential settlement through negotiation and/or litigation. Accruals for tax contingencies are measured using the single best estimate of likely outcome approach.

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 29 to the Financial Statements.

Share-based payments

All plans are assessed and have been classified as equity settled. 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.

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 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

Leases are classified as finance leases if they transfer substantially all the risks and rewards incidental to ownership, otherwise they are classified as operating leases. Assets and liabilities arising on finance leases are initially recognised at fair value or, if lower, the present value of the minimum lease payments. The discount rate used in calculating the present value of the minimum lease payments is the interest rate implicit in the lease. Finance charges under finance leases are allocated to each reporting period so as to produce a constant periodic rate of interest on the remaining balance of the finance liability. Rentals under operating leases are charged to profit on a straight-line basis.

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.

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 products and research and development costs 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 an 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 11.

Financial instruments

The Group's financial instruments include finance leases, 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.

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 profit.

Other investments

Accounting policy applied until 31 December 2017 (IAS 39)

Until 31 December 2017, the investments were classified as available for sale, initially measured at fair value (including direct transaction costs) and subsequently remeasured to fair value at each reporting date. Changes in carrying value due to changes in exchange rates on monetary available for sale investments or impairments were recognised in profit within Other operating income and expense. All other changes in fair value were recognised in Other comprehensive income.

Accounting policy applied from 1 January 2018 (IFRS 9)

On adoption of IFRS 9 'Financial Instruments' on 1 January 2018 the available for sale classification category was eliminated. Investments previously classified as available for sale are now classified as fair value through profit or loss, unless the Group makes an irrevocable election at initial recognition for certain non-current equity investments to present changes in fair value in Other comprehensive income. 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.

Reclassification from available for sale to at fair value through Other comprehensive income

These investments were reclassified from available for sale to assets at fair value through Other comprehensive income. The investments primarily relate to biotech companies and are held to access science rather than to liquidate and realise gains.

Reclassification from available for sale to at fair value through profit or loss

These investments were reclassified from available to sale to assets at fair value through profit or loss. The investments primarily relate to short-term assets invested as part of our cash management strategy to maximise gains on our liquid resources.

For the available for sale assets now at fair value through profit or loss the fair value gain that has gone through profit and loss that under the old classification would have gone to Other comprehensive income is $nil.

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 or 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 profit.

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 profit.

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 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.

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 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 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 profit.

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

IFRS 16 'Leases' is effective for accounting periods beginning on or after 1 January 2019 and will replace IAS 17 'Leases'. It will eliminate the classification of leases as either operating leases or finance leases and, instead, introduce a single lessee accounting model. The standard was endorsed by the EU on 31 October 2017. The adoption of IFRS 16 will result in the Group recognising lease liabilities, and corresponding 'right-of-use' assets for agreements that are currently classified as operating leases. The Group's principal lease arrangements are for property, most notably a portfolio of office premises, and for a global car fleet, utilised primarily by our sales and marketing teams.

The Group will adopt IFRS 16 retrospectively with the cumulative effect of initially applying the standard as an adjustment to the opening balance of Retained earnings at 1 January 2019. The Group has a choice, on a lease-by-lease basis, to measure the right-of-use asset at either its carrying amount as if IFRS 16 had been applied since the commencement of the lease, or an amount equal to the lease liability, adjusted for accruals or prepayments. The Group has assessed the difference between the two methods as immaterial and will measure the right to use asset equal to the right to use liability, after adjusting for accruals and prepayments, recognising approximately $0.7 billion of right-of-use assets and $0.7 billion of lease liabilities upon initial adoption. In applying the Standard retrospectively in this way the Group will use one or more practical expedients, on a lease-by-lease basis, to leases previously classified as operating leases, including electing to not apply the retrospective treatment to leases for which the term ends within 12 months of initial application and excluding initial direct costs from the initial measurement of the right-of-use asset. Key judgements and estimates made in calculating

the initial impact of adoption include assessing whether arrangements contain a lease, determining the lease term, and calculating the discount rate.

The Group will apply IFRS 16's low-value and short-term exemptions prospectively. While the IFRS 16 opening lease liability is calculated differently from the current operating lease commitments, there are no material differences between the positions.

The adoption of IFRS 16 will have no impact on the Group's cash flows except to present cash outflows as financing, instead of operating. There will be an immaterial benefit to Operating profit and a corresponding increase in Finance expense from the presentation of a portion of lease costs as interest costs. Profit before tax and Earnings per share are not expected to be significantly impacted.

IFRIC 23 'Uncertainty Over Income Tax Treatments' is effective for accounting periods beginning on or after 1 January 2019 and provides further clarification on how to apply the recognition and measurement requirements in IAS 12 'Income Taxes'. It is applicable where there is uncertainty over income tax treatments. The EU endorsed IFRIC 23 on 24 October 2018. The adoption of IFRIC 23 will principally result in the Group measuring the effect of uncertainty on income tax positions 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.

The Group will adopt IFRIC 23 retrospectively with the cumulative effect of initially applying the interpretation recognised at 1 January 2019 as an adjustment to the opening balance of Retained earnings. The initial impact of adopting IFRIC 23 is not material. Profit before tax and Earnings per share are not anticipated to be significantly impacted.

In addition, the following amendments and interpretations have been issued:

- Amendments to IFRS 9 'Prepayment Features with Negative Compensation', effective for periods beginning on or after 1 January 2019.
- Amendments to IAS 28 'Long term Interests in Associates and Joint Ventures', effective for periods beginning on or after 1 January 2019.
- Amendments to IAS 19 'Plan Amendment, Curtailment or Settlement', effective for periods beginning on or after 1 January 2019.
- Amendments to IFRS 3 'Business Combinations', effective for period beginning on or after 1 January 2020.
- Amendments to IAS 1 'Presentation of Financial Statements' and IAS 8 'Accounting Policies, Changes in Accounting Estimates and Errors', effective for periods beginning on or after 1 January 2020.

The above amendments and interpretations are not expected to have a significant impact on the Group's net results. The amendments have not yet been endorsed by the EU.

1 Revenue

Product Sales

	2018					2017					2016				
	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	347	869	314	330	1,860	135	405	187	228	955	10	254	76	83	423
Faslodex	154	537	221	116	1,028	115	492	256	78	941	96	438	228	68	830
Zoladex	409	8	133	202	752	353	15	141	226	735	355	35	156	270	816
Lynparza	51	345	190	61	647	18	141	130	8	297	7	127	81	3	218
Imfinzi	6	564	27	36	633	–	19	–	–	19	–	–	–	–	–
Iressa	286	26	109	97	518	251	39	112	126	528	233	23	120	137	513
Arimidex	132	–	31	49	212	118	7	34	58	217	110	14	37	71	232
Casodex	113	1	20	67	201	108	(1)	22	86	215	107	2	27	111	247
Calquence	–	62	–	–	62	–	3	–	–	3	–	–	–	–	–
Others	30	–	8	77	115	28	–	3	83	114	25	–	8	71	104
	1,528	2,412	1,053	1,035	6,028	1,126	1,120	885	893	4,024	943	893	733	814	3,383
Cardiovascular, Renal and Metabolism:															
Crestor	841	170	203	219	1,433	784	373	666	542	2,365	721	1,223	866	591	3,401
Farxiga	336	591	315	149	1,391	232	489	242	111	1,074	133	457	187	58	835
Brilinta	326	588	348	59	1,321	224	509	295	51	1,079	189	348	258	44	839
Seloken/Toprol-XL	641	39	19	13	712	593	37	52	13	695	536	95	90	16	737
Bydureon	8	475	81	20	584	9	458	88	19	574	4	463	100	11	578
Onglyza	172	223	89	59	543	130	320	104	57	611	142	376	132	70	720
Atacand	157	13	70	20	260	178	19	86	17	300	162	36	97	20	315
Byetta	8	74	29	15	126	12	114	34	16	176	24	164	45	21	254
Symlin	–	34	–	–	34	–	48	–	–	48	–	–	–	–	–
Others	206	(1)	76	25	306	205	4	92	43	344	228	40	119	50	437
	2,695	2,206	1,230	579	6,710	2,367	2,371	1,659	869	7,266	2,139	3,202	1,894	881	8,116
Respiratory:															
Symbicort	495	862	773	431	2,561	439	1,099	819	446	2,803	402	1,242	909	436	2,989
Pulmicort	995	116	90	85	1,286	840	156	92	88	1,176	698	174	99	90	1,061
Fasenra	1	218	32	46	297	–	1	–	–	1	–	–	–	–	–
Daliresp/Daxas	5	155	28	1	189	4	167	26	1	198	4	134	15	1	154
Tudorza/Eklira	1	25	74	10	110	2	66	73	9	150	1	77	83	9	170
Duaklir	1	–	91	3	95	–	–	77	2	79	1	–	60	2	63
Bevespi	–	33	–	–	33	–	16	–	–	16	–	–	–	–	–
Others	146	7	141	46	340	103	4	129	47	283	137	11	118	50	316
	1,644	1,416	1,229	622	4,911	1,388	1,509	1,216	593	4,706	1,243	1,638	1,284	588	4,753
Other:															
Nexium	690	306	235	471	1,702	684	499	248	521	1,952	690	554	251	537	2,032
Synagis	1	287	377	–	665	–	317	370	–	687	–	325	352	–	677
Seroquel XR/IR	118	108	107	28	361	151	193	127	37	508	159	572	190	46	967
Losec/Prilosec	161	7	70	34	272	140	11	77	43	271	128	10	83	55	276
FluMist/Fluenz	1	15	91	3	110	(1)	–	76	3	78	1	33	64	6	104
Movantik/Moventig	–	108	–	1	109	–	120	2	–	122	1	90	–	–	91
Others	53	11	67	50	181	294	29	93	122	538	490	48	213	169	920
	1,024	842	947	587	3,400	1,268	1,169	993	726	4,156	1,469	1,632	1,153	813	5,067
Product Sales	6,891	6,876	4,459	2,823	21,049	6,149	6,169	4,753	3,081	20,152	5,794	7,365	5,064	3,096	21,319

Product Sales represents net invoice value less estimated rebates, returns and chargebacks, which are considered to be key estimates. The major market where estimates are seen as significant is the US and 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 in 2018 was 3.2% (2017: 8.9%; 2016: 6.0%).

Externalisation Revenue

	2018 $m	2017 $m	2016 $m
Global co-development and commercialisation of *Lynparza* and selumetinib with MSD	**790**	1,247	–
Licence agreement for *Crestor* in Spain with Almirall	**61**	–	–
Transfer of rights to *Zoladex* in the US and Canada to TerSera	**35**	250	–
Transfer of rights to anaesthetics medicines to Aspen	**–**	150	520
Licence of rights to brodalumab to Valeant and LEO Pharma	**–**	150	–
Co-development and commercialisation of MEDI8897 with Sanofi	**–**	127	–
Commercial rights to *Plendil* in China to CMS	**–**	–	298
Transfer of rights to *Toprol-XL* in the US to Aralez	**–**	–	175
Licence of rights to tralokinumab to LEO Pharma	**–**	–	115
Grant of authorised generic rights to various medicines in Japan	**41**	45	42
Other externalisation upfronts	**10**	114	158
Other externalisation milestones	**4**	87	203
Royalty income	**49**	108	119
Other externalisation revenue	**51**	35	53
	1,041	2,313	1,683

Included with Externalisation Revenue is $35m relating to contract liabilities recognised at 1 January 2018.

2 Operating profit

Operating profit includes the following significant items:

Selling, general and administrative costs

In 2018, Selling, general and administrative costs includes a credit of $482m (2017: charge of $208m; 2016: credit of $999m) 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 2018, Selling, general and administrative costs also includes a credit of $113m (2017: $209m; 2016: $41m) resulting from changes in estimates of the cash flows arising from the put option over the non-controlling interest in Acerta Pharma.

In 2018, Selling, general and administrative costs also includes a credit of $219m (2017: charge of $241m; 2016: charge of $223m) of legal provisions relating to a number of legal proceedings in various jurisdictions in relation to several marketed products.

Further details of impairment charges for 2018, 2017 and 2016 are included in Notes 7 and 9.

Other operating income and expense

	2018 $m	2017 $m	2016 $m
Royalties			
Income	**96**	132	406
Amortisation	**(4)**	(45)	(86)
Gains on disposal of intangible assets	**1,885**	1,518	1,301
Gains on disposal of short-term investments	**–**	161	–
Net (losses)/gains on disposal of other non-current assets	**(8)**	24	29
Impairment of property, plant and equipment	**–**	(78)	–
Legal settlements	**374**	–	–
Other income	**277**	286	146
Other expense	**(93)**	(168)	(141)
Other operating income and expense	**2,527**	1,830	1,655

Royalty amortisation relates to intangible assets recorded in respect of income streams acquired with MedImmune, and upon the restructuring of a historical joint venture with MSD.

Gains on disposal of intangible assets in 2018 includes $695m on the disposal of Europe rights to *Nexium*, $527m on the disposal of rights to *Seroquel* in the UK, China and other international markets, $210m from the sale of rights to *Atacand* in Europe to Cheplapharm, milestone receipts of $172m from the disposal of the anaesthetics portfolio outside the US to Aspen and $139m from the sale of global rights to *Alvesco*, *Omnaris* and *Zetonna* to Covis.

Gains on disposal of intangible assets in 2017 includes $555m on the disposal of the remaining rights to the global anaesthetics portfolio, $301m on disposal of Europe rights to *Seloken* and $193m on disposal of the global rights to *Zomig*.

Gains on disposal of intangible assets in 2016 includes $368m on the disposal of the small molecule antibiotics assets in most markets outside the US, $321m on the disposal of Rest of World rights to *Rhinocort Aqua*, $231m on the disposal of global rights to MEDI2070 and $183m on the disposal of Rest of World rights to *Imdur*.

2 Operating profit *continued*

Restructuring costs

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 20.

	2018 $m	2017 $m	2016 $m
Cost of sales	**432**	181	130
Research and development expense	**94**	201	178
Selling, general and administrative costs	**181**	347	823
Other operating income and expense	**(10)**	78	(24)
Total charge	**697**	807	1,107

	2018 $m	2017 $m	2016 $m
Severance costs	**41**	176	505
Accelerated depreciation and impairment	**259**	141	46
Other	**397**	490	556
Total charge	**697**	807	1,107

Other costs are those incurred in designing and implementing the Group's various restructuring initiatives, including costs of decommissioning sites impacted by changes to our global footprint, temporary lease costs during relocation, internal project costs, and external consultancy fees.

Financial instruments

Included within Operating profit are the following net gains and losses on financial instruments:

	2018 $m	2017 $m	2016 $m
Losses on forward foreign exchange contracts	**(100)**	(6)	(216)
Gains/(losses) on receivables and payables	**43**	(30)	132
Gains on disposal of short-term investments	**–**	161	–
Gains on other available for sale investments	**–**	34	–
Total	**(57)**	159	(84)

3 Finance income and expense

	2018 $m	2017 $m	2016 $m
Finance income			
Returns on fixed deposits and equity securities	**10**	8	8
Returns on short-term deposits	**86**	62	35
Fair value gains on debt and interest rate swaps	**–**	4	–
Net exchange gains	**–**	–	8
Discount unwind on other long-term assets	**6**	10	16
Interest on tax receivables	**36**	29	–
Total	**138**	113	67
Finance expense			
Interest on debt and commercial paper	**(673)**	(612)	(565)
Interest on overdrafts, finance leases and other financing costs	**(68)**	(52)	(52)
Net interest on post-employment defined benefit plan net liabilities (Note 21)	**(52)**	(49)	(63)
Net exchange losses	**(51)**	(148)	–
Discount unwind on contingent consideration arising from business combinations (Note 19)	**(416)**	(402)	(497)
Discount unwind on other long-term liabilities	**(154)**	(245)	(190)
Fair value losses on debt and interest rate swaps	**(2)**	–	(17)
Interest on tax payables	**(3)**	–	–
Total	**(1,419)**	(1,508)	(1,384)
Net finance expense	**(1,281)**	(1,395)	(1,317)

Financial instruments

Included within finance income and expense are the following net gains and losses on financial instruments:

	2018 $m	2017 $m	2016 $m
Interest and fair value adjustments in respect of debt designated at fair value through profit or loss, net of derivatives	**(11)**	8	(14)
Interest and changes in carrying values of debt designated as hedged items in fair value hedges, net of derivatives	**(28)**	(35)	(21)
Interest and fair value changes on fixed and short-term deposits, equity securities, other derivatives and tax balances	**96**	52	74
Interest on debt, overdrafts, finance leases and commercial paper held at amortised cost	**(619)**	(559)	(553)

Fair value losses of $13m (2017: $9m; 2016: $29m) on interest rate fair value hedging instruments and $10m fair value gains (2017: $9m; 2016: $30m) 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 losses of $13m (2017: $10m; 2016: $12m) on derivatives related to debt instruments designated at fair value through profit or loss and $13m fair value gains (2017: $3m; 2016: $9m) 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. Ineffectiveness on the net investment hedge taken to profit was $nil (2017: $nil; 2016: $nil).

4 Taxation

Taxation recognised in the Consolidated Statement of Comprehensive Income is as follows:

	2018 $m	2017 $m	2016 $m
Current tax expense			
Current year	**711**	665	384
Adjustment to prior years	**38**	(287)	(14)
Total	**749**	378	370
Deferred tax expense			
Origination and reversal of temporary differences	**(644)**	(1,113)	(94)
Adjustment to prior years	**(162)**	94	(130)
Total	**(806)**	(1,019)	(224)
Taxation recognised in the profit for the period	**(57)**	(641)	146

Taxation relating to components of Other comprehensive income is as follows:

	2018 $m	2017 $m	2016 $m
Current and deferred tax			
Items that will not be reclassified to profit or loss:			
Remeasurement of the defined benefit liability	**37**	24	110
Share-based payments	**–**	9	51
Net losses on equity investments measured at fair value through other comprehensive income	**30**	–	–
Deferred tax impact of reduction in US, Sweden and other tax rates	**(11)**	(17)	(25)
Total	**56**	16	136
Items that may be reclassified subsequently to profit or loss:			
Foreign exchange arising on consolidation	**69**	(79)	63
Foreign exchange arising on designating borrowings in net investment hedges	**–**	14	83
Net available for sale losses/(gains) recognised in other comprehensive income	**–**	2	(61)
Other	**–**	–	1
Deferred tax impact of reduction in US, Sweden and other tax rates	**(18)**	30	–
Total	**51**	(33)	86
Taxation relating to components of other comprehensive income	**107**	(17)	222

The Reported Tax Rate of (3)% in the year benefitted from a favourable net adjustment of $297m to Deferred taxes, reflecting the recently announced Dutch and Swedish income tax rate reductions, and a favourable adjustment of $188m on the release of provisions for tax contingencies on expiry of statute of limitations and conclusion of tax authority review.

Absent these benefits, the Reported Tax Rate for the year would have been 21%.

The cash tax paid for the year was $537m which was 27% of Profit before tax.

Taxation has been provided at current rates on the profits earned for the periods covered by the Group Financial Statements. The 2018 prior period current tax adjustment relates mainly to net reductions in provisions for tax contingencies and tax accrual to tax return adjustments. The 2017 prior period current tax adjustment relates mainly to net reductions in provisions for tax contingencies totalling $105m and tax accrual to tax return adjustments. The 2016 prior period current tax adjustment relates mainly to net reductions in provisions for tax contingencies totalling $67m and tax accrual to tax return adjustments.

The 2018 and 2017 prior period deferred tax adjustments relate mainly to tax accrual to return adjustments. The 2016 prior period deferred tax adjustments relate mainly to tax accrual to return adjustments and releases in provisions for tax contingencies.

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. No deferred tax has been provided for unremitted earnings of Group companies overseas as these are considered permanently employed in the business of these companies. Unremitted earnings may be liable to overseas taxes and/or UK taxation (after allowing for double tax relief) if distributed as dividends. The aggregate amount of temporary differences associated with investments in subsidiaries and branches for which Deferred tax liabilities have not been recognised totalled approximately $8,144m at 31 December 2018 (2017: $8,359m; 2016: $6,884m).

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.

Details of the material tax exposures and items currently under audit, negotiation and review are set out in Note 29.

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:

	2018 $m	2017 $m	2016 $m
Profit before tax	**1,993**	2,227	3,552
Notional taxation charge at UK corporation tax rate of 19% (2017: 19.25%; 2016: 20%)	**379**	429	710
Differences in effective overseas tax rates	**18**	(212)	(233)
Deferred tax credit relating to reduction in Dutch, Swedish and other tax rates[1]	**(334)**	(616)	(16)
Unrecognised deferred tax asset[2]	**7**	(105)	242
Items not deductible for tax purposes	**167**	203	132
Items not chargeable for tax purposes	**(6)**	(14)	(7)
Other items[3]	**(164)**	(133)	(538)
Adjustments in respect of prior periods[4]	**(124)**	(193)	(144)
Total tax (credit)/charge for the year	**(57)**	(641)	146

[1] The 2018 item relates to the recent reduction in the Dutch and Swedish Corporate Income Tax rates (credit of $297m) and other (credit of $37m). The Dutch Corporate Income Tax rate reduces from 25% to 22.55% effective from 1 January 2020 and to 20.5% effective from 1 January 2021. The Swedish Income Tax rate reduces from 22% to 21.4% effective from 1 January 2019 and to 20.6% effective from 1 January 2021. The 2017 item relates to the reduction in the US Federal Income Tax rate from 35% to 21% effective from 1 January 2018 (credit of $617m) and other (charge of $1m). The 2016 item relates to the reduction in the UK Statutory Corporation Tax rate from 18% to 17% effective from 1 April 2020.
[2] The 2017 item relates to recognition of previously unrecognised net deferred tax assets.
[3] Other items in 2018 relate to a credit of $188m 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 build for transfer pricing and other contingencies (charge $24m). Other items in 2017 relate to the release of tax contingencies following the expiry of the relevant statute of limitations (credit $178m) partially offset by a provision build for transfer pricing and other contingencies (charge $45m). Other items in 2016 relate to the release of tax contingencies following agreements between the Canadian tax authority and UK and Swedish tax authorities in respect of transfer pricing arrangements for the 13 year period from 2004 to 2016 (credit $453m) and release of certain tax contingencies following the expiry of the relevant statute of limitations (credit $280m) partially offset by a provision build for transfer pricing contingencies (charge $195m).
[4] Further details explaining the adjustments in respect of prior periods is set out above on page 163.

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 movements in the net deferred tax balance during the year are as follows:

	Intangibles, property, plant & equipment[1] $m	Pension and post-retirement benefits $m	Inter-company inventory transfers $m	Untaxed reserves[2] $m	Losses and tax credits carried forward[3] $m	Accrued expenses and other $m	Total $m
Net deferred tax balance at 1 January 2016	(3,261)	427	738	(692)	804	613	(1,371)
Taxation expense	(132)	11	314	(53)	151	(67)	224
Other comprehensive income	83	101	–	–	–	(24)	160
Additions through business combinations[4]	(1,827)	–	–	–	50	–	(1,777)
Exchange	(1)	(74)	(38)	48	(1)	(13)	(79)
Other movements[5]	(11)	–	–	–	–	–	(11)
Net deferred tax balance at 31 December 2016	(5,149)	465	1,014	(697)	1,004	509	(2,854)
Income statement	1,393	(8)	(231)	159	(128)	(166)	1,019
Other comprehensive income	(84)	9	–	–	–	35	(40)
Exchange	(12)	43	48	(62)	30	22	69
Net deferred tax balance at 31 December 2017	(3,852)	509	831	(600)	906	400	(1,806)
Net adjustment to the opening balance of Retained earnings	**–**	**–**	**–**	**–**	**–**	**12**	**12**
Income statement	**401**	**(15)**	**179**	**(4)**	**129**	**116**	**806**
Other comprehensive income	**56**	**26**	**–**	**–**	**–**	**31**	**113**
Equity[6]	**–**	**–**	**–**	**–**	**–**	**12**	**12**
Exchange	**27**	**(25)**	**(30)**	**47**	**(27)**	**(36)**	**(44)**
Net deferred tax balance at 31 December 2018[7]	**(3,368)**	**495**	**980**	**(557)**	**1,008**	**535**	**(907)**

[1] Includes deferred tax on contingent liabilities in respect of intangibles.
[2] Untaxed reserves relate to taxable profits where the tax liability is deferred to later periods.
[3] Includes losses and tax credits carried forward which will expire within 1 to 20 years.
[4] The deferred tax liability of $1,777m relates to the acquisition of Acerta Pharma (see Note 25).
[5] Arising on the deconsolidation of Entasis as detailed in Note 10.
[6] Deferred tax movement on share-based payments recorded through equity.
[7] The UK had a net deferred tax asset of $691m as at 31 December 2018, mainly in respect of losses and pensions and post-retirement benefits, which has been recognised on the basis of sufficient forecast future taxable profits against which the deductible temporary differences can be utilised.

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	Inter-company inventory transfers $m	Untaxed reserves $m	Losses and tax credits carried forward $m	Accrued expenses and other $m	Total $m
Deferred tax assets at 31 December 2016	875	465	1,014	–	1,004	629	3,987
Deferred tax liabilities at 31 December 2016	(6,024)	–	–	(697)	–	(120)	(6,841)
Net deferred tax balance at 31 December 2016	(5,149)	465	1,014	(697)	1,004	509	(2,854)
Deferred tax assets at 31 December 2017	1,226	559	1,011	–	957	885	4,638
Deferred tax liabilities at 31 December 2017	(5,078)	(50)	(180)	(600)	(51)	(485)	(6,444)
Net deferred tax balance at 31 December 2017	(3,852)	509	831	(600)	906	400	(1,806)
Deferred tax assets at 31 December 2018	**1,071**	**521**	**1,287**	**–**	**1,103**	**913**	**4,895**
Deferred tax liabilities at 31 December 2018	**(4,439)**	**(26)**	**(307)**	**(557)**	**(95)**	**(378)**	**(5,802)**
Net deferred tax balance at 31 December 2018	**(3,368)**	**495**	**980**	**(557)**	**1,008**	**535**	**(907)**

Analysed in the statement of financial position, after offset of balances within countries, as:

	2018 $m	2017 $m	2016 $m
Deferred tax assets	**2,379**	2,189	1,102
Deferred tax liabilities	**(3,286)**	(3,995)	(3,956)
Net deferred tax balance	**(907)**	(1,806)	(2,854)

Unrecognised deferred tax assets

Deferred tax assets of $444m have not been recognised in respect of deductible temporary differences, which include items which will expire within 1 to 20 years (2017: $420m; 2016: $542m) because it is not probable that future taxable profit will be available against which the Group can utilise the benefits therefrom.

5 Earnings per $0.25 Ordinary Share

	2018	2017	2016
Profit for the year attributable to equity holders ($m)	**2,155**	3,001	3,499
Basic earnings per Ordinary Share	**$1.70**	$2.37	$2.77
Diluted earnings per Ordinary Share	**$1.70**	$2.37	$2.76
Weighted average number of Ordinary Shares in issue for basic earnings (millions)	**1,267**	1,266	1,265
Dilutive impact of share options outstanding (millions)	**–**	1	1
Diluted weighted average number of Ordinary Shares in issue (millions)	**1,267**	1,267	1,266

The earnings figures used in the calculations above are post-tax.

6 Segment information

AstraZeneca is engaged in a single business activity of biopharmaceuticals and the Group does not have multiple operating segments. AstraZeneca's biopharmaceuticals 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.

The SET, established and chaired by the CEO, is the vehicle through which he exercises the authority delegated to him from the Board for the management, development and performance of our business. 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, and manufacturing and supply. All significant operating decisions are taken 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 impacts of being able to develop, produce, deliver and commercialise a wide range of pharmaceutical products drive 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.

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 a single Late Stage Product Committee.

6 Segment information *continued*

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 segment assets, segment assets acquired, net operating assets, and Property, plant and equipment owned by the same companies; export sales and the related profit are included in the area/country where the legal entity resides and from which those sales were made.

	Total Revenue		
	2018 $m	2017 $m	2016 $m
UK	**2,390**	3,240	1,849
Continental Europe			
France	**617**	701	899
Germany	**592**	541	615
Italy	**426**	514	529
Spain	**396**	447	440
Sweden	**477**	842	1,522
Others	**1,312**	1,512	1,575
	3,820	4,557	5,580
The Americas			
Canada	**483**	482	495
US	**7,240**	6,666	7,828
Others	**806**	809	846
	8,529	7,957	9,169
Asia, Africa & Australasia			
Australia	**313**	377	385
China	**3,778**	2,955	2,650
Japan	**1,952**	2,172	2,145
Others	**1,308**	1,207	1,224
	7,351	6,711	6,404
Total Revenue	**22,090**	22,465	23,002

Total revenue outside of the UK totalled $19,700m for the year ended 31 December 2018 (2017: $19,225m; 2016: $21,153m).

	Operating (loss)/profit			(Loss)/profit before tax		
	2018 $m	2017 $m	2016 $m	**2018 $m**	2017 $m	2016 $m
UK	**(66)**	(694)	(526)	**(514)**	(1,146)	(950)
Continental Europe	**3,671**	2,482	3,695	**3,179**	1,918	3,136
The Americas	**(757)**	1,242	1,259	**(1,171)**	822	919
Asia, Africa & Australasia	**539**	647	474	**499**	633	447
Continuing operations	**3,387**	3,677	4,902	**1,993**	2,227	3,552

	Non-current assets[1]			Total assets		
	2018 $m	2017 $m	2016 $m	**2018 $m**	2017 $m	2016 $m
UK	**4,828**	5,371	5,127	**13,573**	12,842	12,704
Continental Europe	**14,529**	16,305	15,731	**17,119**	18,962	18,174
The Americas	**22,191**	24,811	26,044	**26,381**	28,180	28,792
Asia, Africa & Australasia	**976**	1,024	917	**3,578**	3,370	2,856
Continuing operations	**42,524**	47,511	47,819	**60,651**	63,354	62,526

	Assets acquired[2]			Net operating assets[3]		
	2018 $m	2017 $m	2016 $m	**2018 $m**	2017 $m	2016 $m
UK	**556**	400	362	**3,471**	3,351	3,306
Continental Europe	**530**	629	8,494	**8,913**	10,228	8,479
The Americas	**356**	585	688	**18,598**	20,339	20,969
Asia, Africa & Australasia	**105**	138	129	**1,037**	1,198	1,030
Continuing operations	**1,547**	1,752	9,673	**32,019**	35,116	33,784

[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).
[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		
	2018 $m	2017 $m	2016 $m
UK	**1,605**	1,455	1,026
Sweden	**1,456**	1,508	1,142
US	**2,844**	3,055	3,233
Rest of the world	**1,516**	1,597	1,447
Continuing operations	**7,421**	7,615	6,848

Geographic markets

The table below shows Product Sales in each geographic market in which customers are located.

	2018 $m	2017 $m	2016 $m
UK	**469**	489	487
Continental Europe	**4,388**	4,712	4,987
The Americas	**8,177**	7,467	8,717
Asia, Africa & Australasia	**8,015**	7,484	7,128
Continuing operations	**21,049**	20,152	21,319

Product Sales are recognised when control of the goods has been transferred to a third party. In general this is upon delivery of the products to wholesalers. One wholesaler (2017: zero; 2016: one) individually represented greater than 10% of Product Sales. The value of these transactions recorded as Product Sales were $2,704m (2017: N/A; 2016: $2,851m).

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 2016	4,812	7,468	1,568	13,848
Capital expenditure	29	206	1,214	1,449
Transfer of assets into use	222	109	(331)	–
Disposals and other movements	(236)	(700)	(16)	(952)
Exchange adjustments	(211)	(540)	(143)	(894)
At 31 December 2016	4,616	6,543	2,292	13,451
Capital expenditure	39	198	1,074	1,311
Transfer of assets into use	525	567	(1,092)	–
Disposals and other movements	(367)	(577)	–	(944)
Exchange adjustments	210	452	159	821
At 31 December 2017	5,023	7,183	2,433	14,639
Capital expenditure	**25**	**99**	**910**	**1,034**
Transfer of assets into use	**429**	**594**	**(1,023)**	**–**
Disposals and other movements	**50**	**(427)**	**(14)**	**(391)**
Exchange adjustments	**(161)**	**(353)**	**(129)**	**(643)**
At 31 December 2018	**5,366**	**7,096**	**2,177**	**14,639**
Depreciation				
At 1 January 2016	2,253	5,182	–	7,435
Charge for year	185	424	–	609
Impairment	2	–	–	2
Disposals and other movements	(222)	(656)	–	(878)
Exchange adjustments	(126)	(439)	–	(565)
At 31 December 2016	2,092	4,511	–	6,603
Charge for year	182	442	–	624
Impairment	78	–	–	78
Disposals and other movements	(249)	(501)	–	(750)
Exchange adjustments	128	341	–	469
At 31 December 2017	2,231	4,793	–	7,024
Charge for year	**202**	**412**	**–**	**614**
Impairment	**150**	**98**	**43**	**291**
Disposals and other movements	**10**	**(336)**	**(43)**	**(369)**
Exchange adjustments	**(89)**	**(253)**	**–**	**(342)**
At 31 December 2018	**2,504**	**4,714**	**–**	**7,218**
Net book value				
At 31 December 2016	2,524	2,032	2,292	6,848
At 31 December 2017	2,792	2,390	2,433	7,615
At 31 December 2018	**2,862**	**2,382**	**2,177**	**7,421**

Impairment charges in 2018 were recognised for Land and buildings and Plant and equipment as a result of the announcement of the closure of Boulder and Longmont, Colorado manufacturing centres. These charges have been recognised in Cost of sales.

Included within other movements in 2018 is a transfer (cost of $120m and accumulated depreciation of $75m) from Plant and equipment to Land and buildings.

	2018 $m	2017 $m	2016 $m
The net book value of land and buildings comprised:			
Freeholds	**2,567**	2,514	2,326
Leaseholds	**295**	278	198

Included within Plant and equipment are Information Technology assets held under finance leases with a net book value of $nil (2017: $nil; 2016: $43m).

8 Goodwill

	2018 $m	2017 $m	2016 $m
Cost			
At 1 January	**12,143**	11,969	12,113
Additions through business combinations (Note 26)	**–**	–	19
Exchange and other adjustments	**(121)**	174	(163)
At 31 December	**12,022**	12,143	11,969
Amortisation and impairment losses			
At 1 January	**318**	311	313
Exchange and other adjustments	**(3)**	7	(2)
At 31 December	**315**	318	311
Net book value at 31 December	**11,707**	11,825	11,658

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 biopharmaceuticals.

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 2018 (and 31 December 2017 and 31 December 2016).

As a further check, we also perform a discounted cash flow calculation whereby we risk adjust projections of the Group's post-tax cash flows over 10 years. This length of time is considered by the Board as a reasonable period given the long development and life-cycle of a medicine. The projections include assumptions about product launches, competition from rival products and pricing policy as well as the possibility of generics entering the market. In setting these assumptions we consider our past experience, external sources of information (including information on expected increases and ageing of populations in our established markets and the expanding patient populations in newer markets), our knowledge of competitor activity and our assessment of future changes in the pharmaceutical industry. The 10-year period is covered by internal budgets and forecasts. Given that internal budgets and forecasts are prepared for all projections, no general growth rates are used to extrapolate internal budget and forecast amounts. No terminal value is included as the recoverable amount determined by the cash flows exceed the carrying value of net assets without inclusion of a terminal value.

AstraZeneca's post-tax weighted average cost of capital (7.0% for 2018, 2017 and 2016) is used in the calculation to discount the cash flows to reflect the impact of risks relevant to the Group and the time value of money.

No goodwill impairment was identified.

9 Intangible assets

	Product, marketing and distribution rights $m	Other intangibles $m	Software development costs $m	Total $m
Cost				
At 1 January 2016	35,318	2,795	2,019	40,132
Additions through business combinations (Note 26)	7,307	–	–	7,307
Additions – separately acquired	789	32	77	898
Disposals	(339)	(15)	(141)	(495)
Exchange and other adjustments	(1,472)	(232)	(127)	(1,831)
At 31 December 2016	41,603	2,580	1,828	46,011
Additions – separately acquired	397	7	37	441
Disposals	(249)	(67)	(62)	(378)
Exchange and other adjustments	1,162	116	108	1,386
At 31 December 2017	42,913	2,636	1,911	47,460
Additions – separately acquired	**476**	**–**	**37**	**513**
Transferred to assets held for sale (Note 17)	**(2,486)**	**–**	**–**	**(2,486)**
Disposals	**(630)**	**–**	**(16)**	**(646)**
Exchange and other adjustments	**(1,137)**	**(110)**	**(93)**	**(1,340)**
At 31 December 2018	**39,136**	**2,526**	**1,839**	**43,501**
Amortisation and impairment losses				
At 1 January 2016	14,104	1,773	1,609	17,486
Amortisation for year	1,454	162	85	1,701
Impairment	43	1	1	45
Disposals	(25)	(15)	(124)	(164)
Exchange and other adjustments	(481)	(85)	(77)	(643)
At 31 December 2016	15,095	1,836	1,494	18,425
Amortisation for year	1,627	118	84	1,829
Impairment	488	–	3	491
Disposals	(19)	–	(52)	(71)
Exchange and other adjustments	467	50	81	598
At 31 December 2017	17,658	2,004	1,610	21,272
Amortisation for year	**2,016**	**69**	**80**	**2,165**
Impairment	**683**	**–**	**–**	**683**
Transferred to assets held for sale (Note 17)	**(1,504)**	**–**	**–**	**(1,504)**
Disposals	**(294)**	**–**	**(13)**	**(307)**
Exchange and other adjustments	**(652)**	**(38)**	**(77)**	**(767)**
At 31 December 2018	**17,907**	**2,035**	**1,600**	**21,542**
Net book value				
At 31 December 2016	26,508	744	334	27,586
At 31 December 2017	25,255	632	301	26,188
At 31 December 2018	**21,229**	**491**	**239**	**21,959**

Other intangibles consist mainly of research and device technologies.

9 Intangible assets *continued*

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 2016				
Cost of sales	124	–	–	124
Research and development expense	–	48	–	48
Selling, general and administrative costs	1,327	31	85	1,443
Other operating income and expense	3	83	–	86
Total	1,454	162	85	1,701
Year ended 31 December 2017				
Cost of sales	149	–	–	149
Research and development expense	–	43	–	43
Selling, general and administrative costs	1,478	30	84	1,592
Other operating income and expense	–	45	–	45
Total	1,627	118	84	1,829
Year ended 31 December 2018				
Cost of sales	**187**	**–**	**–**	**187**
Research and development expense	**–**	**33**	**–**	**33**
Selling, general and administrative costs	**1,829**	**32**	**80**	**1,941**
Other operating income and expense	**–**	**4**	**–**	**4**
Total	**2,016**	**69**	**80**	**2,165**

Impairment 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 2016				
Research and development expense	32	1	–	33
Selling, general and administrative costs	11	–	1	12
Total	43	1	1	45
Year ended 31 December 2017				
Research and development expense	101	–	–	101
Selling, general and administrative costs	387	–	3	390
Total	488	–	3	491
Year ended 31 December 2018				
Research and development expense	**539**	**–**	**–**	**539**
Selling, general and administrative costs	**144**	**–**	**–**	**144**
Total	**683**	**–**	**–**	**683**

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. Recoverable amount is determined as the higher of value in use or fair value less costs to sell using discounted cash flow calculations where the products' expected post-tax cash flows are risk-adjusted over their estimated remaining useful economic life. The projections are covered by internal budgets and forecasts. The risk-adjusted cash flows are discounted using AstraZeneca's post-tax weighted average cost of capital (7% for 2018, 2017 and 2016).

The estimates used in calculating the recoverable amount are 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;
- amount and timing of projected future cash flows; and
- sales erosion curves following patent expiry.

In 2018, the Group recorded impairment charges of $144m in respect of launched products *Eklira* ($114m, revised carrying value of $396m) and *Movantik* ($30m, revised carrying value of $59m). Impairment charges recorded against products in development related to MEDI0680 ($470m) and other intangible assets ($95m).

In 2017, the Group recorded an impairment charge of $491m in respect of launched products *Byetta* ($92m, revised carrying value of $407m), *FluMist* ($121m, revised carrying value of $267m) and *Movantik* ($174m, revised carrying value of $106m). Impairment charges recorded against products in development related to tralokinumab ($53m) and other intangible assets ($51m).

Impairment charges recorded in 2016 relates to the termination, or reassessment of the likelihood of success, of several individual projects, none of which had significant capitalised values.

The impairments recorded on launched products were a consequence of revised market volume, share and price assumptions and, for *FluMist* in 2017, the US market expected timing of renewed recommendation from the Advisory Committee on Immunization Practices (ACIP) under the Centers for Disease Control and Prevention. These impairments were calculated using value in use models. Impairments recorded on products in development were a consequence of failed or poor performing trials, with the individual assets being fully impaired.

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.

Assets that are particularly sensitive to variations in valuation assumptions include *Byetta* (carrying value as at 31 December 2018 of $316m) and Ardea (carrying value of $1,172m). The *Byetta* valuation, impaired in 2017, is most sensitive to the expected timing of a generic entering the market. Increasing the probability of a generic entry into the market by 20% from our base valuation model would result in an impairment charge of $25m. No impairment charge has been recorded on Ardea, a product in development, with a net book value of $1,172m. The Ardea valuation is particularly sensitive to variations in the probability of technical and regulatory success ('PTRS') assumptions. Sensitivities performed at the year end on the Ardea asset included reducing the PTRS by 5 percentage points. Applying this sensitivity would result in an impairment charge against the Ardea intangible asset of approximately $70m.

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 and none were identified with the exception of a reversal of $28m in respect of an asset previously impaired prior to 2016. This assessment included *FluMist* where an impairment of $121m was taken in 2017 and where currently the uncertainty remains around long term sales potential in the US following the reinstatement of the US recommendation by ACIP in 2018.

Significant assets

	Carrying value $m	Remaining amortisation period
Intangible assets arising from the acquisition of Acerta Pharma	6,745	14 years
Intangible assets arising from the acquisition of ZS Pharma	3,067	13 years
Farxiga/*Forxiga* intangible assets acquired from BMS	1,177	9 years
Intangible assets arising from the acquisition of Ardea[1]	1,172	Not amortised
Intangible assets arising from the restructuring of a historical joint venture with MSD	1,092	1 to 12 years
RSV franchise assets arising from the acquisition of MedImmune	1,068	7 years
Bydureon intangible assets acquired from BMS	988	12 years
Intangible assets arising from the acquisition of Pearl Therapeutics	828	10 years
Other diabetes intangible assets acquired from BMS	795	4 to 7 years
Onglyza intangible assets acquired from BMS	752	5 years
Respiratory intangible assets acquired from Almirall and Actavis	733	1 to 20 years
Intangible assets arising from the acquisition of Omthera[1]	533	Not amortised
Roxadustat intangible assets acquired from FibroGen[1]	327	Not amortised

[1] Assets in development are not amortised but are tested annually for impairment.

All the assets listed above are classified as Product, marketing and distribution rights.

10 Investments in associates and joint ventures

	2018 $m	2017 $m	2016 $m
At 1 January	**103**	99	85
Additions	**187**	76	65
Share of after tax losses	**(113)**	(55)	(33)
Unrecognised profit on transactions with joint ventures	**(64)**	(27)	–
Exchange adjustments	**(24)**	10	(18)
At 31 December	**89**	103	99

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, including MEDI-551, which is an advanced Phase IIb/III asset, and a number of other clinical & pre-clinical assets. AstraZeneca contributed $142m in initial funds and has a 45% interest in the joint venture. Consideration was $142m and a restricted disposal gain of $63m was recognised in Other operating income.

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 meet unmet needs globally, and to bring innovative new medicines to patients in China faster. The agreement resulted in the formation of a joint venture entity based in China, Dizal (Jiangsu) Pharmaceutical Co., Limited. AstraZeneca contributed $55m in initial funds and has a 48% interest in the joint venture. The joint venture entity purchased exclusive rights from AstraZeneca in 2017 to develop and commercialise three potential medicines currently in pre-clinical development in the areas of oncology, cardiovascular and metabolic diseases, and respiratory, resulting in a disposal gain of $28m for AstraZeneca recognised in Other operating income.

In 2015, AstraZeneca established the subsidiaries Entasis Therapeutics Ltd and Entasis Therapeutics Inc. (collectively known as 'Entasis') for the development of early-stage infection assets. In March 2016, Entasis closed a Series B financing, raising $25m from four third party investors. Under the funding agreement, a new board of directors was appointed, and a voting rights agreement was put in place committing to reduce AstraZeneca's voting interest to approximately 49%. The results of Entasis were consequently deconsolidated in 2016 from the Group, with an investment in associate of $24m recognised. There was no gain or loss recognised on deconsolidation. During 2017, the voting interests were further reduced and at 31 December 2017 were approximately 18%. Entasis completed an IPO on 26 September 2018. A gain was made of $25m recognised in profit. After the IPO AstraZeneca's holding was reduced to 16.5% with only one member on an increased board size of 14. As a result, the investment is no longer accounted for as an associate and is now included in equity securities held at FVOCI.

10 Investments in associates and joint ventures *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. AstraZeneca contributed $45m in cash to the joint venture entity and has a 50% interest in the joint venture. An additional contribution of $10m was made in 2016 and additional contributions totalling $20m were made in 2017 with further contributions of $27m made in 2018.

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, with a branch in South Korea. AstraZeneca contributed $70m in cash to the joint venture entity and has a 50% interest in the joint venture. An additional contribution of $30m was made in 2016 and a further $15m in 2018. At the end of the year Archigen had net liabilities of $18m, of which AstraZeneca's share is $9m, and the investment is held at nil value. The Group has made a provision of $5m, within Trade and other payables, for anticipated future costs.

All investments are accounted for using the equity method.

Aggregated summarised financial information for the associate and joint venture entities is set out below:

	2018 $m	2017 $m	2016 $m
Non-current assets	**260**	207	144
Current assets	**233**	158	128
Total liabilities	**(71)**	(41)	(20)
Net assets	**422**	324	252
Amount attributable to AstraZeneca	**104**	117	125
Exchange adjustments	**(15)**	(14)	(26)
Carrying value of investments in associate and joint ventures	**89**	103	99

11 Other investments

	2018 $m	2017 $m	2016 $m
Non-current investments			
Equity securities at fair value through other comprehensive income	**833**	–	–
Equity securities available for sale	**–**	933	727
Total	**833**	933	727
Current investments			
Fixed income securities at fair value through profit and loss	**809**	–	–
Fixed income securities available for sale	**–**	1,150	847
Fixed deposits	**40**	80	37
Total	**849**	1,230	884

Investments classified as available for sale in 2016 and 2017 under IAS 39 have been reclassified in 2018 on adoption of IFRS 9 on 1 January 2018, as either at fair value through Other comprehensive income or at fair value through profit and loss. The financial impact from the reclassification of equity and fixed income investments from available for sale to at fair value through Other comprehensive income and at fair value through profit and loss has been recorded in the Group accounting policies under 'Impact from adoption of IFRS 9'.

Other investments classified as at fair value through Other comprehensive income and at fair value through profit and loss (IFRS 9)

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 for which the Group has not elected to recognise fair value gains through Other comprehensive income.

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.

Other investments previously classified as available for sale in 2017 (IAS 39)

Impairment charges of $14m in respect of available for sale equity securities were included in Other operating income and expense in 2017 (2016: $21m). Equity and fixed income securities available for sale were held at fair value until re-classification.

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 (ie as prices) or indirectly (ie derived from prices).
- Level 3: inputs for the asset or liability that are not based on observable market data (unobservable inputs).

	2018 FVPL $m	**2018 FVOCI $m**	2017 AFS $m	2016 AFS $m
Level 1	**809**	**667**	1,408	933
Level 2	**–**	**–**	–	–
Level 3	**–**	**166**	675	641
Total	**809**	**833**	2,083	1,574

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 calculated by taking costs 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:

	2018 FVOCI $m	2017 AFS $m	2016 AFS $m
At 1 January	**675**	641	352
Additions	**79**	53	210
Revaluations	**(147)**	(1)	110
Transfers out	**(434)**	(12)	(12)
Disposals	**(6)**	(15)	(2)
Impairments and exchange adjustments	**(1)**	9	(17)
At 31 December	**166**	675	641

Assets are transferred in or out of Level 3 on the date of the event or change in circumstances that caused the transfer.

12 Derivative financial instruments

	Non-current assets $m	Current assets $m	Current liabilities $m	Non-current liabilities $m	Total $m
Interest rate swaps designated in a fair value hedge	–	19	–	(2)	17
Interest rate swaps related to instruments designated at fair value through profit and loss	65	–	–	–	65
Cross currency swaps designated in a net investment hedge	278	–	–	–	278
Cross currency swaps designated in a cashflow hedge	–	–	–	(115)	(115)
Other derivatives	–	8	(18)	–	(10)
31 December 2016	343	27	(18)	(117)	235

	Non-current assets $m	Current assets $m	Current liabilities $m	Non-current liabilities $m	Total $m
Interest rate swaps designated in a fair value hedge	–	–	(3)	–	(3)
Interest rate swaps related to instruments designated at fair value through profit and loss	53	–	–	–	53
Cross currency swaps designated in a net investment hedge	223	12	–	(4)	231
Cross currency swaps designated in a cashflow hedge	197	–	–	–	197
Cross currency swaps designated in a fair value hedge	31	–	–	–	31
Other derivatives	–	16	(21)	–	(5)
31 December 2017	504	28	(24)	(4)	504

	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	**40**	**–**	**–**	**–**	**40**
Cross currency swaps designated in a net investment hedge[1]	**–**	**213**	**–**	**(4)**	**209**
Cross currency swaps designated in a cashflow hedge[2]	**101**	**–**	**–**	**–**	**101**
Cross currency swaps designated in a fair value hedge[3]	**16**	**–**	**–**	**–**	**16**
Other derivatives	**–**	**45**	**(27)**	**–**	**18**
31 December 2018	**157**	**258**	**(27)**	**(4)**	**384**

[1] Cross currency swaps designated in a net investment hedge comprise a $750m Japanese yen to US dollar cross currency interest rate swap maturing in 2019 and a $69m Chinese renminbi to US dollar cross currency interest rate swap maturing in 2026. The Japanese to US swap effectively converts $750m of the Group's $1,000m 1.95% 2019 bond into a Japanese yen borrowing, partially hedging the Group's Japanese yen denominated assets and revenues. At 31 December 2018 the fair value of this swap was $213m (2017: $223m; 2016: $242m), the swapped US dollar:Japanese yen rate was 78.01 and the Japanese yen interest rate on the swap was 0.3452%. The Chinese renminbi to US dollar swap hedges inter-company funding provided to Chinese Group entities. At 31 December 2018 the fair value of this swap was $(4)m (2017: $(4)m; 2016: $7m), the swapped US dollar:Chinese renminbi rate was 6.68 and the Chinese renminbi interest rate on the swap was 4.796%. A further $151m Chinese renminbi to US dollar swap matured in December 2018 when the inter-company loan it was hedging was repaid (fair value 2017: $11m; 2016: $29m). Hedge ineffectiveness recognised on swaps designated in a net investment hedge during the period was $nil.

[2] Instruments designated in a cash flow hedge are cross currency swaps with total nominal amounts of euro 2.2bn that effectively convert our fixed rate euro 500m 0.25%, euro 900m 0.75% and euro 800m 1.25% callable bonds repayable in 2021, 2024 and 2028 respectively into fixed rate USD borrowings and hedge the exposure to foreign exchange spot rate and interest rate risk. The fair value of these swaps at 31 December 2018 was $101m (2017: $197m; 2016: $(115)m). The swap maturity dates match the underlying bond maturity dates and the average swapped euro:US dollar exchange rate and swapped interest rates are 1.14 and 2.7% respectively.

[3] 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 maturity date of the cross currency interest rate swap is in 2021 and the swapped euro:US dollar exchange rate and swapped interest rate are 1.09 and three month US dollar libor + 1.27% respectively.

All derivatives are held at fair value and fall within Level 2 of the fair value hierarchy as defined in Note 11. 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 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:

	2018	2017	2016
Derivatives	**(0.4)% to 3.2%**	1.7% to 2.2%	1.5% to 2.2%

13 Non-current other receivables

Non-current other receivables of $515m (2017: $847m; 2016: $901m) include a prepayment of $114m (2017: $180m; 2016: $380m) which represents the long-term element of minimum contractual royalties payable to Shionogi under the global licence agreement for *Crestor*, which was renegotiated in December 2013. The resulting modified royalty structure, which includes fixed minimum and maximum payments in years until 2020, has resulted in the Group recognising liabilities, and corresponding prepayments, for the discounted value of total minimum payments. The current portion of the prepayment is $114m (2017: $181m; 2016: $116m) and is reported in amounts due within one year (see Note 15).

Non-current other receivables also include $146m (2017: $178m; 2016: $178m) prepayments in relation to our research collaboration with Moderna and $nil (2017: $175m; 2016: $175m) receivable related to the disposal of the small molecule antibiotics assets in 2016, as it has been reclassified to amounts due within one year.

14 Inventories

	2018 $m	2017 $m	2016 $m
Raw materials and consumables	**794**	1,024	811
Inventories in process	**1,450**	1,208	1,060
Finished goods and goods for resale	**646**	803	463
Inventories	**2,890**	3,035	2,334

The Group recognised $2,659m (2017: $2,493m; 2016: $2,644m) of inventories as an expense within cost of sales during the year.

Inventory write-offs in the year amounted to $208m (2017: $109m; 2016: $198m).

15 Current trade and other receivables

	2018 $m	2017 $m	2016 $m
Amounts due within one year			
Trade receivables	**3,033**	2,818	2,625
Less: Amounts provided for doubtful debts (Note 27)	**(38)**	(16)	(42)
	2,995	2,802	2,583
Other receivables	**1,143**	793	852
Prepayments and accrued income	**1,363**	1,148	879
	5,501	4,743	4,314
Amounts due after more than one year			
Other receivables	**–**	156	140
Prepayments and accrued income	**73**	110	119
	73	266	259
Trade and other receivables	**5,574**	5,009	4,573

Trade receivables includes $724m (2017: $327m; 2016: $655m) due from customers which are subject to debt factoring agreements, where invoices have currently not been factored and then derecognised.

All financial assets included within current Trade and other receivables are held at amortised cost with carrying value being a reasonable approximation of fair value.

16 Cash and cash equivalents

	2018 $m	2017 $m	2016 $m
Cash at bank and in hand	**893**	784	782
Short-term deposits	**3,938**	2,540	4,236
Cash and cash equivalents	**4,831**	3,324	5,018
Unsecured bank overdrafts	**(160)**	(152)	(94)
Cash and cash equivalents in the cash flow statement	**4,671**	3,172	4,924

The Group holds $86m (2017: $93m; 2016: $91m) of Cash and cash equivalents which is required to meet insurance solvency, capital and security requirements.

Under IAS 39 all Cash and cash equivalents were held at amortised cost with fair value approximating to carrying value. Following the adoption of IFRS 9 Financial Instruments on 1 January 2018 US dollar liquidity fund balances included in Cash and cash equivalents were reclassified from amortised cost to fair value through profit or loss. During 2018 AstraZeneca was invested in constant 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 or loss, although the fair value will be materially the same as amortised cost. The balance reclassified on 1 January 2018 was $1,150m as shown under 'Impact from adoption of IFRS 9' in the Group accounting policies section.

Non-cash and other movements, within operating activities in the Consolidated Statement of Cash Flows, includes:

	2018 $m	2017 $m	2016 $m
Gains on disposal of short-term investments	**–**	(161)	–
Net gains/(losses) on disposal of non-current assets	**8**	(24)	(29)
Changes in fair value of put option (Acerta Pharma)	**(113)**	(209)	(41)
Share-based payments charge for period	**219**	220	241
Settlement of share plan awards	**(212)**	(254)	(281)
Pension contributions	**(174)**	(157)	(192)
Pension charges recorded in operating profit	**128**	74	74
Foreign exchange and other	**(146)**	(13)	(264)
Total operating activities non-cash and other movements	**(290)**	(524)	(492)

17 Assets held for sale

Assets held for sale of $982m (2017: $nil; 2016: $nil) comprise intangible assets relating to the US rights to RSV franchise assets (specifically *Synagis*) arising from the acquisition of MedImmune and to US rights to certain respiratory assets acquired from Almirall and Actavis (including *Tudorza*). In both cases a partial transfer has been made from the respective intangible assets based on the relative values of the portion being disposed of and the portion retained.

AstraZeneca agreed to dispose of the US Rights to *Synagis* to SOBI on 13 November 2018 with completion of the transaction subject to certain contingencies. The transaction closed and control of the assets transferred on 23 January 2019.

In December 2018, Circassia exercised an option right to acquire the remaining rights to *Tudorza* in the US, which was previously part of a strategic collaboration between the two companies. The transaction closed on 1 January 2019.

18 Interest-bearing loans and borrowings

		Repayment dates	2018 $m	2017 $m	2016 $m
Current liabilities					
Bank overdrafts		On demand	**160**	152	94
Bank collateral[1]			**384**	513	–
Finance leases			**–**	5	87
5.9% Callable bond	US dollars	2017	**–**	–	1,769
Floating rate notes	US dollars	2018	**–**	399	–
1.75% Callable bond	US dollars	2018	**–**	998	–
1.95% Callable bond	US dollars	2019	**999**	–	–
Other loans (Commercial paper)		Within one year	**211**	180	357
Total			**1,754**	2,247	2,307
Non-current liabilities					
Finance leases			**–**	–	6
Floating rate notes	US dollars	2018	**–**	–	399
1.75% Callable bond	US dollars	2018	**–**	–	998
1.95% Callable bond	US dollars	2019	**–**	999	998
2.375% Callable bond	US dollars	2020	**1,594**	1,591	1,589
0.875% Non-callable bond	euros	2021	**854**	890	782
0.25% Callable bond	euros	2021	**570**	594	522
Floating rate notes	US dollars	2022	**250**	249	–
2.375% Callable bond	US dollars	2022	**994**	992	–
7% Guaranteed debentures	US dollars	2023	**325**	347	350
Floating rate notes	US dollars	2023	**400**	–	–
3.5% Callable bond	US dollars	2023	**845**	–	–
0.75% Callable bond	euros	2024	**1,022**	1,067	937
3.375% Callable bond	US dollars	2025	**1,980**	1,978	1,976
3.125% Callable bond	US dollars	2027	**743**	742	–
1.25% Callable bond	euros	2028	**903**	941	827
4% Callable bond	US dollars	2029	**992**	–	–
5.75% Non-callable bond	pounds sterling	2031	**443**	468	426
6.45% Callable bond	US dollars	2037	**2,721**	2,720	2,719
4% Callable bond	US dollars	2042	**987**	987	986
4.375% Callable bond	US dollars	2045	**979**	979	979
4.375% Callable bond	US dollars	2048	**736**	–	–
Other loans	US dollars		**21**	16	7
Total			**17,359**	15,560	14,501

[1] In 2017 the Group changed its accounting policy such that collateral receipts were included in interest bearing loans and borrowings. Previously these were included in short term deposits.

All loans and borrowings above are unsecured, except for finance leases which were secured against the Information Technology assets to which they relate (see Note 7).

18 Interest-bearing loans and borrowings *continued*

	Current loans and borrowings $m	Non-current loans and borrowings $m	Total $m
At 31 December 2017	2,247	15,560	17,807
Changes from financing cash flows			
Issue of loans	**–**	**2,971**	**2,971**
Repayment of loans	**(1,400)**	**–**	**(1,400)**
Movement in short-term borrowings	**(98)**	**–**	**(98)**
Total changes in liabilities arising on financing activities	**(1,498)**	**2,971**	**1,473**
Movement in overdrafts	**8**	**–**	**8**
Transfers	**999**	**(999)**	**–**
Exchange and other movements	**(2)**	**(173)**	**(175)**
At 31 December 2018	**1,754**	**17,359**	**19,113**

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[3] $m	Amortised cost[4] $m	Total carrying value $m	Fair value $m
2016						
Overdrafts	–	–	–	94	94	94
Finance leases due within one year	–	–	–	87	87	87
Finance leases due after more than one year	–	–	–	6	6	6
Loans due within one year	770	–	–	1,356	2,126	2,161
Loans due after more than one year	598	350	2,286	11,261	14,495	15,826
Total at 31 December 2016	1,368	350	2,286	12,804	16,808	18,174
2017						
Overdrafts	–	–	–	152	152	152
Finance leases due within one year	–	–	–	5	5	5
Loans due within one year	596	–	–	1,494	2,090	2,092
Loans due after more than one year	304	347	2,602	12,307	15,560	17,031
Total at 31 December 2017	900	347	2,602	13,958	17,807	19,280
2018						
Overdrafts	**–**	**–**	**–**	**160**	**160**	**160**
Finance leases due within one year	**–**	**–**	**–**	**–**	**–**	**–**
Loans due within one year	**–**	**–**	**–**	**1,594**	**1,594**	**1,587**
Loans due after more than one year	**346**	**325**	**2,495**	**14,193**	**17,359**	**17,841**
Total at 31 December 2018	**346**	**325**	**2,495**	**15,947**	**19,113**	**19,588**

[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. The accumulated amount of fair value hedge adjustments to the bond is a loss of $19m and hedge ineffectiveness recognised during the period was nil.
[2] Instruments designated at fair value through profit or loss include the US dollar 7% guaranteed debentures repayable in 2023.
[3] Instruments designated in a cash flow hedge include the euro 500m 0.25%, euro 900m 0.75% and euro 800m 1.25% Callable bonds repayable in 2021, 2024 and 2028 respectively. Hedge ineffectiveness recognised during the period was nil.
[4] Included within borrowings held at amortised cost are amounts designated as hedges of net investments in foreign operations of $954m at 31 December 2018 (2017: $1,054m; 2016: $1,208m). The fair value of these borrowings was $1,106m at 31 December 2018 (2017: $1,206m; 2016: $1,400m). These borrowings comprise our £350m 5.75% 2031 non-callable bond and a euro 450m portion of our euro 750m 0.875% 2021 non-callable bond and have been designated as hedges of net investments in the Group's UK and Euro operations respectively. Also included within borrowings held at amortised cost is the Group's $1bn 1.95% 2019 bond, $750m of which has been swapped to Japanese yen. The US dollar to Japanese yen cross currency interest rate swap has been designated as a hedge of net investments in the Group's Japanese operations. Hedge ineffectiveness recognised on borrowings designated in a net investment hedge during the period was nil.

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 11. 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 11, with the exception of overdrafts and finance leases, where fair value approximates to carrying values.

A gain of $8m was made during the year on the fair value of bonds designated at fair value through profit or loss, due to increased credit risk. A gain of $34m 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:

	2018	2017	2016
Loans and borrowings	**2.3% to 2.4%**	1.9% to 2.2%	1.5% to 2.2%

19 Trade and other payables

	2018 $m	2017 $m	2016 $m
Current liabilities			
Trade payables	**1,720**	2,285	1,680
Value added and payroll taxes and social security	**204**	243	240
Rebates, chargebacks, returns and other revenue accruals	**4,043**	3,264	3,601
Clinical trial accruals	**993**	922	696
Other accruals	**3,951**	3,324	2,714
Externalisation revenue contract liabilities	**92**	–	–
Contingent consideration	**867**	555	527
Other payables	**971**	1,048	1,028
Total	**12,841**	11,641	10,486
Non-current liabilities			
Accruals	**7**	143	292
Externalisation revenue contract liabilities	**78**	–	–
Contingent consideration	**4,239**	4,979	4,930
Acerta Pharma put option liability (Note 25)	**1,838**	1,823	1,901
Other payables	**608**	895	2,365
Total	**6,770**	7,840	9,488

The Group has revised the presentation of Trade and other payables in 2018 to separately present clinical trial accruals, returns and other revenue accruals that have historically been presented within Trade payables (see the Group Accounting policies section from page 153). The Group has also separately presented the Acerta put option that has historically been presented within Other payables.

Included within Rebates, chargebacks, returns and other revenue accruals are contract liabilities of $126m (1 January 2018: $138m). The revenue recognised in the year for contract liabilities is $139m, comprising $104m relating to other revenue accruals and $35m Externalisation Revenue contract liabilities.

Trade payables includes $166m (2017: $64m; 2016: $nil) due to suppliers that have signed up to a supply chain financing programme, under which the suppliers can elect on a invoice by invoice basis to receive a discounted early payment from the partner 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 partner 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 2018 the payables met the criteria of Trade payables.

The Acerta Pharma put option liability is remeasured each period, based on the latest assessment of the expected redemption amount with remeasurements taken to Selling, general and administrative costs (see Note 2). Interest arising from amortising the liability is included within Finance expense (see Note 3). The expected redemption amount is dependent on the accumulated profits of *Calquence* to the point of redemption, which may vary materially dependent on factors such as revenues earned, research and development expenditure, regulatory approvals received, and certain other expenses of Acerta Pharma B.V. and its subsidiaries.

The Group has adopted IFRS 15 Revenue from Contracts with Customers from 1 January 2018 under the modified retrospective method. Consequently, the Group has presented Externalisation revenue contract liabilities prospectively from that date.

With the exception of Contingent consideration payables of $5,106m (2017: $5,534m; 2016: $5,457m) which are held at fair value within Level 3 of the fair value hierarchy as defined in Note 11, all other financial liabilities are held at amortised cost with carrying value being a reasonable approximation of fair value.

Contingent consideration

	2018 $m	2017 $m	2016 $m
At 1 January	**5,534**	5,457	6,411
Settlements	**(349)**	(434)	(293)
Revaluations	**(495)**	109	(1,158)
Discount unwind (Note 3)	**416**	402	497
At 31 December	**5,106**	5,534	5,457

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 costs and include a decrease of $482m in 2018 (2017: an increase of $208m; 2016: a decrease of $999m) 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).

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 therapeutic area and expected pricing for launched products, may cause the calculated fair value of the above contingent consideration to vary materially in future years.

The contingent consideration balance relating to BMS's share of Global Diabetes Alliance of $3,983m (2017: $4,477m; 2016: $4,240m) would increase/decrease by $398m with an increase/decrease in sales of 10% as compared with the current estimates.

19 Trade and other payables *continued*

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	216
Amplimmune	2013	Milestones	275
Omthera	2013	Milestones	120
Pearl Therapeutics	2013	Milestones	390
BMS's share of Global Diabetes Alliance[1]	2014	Milestones and royalties	600
Almirall[1]	2014	Milestones and royalties	620
Definiens[1]	2014	Milestones	150

[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.

20 Provisions

	Severance $m	Environmental $m	Employee benefits $m	Legal $m	Other provisions $m	Total $m
At 1 January 2016	403	67	158	357	257	1,242
Charge for year	578	11	6	223	170	988
Cash paid	(433)	(19)	(21)	(126)	(87)	(686)
Reversals	(40)	–	–	–	(39)	(79)
Exchange and other movements	(21)	–	–	(16)	(10)	(47)
At 31 December 2016	487	59	143	438	291	1,418
Charge for year	225	11	30	281	55	602
Cash paid	(324)	(20)	(43)	(48)	(37)	(472)
Reversals	(75)	–	(10)	(40)	(44)	(169)
Exchange and other movements	45	9	6	23	6	89
At 31 December 2017	358	59	126	654	271	1,468
Charge for year	**94**	**65**	**1**	**11**	**30**	**201**
Cash paid	**(152)**	**(24)**	**(9)**	**(232)**	**(28)**	**(445)**
Reversals	**(58)**	**–**	**–**	**(230)**	**(28)**	**(316)**
Exchange and other movements	**(16)**	**(3)**	**1**	**(5)**	**6**	**(17)**
At 31 December 2018	**226**	**97**	**119**	**198**	**251**	**891**

	2018 $m	2017 $m	2016 $m
Due within one year	**506**	1,121	1,065
Due after more than one year	**385**	347	353
Total	**891**	1,468	1,418

AstraZeneca is undergoing a global restructuring initiative which involves rationalisation of the global supply chain, the sales and marketing organisation, IT and business support infrastructure, and R&D. Employee costs in connection with the initiatives are recognised in severance provisions. Final severance costs are often subject to the completion of the requisite consultations on the areas impacted.

Details of the environmental and legal provisions are provided in Note 29. Two payments totalling $145m were paid out of the legal provision during January 2019.

Employee benefit provisions include the Deferred Bonus Plan. Further details are included in Note 28.

Other provisions comprise amounts relating to specific contractual or constructive obligations and disputes.

No provision has been released or applied for any purpose other than that for which it was established.

21 Post-retirement benefits

Pensions

Background

The Company and most of its subsidiaries offer retirement plans which cover the majority of employees in the Group. 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 defined benefit plans are now 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 defined benefit members of the UK Pension Fund. The number of active members in the Fund continues to decline and is now approximately 700 employees. In November 2017, the Group closed the qualified and non-qualified US defined benefit pension plans to future accrual (and removed any salary link) from 31 December 2017.

The major defined benefit 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 rigorously by the Group and local fiduciaries, taking into account: the Group's credit rating; local regulation; cash flows; and the solvency and maturity of the relevant pension scheme.

Financing principles

Ninety one per cent of the Group's defined benefit obligations at 31 December 2018 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. There have been no fundamental changes to these principles during 2018. The Group believes:

- In funding the benefits it promises to employees and meeting its obligations.
- That the pension arrangements should be considered in the context of its broader capital structure. In general, it does not believe in committing excessive capital for funding when the Group might use the capital elsewhere to reinvest in the wider business, nor does it wish to generate surpluses.
- In taking some measured and rewarded risks with the investments underlying the funding, subject to a long-term plan to reduce those risks when opportunities arise.
- That holding certain investments may cause volatility in the funding position. However, the Group would not wish to amend its contribution level for relatively small deviations from its preferred funding level, because it is expected that there will be short-term volatility, but it is prepared to react appropriately to more significant deviations.
- That proactive engagement with local Fiduciary Bodies is necessary and helpful to provide robust oversight and input in relation to funding and investment strategy and to facilitate liability management exercises appropriate to each pension plan.
- In considering the use of alternative methods of providing security that do not require immediate cash funding but help mitigate exposure of the pension arrangement to the credit risk of the Group.

These principles are appropriate at the present date but they are kept under ongoing review, should circumstances change these principles may also be subject to change.

The Group has developed a long-term funding framework to implement these principles, which targets full funding on a low risk funding measure over the long term as the pension funds mature, with affordable long-term de-risking of investment strategy over time. Unless local regulation dictates otherwise, this framework determines the cash contributions payable to the pension funds. A key element of this funding framework is the investment strategy used to grow existing assets and hedge against changes in liability values. The Group provides regular input to local fiduciary boards with the aim of ensuring that an appropriate investment return is targeted over the long term in a risk-controlled manner.

UK

The UK defined benefit pension fund represents approximately 62% of the Group's defined benefit obligations at 31 December 2018. The financing principles are modified in light of the UK regulatory requirements (summarised below) and resulting discussions with the Pension Fund Trustee.

Role of Trustees and Regulation (UK)

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 the asset investment policy 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 (see below).

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.

Funding requirements (UK)

UK legislation requires that pension schemes are funded prudently. On a triennial basis, the Trustee and the Group must agree the contributions required (if any) to ensure the Fund is fully funded over an appropriate time-period and on a suitably prudent measure. The last full actuarial valuation of the AstraZeneca Pension Fund was carried out by a qualified actuary as at 31 March 2016 and following discussions between the Group and Trustee was finalised and accepted by The Pensions Regulator in 2017. The next actuarial valuation is due to take place as at 31 March 2019, with a likely timescale for completion in early to mid-2020.

In relation to deficit recovery contributions, a lump sum contribution of £51m ($68m) was made in March 2018, with a further £51m contribution due before 31 March 2019. In addition, a contribution of £26m ($35m) was made in March 2018, with a further contribution of £27m due before 31 March 2019, 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 payment of approximately £126m which was due in 2017. This contribution will now be paid in five instalments (with interest added each year) from March 2018 to March 2022. The letter of credit underwriting these payments will be renewed each year, but will reduce in value as each annual payment is made.

The Group entered into a long-term funding agreement with the Trustee in October 2016 under which the Group will grant a charge in favour of the Trustee over certain land and buildings at the Cambridge Biomedical Campus, which would crystallise only in the event of the Group's insolvency. This charge will provide security in respect of future UK Pension Fund contributions.

Under the funding assumptions used to set the statutory funding target, the key assumptions from the actuarial valuation as at 31 March 2016 were as follows: long-term UK price inflation set at 2.6% per annum; salary increases at 0% per annum (as a result of pensionable pay levels being frozen in 2010); pension increases at 2.85% per annum; and discount rate at 3.71% per annum. The resulting valuation of the Fund's liabilities on that basis were £5,265m ($6,710m) compared to a market value of assets at 31 March 2016 of £4,492m ($5,724m).

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. As such, there are no adjustments required in respect of IFRIC 14 'IAS 19 – The Limit on a Defined Benefit Asset, Minimum Funding Requirements and their Interaction'.

21 Post-retirement benefits *continued*

GMP Equalisation (UK)

A UK High Court judgment was issued on 26 October 2018 relating to Guaranteed Minimum Pensions ('GMP'). Although the ruling relates to the Lloyds Banking Group pension schemes, it is expected to create a precedent for other UK defined benefit pension schemes. The ruling requires the equalisation of member benefits earned between 1990 and 1997 to address gender inequality in instances where GMP benefits are currently unequal. While there remains some uncertainty, the Group has made a provision for the estimated financial impact of this ruling on the UK Pension Fund, based on a comparison of the cumulative value of members' benefits with the benefits of a notional member of the opposite gender (method C2 under the terminology of the High Court Judgement). The estimated impact is based on the broad profile of the Fund (ie age profile, service profile and GMP proportion) and a past service cost of £17m ($23m) has been recognised in the year ended 31 December 2018. Further work will be carried out with the Trustee over 2019 to determine the exact impact.

Rest of Group

The IAS 19 positions for the US and Sweden as at 31 December 2018 are shown below. These plans account for 29% of the Group's defined benefit obligations. The US and Sweden pension funds are governed by Fiduciary Bodies with responsibility for the investment policies of those funds. These plans are funded in line with the Group's financing principles and contributions are paid as prescribed by the long-term funding framework (subject to local regulations being met).

The US defined benefit pension plans were actuarially revalued at 31 December 2018, when plan obligations were $1,463m and plan assets were $1,379m. This includes obligations in respect of the non-qualified plan which is unfunded. There has been an improvement in the funding position of the qualified US pension plan and it is now close to being fully funded on the IAS 19 basis. As the funding position improved over 2018, the investment strategy was de-risked, reducing equity exposure and increasing the interest rate hedge.

The Swedish defined benefit pension plans were actuarially valued at 31 December 2018, when plan obligations were estimated to amount to $1,872m and plan assets were $1,017m. It should be noted that the Swedish plans have a funding surplus on the local GAAP accounting basis and this influences contribution policy.

On current bases, it is expected that ongoing contributions (excluding those in respect of past service deficit contributions) during the year ending 31 December 2019 for the three main countries will be approximately $32m.

Post-retirement benefits other than pensions

In the US, and to a lesser extent in certain other countries, AstraZeneca's employment practices include the provision of healthcare and life assurance benefits for retired employees. As at 31 December 2018, some 3,215 retired employees and covered dependants currently benefit from these provisions and some 2,231 current employees will be eligible on their retirement. AstraZeneca 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.

The cost of post-retirement benefits other than pensions for the Group in 2018 was $5m (2017: $14m; 2016: $17m). Plan assets were $260m and plan obligations were $263m at 31 December 2018. 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 of the major defined benefit schemes operated by the Group to 31 December 2018. 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 were as follows:

	2018		2017	
	UK	**Rest of Group**	UK	Rest of Group
Inflation assumption	**3.2%**	**1.1%**	3.1%	2.2%
Rate of increase in salaries	**–**[1]	**2.0%**	–[1]	3.1%
Rate of increase in pensions in payment	**3.0%**	**1.1%**	2.9%	1.1%
Discount rate – defined benefit obligation	**2.8%**[2]	**3.0%**	2.5%[2]	3.0%
Discount rate – interest cost[2]	**2.4%**[3]	**2.5%**	2.5%[3]	2.7%
Discount rate – service cost[2]	**2.5%**[3]	**2.9%**	2.7%[3]	3.5%

[1] Pensionable pay frozen at 30 June 2010 levels following UK fund changes.
[2] Group defined benefit obligation as at 31 December 2018 calculated using discount rates based on market conditions as at 31 December 2018.
[3] 2018 interest costs and service costs calculated using discount rates based on market conditions as at 31 December 2017.

In the UK, a new assumption has been made that 30% of members will transfer out of the defined benefit section of the AstraZeneca Pension Fund at the point of retirement. This assumption is based on Fund experience since pensions freedoms legislation came into effect in April 2015 and will be reviewed each year to ensure it remains appropriate. The assumption has the impact of reducing liabilities by approximately £53m ($70m) and has been recorded in Other comprehensive income.

The weighted average duration of the post-retirement scheme obligations in the UK is 16 years and 15 years in the Rest of Group.

Demographic assumptions

The mortality assumptions are based on country-specific mortality tables. These are compared to actual experience and adjusted where sufficient data is 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 members retiring in 2018 and male members expected to retire in 2038 (2017: 2017 and 2037 respectively).

	Life expectancy assumption for a male member retiring at age 65			
Country	**2018**	2038	2017	2037
UK	**23.2**	24.7	23.7	24.8
US	**22.2**	22.8	20.8	23.0
Sweden	**21.9**	23.6	21.9	23.6

The Group adopted the CMI 2017 Mortality Projections Model with a 1% long-term improvement rate in 2018 in the UK.

Risks associated with the Group's defined benefit pensions

The UK defined benefit plan accounts for 62% 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 continue to evolve to further improve the expected risk/return profile as opportunities arise. The Trustee has hedged the majority (over 80%) 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 85% of total assets and protects to some degree against falls in long-term interest rates (approximately 80% hedged at the end of 2017). There is a framework in place to gradually increase the level of interest rate hedging to 100% of assets over time, via a combination of liability management exercises and additional market-based hedging. 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	A significant proportion of the DBO is indexed in line with price inflation (mainly inflation as measured by the UK Retail Price Index (RP') 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%).	The UK Pension Fund holds index-linked gilts and derivative instruments such as swaps. The inflation hedge of the UK Pension Fund is set at approximately 88% of total assets and protects to some degree against higher-than-expected inflation increases on the DBO (approximately 85% hedged at the end of 2017). 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 $2.1bn of the UK Pension Fund's liabilities. A one-year increase in life expectancy will result in a $217m increase in pension fund assets.

Other risks

There are a number of other risks of running the UK Pension Fund including counterparty risks from using derivatives (mitigated by using 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 manner, with the local fiduciary bodies investing in a diversified growth portfolio and employing a framework to hedge interest rate risk.

Post-retirement scheme deficit

The assets and obligations of the defined benefit schemes operated by the Group at 31 December 2018, as calculated in accordance with IAS 19, are shown overleaf. 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.

21 Post-retirement benefits *continued*

Scheme assets

	UK		Rest of Group		Total		2017
	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Quoted $m	Unquoted $m	Total $m
Government bonds[1]	2,056	–	79	45	2,135	45	2,180
Corporate bonds[2]	–	37	849	–	849	37	886
Derivatives[3]	–	(237)	(12)	26	(12)	(211)	(223)
Investment funds: Listed Equities	–	1,174	371	421	371	1,595	1,966
Investment funds: Global Macro Hedge[4]	–	1,004	–	396	–	1,400	1,400
Investment funds: Diversified growth/Multi Strategy[4]	–	1,921	–	416	–	2,337	2,337
Investment funds: Multi-asset credit[4]	–	633	–	268	–	901	901
Cash and cash equivalents	40	121	23	23	63	144	207
Other	–	–	2	266	2	266	268
Total fair value of scheme assets[5]	2,096	4,653	1,312	1,861	3,408	6,514	9,922

	UK		**Rest of Group**		**Total**		**2018**
	Quoted $m	**Unquoted $m**	**Quoted $m**	**Unquoted $m**	**Quoted $m**	**Unquoted $m**	**Total $m**
Government bonds[1]	**1,725**	**–**	**199**	**–**	**1,924**	**–**	**1,924**
Corporate bonds[2]	**–**	**–**	**870**	**–**	**870**	**–**	**870**
Derivatives[3]	**–**	**(189)**	**3**	**145**	**3**	**(44)**	**(41)**
Investment funds: Listed Equities	**–**	**1,197**	**201**	**190**	**201**	**1,387**	**1,588**
Investment funds: Global Macro Hedge[4]	**–**	**733**	**–**	**280**	**–**	**1,013**	**1,013**
Investment funds: Diversified growth/Multi Strategy[4]	**–**	**1,712**	**–**	**449**	**–**	**2,161**	**2,161**
Investment funds: Multi-asset credit[4]	**–**	**596**	**–**	**191**	**–**	**787**	**787**
Cash and cash equivalents	**39**	**176**	**81**	**5**	**120**	**181**	**301**
Other	**–**	**–**	**1**	**250**	**1**	**250**	**251**
Total fair value of scheme assets[5]	**1,764**	**4,225**	**1,355**	**1,510**	**3,119**	**5,735**	**8,854**

[1] Predominantly developed markets in nature.
[2] Predominantly developed markets in nature and investment grade (AAA-BBB).
[3] Includes interest rate swaps, inflation swaps, longevity swap, equity total return swaps and other contracts.
[4] 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 across the world), Multi-asset credit (bonds and debt including a range of investment grade and non-investment grade credit across the world), Diversified growth/Multi Strategy (multi-asset exposure both across and within traditional and alternative asset classes), and Global Macro Hedge funds (Discretionary/Fundamental Macro and managed futures).
[5] Included in scheme assets is $nil (2017: $nil) of the Group's own assets.

Scheme obligations

			2018			2017
	UK $m	**Rest of Group $m**	**Total $m**	UK $m	Rest of Group $m	Total $m
Present value of scheme obligations in respect of:						
Active membership	**(751)**	**(1,468)**	**(2,219)**	(814)	(1,018)	(1,832)
Deferred membership	**(1,665)**	**(1,215)**	**(2,880)**	(1,998)	(1,688)	(3,686)
Pensioners	**(4,636)**	**(1,630)**	**(6,266)**	(5,220)	(1,767)	(6,987)
Total value of scheme obligations	**(7,052)**	**(4,313)**	**(11,365)**	(8,032)	(4,473)	(12,505)

Net deficit in the scheme

			2018			2017
	UK $m	**Rest of Group $m**	**Total $m**	UK $m	Rest of Group $m	Total $m
Total fair value of scheme assets	**5,989**	**2,865**	**8,854**	6,749	3,173	9,922
Total value of scheme obligations	**(7,052)**	**(4,313)**	**(11,365)**	(8,032)	(4,473)	(12,505)
Deficit in the scheme as recognised in the Consolidated Statement of Financial Position	**(1,063)**	**(1,448)**	**(2,511)**	(1,283)	(1,300)	(2,583)

Fair value of scheme assets

			2018			2017
	UK $m	**Rest of Group $m**	**Total $m**	UK $m	Rest of Group $m	Total $m
At beginning of year	**6,749**	**3,173**	**9,922**	6,137	2,979	9,116
Interest income on scheme assets	**156**	**79**	**235**	159	81	240
Expenses	**(5)**	**(9)**	**(14)**	(6)	(12)	(18)
Actuarial gains	**(351)**	**(123)**	**(474)**	45	188	233
Exchange and other adjustments	**(349)**	**(23)**	**(372)**	596	176	772
Employer contributions	**143**	**31**	**174**	123	34	157
Participant contributions	**2**	**1**	**3**	3	–	3
Benefits paid	**(356)**	**(264)**	**(620)**	(308)	(273)	(581)
Scheme assets' fair value at end of year	**5,989**	**2,865**	**8,854**	6,749	3,173	9,922

The actual return on the plan assets was a loss of $239m (2017: gain of $473m).

Movement in post-retirement scheme obligations

	2018			2017		
	UK $m	Rest of Group $m	Total $m	UK $m	Rest of Group $m	Total $m
Present value of obligations in scheme at beginning of year	**(8,032)**	**(4,473)**	**(12,505)**	(7,118)	(4,184)	(11,302)
Current service cost	**(23)**	**(51)**	**(74)**	(23)	(64)	(87)
Past service (cost)/credit	**(34)**	**(6)**	**(40)**	(39)	70	31
Participant contributions	**(2)**	**(1)**	**(3)**	(3)	–	(3)
Benefits paid	**356**	**264**	**620**	308	273	581
Interest expense on post-retirement scheme obligations	**(185)**	**(102)**	**(287)**	(184)	(105)	(289)
Actuarial losses	**472**	**(44)**	**428**	(272)	(202)	(474)
Exchange and other adjustments	**396**	**100**	**496**	(701)	(261)	(962)
Present value of obligations in scheme at end of year	**(7,052)**	**(4,313)**	**(11,365)**	(8,032)	(4,473)	(12,505)

The obligations arise from the following plans:

	2018			2017		
	UK $m	Rest of Group $m	Total $m	UK $m	Rest of Group $m	Total $m
Funded – pension schemes	**(7,034)**	**(3,584)**	**(10,618)**	(8,013)	(3,698)	(11,711)
Funded – post-retirement healthcare	**–**	**(230)**	**(230)**	–	(245)	(245)
Unfunded – pension schemes	**–**	**(483)**	**(483)**	–	(515)	(515)
Unfunded – post-retirement healthcare	**(18)**	**(16)**	**(34)**	(19)	(15)	(34)
Total	**(7,052)**	**(4,313)**	**(11,365)**	(8,032)	(4,473)	(12,505)

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 2018, are set out below.

	2018			2017		
	UK $m	Rest of Group $m	Total $m	UK $m	Rest of Group $m	Total $m
Operating profit						
Current service cost	**(23)**	**(51)**	**(74)**	(23)	(64)	(87)
Past service (cost)/credit	**(34)**	**(6)**	**(40)**	(39)	70	31
Expenses	**(5)**	**(9)**	**(14)**	(6)	(12)	(18)
Total charge to operating profit	**(62)**	**(66)**	**(128)**	(68)	(6)	(74)
Finance expense						
Interest income on scheme assets	**156**	**79**	**235**	159	81	240
Interest expense on post-retirement scheme obligations	**(185)**	**(102)**	**(287)**	(184)	(105)	(289)
Net interest on post-employment defined benefit plan liabilities	**(29)**	**(23)**	**(52)**	(25)	(24)	(49)
Charge before taxation	**(91)**	**(89)**	**(180)**	(93)	(30)	(123)
Other comprehensive income						
Difference between the actual return and the expected return on the post-retirement scheme assets	**(351)**	**(123)**	**(474)**	45	188	233
Experience gains/(losses) arising on the post-retirement scheme obligations	**(26)**	**(46)**	**(72)**	(50)	(4)	(54)
Changes in financial assumptions underlying the present value of the post-retirement scheme obligations	**389**	**4**	**393**	(261)	(214)	(475)
Changes in demographic assumptions	**109**	**(2)**	**107**	39	15	54
Remeasurement of the defined benefit liability	**121**	**(167)**	**(46)**	(227)	(15)	(242)

Past service cost in 2018 includes a charge to Operating Profit of $23m arising from the expected impact of the UK High Court judgment relating to Guaranteed Minimum Pensions on the UK Pension Fund, as referred to in the UK section on page 179. The past service cost in 2018 also includes costs predominantly related to enhanced pensions in early retirement in the UK and Sweden.

Group costs in respect of defined contribution schemes during the year were $341m (2017: $304m).

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.

	2018		2017	
	+0.5%	–0.5%	+0.5%	–0.5%
Discount rate				
UK ($m)	**520**	**(586)**	618	(703)
US ($m)	**78**	**(83)**	95	(101)
Sweden ($m)	**152**	**(174)**	147	(168)
Total ($m)	**750**	**(843)**	860	(972)

21 Post-retirement benefits *continued*

	2018		2017	
	+0.5%	**–0.5%**	+0.5%	–0.5%
Inflation rate[1]				
UK ($m)	**(444)**	**421**	(526)	495
US ($m)	**–**	**–**	–	–
Sweden ($m)	**(171)**	**151**	(165)	146
Total ($m)	**(615)**	**572**	(691)	641

	2018		2017	
	+0.5%	**–0.5%**	+0.5%	–0.5%
Rate of increase in salaries				
UK ($m)	**–**	**–**	–	–
US ($m)	**–**	**–**	–	–
Sweden ($m)	**(52)**	**48**	(51)	47
Total ($m)	**(52)**	**48**	(51)	47

	2018		2017	
	+1 year	**–1 year**	+1 year	–1 year
Mortality rate				
UK ($m)	**(301)**[2]	**302**[3]	(337)	337
US ($m)	**(24)**	**24**	(26)	27
Sweden ($m)	**(68)**	**68**	(63)	64
Total ($m)	**(393)**	**394**	(426)	428

[1] Rate of increase in pensions in payment follows inflation.
[2] Of the $301m increase, $217m is covered by the longevity swap.
[3] Of the $302m decrease, $212m 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 sensitivity to the life expectancy assumption has been estimated based on the distribution of the plan cash flows.

22 Reserves

Retained earnings

The cumulative amount of goodwill written off directly to reserves resulting from acquisitions, net of disposals, amounted to $619m (2017: $631m; 2016: $613m) using year-end rates of exchange.

At 31 December 2018, 456,792 shares, at a cost of $22m, have been deducted from retained earnings (2017: 476,504 shares, at a cost of $22m; 2016: 276,303 shares, at a cost of $19m) 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).

	2018 $m	2017 $m	2016 $m
Cumulative translation differences included within retained earnings			
At 1 January	**(1,017)**	(2,028)	(372)
Foreign exchange arising on consolidation	**(450)**	536	(1,050)
Exchange adjustments on goodwill (recorded against other reserves)	**(12)**	18	(11)
Foreign exchange arising on designating borrowings in net investment hedges[1]	**(520)**	505	(591)
Fair value movement on derivatives designated in net investment hedges[2]	**(8)**	(48)	(4)
Net exchange movement in retained earnings	**(990)**	1,011	(1,656)
At 31 December	**(2,007)**	(1,017)	(2,028)

[1] Foreign exchange arising on designated borrowings in net investment hedges includes $45m in respect of designated bonds and $(565)m in respect of designated contingent consideration liabilities. The change in value of designated bonds relates to $25m in respect of our £350m 5.75% 2031 non-callable bond and $20m in respect of a €450m portion of our €750m 0.875% 2021 non-callable bond. The change in value of designated contingent consideration liabilities relates to $(358)m in respect of BMS' share of Global Diabetes Alliance, $(32)m in respect of Almirall and $(6)m in respect of Definiens and $(169)m in relation to the put option liability in Acerta Pharma.
[2] Fair value movement on derivatives designated in net investment hedges comprises $(13)m in respect of our $750m Japanese yen to US dollar cross currency interest rate swap, $(1)m in respect of our $69m Chinese renminbi to US dollar cross currency interest rate swap and $6m in respect of our matured $151m Chinese renminbi to US dollar cross currency interest rate swap.

Cumulative amounts with respect to cash flow hedges included within retained earnings are $37m (2017: $76m; 2016: $80m). With effect from 1 January 2018, the Company has disclosed separately the costs of hedging of cross currency interest rate swaps in cash flow hedges and net investment hedges. The cumulative gain with respect to costs of hedging is $47m and the loss during the year was $54m.

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 £154m.

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 ($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.

23 Share capital of the Company

	Allotted, called-up and fully paid		
	2018 $m	2017 $m	2016 $m
Issued Ordinary Shares ($0.25 each)	**317**	317	316
Redeemable Preference Shares (£1 each – £50,000)	**–**	–	–
At 31 December	**317**	317	316

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		
	2018	2017	2016
At 1 January	**1,266,221,605**	1,265,229,424	1,264,122,670
Issues of shares (share schemes)	**817,831**	992,181	1,106,754
At 31 December	**1,267,039,436**	1,266,221,605	1,265,229,424

Share repurchases

No Ordinary Shares were repurchased by the Company in 2018 (2017: nil; 2016: nil).

Shares held by subsidiaries

No shares in the Company were held by subsidiaries in any year.

24 Dividends to shareholders

	2018 Per share	2017 Per share	2016 Per share	**2018 $m**	2017 $m	2016 $m
Second interim (March 2018)	**$1.90**	$1.90	$1.90	**2,402**	2,404	2,402
Interim (September 2018)	**$0.90**	$0.90	$0.90	**1,139**	1,139	1,138
Total	**$2.80**	$2.80	$2.80	**3,541**	3,543	3,540

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 over past 12 years be forfeited. $2m of unclaimed dividends have been adjusted for in retained earnings in 2018.

The 2017 second interim dividend of $1.90 per share was paid on 19 March 2018.

Reconciliation of dividend charged to equity to cash flow statement:

	2018 $m	2017 $m	2016 $m
Dividends charged to equity	**3,541**	3,543	3,540
Exchange losses/(gains) on payment of dividend	**10**	(4)	3
Hedge contracts relating to payment of dividends (cash flow statement)	**(67)**	(20)	18
Dividends paid (cash flow statement)	**3,484**	3,519	3,561

25 Non-controlling interests

Following the acquisition of a majority stake in Acerta Pharma on 2 February 2016, the Group Financial Statements at 31 December 2018 reflect equity of $1,567m (2017: $1,676m; 2016: $1,808m) and total comprehensive losses of $109m (2017: losses of $132m; 2016: losses of $95m) attributable to the non-controlling interests, held by other parties, of Acerta Pharma B.V. and its subsidiaries. The following summarised financial information, for Acerta Pharma B.V. and its subsidiaries, is presented on a stand-alone basis since the acquisition date, and before the impact of Group-related adjustments, some of which are incorporated into this calculation of the loss attributable to the non-controlling interests:

	2018 $m	2017 $m	2016 $m
Total Revenue	**–**	–	–
(Loss)/profit after tax	**(9)**	412	(212)
Other comprehensive income	**–**	–	–
Total comprehensive (loss)/income	**(9)**	412	(212)

	2018 $m	2017 $m	2016 $m
Non-current assets	**16**	3	73
Current assets	**526**	904	79
Total assets	**542**	907	152
Current liabilities	**(63)**	(417)	(171)
Total liabilities	**(63)**	(417)	(171)
Net assets/(liabilities)	**479**	490	(19)

	2018 $m	2017 $m	2016 $m
Net cash inflow/(outflow) from operating activities	**7**	5	(223)
Net cash (outflow)/inflow from investing activities	**(4)**	–	139
Increase/(decrease) in cash and cash equivalents in the year	**3**	5	(84)

25 Non-controlling interests *continued*

The non-controlling interest in Acerta Pharma is subject to a put option, exercisable by the minority shareholders at certain points in the future, not earlier than the commercial launch of *Calquence* (acalabrutinib) in both the US and Europe and when the extent of the commercial opportunity has been fully established. This put option gives rise to a liability which is recorded at the present value of the expected redemption amount, calculated using a probability-weighted model based on forecast revenue and earnings of Acerta Pharma, and is recorded within Non-current other payables (see Note 19). The forecast revenue and earnings of Acerta Pharma will particularly be affected by the outcome of ongoing clinical trials and regulatory submissions relating to *Calquence*. If actual earnings are lower than forecast, the liability for the put option will decrease. Similarly, if actual earnings are higher than forecast, the liability for the put option will increase. The value of the liability is also sensitive to the expected timing of exercise. The amount of the liability is not directly correlated to time until the expected date of exercise. During the year, the liability was remeasured due to a change in the expected timing of the exercise of the put option, while during 2017, *Calquence* received regulatory approval in the US for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. This approval has changed the weighted probability of certain outcomes in respect of the forecast earnings of Acerta Pharma and has brought forward the weighted average expected exercise date of the put option. The changes to these assumptions resulted in a decrease (2017: decrease; 2016 decrease) in the liability for the year before the effect of interest costs. On exercise of the put option, the associated cash flows will be disclosed as financing activities within the Consolidated Statement of Cash Flows.

26 Acquisitions of business operations

There were no acquisitions of business operations in 2018 or 2017.

2016 Acquisitions

Acerta Pharma

On 2 February 2016, AstraZeneca completed an agreement to invest in a majority equity stake in Acerta Pharma, a privately-owned biopharmaceutical company based in the Netherlands and US. The transaction provides AstraZeneca with a potential best-in-class irreversible oral Bruton's tyrosine kinase (BTK) inhibitor, *Calquence*, currently in Phase III development for B-cell blood cancers and in Phase I/II clinical trials in multiple solid tumours. Acerta Pharma has approximately 150 employees.

Under the terms of the agreement, AstraZeneca has acquired 55% of the issued share capital of Acerta Pharma for an upfront payment of $2.5bn. A further payment of $1.5bn was due either on receipt of the first regulatory approval for *Calquence* for any indication in the US, or the end of 2018, depending on which was first. This was paid in 2017 on receipt of first regulatory approval in the US. The agreement also includes options which, if exercised, provide the opportunity for Acerta Pharma's shareholders to sell, and AstraZeneca to buy, the remaining 45% of shares in Acerta Pharma. The options can be exercised at various points in time, conditional on the first approval of *Calquence* in both the US and Europe and when the extent of the commercial opportunity has been fully established, at a price of approximately $3bn net of certain costs and payments incurred by AstraZeneca and net of agreed future adjusting items, using a pre-agreed pricing mechanism.

The acquiring entity within the Group was a Swedish krona functional currency subsidiary. Foreign currency risk arises from the retranslation of the US dollar denominated liabilities arising from the transaction. To manage this foreign currency risk these liabilities have been designated as the hedge instrument in a net investment hedge of the Group's underlying US dollar net investments. 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.

AstraZeneca's 55% holding is a controlling interest and Acerta Pharma's combination of intangible product rights with an established workforce and their operating processes requires that the transaction is accounted for as a business combination in accordance with IFRS 3.

Goodwill is principally attributable to the value of the specialist know-how inherent in the acquired workforce and the accounting for deferred taxes. Goodwill is not expected to be deductible for tax purposes.

Acerta Pharma's results have been consolidated into the Group's results from 2 February 2016. From the period from acquisition to 31 December 2016, Acerta Pharma had no revenues and its loss after tax was $212m.

If the acquisition had taken effect at the beginning of the reporting period in which the acquisition occurred (1 January 2016), on a *pro forma* basis, the revenue of the combined Group for 2016 would have been unchanged and the profit after tax would have been $3,367m. 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 2016 and should not be taken to be representative of future results.

The fair values assigned to the Acerta Pharma business combination completed in 2016 were:

	Fair value $m
Non-current assets	
Intangible assets (Note 9)	7,307
Current assets	253
Current liabilities	(90)
Non-current liabilities	
Deferred tax liabilities	(1,777)
Total net assets acquired	5,693
Non-controlling interests	(1,903)
Goodwill (Note 8)	19
Fair value of total consideration	3,809
Less: fair value of deferred consideration	(1,332)
Total upfront consideration	2,477
Less: cash and cash equivalents acquired	(94)
Net cash outflow	2,383

Acquisition costs were immaterial.

27 Financial risk management objectives and policies

The Group's principal financial instruments, other than derivatives, comprise bank overdrafts, finance leases, loans, 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 are set out below.

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.

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.

Capital management

The capital structure of the Group consists of shareholders' equity (Note 23), debt (Note 18), other current investments (Note 11) and cash (Note 16). 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.

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 15.

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 $12,679m at the beginning of the year to a net debt position of $13,003m at 31 December 2018.

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 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. The Group is 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 is A3 negative outlook by Moody's and BBB+ stable outlook by Standard and Poor's.

In addition to Cash and cash equivalents of $4,831m, short-term fixed income investments of $809m, fixed deposits of $40m, less overdrafts of $160m at 31 December 2018, the Group has committed bank facilities of $4.1bn available to manage liquidity. At 31 December 2018, the Group has issued $3,792m under a Euro Medium Term Note programme and $14,546m under a SEC-registered programme. The Group increased its committed bank facilities by $1.1bn in the year to a total of $4.1bn at 31 December 2018. $0.2bn of the new facilities mature in December 2019 but have a one-year extension option, exercisable by the Group. $0.5bn of the new facilities mature in December 2020 but have a one-year extension option, exercisable by the Group. $0.4bn of the new facilities, together with the existing $3bn of facilities, mature in April 2022. The funds made available under these facility agreements may be used for the general corporate purposes of the Group. 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 the revolving facilities bear an interest rate per annum based on LIBOR (or other relevant benchmark rate) plus a margin. The facility agreements contain no financial covenants. At 31 December 2018 the facilities were undrawn.

27 Financial risk management objectives and policies *continued*

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	Finance leases $m	Trade and other payables $m	Total non-derivative financial instruments $m	Interest rate swaps $m	Cross-currency swaps $m	Total derivative financial instruments $m	Total $m
Within one year	455	2,374	42	10,566	13,437	(54)	32	(22)	13,415
In one to two years	–	1,921	24	4,986	6,931	(19)	12	(7)	6,924
In two to three years	–	1,500	16	1,144	2,660	(15)	(216)	(231)	2,429
In three to four years	–	2,080	10	1,666	3,756	(15)	47	32	3,788
In four to five years	7	1,756	3	877	2,643	(15)	86	71	2,714
In more than five years	–	14,796	–	3,624	18,420	(30)	320	290	18,710
	462	24,427	95	22,863	47,847	(148)	281	133	47,980
Effect of interest	(4)	(8,111)	(2)	–	(8,117)	148	(351)	(203)	(8,320)
Effect of discounting, fair values and issue costs	–	(59)	–	(2,889)	(2,948)	(82)	(93)	(175)	(3,123)
31 December 2016	458	16,257	93	19,974	36,782	(82)	(163)	(245)	36,537

	Bank overdrafts and other loans $m	Bonds $m	Finance leases $m	Trade and other payables $m	Total non-derivative financial instruments $m	Interest rate swaps $m	Cross-currency swaps[1] $m	Total derivative financial instruments[1] $m	Total $m
Within one year	859	1,985	5	11,840	14,689	(10)	32	22	14,711
In one to two years	–	1,564	–	1,976	3,540	(12)	(190)	(202)	3,338
In two to three years	–	2,144	–	1,586	3,730	(12)	53	41	3,771
In three to four years	16	2,000	–	3,240	5,256	(12)	(11)	(23)	5,233
In four to five years	–	1,736	–	1,112	2,848	(12)	37	25	2,873
In more than five years	–	15,575	–	2,808	18,383	(12)	31	19	18,402
	875	25,004	5	22,562	48,446	(70)	(48)	(118)	48,328
Effect of interest	(14)	(7,969)	–	–	(7,983)	70	(504)	(434)	(8,417)
Effect of discounting, fair values and issue costs	–	(94)	–	(3,081)	(3,175)	(50)	93	43	(3,132)
31 December 2017	861	16,941	5	19,481	37,288	(50)	(459)	(509)	36,779

[1] The 2017 disclosures have been revised with the within one year outflow reducing to $32m from $420m, the in one to two years inflow increasing to $190m from $100m, the in two to three years outflow reducing to $53m from $295m, the in three to four years inflow reducing to $11m from $747m, the in four to five years outflow increasing to $37m from $34m and the in more than five years outflow increasing to $31m from $26m.

	Bank overdrafts and other loans $m	**Bonds $m**	**Finance leases $m**	**Trade and other payables $m**	**Total non-derivative financial instruments $m**	**Interest rate swaps $m**	**Cross-currency swaps $m**	**Total derivative financial instruments $m**	**Total $m**
Within one year	**774**	**1,629**	**–**	**13,029**	**15,432**	**(10)**	**(172)**	**(182)[1]**	**15,250**
In one to two years	**7**	**2,210**	**–**	**1,688**	**3,905**	**(9)**	**57**	**48[2]**	**3,953**
In two to three years	**14**	**2,002**	**–**	**833**	**2,849**	**(9)**	**33**	**24[3]**	**2,873**
In three to four years	**–**	**1,813**	**–**	**3,340**	**5,153**	**(9)**	**37**	**28[4]**	**5,181**
In four to five years	**–**	**2,069**	**–**	**776**	**2,845**	**(9)**	**37**	**28[5]**	**2,873**
In more than five years	**–**	**17,405**	**–**	**2,084**	**19,489**	**–**	**69**	**69[6]**	**19,558**
	795	**27,128**	**–**	**21,750**	**49,673**	**(46)**	**61**	**15**	**49,688**
Effect of interest	**(2)**	**(8,669)**	**–**	**–**	**(8,671)**	**46**	**(304)**	**(258)**	**(8,929)**
Effect of discounting, fair values and issue costs	**(17)**	**(122)**	**–**	**(2,139)**	**(2,278)**	**(40)**	**(83)**	**(123)**	**(2,401)**
31 December 2018	**776**	**18,337**	**–**	**19,611**	**38,724**	**(40)**	**(326)**	**(366)**	**38,358**

[1] Total derivative financial instruments within one year excludes Other current derivatives of $(18)m (2017: $5m; 2016: $10m). Total derivative financial instruments within one year and Other current derivatives reflect receivables of $10.207bn (2017: $6.738bn) and payables of $10.007bn (2017: $6.765bn).
[2] Total derivative financial instruments in one to two years reflects receivables of $35m (2017: $803m) and payables of $83m (2017: $601m).
[3] Total derivative financial instruments in two to three years reflects receivables of $950m (2017: $39m) and payables of $974m (2017: $80m).
[4] Total derivative financial instruments in three to four years reflects receivables of $30m (2017: $994m) and payables of $58m (2017: $971m).
[5] Total derivative financial instruments in four to five years reflects receivables of $30m (2017: $34m) and payables of $58m (2017: $59m).
[6] Total derivative financial instruments in more than five years reflects receivables of $2.084bn (2017: $2.198bn) and payables of $2.153bn (2017: $2.217bn).

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.

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 $5,106m of contingent consideration and $1,838m arising from the put option over the non-controlling interest in Acerta Pharma, both held within Other payables (see Note 19).

Market risk

Interest rate risk

The Group maintains a mix of fixed and floating rate debt. The portion of fixed rate debt was approved by the Board and any variation requires Board approval.

A significant portion of the long-term debt is held at fixed rates of interest. The Group uses interest rate swaps and forward rate agreements to manage this mix. During the year, the Group issued $1.25bn of bonds maturing in 2023, $1.0bn in 2029 and $0.75bn in 2048. These were to refinance the $1.4bn of bonds maturing in 2018 and for general corporate purposes.

At 31 December 2018, the Group held interest rate swaps with a notional value of $0.29bn, converting the 7% guaranteed debentures payable in 2023 to floating rates. No new interest rate swaps were entered into during 2018. At 31 December 2018, swaps with a notional value of $0.29bn related to debt designated as fair value through profit or loss. 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 157.

The majority of surplus cash is currently invested in US dollar liquidity funds, fully collateralised repurchase arrangements and investment grade fixed income securities.

The interest rate profile of the Group's interest-bearing financial instruments, as at 31 December 2018, 31 December 2017 and 31 December 2016, is 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.

	2018			2017			2016		
	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	**999**	**755**	**1,754**	404	1,843	2,247	1,086	1,221	2,307
Non-current	**16,038**	**1,321**	**17,359**	14,608	952	15,560	13,154	1,347	14,501
Total	**17,037**	**2,076**	**19,113**	15,012	2,795	17,807	14,240	2,568	16,808
Financial assets									
Fixed deposits	**40**	**–**	**40**	–	80	80	–	37	37
Cash and cash equivalents	**–**	**4,831**	**4,831**	–	3,324	3,324	–	5,018	5,018
Total	**40**	**4,831**	**4,871**	–	3,404	3,404	–	5,055	5,055

In addition to the financial assets above, there are $6,195m (2017: $6,366m; 2016: $5,519m) of other current and non-current asset investments and other financial assets on which no interest is received.

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 67% of Group external sales in 2018 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 2018, before impact of derivatives, 2.4% of interest-bearing loans and borrowings were denominated in pounds sterling and 18.3% 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 hyper inflationary. As at 31 December 2018, the Group operates in two countries designated as hyper inflationary being Argentina and Venezuela.

The foreign exchange risk to the Group from Argentina is immaterial.

At the start of 2018 Venezuela operated a two tier exchange rate system with a heavily subsidised DIPRO rate for essential goods and services and a second rate, DICOM, to cover all other non-essentials. During 2017 the Group had begun to use the DICOM rate for the consolidation of its financial statements, believing that this was the best expectation of the rate at which profits would be remitted. As a result of this the Group was unaffected by the elimination of the DIPRO rate in early 2018. The foreign exchange risk to the Group from Venezuela is 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, are hedged, where practicable, using forward foreign exchange contracts against individual Group companies' reporting currency. 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.

Sensitivity analysis

The sensitivity analysis set out overleaf 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.

27 Financial risk management objectives and policies *continued*

The sensitivity analysis assumes an instantaneous 100 basis point change in interest rates in all currencies from their levels at 31 December 2018, with all other variables held constant. Based on the composition of our long-term debt portfolio as at 31 December 2018, a 1% increase in interest rates would result in an additional $17m in interest expense being incurred per year. The exchange rate sensitivity analysis assumes an instantaneous 10% change in foreign currency exchange rates from their levels at 31 December 2018, 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 2016	+1%	–1%	+10%	–10%
Increase/(decrease) in fair value of financial instruments ($m)	1,249	(1,390)	180	(180)
Impact on profit: (loss)/gain ($m)	–	–	(24)	24
Impact on equity: gain/(loss) ($m)	–	–	204	(204)

	Interest rates		Exchange rates	
31 December 2017	+1%	–1%	+10%	–10%
Increase/(decrease) in fair value of financial instruments ($m)	1,329	(1,293)	198	(198)
Impact on profit: (loss)/gain ($m)	–	–	(123)	123
Impact on equity: gain/(loss) ($m)	–	–	321	(321)

	Interest rates		Exchange rates	
31 December 2018	**+1%**	**–1%**	+10%	–10%
Increase/(decrease) in fair value of financial instruments ($m)	**1,130**	**(1,267)**	**(146)**	**161**
Impact on profit: (loss)/gain ($m)	**–**	**–**	**(299)**	**348**
Impact on equity: gain/(loss) ($m)	**–**	**–**	**153**	**(187)**

In 2018 the Group changed the method for assessing a 10% change in foreign currency exchange rates. In 2017 and 2016 the sensitivity was calculated as 10% of year end exposure. The sensitivity is now calculated by dividing the non-USD balances by adjusted foreign rates. This does not have a material impact on results but has resulted in the weakening and strengthening values no longer being symmetrical. There have been no other changes in the methods and assumptions used in preparing the sensitivity analysis.

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 Group records 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 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 2018 were as follows:

Current assets

	2018 $m	2017 $m	2016 $m
Cash at bank and in hand	**893**	784	782
Money market liquidity fund	**3,435**	1,150	3,440
Collateralised repurchase agreement	**400**	1,150	950
Bank collateral[1]	**–**	–	(242)
Other short-term cash equivalents	**103**	240	88
Total Cash and cash equivalents (Note 16)	**4,831**	3,324	5,018
Fixed income securities at fair value through profit and loss (Note 11)	**809**	–	–
Fixed income securities available for sale (Note 11)	**–**	1,150	847
Fixed deposits (Note 11)	**40**	80	37
Total derivative financial instruments (Note 12)	**258**	28	27
Current assets subject to credit risk	**5,938**	4,582	5,929

[1] In 2017 the Group changed its accounting policy such that collateral receipts were included in interest bearing loans and borrowings.

Non-current assets

	2018 $m	2017 $m	2016 $m
Equity securities at fair value through other comprehensive income (Note 11)	**833**	–	–
Equity securities available for sale (Note 11)	**–**	933	727
Derivative financial instruments (Note 12)	**157**	504	343
Non-current assets subject to credit risk	**990**	1,437	1,070

The Group may hold significant cash balances as part of its normal operations, with the amount of cash held at any point reflecting the level of cash flow generated by the business and the timing of the use of that cash. The majority of excess cash is centralised within the Group treasury entity and is subject to counterparty risk on the principal invested. This 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 majority of the Group's cash is invested in US dollar AAA-rated liquidity funds, fully collateralised repurchase agreements and short-term bank deposits.

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 are fully collateralised investments. The collateral is fixed income in nature and is held by a third party custodian and represents approximately 101% of the value of the cash deposited. The minimum long term credit rating of the collateral is BBB minus. In the event of any default, ownership of the collateral would revert to the Group, and would be readily convertible to cash. The value of the collateral held at 31 December 2018 was $403m (2017: $1,151m; 2016: $951m).

The fixed income securities are managed by four external third-party fund managers. The long term rating of these securities was BBB minus 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 2018 was $384m (2017: $513m; 2016: $322m) and the carrying value of each cash collateral posted by the Group at 31 December 2018 was $14m (2017: $nil; 2016: $80m).

The impairment provision for other financial assets at 31 December 2018 was immaterial.

Equity securities represent non-controlling investments in third-party pharmaceutical companies.

Trade and other 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. Following the adoption of IFRS 9 on 1 January 2018 the Group introduced the expected credit loss approach to establish an allowance for impairment that represents its estimate of expected losses in respect of Trade and other receivables. Given the general quality and short-term nature of our trade receivables, there was no material impact assessed arising from the introduction of this method.

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 2018 or 1 January 2018 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.

On that basis, the loss allowance as at 31 December 2018 and 1 January 2018 was determined as follows:

31 December 2018	Current	0-90 days past due	90-180 days past due	Over 180 days past due	Total
Expected loss rate	0.05%	0.75%	10%	47%	
Gross carrying amount	2,854	82	27	70	3,033
Loss allowance	1	1	3	33	38

1 January 2018	Current	0-90 days past due	90-180 days past due	Over 180 days past due	Total
Expected loss rate	0.05%	0.75%	5%	33%	
Gross carrying amount	2,490	262	31	35	2,818
Loss allowance	1	2	1	12	16

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 88% of US sales (2017: three wholesalers accounted for approximately 60%; 2016: three wholesalers accounted for approximately 83%).

27 Financial risk management objectives and policies *continued*

The ageing of trade receivables at the reporting date was:

	2018 $m	2017 $m	2016 $m
Not past due	**2,853**	2,488	2,559
Past due 0–90 days	**81**	260	14
Past due 90–180 days	**24**	31	–
Past due > 180 days	**37**	23	10
	2,995	2,802	2,583

	2018 $m	2017 $m	2016 $m
Movements in provisions for trade receivables			
At 1 January	**16**	42	52
Income statement	**22**	(26)	–
Amounts utilised, exchange and other movements	**–**	–	(10)
At 31 December	**38**	16	42

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 Selling, general and administrative costs.

28 Employee costs and share plans for employees

Employee costs

The 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.

	2018	2017	2016
Employees			
UK	**7,200**	6,900	7,000
Continental Europe	**14,800**	14,500	14,700
The Americas	**16,700**	16,300	17,800
Asia, Africa & Australasia	**24,500**	22,300	22,000
Continuing operations	**63,200**	60,000	61,500

Geographical distribution described in the table above is by location of legal entity employing staff. Certain staff will spend some or all of their activity in a different location.

The number of people employed by the Group at the end of 2018 was 64,400 (2017: 61,100; 2016: 59,700).

The costs incurred during the year in respect of these employees were:

	2018 $m	2017 $m	2016 $m
Salaries	**5,370**	5,004	4,664
Social security costs	**626**	570	584
Pension costs	**469**	378	426
Other employment costs	**505**	534	610
Total	**6,970**	6,486	6,284

Severance costs of $94m are not included above (2017: $225m; 2016: $578m).

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. 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 123 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 $219m (2017: $220m; 2016: $241m). 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 £1,800 over a 12-month accumulation period and purchase Partnership Shares in the Company with the total proceeds at the end of the period. The purchase price for the shares is the lower of the price at the beginning or the end of the 12-month period. 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 (PSP)
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 2018, 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. The main grant of awards in 2018 under the plan took place in March with further grants in May and August.

	Shares '000	WAFV[1] pence	WAFV[1] $
Shares awarded in March 2016	2,673	1962	28.19
Shares awarded in May 2016	24	1935	28.64
Shares awarded in August 2016	67	2536	33.58
Shares awarded in March 2017	2,359	2440	30.88
Shares awarded in May 2017	10	2607	34.20
Shares awarded in August 2017	44	2234	29.11
Shares awarded in March 2018	3,400	2427	34.62
Shares awarded in May 2018	18	2651	36.42
Shares awarded in August 2018	92	2982	38.46

[1] Weighted average fair value.

The AstraZeneca Investment Plan (AZIP)
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 between three and eight years.

	Shares '000	WAFV pence	WAFV $
Shares awarded in March 2016	84	3923	56.38

The AstraZeneca Global Restricted Stock Plan
This plan was introduced in 2010. The main grant of awards in 2018 under the plan was in March, with further, smaller grants in May, August and November. 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.

	Shares '000	WAFV pence	WAFV $
Shares awarded in March 2016	2,695	3923	56.38
Shares awarded in August 2016	122	5071	67.16
Shares awarded in March 2017	2,502	4880	61.76
Shares awarded in May 2017	78	5214	68.40
Shares awarded in August 2017	31	4468	58.22
Shares awarded in November 2017	77	4942	66.24
Shares awarded in March 2018	4,474	4853	69.24
Shares awarded in August 2018	40	5964	76.92
Shares awarded in November 2018	3	6300	82.86

28 Employee costs and share plans for employees *continued*

The AstraZeneca Restricted Share Plan

This plan was introduced in 2008 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 2018 to make awards to 252 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.

	Shares '000	WAFV pence	WAFV $
Shares awarded in March 2016	809	3923	56.38
Shares awarded in May 2016	335	3869	57.28
Shares awarded in August 2016	37	5071	67.16
Shares awarded in November 2016	14	4233	53.42
Shares awarded in February 2017	205	4293	55.50
Shares awarded in March 2017	134	4880	61.76
Shares awarded in May 2017	8	5214	68.40
Shares awarded in August 2017	26	4468	58.22
Shares awarded in September 2017	31	4765	65.60
Shares awarded in November 2017	23	4942	66.24
Shares awarded in March 2018	148	4853	69.24
Shares awarded in May 2018	45	5301	72.84
Shares awarded in August 2018	37	5964	76.92
Shares awarded in November 2018	38	6300	82.86

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.

	Shares '000	WAFV pence	WAFV $
Shares awarded in March 2018	163	4853	69.24
Shares awarded in August 2018	116	5964	76.92
Shares awarded in November 2018	24	6300	82.86

The fair values were determined using a modified version of the Monte Carlo model. This method incorporated expected dividends but no other features into the measurements of fair value. The grant date fair values of share awards disclosed in this section do not take account of service and non-market related performance conditions.

29 Commitments and contingent liabilities

Commitments	**2018 $m**	2017 $m	2016 $m
Contracts placed for future capital expenditure on Property, plant and equipment and software development costs not provided for in these accounts	**586**	570	629

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 intangible assets 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	**6,881**	**425**	**966**	**1,395**	**4,095**
Future potential revenue milestone payments	**6,011**	**68**	**718**	**271**	**4,954**

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 (eg 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 2018.

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 220, 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 2016, 2017 or 2018.

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 approximately 13 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.

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 nearing completion. 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 2018 in the aggregate of $97m (2017: $59m; 2016: $59m), 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: (1) the nature and extent of claims that may be asserted in the future; (2) whether AstraZeneca has or will have any legal obligation with respect to asserted or unasserted claims; (3) the type of remedial action, if any, that may be selected at sites where the remedy is presently not known; (4) the potential for recoveries from or allocation of liability to third parties; and (5) the length of time that the environmental investigation, remediation and liability allocation process can take. As per our accounting policy on page 158, 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 $71m and $118m (2017: $87m and $144m; 2016: $85m and $141m), 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/or 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 an estimate of the amount of any loss is difficult to ascertain. Consequently, for a majority of these claims, it is not possible to make a reasonable estimate of the expected financial effect, if any, that will result from ultimate resolution of the proceedings. In these cases, AstraZeneca discloses information with respect to the nature and facts of the cases.

With respect to each of the legal proceedings described below, other than those for which provision has been made, we are unable to make estimates of the possible loss or range of possible losses at this stage, other than as set forth in this section. We also do not believe that disclosure of the amount sought by plaintiffs, if known, would be meaningful with respect to those legal proceedings. This is due to a number of factors, including (1) the stage of the proceedings (in many cases trial dates have not been set) and the overall length and extent of pre-trial discovery; (2) the entitlement of the parties to an action to appeal a decision; (3) clarity as to theories of liability, damages and governing law; (4) uncertainties in timing of litigation; and (5) 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 29, 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. 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.

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 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 2018, 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

Brilinta (ticagrelor)

US patent proceedings

In 2015 and subsequently, 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 (the District Court) relating to patents listed in the FDA Orange Book with reference to *Brilinta*. In 2018, AstraZeneca entered into several separate settlements and the District Court entered consent judgments to dismiss several of the litigations. Additional proceedings are ongoing in the District Court. No trial date has been set.

Patent proceedings outside the US

In Canada, in June 2017, Teva Canada Limited (Teva) challenged the patents listed on the Canadian Patent Register with reference to *Brilinta*. In September 2017, Apotex Inc. (Apotex) did the same. AstraZeneca discontinued the proceeding against Teva in June 2018 after Teva withdrew its challenge. The hearing in the Apotex matter is scheduled for May 2019. In October 2018, Taro Pharmaceuticals Inc. (Taro) also challenged the patents. AstraZeneca commenced an infringement action against Taro in November 2018.

In China, in October 2017, the Chinese Patent Office issued a decision invalidating one of AstraZeneca's Chinese substance patents relating to *Brilinta*. AstraZeneca appealed and, in December 2018, the Beijing High People's Court vacated the invalidation decision and remanded the case back to the Chinese Patent Office for further processing in view of the Court's decision. The patent, Chinese Patent No. ZL99815926.3, is due to expire in December 2019.

Calquence (acalabrutinib)

US patent proceedings

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

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

Crestor (rosuvastatin calcium)

Patent proceedings outside the US

In Australia, AstraZeneca had taken a provision in respect of damages claims from generic entities and the Commonwealth of Australia in relation to alleged losses suffered in connection with AstraZeneca's enforcement of *Crestor* patents which were subsequently found invalid. In February 2018, AstraZeneca settled the claim from Apotex Pty Ltd (and other related Apotex entities) which was the last generic claim outstanding with respect to this matter. In May 2018, AstraZeneca settled the claim from the Commonwealth of Australia and, as a result, all of the claims related to this matter have now been resolved and the matter is now closed.

In France, patent infringement proceedings are now resolved against Biogaran S.A.S. in relation to the *Crestor* substance patent (European Patent No. EP 0,521,471).

In Japan, patent invalidity proceedings are now resolved against Nippon Chemiphar Co. Ltd (Nippon) in relation to the *Crestor* substance patent (Japanese Patent No. JP 2648897). The patent was found valid by the Japanese Patent Office in 2016 and an appeal from Nippon has been dismissed.

In the Netherlands, in 2016, Resolution Chemicals Ltd. (Resolution) appealed a lower court's decision that Resolution's rosuvastatin zinc product infringed the supplementary protection certificate related to AstraZeneca's European Patent No. EP 0,521,471 to the Supreme Court of the Netherlands (the Supreme Court). In 2018, the Supreme Court dismissed Resolution's appeal and upheld Resolution's product as infringing AstraZeneca's patent rights in the Netherlands. The matter is now closed.

In Spain, in 2017, AstraZeneca initiated patent infringement proceedings against ratiopharm España, S.A. (ratiopharm) in reference to ratiopharm's rosuvastatin zinc product. In 2018, AstraZeneca settled the proceedings against ratiopharm and the matter is now closed.

Daliresp (roflumilast)

US patent proceedings

In 2015 and subsequently, in response to Paragraph IV notices from multiple 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 2018, AstraZeneca entered into several separate settlements and the District Court entered consent judgments to dismiss several of the litigations. Additional proceedings are ongoing in the District Court. No trial date has been set.

Farxiga (dapagliflozin)

US patent proceedings

In May 2018, AstraZeneca initiated ANDA litigation against Zydus Pharmaceuticals (USA) Inc. (Zydus) in the US District Court for the District of Delaware. In its complaint, AstraZeneca alleged that Zydus' generic version of *Farxiga*, if approved and marketed, would infringe AstraZeneca's US Patents Nos. 6,414,126 and 6,515,117. In June 2018, Zydus filed its answer and counterclaims for non-infringement of AstraZeneca's US Patent Nos. 7,851,502; 7,919,598; 8,221,786; 8,361,972; 8,501,698; 8,685,934; and 8,716,251. Trial is scheduled for February 2021.

Faslodex (fulvestrant)

US patent proceedings

AstraZeneca has filed patent infringement lawsuits in the US District Court for the District of New Jersey (the District Court) relating to four patents listed in the FDA Orange Book with reference to *Faslodex* after receiving a number of Paragraph IV notices relating to multiple ANDAs or NDAs submitted pursuant to 21 U.S.C. § 355(b)(2) seeking FDA approval to market generic versions of *Faslodex* prior to the expiration of AstraZeneca's patents. In July 2016, AstraZeneca settled one of these, the lawsuit brought against Sandoz, Inc (Sandoz), and the District Court entered a consent judgment, which included an injunction preventing Sandoz from launching a generic fulvestrant product until March 2019, or earlier in certain circumstances. Between 2016 and 2018, AstraZeneca resolved all of the remaining lawsuits, and the District Court also entered consent judgments ending those lawsuits. In December 2018, AstraZeneca filed a new patent infringement lawsuit in the District Court relating to all four listed-patents after receiving a new Paragraph IV notice relating to an ANDA seeking FDA approval to market generic versions of *Faslodex* prior to the expiration of AstraZeneca's patents.

Patent proceedings outside the US

In France, in June 2018, the Commercial Court of Nanterre denied AstraZeneca's request for a preliminary injunction against Sandoz SAS (Sandoz) to prevent a potential launch of its generic *Faslodex* in France. Additionally, in June 2018, Sandoz served AstraZeneca with an invalidation writ against European Patent Nos. EP 2,266,573; EP 1,250,138; and EP 1,272,195.

In Italy, in February 2015, Actavis Group Ptc ehf and Actavis Italy S.p.A. filed an action alleging that AstraZeneca's European Patent No. EP 1,250,138 (the '138 patent) was invalid. In July 2018, the Court of Turin determined that the '138 patent is invalid.

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

Imfinzi (durvalumab)

US patent proceedings

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

Losec/Prilosec (omeprazole)

Patent proceedings outside the US

In Canada, in 2004, AstraZeneca brought proceedings against Apotex Inc. (Apotex) for infringement of several patents related to *Losec*. In February 2015, the Federal Court of Canada (the Federal Court) found that Apotex had infringed the *Losec* formulation patent (Canadian Patent No. 1,292,693). In July 2017, after a reference to account for Apotex's profits earned as a result of the infringement, the Federal Court issued its decision describing how the quantification of monies owed to AstraZeneca should proceed. Apotex appealed. In February 2018, AstraZeneca and Apotex entered into a settlement agreement under which Apotex agreed to pay AstraZeneca CAD 435m ($352m), concluding all *Losec* patent litigation in Canada.

Movantik (naloxegol)

US patent proceedings

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

Nexium (esomeprazole magnesium)

Patent proceedings outside the US

In Canada, in July 2014, the Federal Court of Canada found the *Nexium* substance patent (Canadian Patent No. 2,139,653 (the '653 patent)) invalid and not infringed by Apotex Inc. (Apotex). In July 2015, AstraZeneca's appeal was dismissed. AstraZeneca was granted leave to appeal to the Supreme Court of Canada (the Supreme Court). In June 2017, the Supreme Court granted AstraZeneca's appeal and found the '653 patent valid. Apotex appealed the Supreme Court's decision. AstraZeneca commenced proceedings to collect damages. In June 2018, the parties settled all outstanding proceedings. The matter is now closed.

Onglyza (saxagliptin) and *Kombiglyze* (saxagliptin and metformin)

US patent proceedings

In February 2017, the US District Court for the District of Delaware (the District Court) issued a decision upholding the validity of US Patent No. RE44,186 (the '186 patent), listed in the FDA Orange Book with reference to *Onglyza* and/or *Kombiglyze* XR. In August 2017, the US Patent and Trademark Office (USPTO) issued a decision in an inter partes review upholding the challenged claims of the '186 patent. Mylan Pharmaceuticals Inc. (Mylan) appealed the District Court's decision and the USPTO's decision to the US Court of Appeals for the Federal Circuit. In May 2018, AstraZeneca and Mylan settled these two appeals. The matter is now closed.

Pulmicort Respules (budesonide inhalation suspension)

US patent proceedings

In February 2015, the US District Court for the District of New Jersey (the District Court) determined that the asserted claims of US Patent No. 7,524,834, which covered *Pulmicort Respules*, were invalid following challenges brought by Apotex, Inc. and Apotex Corp., Breath Limited, Sandoz, Inc. and Watson Laboratories, Inc. (together, the Generic Challengers). In May 2015, the US Court of Appeals for the Federal Circuit affirmed the District Court's decision. Since 2009, various injunctions were issued in this matter. Damages claims based on those injunctions were filed by the Generic Challengers. In June 2018, AstraZeneca and the Generic Challengers settled these claims. The matter is now closed.

Roxadustat

Patent proceedings outside the US

In Canada, in May 2018, Akebia Therapeutics, Inc. (Akebia) filed an impeachment action in the Federal Court alleging invalidity of several of FibroGen, Inc.'s (FibroGen) method of use patents (Canadian Patent Nos. 2467689; 2468083; and 2526496) related to HIF prolyl hydroxylase inhibitors. AstraZeneca is the exclusive licensee of FibroGen in Canada. AstraZeneca and FibroGen are defending the action.

Symbicort (budesonide/formoterol fumarate dihydrate)

US patent proceedings

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

In November 2018, AstraZeneca filed an amended complaint in the Teva action to add Catalent Pharma Solutions LLC (Catalent) as a party. In December 2018, Teva and Catalent responded to the amended complaint and alleged that their proposed generic product does not infringe the asserted patents and/or that the asserted patents are invalid and/or unenforceable. Teva also asserted counterclaims in which it alleged that the proposed generic product does not infringe five additional patents that AstraZeneca did not assert in its complaint, namely US Patents Nos. 7,587,988; 8,528,545; 8,387,615; 8,616,196; and 8,875,699.

In December 2018, AstraZeneca filed an amended complaint in the Mylan Delaware action to add 3M Company as a party. In January 2019, in the Mylan Delaware action, Mylan Laboratories Limited, Mylan Inc., and Mylan N.V. filed a motion to dismiss for failure to state a claim and MPI filed a motion to dismiss for improper venue.

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

Product liability litigation

Byetta/Bydureon (exenatide)

In the US, Amylin Pharmaceuticals, LLC, a wholly-owned subsidiary of AstraZeneca, and/or 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 pancreatitis, pancreatic cancer, thyroid cancer, and kidney 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 co-ordinated proceeding has been established in Los Angeles, California in regard to the various lawsuits in California state courts.

In November 2015, the District Court granted the defendants' motion for summary judgment and dismissed all claims alleging pancreatic cancer that accrued prior to 11 September 2015. In November 2017, the US Court of Appeals for the Ninth Circuit vacated the District Court's order and remanded for further discovery. In November 2018, the Court of Appeal for the State of California annulled the judgment from the California state co-ordinated proceeding and remanded for further discovery.

Farxiga (dapagliflozin) and *Xigduo* (dapagliflozin/metformin HCl)

In the US, AstraZeneca has been named as a defendant in lawsuits involving plaintiffs claiming physical injury, including diabetic ketoacidosis and kidney injury/failure, from treatment with *Farxiga* and/or *Xigduo* XR. In April 2017, the Judicial Panel on Multidistrict Litigation ordered transfer of any currently pending cases as well as any similar, subsequently filed cases to a co-ordinated and consolidated pre-trial multidistrict litigation proceeding in the US District Court for the Southern District of New York.

Nexium (esomeprazole magnesium) and *Losec/Prilosec* (omeprazole)

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,

including *Nexium* and *Prilosec*. 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 co-ordinated 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.

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

Onglyza (saxagliptin) and
Kombiglyze (saxagliptin and metformin)
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 Eastern District of Kentucky (the District) for consolidated pre-trial proceedings with the federal actions pending in the District. The previously disclosed California state court co-ordinated proceeding remains pending in California.

Seroquel (quetiapine fumarate)
In the US, in June 2018, AstraZeneca was named in a lawsuit filed in Illinois involving one plaintiff alleging Brugada Syndrome from treatment with *Seroquel*. In September 2018, the US District Court for the Southern District of Illinois entered judgment in favour of AstraZeneca and terminated AstraZeneca as a party to the action.

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

Commercial litigation

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.

Array BioPharma
In the US, in December 2017, AstraZeneca was served with a complaint filed in New York State court by Array BioPharma, Inc. (Array) that alleged, among other things, breaches of contractual obligations relating to a 2003 collaboration agreement between AstraZeneca and Array.

Nexium settlement anti-trust litigation
In the US, AstraZeneca was a defendant in a multidistrict litigation class action and individual lawsuit alleging that AstraZeneca's settlements of certain patent litigation in the US relating to *Nexium* violated US anti-trust law and various state laws. A trial in the US District Court for the District of Massachusetts returned a verdict in favour of AstraZeneca, and the federal appeals for this verdict were subsequently concluded. Two lawsuits with similar allegations were filed in Pennsylvania state court by various indirect purchasers of *Nexium*. These cases had been stayed pending the outcome of the federal court litigation, but AstraZeneca was informed in June 2018 that both matters were administratively closed by the state court. This matter is accordingly concluded.

Ocimum lawsuit
In the US, in December 2015, AstraZeneca was served with a complaint filed by Ocimum Biosciences, Ltd. (Ocimum) in the Superior Court for the State of Delaware that alleges, 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.

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

Other commercial litigation
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 by US nationals (or their estates, survivors, or heirs) who were killed or wounded in Iraq between 2005 and 2011. 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.

Telephone Consumer Protection Act litigation
In the US, in December 2016, AstraZeneca and several other entities were served with a complaint filed in the US District Court for the Southern District of Florida that alleges, among other things, violations of the Telephone Consumer Protection Act caused by the sending of unsolicited advertisements by facsimile. This matter has been dismissed.

Government investigations/proceedings

Iraq Ministry of Health Anti-Corruption Probe
In July 2018, AstraZeneca, along with other companies, received an inquiry from the DOJ pursuant to the Foreign Corrupt Practices Act in connection with an anti-corruption investigation relating to activities in Iraq, including interactions with the Iraqi government. AstraZeneca is cooperating with the inquiry.

Crestor (rosuvastatin calcium)
Qui tam litigation
In the US, in January and February 2014, AstraZeneca was served with lawsuits filed in the US District Court for the District of Delaware under the *qui tam* (whistleblower) provisions of the federal False Claims Act and related state statutes, alleging that AstraZeneca directed certain employees to promote *Crestor* off-label and provided unlawful remuneration to physicians in connection with the promotion of *Crestor*. The DOJ and all US states have declined to intervene in the lawsuits. This litigation is ongoing.

Texas Attorney General litigation
In the US, in January 2015, AstraZeneca was served with a lawsuit in which the Texas Attorney General's office intervened in a state whistleblower action pending in Travis County Court, Texas. The lawsuit alleged that AstraZeneca engaged in inappropriate promotion of *Crestor* and improperly influenced the formulary status of *Crestor*. In July 2018, this matter was resolved and is now concluded.

Seroquel IR (quetiapine fumarate) and
Seroquel XR (quetiapine fumarate)
Qui tam litigation in New York
In the US, in September 2015, AstraZeneca was served with a lawsuit filed in US Federal Court in New York under the *qui tam* (whistleblower) provisions of the federal and certain state False Claims Acts. The lawsuit alleges that AstraZeneca misrepresented the safety profile of, and improperly promoted, *Seroquel*. In July 2018, this matter was resolved and is now concluded.

Qui tam litigation in Delaware
In the US, in April 2014, AstraZeneca was served with lawsuits filed in the US District Court for the District of Delaware under the *qui tam* (whistleblower) provisions of the federal False Claims Act and related state statutes, alleging that AstraZeneca directed certain employees to promote *Seroquel* off-label and provided unlawful remuneration to physicians in connection with the promotion of *Seroquel*. In July 2018, this matter was resolved and is now concluded.

Texas Attorney General litigation
In the US, in October 2014, the Texas Attorney General's Office intervened in a state whistleblower action pending in Travis County Court, Texas. The lawsuit alleged that

AstraZeneca engaged in inappropriate promotion and made improper payments intended to influence the formulary status of *Seroquel*. In July 2018, this matter was resolved and is now concluded.

Synagis (palivizumab)

Litigation in New York

In the US, in June 2011, MedImmune received a demand from the US Attorney's Office for the Southern District of New York requesting certain documents related to the sales and marketing activities of *Synagis*. In July 2011, MedImmune received a similar court order to produce documents from the Office of the Attorney General for the State of New York Medicaid and Fraud Control Unit pursuant to what the government attorneys advised was a joint investigation. MedImmune has cooperated with these inquiries. In March 2017, MedImmune was served with a lawsuit filed in US Federal Court in New York by the Attorney General for the State of New York alleging that MedImmune inappropriately provided assistance to a single specialty care pharmacy. In September 2018, the US Federal Court in New York denied MedImmune's motion to dismiss the lawsuit brought by the Attorney General for the State of New York.

In June 2017, MedImmune was served with a lawsuit in US Federal Court in New York by a relator under the *qui tam* (whistleblower) provisions of the federal and certain state False Claims Acts. The lawsuit was originally filed under seal in April 2009 and alleges that MedImmune made false claims about *Synagis*. In November 2017, MedImmune was served with an amended complaint in which relator set forth additional false claims allegations relating to *Synagis*. In September 2018, the US Federal Court in New York dismissed the relator's lawsuit.

Florida Attorney General investigation

In May 2012, MedImmune received a *subpoena duces tecum* from the Office of Attorney General for the State of Florida Medicaid and Fraud Control Unit requesting certain documents related to the sales and marketing activities of *Synagis*. MedImmune accepted receipt of the request and has co-ordinated with the Florida government to provide the appropriate responses and cooperate with any related investigation. AstraZeneca is unaware of the nature or focus of the investigation, however, based on the requests, it appears to be similar to the inquiry from the State of New York (which is described above).

Toprol-XL (metoprolol succinate)

Louisiana Attorney General litigation

In the US, in March 2015, AstraZeneca was served with a state court complaint filed by the Attorney General for the State of Louisiana (the State) alleging that, in connection with enforcement of its patents for *Toprol-XL*, it had engaged in unlawful monopolisation and unfair trade practices, causing the State government to pay increased prices for *Toprol-XL*. In February 2016, a Louisiana state court (the Trial Court) granted AstraZeneca's motion to dismiss the lawsuit, but the State appealed and, in April 2018, the Louisiana Court of Appeals for the First Circuit (the Appellate Court) reversed the dismissal and remanded the case back to the Trial Court for further proceedings. In May 2018, AstraZeneca filed a writ with the Louisiana Supreme Court seeking review of the Appellate Court's decision. In September 2018, the Louisiana Supreme Court denied that writ and declined to review the Appellate Court's decision.

Multi-product litigation

Litigation in Washington State

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

Other government investigations/proceedings

US Congressional Inquiry

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

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

Where tax exposures can be quantified, an accrual is made based on best estimates and management's judgement. Details of the movements in relation to material tax exposures are discussed below. As 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.

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 estimates and judgements with respect to the ultimate outcome of a tax audit, 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 $212m, a decrease of $23m compared with 2017 mainly due to a reduction in accruals for transfer pricing contingencies as a result of the conclusion of tax authority review.

Management continues to believe that AstraZeneca's positions on all its transfer pricing audits and disputes are robust, and that AstraZeneca is appropriately provided, including the assessment where corresponding relief will be available. For transfer pricing audits where AstraZeneca and the tax authorities are in dispute, AstraZeneca estimates the potential for reasonably possible additional losses above and beyond the amount provided to be up to $357m (2017: $30m; 2016: $184m) including associated interest. However, management believes that it is unlikely that these additional losses will arise. It is possible that some of these contingencies may reduce in the future to the extent that any tax authority challenge is unsuccessful, or matters lapse following expiry of the relevant statutes of limitation resulting in a reduction in the tax charge in future periods.

Other tax contingencies

Included in the tax accrual is $730m relating to a number of other tax contingencies, a decrease of $201m mainly due to releases following expiry of statute of limitations and on conclusion of tax authority review, exchange rate effects, partially offset by the impact of an additional year of transactions relating to contingencies for which accruals had already been established. For these tax exposures, AstraZeneca estimates the potential for reasonably possible additional losses above and beyond the amount provided to be up to $253m (2017: $nil; 2016: $nil) including associated interest. It is, however, possible that some of these contingencies may reduce in the future if any tax authority challenge is unsuccessful or matters lapse following expiry of the relevant statutes of limitation resulting in a reduction in the tax charge in future periods.

In addition to the above tax exposures, the European Commission (EC) announced in 2017 that it had opened a State aid investigation into the UK's Controlled Foreign Company (CFC) Group Financing Exemption. The EC's decision is anticipated in 2019 although any decision would be subject to appeal.

Timing of cash flows and interest

It is not possible to estimate the timing of tax cash flows in relation to each outcome. However, it is anticipated that a number of significant disputes may be resolved over the next one to two years.

Included within Trade and other payables is an amount of interest arising on tax contingencies of $116m.

30 Operating leases

Total rentals under operating leases charged to profit were as follows:

	2018 $m	2017 $m	2016 $m
Operating leases	**188**	175	174

The Group has revised the presentation of operating leases from 2017 to include operating leases that have been identified during the transition to IFRS 16 as having previously been omitted from this disclosure. This resulted in an increase in 2017 from $137m to $175m.

The future minimum lease payments under operating leases that have initial or remaining terms in excess of one year at 31 December 2018 were as follows:

	2018 $m	2017 $m	2016 $m
Obligations under leases comprise:			
Not later than one year	**188**	151	98
Later than one year and not later than five years	**360**	345	247
Later than five years	**136**	118	96
Total future minimum lease payments	**684**	614	441

The Group has revised the presentation of operating leases from 2017 to include operating leases that have been identified during the transition to IFRS 16 as having previously been omitted from this disclosure. This resulted in an increase in 2017 from $523m to $614m.

31 Statutory and other information

	2018 $m	2017 $m	2016 $m
Fees payable to PricewaterhouseCoopers LLP and its associates:			
Group audit fee	**3.8**	3.0	–
Fees payable to PricewaterhouseCoopers LLP and its associates for other services:			
The audit of subsidiaries pursuant to legislation	**9.4**	5.7	–
Attestation under s404 of Sarbanes-Oxley Act 2002	**2.0**	2.0	–
Audit-related assurance services	**0.8**	0.4	–
Tax compliance services	**0.1**	–	–
Other assurance services	**0.9**	–	–
Fees payable to PricewaterhouseCoopers Associates in respect of the Group's pension schemes:			
The audit of subsidiaries' pension schemes	**0.4**	–	–
	17.4	11.1	–

$3.2m of fees payable in 2018 are in respect of the 2017 Group audit and audit of subsidiaries.

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.

	2018 $'000	2017 $'000	2016 $'000
Short-term employee benefits	**32,523**	28,274	23,725
Post-employment benefits	**2,387**	2,469	2,407
Share-based payments	**23,605**	16,452	20,377
	58,515	47,195	46,509

Total remuneration is included within employee costs (see Note 28).

32 Subsequent events

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

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

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

Consideration attributable to the sale of US rights to *Synagis* will be treated as Other operating income and expense in the Group in 2019, net of the derecognition of $893m of the related intangible asset, which has been transferred to assets held for sale at 31 December 2018.

The right to participate in payments from the US profits and losses for MEDI8897 will be treated as a financial liability at amortised cost, recognised initially at fair value. The valuation of this financial liability was not finalised at the date of signing of these Financial Statements. Any difference between the amount of consideration received and the fair value recognised will be recognised within Other operating income and expense in 2019.

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 2018 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 2018.

At 31 December 2018	Group Interest
Wholly owned subsidiaries	
Argentina	
AstraZeneca S.A.	100%
Nicolas de Vedia 3616, Piso 8, Ciudad Autónoma de Buenos Aires, Argentina	
Australia	
AstraZeneca Holdings Pty Limited	100%
AstraZeneca PTY Limited	100%
Pharmaceutical Manufacturing Company Pty Limited	100%
Pharmaceutical Manufacturing Division Pty Limited	100%
66 Talavera Road, Macquarie Park, NSW 2113, Australia	
Austria	
AstraZeneca Österreich GmbH	100%
A-1030 Wien, Landstraßer Hauptstraße 1A, Austria	
Belgium	
AstraZeneca S.A. / N.V.	100%
Alfons Gossetlaan 40 bus 201 at 1702 Groot-Bijgaarden, Belgium	
Brazil	
AstraZeneca do Brasil Limitada	100%
Rod. Raposo Tavares, KM 26, 9, Cotia, 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	
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 New District, China	
AstraZeneca (Wuxi) Trading Co. Ltd	100%
Building E (Building No. 5), Huirong Commercial Plaza, East Jinghui Road, Xinwu District, Wuxi, China	
AstraZeneca Investment (China) Co., Ltd	100%
No. 199 Liangjing Road, China (Shanghai) Pilot Free Trade Zone, Shanghai, China	
AstraZeneca Pharmaceutical (China) Co. Ltd	100%
No. 88 Yaocheng Avenue, Taizhou, Jiangsu Province, China	
AstraZeneca Pharmaceuticals Technologies (Beijing) Co., Ltd	100%
Unit 2203, 22F, No 8, Jianguomenwai Avenue, Chaoyang District, Beijing, China	
Colombia	
AstraZeneca Colombia S.A.S.	100%
Carrera 7 No. 71-21, Torre A, Piso 19, 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	
Denmark	
AstraZeneca A/S	100%
Arne Jacobsens Allé 13, DK-2300, Copenhagen S, Denmark	
Egypt	
AstraZeneca Egypt for Pharmaceutical Industries JSC	100%
Villa 133, Road 90 North, New Cairo, Egypt	
AstraZeneca Egypt for Trading LLC	100%
14C Ahmed Kamel Street, New Maadi, Cairo, Egypt	
Drimex LLC	100%
Villa 47, Road 270, New Maadi, Cairo 11435, 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%
AstraZeneca Finance S.A.S.	100%
AstraZeneca Holding France 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	
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	
Definiens AG[2]	100%
Bernhard-Wicki-Straße 5, 80636, Munich, Germany	
Greece	
AstraZeneca S.A.	100%
Theotokopoulou 4 & Astronafton, Athens, 151 25, Greece	
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	
Iran	
AstraZeneca Pars Company	100%
Suite 1, 1st Floor No. 39, Alvand Ave., Argantin Sq., Tehran 1516673114, Iran	
Ireland	
AstraZeneca Pharmaceuticals (Ireland) Designated Activity Company	100%
4th Floor, South Bank House, Barrow Street, Dublin, 4, Republic of Ireland	
Israel	
AstraZeneca (Israel) Ltd	100%
6 Hacharash St., Hod Hasharon 4524075, Israel	
Italy	
Simesa SpA	100%
AstraZeneca SpA	100%
Palazzo Ferraris, via Ludovico il Moro 6/c 20080, Basiglio (Milan), Italy	
Japan	
AstraZeneca K.K.	100%
3-1, Ofuka-cho, Kita-ku, Osaka, 530-0011, Japan	
Kenya	
AstraZeneca Pharmaceuticals Limited	100%
L.R. No.1/1327, Avenue 5, 1F, Rose Avenue, Nairobi, Kenya	

Group Subsidiaries and Holdings
continued

At 31 December 2018	Group Interest

Latvia

AstraZeneca Latvija SIA	100%
Skanstes iela 50, Riga, LV-1013, Latvia	

Lithuania

AstraZeneca Lietuva UAB	100%
Jasinkio 16A, Vilnius, LT-03163, Lithuania	

Luxembourg

AstraZeneca Luxembourg S.A.	100%
Am Brill 7 B – L-3961 Ehlange – Grand Duchy du Luxembourg, Luxembourg	

Malaysia

AstraZeneca Asia-Pacific Business Services Sdn Bhd	100%
Level 8, Unit 8.01-8.05 Menara UAC, Jalan PJU 7/5, Mutiara Damansara, 47800 Petaling Jaya, Selangor, Malaysia	
AstraZeneca Sdn Bhd	100%
Lot 6.05, Level 6, KPMG Tower, 8 First Avenue, Bandar Utama, 47800 Petaling Jaya, Selangor Darul Ehsan, Malaysia	

Mexico

AstraZeneca, S.A. de C.V.	100%
Av. Periferico Sur 4305 interior 5, Colonia Jardines en la Montana, Mexico City, Tlalpan Distrito Federal, CP 14210, Mexico	
AstraZeneca Health Care Division, S.A. de C.V.	100%
Avenida Lomas Verdes 67 Colonia Lomas Verdes, Naucalpan de Juarez, CP 53120, 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%
Prinses Beatrixlaan 582, 2595BM, The Hague, The Netherlands	
MedImmune Pharma B.V.	100%
Lagelandseweg 78, 6545 CG Nijmegen, 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	

At 31 December 2018	Group Interest

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%
Av. El Derby 055, Torre 2. Piso 5. Of. 503. Santiago de Surco, 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 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	

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%
AstraZeneca Pharmaceuticals, LLC	100%
125284, Begovaya Str, 3, Block 1, Moscow, Russian Federation	

Singapore

AstraZeneca Singapore Pte Limited	100%
10 Kallang Avenue #12-10, Aperia Tower 2, 339510, Singapore	

At 31 December 2018	Group Interest

South Africa

AstraZeneca Pharmaceuticals (Pty) Limited	100%
17 Georgian Crescent West, Northdowns Office Park, Bryanston, 2041, South Africa	

South Korea

AstraZeneca Korea Co. Ltd	100%
17th Floor, Luther Building, 42, Olympic-ro 35da-gil Songpa-gu, Seoul, South Korea	

Spain

AstraZeneca Farmaceutica Spain S.A.	100%
AstraZeneca Farmaceutica Holding Spain, S.A.	100%
Laboratorio Beta, S.A.	100%
Laboratorio Lailan, S.A.	100%
Laboratorio Odin, S.A.	100%
Laboratorio Tau S.A.	100%
Parque Norte, Edificio Álamo, C/Serrano Galvache no 56., 28033 Madrid, 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[6]	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	
Aktiebolaget Hassle	100%
Symbicom Aktiebolag[6]	100%
431 83 Molndal, Sweden	
Astra Tech International Aktiebolag	100%
Box 14, 431 21 Molndal, Sweden	

Switzerland

AstraZeneca AG	100%
Neuhofstrasse 34, 6340 Baar, Switzerland	
Spirogen Sarl[6]	100%
Rue du Grand-Chêne 5, CH-1003 Lausanne, Switzerland	

Taiwan

AstraZeneca Taiwan Limited[7]	100%
21st Floor, Taipei Metro Building 207, Tun Hwa South Road, SEC 2 Taipei, Taiwan, Republic of China	

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 n°1.5.5 les jardins du lac, bloc B les berges du lac Tunis, Tunisia	

At 31 December 2018	Group Interest
Turkey	
AstraZeneca Ilac Sanayi ve Ticaret Limited Sirketi	100%
YKB Plaza, B Blok, Kat:3-4, Levent/Beşiktaş, Istanbul, Turkey	
Zeneca Ilac Sanayi Ve Ticaret Anonim Sirketi	100%
Büyükdere Cad., Y.K.B. Plaza, B Blok, Kat:4, Levent/ Beşiktaş, Istanbul, Turkey	
Ukraine	
AstraZeneca Ukraina LLC	100%
13, Pymonenko Street, building 1, Kiev, 04050, Ukraine	
United Arab Emirates	
AstraZeneca FZ-LLC	100%
P.O. Box 505070, Block D, Dubai Healthcare City, Oud Mehta Road, 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	

At 31 December 2018	Group Interest
United States	
Amylin Pharmaceuticals, LLC[8]	100%
AstraZeneca Collaboration Ventures, LLC[8]	100%
AstraZeneca Pharmaceuticals LP[9]	100%
Atkemix Nine Inc.	100%
Atkemix Ten Inc.	100%
BMS Holdco, Inc.	100%
Corpus Christi Holdings Inc.	100%
Omthera Pharmaceuticals, Inc.	100%
Stauffer Management Company LLC[8]	100%
Zeneca Holdings Inc.	100%
Zeneca Inc.	100%
Zeneca Wilmington 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[8]	100%
333 Parkland Plaza, Suite 5, Ann Arbor, MI 48103, United States	
Amylin Ohio LLC[8]	100%
8814 Trade Port Drive, West Chester, OH 45011, United States	
Ardea Biosciences, Inc.	100%
4939 Directors Place, San Diego, CA 92121, 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 Biologics, Inc.	100%
MedImmune, LLC[8]	100%
MedImmune Ventures, Inc.	100%
One MedImmune Way, Gaithersburg, MD 20878, United States	
Optein, Inc.	100%
2711 Centerville Road, Suite 400, Wilmington, DE 1989, United States	
Pearl Therapeutics, Inc.	100%
200 Cardinal Way, Redwood City, CA 94063, United States	
Uruguay	
AstraZeneca S.A.[7]	100%
Yaguarón 1407 of 1205, 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 2018	Group Interest
Subsidiaries where the effective interest is less than 100%	
Algeria	
SPA AstraZeneca Al Djazair[10]	65.77%
No 20 Zone Macro Economique, dar El Medina-Hydra, Alger, Algeria	
India	
AstraZeneca Pharma India Limited[5]	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	
The Netherlands	
Acerta Pharma B.V.	55%
Aspire Therapeutics B.V.	55%
Kloosterstraat 9, 5349 AB, Oss, The Netherlands	
United States	
Acerta Pharma LLC[8]	55%
121 Oyster Point Boulevard, South San Francisco, CA 94080, United States	
Joint Ventures	
Hong Kong	
WuXi MedImmune Biopharmaceutical Co., Limited	50%
Room 1902, 19/F, Lee Garden One, 33 Hysan Avenue, Causeway Bay, Hong Kong	
United Kingdom	
Archigen Biotech Limited[10]	50%
Centus Biotherapeutics Limited[10]	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	
Significant Holdings	
Australia	
Armaron Bio Ltd[11]	22.07%
MPR Group, HWT Tower, Level 19, 40 City Rd, Southbank, VIC 3006, Australia	
China	
Dizal (Jiangsu) Pharmaceutical Co., Ltd.[12]	48.3%
Suite 4105, Building E (Building No.5) of Huirong Plaza, East Jinghui Road, Xinwu District, Wuxi, Jiangsu Province, China	
United Kingdom	
Apollo Therapeutics LLP[8]	25%
Stevenage Biosciences Catalyst, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2FX, United Kingdom	

Group Subsidiaries and Holdings
continued

At 31 December 2018	Group Interest
United States	
C.C. Global Chemicals Company[9]	37.5%
PO Box 7, MS2901, Texas, TX76101-0007, United States	
Viela Bio, Inc.[13]	40.9%
One MedImmune Way, Fifth Floor, Suite Area Two, Gaithersburg, MD 20878, United States	
Associated Holdings	
Australia	
Adherium Limited	4.64%
Collins Square, Tower Four, Level 18, 727 Collins Street, Melbourne VIC 3008, Australia	
France	
Innate Pharma S.A.	9.8%
117 Avenue de Luminy, 13009 Marseille, France	
Switzerland	
ADC Therapeutics Sàrl[14]	7.23%
Biopôle, Route de la Corniche 3B, 1066 Epalinges, Switzerland	
United Kingdom	
Circassia Pharmaceuticals PLC	19.9%
The Magdalen Centre, Robert Robinson Avenue, Oxford Science Park, Oxford, Oxfordshire, OX4 4GA, United Kingdom	
Datapharm Communications Limited[8,15]	12.5%
Ground Floor, Pascal Place, Randalls Way, Leatherhead, Surrey, KT22 7TW, United Kingdom	
Mereo Biopharma Group PLC	0.69%
4th Floor, One, Cavendish Place, London, W1G 0QF, United Kingdom	
Silence Therapeutics PLC	0.17%
27 Eastcastle Street, London, W1W 8DH, United Kingdom	
United States	
AbMed Corporation[16]	18%
65 Cummings Park Drive, Woburn, MA 01801, United States	
Affinita Biotech, Inc.[17]	16.23%
329 Oyster Point Blvd., 3rd Floor, South San Francisco, CA 94080, United States	
Albireo Pharma, Inc.	4.25%
10 Post Office Square, Suite 502 South, Boston, MA 02109, United States	
Arcutis, Inc.[18]	2.22%
70 Willow Road, Suite 200, Menlo Park, CA 94025, United States	
Aristea Therapeutics, Inc.[19]	15%
16652 Maverick Lane, Poway, CA 92064, United States	
Biodesix Inc.[20]	0.05%
2970 Wilderness Place, Suite 100, Boulder, CO 80301, United States	

At 31 December 2018	Group Interest
Biohaven Pharmaceutical Holding Company Ltd.	0.25%
234 Church Street, New Haven, CT 06510, United States	
BlinkBio, Inc.	0.38%
P.O. Box 1966, Jupiter, FL 33468, United States	
Cerapedics, Inc.[21]	7.09%
11025 Dover St #1600, Broomfield, CO 80021, United States	
Corvidia Corporation[22]	11.98%
35 Gatehouse Drive, Waltham, MA 02451, United States	
Elusys Therapeutics, Inc.[23]	7.51%
25 Riverside Drive, Unit One, Pine Brook, NJ 07058, United States	
Entasis Therapeutics Holdings Inc.	16.53%
35 Gatehouse Drive, Waltham, MA 02451, United States	
FibroGen, Inc.	0.65%
409 Illinois St., San Francisco, CA 94158, United States	
G1 Therapeutics, Inc.	7.93%
79 T.W. Alexander Drive, 4401 Research Commons, Suite 105, Research Triangle Park, NC 7709, United States	
Hydra Biosciences Inc.	4.27%
405 Concord Avenue, PO Box 147, Belmont, MA 02478, United States	
Millendo Therapeutics, Inc.	3.08%
301 North Main Street, Suite 100, Ann Arbor, MI 48104, United States	
Moderna, Inc.	7.75%
200 Technology Square, Cambridge, MA 02139, United States	
Myotherix Inc.[11]	8.27%
2600 Tenth St., #435, Berkeley, CA 94710, United States	
Nano Precision Medical, Inc.	4.83%
5858 Horton St Suite 393, Emeryville, CA 94608, United States	
PhaseBio Pharmaceuticals, Inc.	12.26%
One Great Valley, Parkway, Suite 30, Malvern, PA 19355, United States	
Rani Therapeutics, LLC[24]	0.97%
2051 Ringwood Ave, San Jose, CA 95116, United States	
Regulus Therapeutics Inc.	3.35%
10614 Science Center Dr., San Diego, CA 92121, United States	
Rocket Pharmaceuticals Inc.	1.07%
350 Fifth Avenue, Suite 7530, New York, NY 10118, United States	

[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 in common shares and special shares.
[8] Ownership held as membership interest.
[9] Ownership held as partnership interest.
[10] Ownership held in class A shares.
[11] Ownership held in class B preference shares.
[12] Voting rights and percentages vary depending on the subject matter and business to be voted on.
[13] Ownership held in common stock and series A-1 preferred stock.
[14] Ownership held in class B preference shares, class C preference shares, class D preference shares and class E preference shares.
[15] A company limited by guarantee.
[16] Ownership held in common shares and series A preferred shares.
[17] Ownership held in Class A voting and Class A non-voting shares.
[18] Ownership held in series B preferred stock.
[19] Ownership held in series A-1 preferred stock.
[20] Ownership held in series A preferred stock.
[21] Ownership held in class C preference shares and class D preference shares.
[22] Ownership held in series A preferred stock and series B preferred stock.
[23] Ownership held in class D preference shares.
[24] Ownership held in class C-1 preference shares.

Company Balance Sheet
at 31 December

AstraZeneca PLC

	Notes	2018 $m	2017 $m
Fixed assets			
Fixed asset investments	1	**33,244**	31,482
Current assets			
Debtors – other		**–**	11
Debtors – amounts owed by Group undertakings		**4,466**	7,995
		4,466	8,006
Creditors: Amounts falling due within one year			
Non-trade creditors	2	**(383)**	(325)
Interest-bearing loans and borrowings	3	**(999)**	(1,397)
		(1,382)	(1,722)
Net current assets		**3,084**	6,284
Total assets less current liabilities		**36,328**	37,766
Creditors: Amounts falling due after more than one year			
Amounts owed to Group undertakings	3	**(283)**	(283)
Interest-bearing loans and borrowings	3	**(17,013)**	(15,197)
		(17,296)	(15,480)
Net assets		**19,032**	22,286
Capital and reserves			
Called-up share capital	4	**317**	317
Share premium account		**4,427**	4,393
Capital redemption reserve		**153**	153
Other reserves		**2,533**	2,549
Profit and loss account		**11,602**	14,874
Shareholders' funds		**19,032**	22,286

$m means millions of US dollars.

The Company's profit for the year was $266m (2017: $3,109m).

The Company Financial Statements from page 205 to 209 were approved by the Board and were signed on its behalf by

Pascal Soriot
Director

Marc Dunoyer
Director

14 February 2019

Company's registered number 02723534

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 $m	Profit and loss account $m	Total equity $m
At 1 January 2017	316	4,351	153	2,583	15,307	22,710
Total comprehensive income for the period						
Profit for the period	–	–	–	–	3,109	3,109
Amortisation of loss on cash flow hedge	–	–	–	–	1	1
Total comprehensive income for the period	–	–	–	–	3,110	3,110
Transactions with owners, recorded directly in equity						
Dividends	–	–	–	–	(3,543)	(3,543)
Capital contributions for share-based payments	–	–	–	(34)	–	(34)
Issue of Ordinary Shares	1	42	–	–	–	43
Total contributions by and distributions to owners	1	42	–	(34)	(3,543)	(3,534)
At 31 December 2017	317	4,393	153	2,549	14,874	22,286
Total comprehensive income for the period						
Profit for the period	**–**	**–**	**–**	**–**	**266**	**266**
Amortisation of loss on cash flow hedge	**–**	**–**	**–**	**–**	**1**	**1**
Total comprehensive income for the period	**–**	**–**	**–**	**–**	**267**	**267**
Transactions with owners, recorded directly in equity						
Dividends	**–**	**–**	**–**	**–**	**(3,539)**	**(3,539)**
Capital contributions for share-based payments	**–**	**–**	**–**	**(16)**	**–**	**(16)**
Issue of Ordinary Shares	**–**	**34**	**–**	**–**	**–**	**34**
Total contributions by and distributions to owners	**–**	**34**	**–**	**(16)**	**(3,539)**	**(3,521)**
At 31 December 2018	**317**	**4,427**	**153**	**2,533**	**11,602**	**19,032**

At 31 December 2018, $11,602m (2017: $14,874m) of the Profit and loss account reserve was available for distribution, subject to filing these Financial Statements with Companies House. Included in Other reserves is a special reserve of $157m (2017: $157m), arising on the redenomination of share capital in 1999. The other reserves arose from the cancellation of share premium by the Company in 1993.

Included within Other reserves at 31 December 2018 is $692m (2017: $708m) in respect of cumulative share-based payment awards.

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 EU (Adopted IFRSs), but makes amendments where necessary in order to comply with the Companies Act 2006 and has set out below where advantage of the FRS 101 disclosure exemptions has been taken.

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 135 to 193) 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 Instrument Disclosures'.

No individual profit and loss account is prepared as provided by section 408 of the Companies Act 2006.

The accounting policies set out below have, unless otherwise stated, been applied consistently to all periods presented in these financial statements.

Basis of accounting

The Company Financial Statements are prepared under the historical cost convention, in accordance with the Companies Act 2006.

The following paragraphs describe the main accounting policies, which have been applied consistently.

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 interest payable. Exchange differences on all other transactions are taken to 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 sustained based upon management's interpretation of applicable laws and regulations and the likelihood of settlement.

Once considered probable of not being sustained, management reviews each material tax benefit to assess whether a provision should be taken against full recognition of the benefit on the basis of potential settlement through negotiation and/or litigation. Accruals for tax contingencies are measured using the single best estimate of likely outcome approach.

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.

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 2018	**15,996**	**15,486**	**31,482**
Additions	**–**	**2,974**	**2,974**
Transfer to current assets	**–**	**(999)**	**(999)**
Capital reimbursement	**(16)**	**–**	**(16)**
Exchange	**–**	**(174)**	**(174)**
Amortisation	**–**	**15**	**15**
Impairment	**(38)**	**–**	**(38)**
At 31 December 2018	**15,942**	**17,302**	**33,244**

A list of subsidiaries is included on pages 201 to 204.

2 Non-trade creditors

	2018 $m	2017 $m
Amounts due within one year		
Short-term borrowings	**211**	199
Other creditors	**165**	119
Amounts owed to Group undertakings	**7**	7
	383	325

3 Loans

		Repayment dates	**2018 $m**	2017 $m
Amounts due within one year				
Interest-bearing loans and borrowings (unsecured)				
Floating rate notes	US dollars	2018	**–**	399
1.75% Callable bond	US dollars	2018	**–**	998
1.95% Callable bond	US dollars	2019	**999**	–
			999	1,397
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)				
1.95% Callable bond	US dollars	2019	**–**	999
2.375% Callable bond	US dollars	2020	**1,594**	1,591
0.875% Non-callable bond	euros	2021	**854**	890
0.25% Callable bond	euros	2021	**570**	594
Floating rate note	US dollars	2022	**250**	249
2.375% Callable bond	US dollars	2022	**994**	992
3.5% Callable bond	US dollars	2023	**845**	–
Floating rate note	US dollars	2023	**400**	–
0.75% Callable bond	euros	2024	**1,022**	1,067
3.375% Callable bond	US dollars	2025	**1,980**	1,978
3.125% Callable bond	US dollars	2027	**743**	742
1.25% Callable bond	euros	2028	**903**	941
4% Callable bond	US dollars	2029	**992**	–
5.75% Non-callable bond	Pounds sterling	2031	**443**	468
6.45% Callable bond	US dollars	2037	**2,721**	2,720
4% Callable bond	US dollars	2042	**987**	987
4.375% Callable bond	US dollars	2045	**979**	979
4.375% Callable bond	US dollars	2048	**736**	–
Total amounts due after more than one year			**17,296**	15,480
Total loans			**18,295**	16,877

	2018 $m	2017 $m
Loans are repayable:		
After five years from balance sheet date	**11,506**	10,165
From two to five years	**4,196**	4,316
From one to two years	**1,594**	999
Within one year	**999**	1,397
Total unsecured	**18,295**	16,877

With the exception of the 2018, 2022 and 2023 floating rate notes, all loans are at fixed interest rates. Accordingly the fair values of the loans will change as market rates change. However, since the loans are 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. IFRS 9 has been adopted from 1 January 2018. The recoverability of all inter-company loans has been assessed in accordance with IFRS 9. No impairment was identified and thus, no provision has been made. The inter-company balances are considered to have low credit risk and the loss allowance is therefore limited to 12 month expected credit losses. In 2018 there have been no credit losses.

4 Share capital

Details of share capital movements in the year are included in Note 23 to the Group Financial Statements.

5 Contingent liabilities

The Company is named as a party to legal proceedings in the Array BioPharma Inc. commercial litigation, which is described more fully in Note 29 to the Group Financial Statements.

Other

The Company has guaranteed the external borrowing of a subsidiary in the amount of $286m (2017: $286m).

6 Statutory and other information

The Directors were paid by another Group company in 2018 and 2017.

7 Subsequent events

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

Group Financial Record

For the year ended 31 December	2014 $m	2015 $m	2016 $m	2017 $m	**2018 $m**
Revenue and profits					
Product Sales	26,095	23,641	21,319	20,152	**21,049**
Externalisation Revenue	452	1,067	1,683	2,313	**1,041**
Cost of sales	(5,842)	(4,646)	(4,126)	(4,318)	**(4,936)**
Distribution costs	(324)	(339)	(326)	(310)	**(331)**
Research and development expense	(5,579)	(5,997)	(5,890)	(5,757)	**(5,932)**
Selling, general and administrative costs	(13,000)	(11,112)	(9,413)	(10,233)	**(10,031)**
Other operating income and expense	335	1,500	1,655	1,830	**2,527**
Operating profit	2,137	4,114	4,902	3,677	**3,387**
Finance income	78	46	67	113	**138**
Finance expense	(963)	(1,075)	(1,384)	(1,508)	**(1,419)**
Share of after tax losses in associates and joint ventures	(6)	(16)	(33)	(55)	**(113)**
Profit before tax	1,246	3,069	3,552	2,227	**1,993**
Taxation	(11)	(243)	(146)	641	**57**
Profit for the period	1,235	2,826	3,406	2,868	**2,050**
Other comprehensive income for the period, net of tax	(1,506)	(338)	(1,778)	639	**(1,059)**
Total comprehensive income for the period	(271)	2,488	1,628	3,507	**991**
Profit attributable to:					
Owners of the Parent	1,233	2,825	3,499	3,001	**2,155**
Non-controlling interests	2	1	(93)	(133)	**(105)**
Earnings per share					
Basic earnings per $0.25 Ordinary Share	$0.98	$2.23	$2.77	$2.37	**$1.70**
Diluted earnings per $0.25 Ordinary Share	$0.98	$2.23	$2.76	$2.37	**$1.70**
Dividends	$2.80	$2.80	$2.80	$2.80	**$2.80**
Return on revenues					
Operating profit as a percentage of Total Revenue	8.0%	16.7%	21.3%	16.4%	**15.3%**
Ratio of earnings to fixed charges	6.1	11.3	8.9	4.4	**3.7**

At 31 December	2014 $m	2015 $m	2016 $m	2017 $m	**2018 $m**
Statement of Financial Position					
Property, plant and equipment, goodwill and intangible assets	38,541	40,859	46,092	45,628	**41,087**
Other investments and non-current receivables	2,138	1,896	2,070	2,387	**1,594**
Deferred tax assets	1,219	1,294	1,102	2,189	**2,379**
Current assets	16,697	16,007	13,262	13,150	**15,591**
Total assets	58,595	60,056	62,526	63,354	**60,651**
Current liabilities	(17,330)	(14,869)	(15,256)	(16,383)	**(16,292)**
Deferred tax liabilities	(1,796)	(2,665)	(3,956)	(3,995)	**(3,286)**
Other non-current liabilities	(19,823)	(24,013)	(26,645)	(26,334)	**(27,029)**
Net assets	19,646	18,509	16,669	16,642	**14,044**
Share capital	316	316	316	317	**317**
Reserves attributable to equity holders of the Company	19,311	18,174	14,538	14,643	**12,151**
Non-controlling interests	19	19	1,815	1,682	**1,576**
Total equity and reserves	19,646	18,509	16,669	16,642	**14,044**

For the year ended 31 December	2014 $m	2015 $m	2016 $m	2017 $m	**2018 $m**
Cash flows					
Net cash inflow/(outflow) from:					
Operating activities	7,058	3,324	4,145	3,578	**2,618**
Investing activities	(7,032)	(4,239)	(3,969)	(2,328)	**963**
Financing activities	(2,705)	878	(1,324)	(2,936)	**(2,044)**
	(2,679)	(37)	(1,148)	(1,686)	**1,537**

For the purpose of computing the ratio of earnings to fixed charges, earnings consist of the income from continuing ordinary activities before taxation of Group companies and income received from companies owned 50% or less, plus fixed charges. Fixed charges consist of interest on all indebtedness, amortisation of debt discount and expense, and that portion of rental expense representative of the interest factor.

Additional Information

Development Pipeline as at 31 December 2018

AstraZeneca-sponsored or -directed trials

New Molecular Entities (NMEs) and significant indications

Regulatory submission dates shown for assets in Phase III and beyond. As disclosure of compound information is balanced by the business need to maintain confidentiality, information in relation to some compounds listed here has not been disclosed at this time.

Phase I

Compound	Mechanism	Area Under Investigation
Oncology		
AZD0156	ATM inhibitor	solid tumours
AZD1390	ATM inhibitor	glioblastoma
AZD4573	CDK9 inhibitor	haematological malignancies
AZD4785	KRAS inhibitor	solid tumours
AZD5153	BRD4 inhibitor	solid tumours
AZD5991	MCL1 inhibitor	haematological malignancies
AZD9496	selective oestrogen receptor degrader	oestrogen receptor +ve breast cancer
Calquence + AZD6738	BTK inhibitor + ATR inhibitor	haematological malignancies
Calquence + danvatirsen	BTK inhibitor + STAT3 inhibitor	haematological malignancies
Imfinzi + adavosertib	PD-L1 mAb + Wee1 inhibitor	solid tumours
Imfinzi + azacitidine	PD-L1 mAb + azacitidine	myelodysplastic syndrome
Imfinzi + dabrafenib + trametinib	PD-L1 mAb + BRAF inhibitor + MEK inhibitor	melanoma
Imfinzi + *Iressa*	PD-L1 mAb + EGFR inhibitor	non-small cell lung cancer (NSCLC)
Imfinzi + RT (platform) (CLOVER)	PD-L1 mAb + RT	locally-advanced head and neck squamous cell carcinoma, NSCLC, small cell lung cancer
Imfinzi + selumetinib	PD-L1 + MEK inhibitor	solid tumours
Imfinzi + tremelimumab	PD-L1 mAb + CTLA-4 mAb	solid tumours
Imfinzi + tremelimumab + chemotherapy	PD-L1 mAb + CTLA-4 mAb + chemotherapy	1st line pancreatic ductal adenocarcinoma, oesophageal and small cell lung cancer
MEDI2228	BCMA antibody drug conjugate	multiple myeloma
MEDI3726	PSMA antibody drug conjugate	prostate cancer
MEDI5083	CD40 ligand fusion protein	solid tumours
MEDI5752	PD-1/CTLA-4 bispecific mAb	solid tumours
MEDI7247	ASCT2 antibody drug conjugate	haematological malignancies
oleclumab	CD73 mAb	solid tumours
oleclumab + AZD4635	CD73 mAb + A2aR inhibitor	EGFRm NSCLC
oleclumab + *Tagrisso*	CD73 mAb + EGFR inhibitor	EGFRm NSCLC
CVRM		
AZD9977	MCR	CV disease
AZD8233	hypercholesterolaemia	CV disease
MEDI6570	LOX-1 mAb	CV disease
MEDI7219	anti-diabetic	type-2 diabetes
Respiratory		
AZD0449	inhaled JAK inhibitor	asthma
AZD1402	inhaled IL-4Ra	asthma
AZD5634	inhaled ENaC	cystic fibrosis
AZD8154	inhaled PI3Kgd	asthma
MEDI3506	IL-33 mAb	chronic obstructive pulmonary disease (COPD)
Other		
AZD0284	RORg	psoriasis/respiratory
MEDI0700	BAFF/B7RP1 bispecific mAb	systemic lupus erythematosus
MEDI1341	alpha synuclein mAb	Parkinson's disease
MEDI1814	amyloid beta mAb	Alzheimer's disease

Phase II

Compound	Mechanism	Area Under Investigation
Oncology		
adavosertib + chemotherapy	Wee1 inhibitor + chemotherapy	ovarian cancer
AZD2811	Aurora B inhibitor	solid tumours
AZD4547	FGFR inhibitor	solid tumours
AZD4635	A2aR inhibitor	solid tumours
AZD6738	ATR inhibitor	solid tumours
AZD8186	PI3K inhibitor	solid tumours
capivasertib	AKT inhibitor	breast cancer
Imfinzi + AZD5069 or *Imfinzi* + danvatirsen	PD-L1 mAb + CXCR2 antagonist or PD-L1 mAb + STAT3 inhibitor	head and neck squamous cell carcinoma, bladder and NSCLC
Imfinzi + *Lynparza* (BAYOU)	PD-L1 mAb + PARP inhibitor	1st line unresectable stage 4 bladder cancer
Imfinzi + MEDI0457	PD-L1 mAb + DNA HPV vaccine	head and neck squamous cell carcinoma
Imfinzi + MEDI0680	PD-L1 mAb + PD-1 mAb	solid tumours
Imfinzi + monalizumab	PD-L1 mAb + NKG2a mAb	solid tumours
Imfinzi + oleclumab	PD-L1 mAb + CD73 mAb	solid tumours
Imfinzi + tremelimumab	PD-L1 mAb + CTLA-4 mAb	biliary tract, oesophageal
Imfinzi + tremelimumab	PD-L1 mAb + CTLA-4 mAb	gastric cancer
Lynparza + adavosertib	PARP inhibitor + Wee1 inhibitor	solid tumours
Lynparza + AZD6738	PARP inhibitor + ATR inhibitor	gastric cancer
Lynparza + AZD6738 or *Lynparza* + adavosertib (VIOLETTE)	PARP inhibitor + ATR inhibitor or PARP inhibitor + Wee1 inhibitor	breast cancer
Lynparza + *Imfinzi* (MEDIOLA)	PARP inhibitor + PD-L1 mAb	ovarian cancer, breast cancer, gastric cancer and small cell lung cancer
Tagrisso + (selumetinib or savolitinib) (TATTON)	EGFR inhibitor + (MEK inhibitor or MET inhibitor)	advanced EGFRm NSCLC
CVRM		
AZD4831	myeloperoxidase	heart failure with a preserved ejection fraction
AZD5718	FLAP	coronary artery disease
AZD8601	VEGF-A	CV disease
cotadutide (MEDI0382)	GLP-1/glucagon dual agonist	type-2 diabetes/obesity
MEDI5884	cholesterol modulation	CV disease
MEDI6012	LCAT	CV disease
verinurad	URAT1 inhibitor	chronic kidney disease (CKD)
Respiratory		
abediterol	LABA	asthma/COPD
AZD1419	inhaled TLR9 agonist	asthma
AZD7594	inhaled SGRM	asthma/COPD
AZD7986	DPP1	COPD
AZD8871	MABA	COPD
AZD9567	oral SGRM	rheumatoid arthritis/respiratory
PT010	LABA/LAMA/ICS	asthma
tezepelumab	TSLP mAb	atopic dermatitis
Other		
anifrolumab	Type I IFN receptor mAb	lupus nephritis
anifrolumab	Type I IFN receptor mAb	systemic lupus erythematosus (subcutaneous)
MEDI3902	Psl/PcrV bispecific mAb	prevention of nosocomial Pseudomonas aeruginosa pneumonia
MEDI7352	NGF/TNF bispecific mAb	osteoarthritis pain/painful diabetic neuropathy
MEDI8852	influenza A mAb	influenza A treatment
MEDI8897	RSV mAb-YTE	passive RSV prophylaxis
prezalumab	B7RP1 mAb	primary Sjögren's syndrome
suvratoxumab	mAb binding to S. aureus toxin	prevention of nosocomial Staphylococcus aureus pneumonia

Development Pipeline
continued

Phase III/Pivotal Phase II/Registration

Compound	Mechanism	Area Under Investigation	Estimated Filing US	EU	Japan	China
Oncology						
Calquence	BTK inhibitor	relapsed/refractory mantle cell lymphoma	Launched			
Imfinzi + tremelimumab + chemotherapy (POSEIDON)	PD-L1 mAb + CTLA-4 mAb + chemotherapy	1st line NSCLC	H2 2019	H2 2019	H2 2019	2020
Imfinzi + tremelimumab + CRT (ADRIATIC)	PD-L1 mAb + CTLA-4 mAb + CRT	Limited disease small cell lung cancer	2020+	2020+	2020+	2020+
Imfinzi + tremelimumab + SoC (CASPIAN)	PD-L1 mAb + CTLA-4 mAb + SoC	1st line small cell lung cancer	H2 2019	H2 2019	H2 2019	2020
Imfinzi + tremelimumab + SoC (NILE)	PD-L1 mAb + CTLA-4 mAb + SoC	1st line urothelial cancer	2020+	2020+	2020+	
Imfinzi + tremelimumab (DANUBE)	PD-L1 mAb + CTLA-4 mAb	1st line bladder cancer	H2 2019	H2 2019	H2 2019	
Imfinzi + tremelimumab (HIMALAYA)	PD-L1 mAb + CTLA-4 mAb	1st line hepatocellular carcinoma	2020+	2020+	2020+	2020+
Imfinzi + tremelimumab (KESTREL)	PD-L1 mAb + CTLA-4 mAb	1st line head and neck squamous cell carcinoma	H1 2019	H2 2019	H2 2019	
Imfinzi + tremelimumab (NEPTUNE)	PD-L1 mAb + CTLA-4 mAb	1st line NSCLC	H2 2019	H2 2019	H2 2019	2020
Lumoxiti (PLAIT)	anti-CD22 recombinant immunotoxin	3rd line hairy cell leukaemia	Launched (Orphan Drug, Priority Review)	2020		
Lynparza + cediranib (CONCERTO)	PARP inhibitor + VEGF inhibitor	recurrent platinum-resistant ovarian cancer	2020			
savolitinib (SAVOIR)	MET inhibitor	papillary renal cell carcinoma	2020	2020		
selumetinib (SPRINT)	MEK inhibitor	paediatric neurofibromatosis type-1	H2 2019 (Orphan Drug)	H2 2019 (Orphan Drug)		
CVRM						
Epanova	omega-3 carboxylic acids	severe hypertriglyceridaemia	Approved			
Lokelma	potassium binder	hyperkalaemia	Approved	Approved	H2 2019	2020
roxadustat (OLYMPUS, ROCKIES)	hypoxia-inducible factor prolyl hydroxylase inhibitor	anaemia in CKD/end-stage renal disease	H1 2019			Approved
Respiratory						
Bevespi Aerosphere (PT003)	LABA/LAMA	COPD	Launched	Approved	Accepted	Accepted
Fasenra (CALIMA, SIROCCO, ZONDA, BISE, BORA, GREGALE)	IL-5R mAb	severe, uncontrolled asthma	Launched	Launched	Launched	2020+
PT010	LABA/LAMA/ICS	COPD	2019	2019	Accepted	Accepted
PT027	ICS/SABA	asthma	2020+			
tezepelumab (NAVIGATOR, SOURCE)	TSLP mAb	severe, uncontrolled asthma	2020+	2020+	2020+	
Other						
anifrolumab (TULIP)	Type I IFN receptor mAb	systemic lupus erythematosus	2020 (Fast Track designation)	2020	2020	

Significant Life-cycle Management

Compound	Mechanism	Area Under Investigation	Estimated Filing US	EU	Japan	China
Oncology						
Calquence	BTK inhibitor	1st line chronic lymphocytic leukaemia	2020 (Orphan Drug)	2020 (Orphan Drug)		2020+
Calquence	BTK inhibitor	relapsed/refractory chronic lymphocytic leukaemia	2020 (Orphan Drug)	2020 (Orphan Drug)		
Calquence	BTK inhibitor	relapsed/refractory chronic lymphocytic leukaemia, high risk	H2 2019 (Orphan Drug)	H2 2019 (Orphan Drug)		
Calquence	BTK inhibitor	haematological malignancies				
Calquence	BTK inhibitor	1st line mantle cell lymphoma	2020+ (Orphan Drug)	2020+		2020+
Imfinzi	PD-L1 mAb	solid tumours				
Imfinzi (PEARL, China)	PD-L1 mAb	1st line NSCLC	N/A	N/A	N/A	2020
Imfinzi (PACIFIC)	PD-L1 mAb	locally advanced (stage 3) NSCLC	Approved (Breakthrough designation, Priority Review)	Approved	Approved	Accepted
Imfinzi (POTOMAC)	PD-L1 mAb	non-muscle invasive bladder cancer	N/A	2020+	2020+	N/A
Imfinzi + CRT (PACIFIC-2)	PD-L1 mAb + CRT	locally-advanced (stage 3) NSCLC	2020+	2020+	2020+	
Imfinzi + CRT (PACIFIC-5, China)	PD-L1 mAb + CRT	locally-advanced (stage 3) NSCLC	N/A	N/A	N/A	2020+
Imfinzi + CTx neoadjuvant (AEGEAN)	PD-L1 mAb + CTx	locally-advanced (stage 3) NSCLC	2020+	2020+	2020+	
Imfinzi + CTx (NIAGARA)	PD-L1 mAb + CTx	muscle invasive bladder cancer	2020+	2020+	2020+	
Imfinzi + VEGF + TACE (EMERALD-1)	PD-L1 mAb + VEGF + TACE	locoregional hepatocellar carcinoma	2020+	2020+	2020+	2020+
Lynparza (OlympiA)	PARP inhibitor	gBRCA adjuvant breast cancer	2020+	2020+	2020+	
Lynparza (OlympiAD)	PARP inhibitor	gBRCA metastatic breast cancer	Launched (Priority Review)	Accepted	Approved (Orphan Drug, Priority Review)	H1 2019
Lynparza (POLO)	PARP inhibitor	pancreatic cancer	H2 2019 (Orphan Drug)	H2 2019		
Lynparza (SOLO-3)	PARP inhibitor	gBRCA PSR ovarian cancer	H2 2019			
Lynparza + abiraterone (PROpel)	PARP inhibitor + NHA	prostate cancer	2020+	2020+	2020+	2020+
Lynparza (PROfound)	PARP inhibitor	prostate cancer	2020 (Breakthrough designation)	2020	2020	2020+
Lynparza (SOLO-1)	PARP inhibitor	1st line BRCAm ovarian cancer	Approved (Priority Review)	Accepted	Accepted	Accepted (Priority Review)
Lynparza (SOLO-2)	PARP inhibitor	2nd line or greater BRCAm PSR ovarian cancer, maintenance monotherapy	Approved (Priority Review)	Approved	Approved (Orphan Drug)	Approved
Tagrisso (LAURA)	EGFR inhibitor	stage 3 EGFRm NSCLC	2020+	2020+	2020+	2020+
Tagrisso (ADAURA)	EGFR inhibitor	adjuvant EGFRm NSCLC	2020+	2020+	2020+	2020+
Tagrisso (FLAURA)	EGFR inhibitor	1st line advanced EGFRm NSCLC	Approved (Breakthrough designation)	Approved	Approved	Accepted

Development Pipeline
continued

Significant Life-cycle Management *continued*

Compound	Mechanism	Area Under Investigation	Estimated Filing US	EU	Japan	China
CVRM						
Brilinta/Brilique (HESTIA)	P2Y12 receptor antagonist	prevention of vaso-occlusive crises in paediatric patients with sickle cell disease	2020+	2020+		
Brilinta/Brilique (THEMIS)	P2Y12 receptor antagonist	CV outcomes trial in patients with coronary artery disease and type-2 diabetes without a previous history of myocardial infarction or stroke	H2 2019	H2 2019	H2 2019	H2 2019
Brilinta/Brilique (THALES)	P2Y12 receptor antagonist	acute ischaemic stroke or transient ischaemic attack	2020	2020		2020
Bydureon (EXSCEL)	GLP-1 receptor agonist	type-2 diabetes outcomes study	Accepted	Approved	N/A	Accepted
Bydureon BCise (autoinjector)	GLP-1 receptor agonist	type-2 diabetes	Launched	Approved		
Epanova (STRENGTH)	omega-3 carboxylic acids	CV outcomes study in statin-treated patients at high CV risk, with persistent hypertriglyceridaemia plus low HDL-cholesterol	2020	2020	2020	2020
Farxiga/Forxiga Dapa-HF	SGLT-2 inhibitor	worsening heart failure or CV death in patients with chronic heart failure (HFrEF)	2020	2020	2020	2020
Farxiga/Forxiga (DELIVER)	SGLT-2 inhibitor	worsening heart failure or CV death in patients with chronic heart failure (HFpEF)	2020+	2020+	2020+	2020+
Farxiga/Forxiga Dapa-CKD	SGLT-2 inhibitor	renal outcomes and CV mortality in patients with CKD	2020+	2020+	2020+	2020+
Farxiga/Forxiga (DEPICT)	SGLT-2 inhibitor	type-1 diabetes	Accepted	Accepted	Accepted	
Farxiga/Forxiga (DECLARE)	SGLT-2 inhibitor	CV outcomes trial in patients with type-2 diabetes	H1 2019	H1 2019		H1 2019
Qtern	DPP-4 inhibitor/SGLT-2 inhibitor FDC	type-2 diabetes	Launched	Launched		
roxadustat	hypoxia-inducible factor prolyl hydroxylase inhibitor	anaemia in myelodysplastic syndrome	2020+			2020+
saxagliptin/dapagliflozin metformin	DPP-4 inhibitor/SGLT-2 inhibitor	type-2 diabetes	Accepted	Accepted		
Xigduo XR/*Xigduo*	SGLT-2 inhibitor/ metformin FDC	type-2 diabetes	Launched	Launched		2020
Respiratory						
Duaklir Genuair	LAMA/LABA	COPD	Accepted	Launched		2020
Fasenra (TERRANOVA, GALATHEA)	IL-5R mAb	COPD				
Fasenra (OSTRO)	IL-5R mAb	nasal polyposis	2020	2020		
Symbicort (SYGMA)	ICS/LABA	as-needed use in mild asthma	N/A	Accepted	N/A	H2 2019
Other						
Linzess (linaclotide)	GC-C receptor peptide agonist	irritable bowel syndrome with constipation				Approved
Nexium	proton pump inhibitor	stress ulcer prophylaxis				Accepted

Patent Expiries of Key Marketed Products

Patents covering our products are or may be challenged by third parties. Generic products may be launched 'at risk' and our patents may be revoked, circumvented or found not to be infringed. For more information, please see Risk from page 220. Many of our products are subject to challenges by third parties. Details of material challenges by third parties can be found in Note 29 to the Financial Statements from page 196. The expiry dates shown below include granted SPC/PTE and/or Paediatric Exclusivity periods (as appropriate). In Europe, the exact SPC situation may vary by country as different Patent Offices grant SPCs at different rates. Expiry dates in red relate to new molecular entity patents, the remaining dates relate to other patents. The expiry dates of relevant regulatory data exclusivity periods are not represented in the table below. A number of our products are subject to generic competition in one or more markets.

Key marketed products	Description	US	China	EU[1]	Japan	US Product Sales ($m)			Aggregate Revenue for China, Japan and Europe[2] Product Sales ($m)		
						2018	2017	2016	**2018**	2017	2016
Atacand[3] (candesartan cilexitil)	An angiotensin II antagonist for the 1st line treatment of hypertension and symptomatic heart failure	expired	[4]	expired	[4]	**13**	19	36	**62**	86	97
Bevespi Aerosphere (glycopyrrolate/ formoterol)	A combination of a long-acting muscarinic antagonist (LAMA) and a long-acting beta2-agonist (LABA) used for the long-term maintenance treatment of airflow obstruction in COPD	2030-2031	2030	2030	2030	**33**	16	2	**–**	–	–
Brilinta/ *Brilique* (ticagrelor)	An oral P2Y12 platelet inhibitor for acute coronary syndromes (ACS) (ticagrelor 90mg) or continuation therapy in high-risk patients (ticagrelor 60mg) with a history of myocardial infarction (MI)	2018-2024[5], 2021-2030	2018, 2019[6], 2021[7]	2018-2024, 2021[8]-2027[9]	2023-2024, 2025-2030	**588**	509	348	**532**	402	347
Bydureon/ *Bydureon BCise* (exenatide XR injectable suspension)	A once-weekly injectable glucagon-like peptide-1 (GLP-1) receptor agonist available as a single-dose tray, a single-dose pen or autoinjector device indicated as monotherapy and as part of combination therapy adjunct to diet and exercise to improve glycaemic control in adults with type-2 diabetes	2018-2028, 2030[10]	2020-2028, 2029[10]	2018-2028, 2029[10]	2018-2028, 2029[10]	**475**	458	463	**85**	93	109
Byetta (exenatide injection)	A twice-daily injectable GLP-1 receptor agonist indicated to improve glycaemic control in adults with type-2 diabetes	2018-2020[11]	2020	2018-2021	2018-2020	**74**	114	164	**34**	39	62
Calquence (acalabrutinib)	A selective inhibitor of Bruton's tyrosine kinase indicated for the treatment of mantle cell lymphoma (MCL) and in development for the treatment of multiple B-cell malignancies and other cancers	2026-2032, 2036	2032	2032	2032	**62**	–	–	**–**	–	–
Crestor (rosuvastatin calcium)	A statin for dyslipidaemia and hypercholesterolaemia	2018-2022[12]	2020-2021	2020	2023	**170**	373	1,223	**825**	1,528	1,698
Daliresp/ *Daxas* (roflumilast)	An oral phosphodiesterase-4 inhibitor for adults with severe COPD to decrease their number of exacerbations	2020, 2023-2024	2023	2019[13], 2023		**155**	167	134	**28**	26	15
Duaklir (aclidinium/ formoterol)	A fixed-dose combination of a LAMA and a LABA for the maintenance treatment of COPD	2020, 2025, 2022-2029[14]	2020, 2022-2027	2025, 2022-2029	2025, 2021-2029	**–**	–	–	**91**	77	62
Fasenra (benralizumab)	A monoclonal antibody for add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype, which directly targets and depletes eosinophils by recruiting natural killer cells and inducing apoptosis (programmed cell death)	2020, 2028-2034	2021, 2028	2020, 2028	2020	**218**	–	–	**77**	–	–
Faslodex (fulvestrant)	An injectable oestrogen receptor antagonist. Used for the treatment of hormone receptor positive advanced breast cancer that has progressed following treatment with prior endocrine therapy	2021[15]		2021	2026	**537**	492	438	**382**	352	311
Farxiga/ *Forxiga* (dapagliflozin)	A selective inhibitor of human sodium-glucose co-transporter 2 (SGLT-2 inhibitor) indicated as monotherapy, and as part of combination therapy, adjunct to diet and exercise to improve glycaemic control in adult patients with type-2 diabetes	2020, 2025*, 2020-2030	2020-2023, 2028	2020-2027	2024-2025, 2028	**591**	355	358	**394**	245	175
Fluenz Tetra/ *FluMist* Quadrivalent (live attenuated influenza vaccine)	A live attenuated vaccine indicated for active immunisation for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine	2018-2026	2020-2025	2020-2026	2020-2025	**15**	–	33	**91**	76	65

Patent Expiries of Key Marketed Products *continued*

Key marketed products	Description	US	China	EU[1]	Japan	US Product Sales ($m)			Aggregate Revenue for China, Japan and Europe[2] Product Sales ($m)		
						2018	2017	2016	**2018**	2017	2016
Imfinzi (durvalumab)	A human monoclonal antibody that blocks PD-L1 interaction with PD-1 and CD80 on T cells, countering the tumour's immune-evading tactics and inducing an immune response. It is currently indicated for the treatment of locally advanced or metastatic urothelial carcinoma and unresectable stage 3 non-small cell lung cancer (NSCLC)	2030	2030	2030	2030	**564**	19	–	**62**	–	–
Iressa (gefitinib)	An epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) that acts to block signals for cancer cell growth and survival in advanced NSCLC	[16]	2023	2019[17], 2023	2018, 2023	**26**	39	23	**376**	367	358
Komboglyze/ Kombiglyze XR[18] (saxagliptin/ metformin)	Combines saxagliptin and metformin as either *Komboglyze* – a twice-daily tablet for type-2 diabetes, or *Kombiglyze* XR – an extended release once-daily tablet for type-2 diabetes	2023, 2025	2021, 2025	2021-2026, 2025	[19]	**–**	111	145	**–**	–	–
Lokelma (sodium zirconium cyclosilicate)	An insoluble, non-absorbed sodium zirconium silicate, formulated as a powder for oral suspension, that acts as a highly-selective potassium-removing agent for the treatment of hyperkalaemia	2019, 2032-2033, 2035	2033	2032	2032-2033	**–**	–	–	**–**	–	–
Lumoxiti (moxetumomab pasudotox-tdfk)	A CD22-directed cytotoxin and a first-in-class treatment in the US for adult patients with relapsed or refractory hairy cell leukaemia (HCL)	2022-2024, 2031-2032	2031	2022, 2031	2031	**–**	–	–	**–**	–	–
Lynparza (olaparib)	An oral poly ADP-ribose polymerase (PARP) inhibitor that may exploit tumour DNA damage response (DDR) pathway deficiencies to potentially kill cancer cells. It is indicated for the treatment of women with BRCAm ovarian cancer and metastatic breast cancer	2022-2024, 2028*, 2029[20], 2024-2031	2021-2024, 2024-2027, 2029[20], 2024	2021-2029, 2024-2027, 2029[20], 2024	2021-2029, 2024-2027, 2029[20], 2024	**345**	141	127	**250**	130	81
Movantik/ Moventig (naloxegol)	A once-daily, peripherally acting mu-opioid receptor antagonist approved for the treatment of opioid-induced constipation (OIC) in adult patients. The indication varies by jurisdiction	2022-2027, 2028*, 2032	2024, 2031	2022-2024, 2029*[21], 2031	2022-2024, 2031	**108**	120	90	**–**	2	–
Nexium (esomeprazole)	A proton pump inhibitor used to treat acid-related diseases	2018-2020[22]	2018-2019	2018	2018, 2018-2019	**287**	499	526	**955**	973	975
Onglyza (saxagliptin)	An oral dipeptidyl peptidase 4 (DPP-4) inhibitor for type-2 diabetes	2023, 2028	2021, 2025	2024, 2025	[19]	**109**	209	231	**95**	114	120
Pulmicort (budesonide)	An inhaled corticosteroid for maintenance treatment of asthma	2018-2019[23]	2018[24]	2018[24]	2018[24]	**116**	156	174	**975**	847	732
Qtern (dapagliflozin/ saxagliptin)	A once-daily oral treatment combination of dapagliflozin (10mg) and saxagliptin (5mg) indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type-2 diabetes who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin	2020, 2025*, 2020-2029	2020-2023	2020-2027	2024-2025	**–**	4	–	**5**	–	–
Seloken/ Toprol-XL (metoprolol succinate)	A beta-blocker once-daily tablet for control of hypertension, heart failure and angina	expired	expired	expired	expired	**39**	37	95	**488**	470	462
Seroquel XR (quetiapine)	Generally approved for the treatment of schizophrenia, bipolar disorder, major depressive disorder and, on a more limited basis, for generalised anxiety disorder	expired	expired[25]	expired	[26]	**73**	175	515	**70**	82	134
Symbicort (budesonide/ formoterol)	A combination of an inhaled corticosteroid and a fast onset LABA for maintenance treatment of asthma and COPD either as *Symbicort Turbuhaler* or *Symbicort* pMDI (pressurised metered-dose inhaler)	2019-2029[27]	2018[28]	2018-2019[28]	2019-2020[28]	**862**	1,099	1,242	**1,220**	1,201	1,276

Key marketed products	Description	US	China	EU[1]	Japan	US Product Sales ($m)			Aggregate Revenue for China, Japan and Europe[2] Product Sales ($m)		
						2018	2017	2016	**2018**	2017	2016
Synagis (palivizumab)	A humanised mAb used to prevent serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in paediatric patients at high risk of acquiring RSV disease	2023		2023	2023	**287**	317	325	**377**	370	352
Tagrisso (osimertinib)	An EGFR-TKI indicated for patients with metastatic EGFR T790M mutation-positive NSCLC	2032	2032	2032	2034	**869**	405	254	**808**	486	158
Tudorza/Eklira Genuair (aclidinium)	A LAMA for the maintenance treatment of COPD	2020, 2025, 2022-2029	2020, 2022-2027	2025, 2022-2029	2025, 2021-2029	**25**	66	77	**75**	74	84
Xigduo/Xigduo XR (dapagliflozin/ metformin)	Combines dapagliflozin and metformin as either *Xigduo* – a twice-daily tablet to improve glycaemic control in adult patients with type-2 diabetes who are inadequately controlled on metformin alone or *Xigduo* XR – an extended release once-daily tablet to improve glycaemic control in adult patients with type-2 diabetes who are inadequately controlled on metformin alone	2020, 2025*, 2020-2030	2020-2023	2020-2028	2024-2025, 2030	**114**	134	99	**83**	58	37
Zoladex (goserelin acetate implant)	A luteinising hormone-releasing hormone (LHRH) agonist used to treat prostate cancer, breast cancer and certain benign gynaecological disorders	2022[29]	2021	2021	2021	**8**	15	35	**508**	483	498

* Date represents expiry of a pending SPC/PTE and/or Paediatric Exclusivity period.

1 Expiry in major EU markets.

2 The Product Sales reflected are for Europe Region as defined in Market definitions on page 239.

3 *Atacand HCT* in US.

4 Takeda retained rights.

5 Separate settlements with ANDA challengers for a licensed entry date corresponding to the expiry of US Patent No. RE46,276, subject to regulatory approval.

6 The patent was invalidated during invalidation proceedings at the Chinese Patent Office (CNIPA). In December 2018, however, the Beijing High People's Court vacated the invalidation decision and remanded the case back to the CNIPA for further processing in view of the Court's decision upholding the validity of the patent.

7 The patent was invalidated during invalidation proceedings at the CNIPA. The patentee has appealed that decision.

8 The patent was revoked during opposition proceedings at the European Patent Office (EPO). The patentee has appealed that decision.

9 The patent is the subject of a pending opposition proceeding at the EPO.

10 Patent expiry date relates to *BCise*.

11 Separate settlements with ANDA challengers for a licensed entry date of 15 October 2017, or later, subject to regulatory approval.

12 A settlement agreement in the US permitted Watson Laboratories, Inc. and Actavis, Inc. (together, Watson) to begin selling its generic version of *Crestor* and its rosuvastatin zinc product from 2 May 2016.

13 There is eight years' data exclusivity and two years' market exclusivity for *Daxas* in the EU to 5 July 2020.

14 NDA filed 31 May 2018.

15 Settled with various generic companies for licensed entry dates of 25 March 2019 or later.

16 In the US, *Iressa* has seven years' Orphan Drug exclusivity to 13 July 2022.

17 SPCs expire 2 March 2019. There is eight years' data exclusivity and two years' market exclusivity for *Iressa* in the EU to 24 June 2019.

18 *Komboglyze/Kombiglyze* XR revenue is included in the *Onglyza* revenue figure.

19 AstraZeneca does not have commercialisation rights.

20 Patent expiry date relates to the tablet formulation.

21 ProStrakan Group (a subsidiary of Kyowa Hakko Kirin) is exclusively licensed in the EU, Iceland, Norway, Switzerland and Liechtenstein.

22 Licence agreements have allowed generic companies to launch generic capsule versions in the US.

23 A licence agreement with Teva permits its ongoing sale in the US of a generic version from December 2009. The 2018 expiry relates to the Flexhaler device, while the 2019 expiry relates to the formulation in the Flexhaler presentation and also to *Respules*.

24 The 2018 expiry relates to the formulation in the *Turbuhaler* presentation and to a process useful for the *Respules* product.

25 Rights licensed to Luye Pharma.

26 Rights licensed to Astellas.

27 Patent expiry dates relate to the *Symbicort* pMDI product, including any granted Paediatric Exclusivity term.

28 Patent expiry dates relate to the *Symbicort Turbuhaler* product.

29 Rights licensed to TerSera.

Risks and uncertainties

Operating in the pharmaceutical sector carries various inherent risks and uncertainties that may affect our business. In this section, we describe the risks and uncertainties that we consider material to our business in that they may have a significant effect on our financial condition, results of operations, and/or reputation.

These risks are not listed in any particular order of priority and have been categorised consistently with the Principal Risks detailed from page 72, which are included below along with the other risks that we face. We believe that the forward-looking statements about AstraZeneca in this Annual Report, identified by words such as 'anticipates', 'believes', 'expects' and 'intends', and that include, among other things, Future prospects in the Financial Review on page 86, are based on reasonable assumptions. However, forward-looking statements involve inherent risks and uncertainties such as those summarised below. They relate to events that may occur in the future, that may be influenced by factors beyond our control and that may have actual outcomes materially different from our expectations. Therefore, other risks, unknown or not currently considered material, could have a material adverse effect on our financial condition or results of operations.

Product pipeline and IP risks	Impact
Failure or delay in delivery of pipeline or launch of new products	
Our continued success depends on the development and successful launch of innovative new drugs. The development of pharmaceutical product candidates is a complex, risky and lengthy process involving significant financial, R&D and other resources. A project may fail at any stage of the process due to various factors, including failure to obtain the required regulatory or marketing approvals for the product candidate or for its manufacturing facilities, unfavourable clinical efficacy data, safety concerns, failure to demonstrate adequate cost-effective benefits to regulatory authorities and/or payers and the emergence of competing products. More details of projects that have suffered setbacks or failures during 2018 can be found in the Therapy Area Review. The anticipated launch dates of major new products significantly affect our business, including investment in large clinical studies, the manufacture of pre-launch product stocks, investment in marketing materials pre-launch, sales force training and the timing of anticipated future revenue streams from new Product Sales. Launch dates are primarily driven by our development programmes and the demands from various factors, including adverse findings in pre-clinical or clinical studies, regulatory demands, price negotiation, competitor activity and technology transfer. More complex and stringent regulations govern the manufacturing and supply of biologics products, thus impacting the production and release schedules of such products more significantly. In addition to developing products in-house, we also expand our product portfolio and geographical presence through licensing arrangements and strategic collaborations, which are key to growing and strengthening our business. The success of such arrangements is largely dependent on the technology and other IP rights we acquire or license, and the resources, efforts and skills of our partners. Disputes or difficulties in our relationship with our collaborators or partners may arise, for example, due to conflicting priorities or conflicts of interest between parties. In many cases we make milestone payments well in advance of the commercialisation of the products, with no assurance that we will recoup these payments. We experience strong competition from other pharmaceutical companies in respect of licensing arrangements, strategic collaborations, and acquisition targets.	Failure or delay in development of new product candidates that achieve the expected commercial success could frustrate the achievement of development targets, adversely affect the reputation of our R&D capabilities, and is likely to materially adversely affect our business and results of operations. See also Failure to achieve strategic plans or meet targets and expectations on page 229. Since our business model and strategy rely on the success of relatively few compounds, the failure of any compound in our late-stage pipeline or in-line products may have a significant negative effect on our business or results of operations. Significant delays to anticipated launch dates of new products could have a material adverse effect on our financial position and/or results of operations. For example, for the launch of products that are seasonal in nature, delays in regulatory approvals or manufacturing difficulties may delay launch to the next season which, in turn, may significantly reduce the return on costs incurred in preparing for the launch for that season. Furthermore, in immuno-oncology for example, speed to market is critical given the large number of clinical trials being conducted by other companies. In addition, a delayed launch may lead to increased costs if, for example, marketing and sales efforts need to be rescheduled or performed for longer than expected. Failure to complete collaborative projects in a timely, cost-effective manner may limit our ability to access a greater portfolio of products, IP, technology and shared expertise. Disputes and difficulties with our partners may erode or eliminate the benefits of our alliances and collaborations. In addition, failure to perform on the part of parties to externalisation transactions may diminish the future value of those transactions or, in some cases, allow a competitor to beat us to market with a similar or first-in-class product. Delay of launch can also erode the term of patent exclusivity. Competition from other pharmaceutical companies means that we may be unsuccessful in implementing some of our intended projects or we may have to pay a significant premium over book or market values for our acquisitions.

Product pipeline and IP risks	Impact

Difficulties in obtaining or maintaining regulatory drug approval for products

We are subject to strict controls on the commercialisation processes for our pharmaceutical products, including their development, manufacture, distribution and marketing. The criteria for establishing safety, efficacy and quality, which are essential for securing marketing approvals, vary by country and by region. Regulators can refuse to grant approval or may require additional data before approval is granted or as a post-approval commitment, even though the medicine may already be approved or launched in other countries.

Factors, including advances in science and technology, evolving regulatory science, new laws and policies, and different approaches to benefit/risk tolerance by regulatory authorities, the general public, and other third-party public interest groups are known to influence the approvability of new drugs. While we seek to manage most of these risks, unanticipated and unpredictable policymaking by governments and regulators, limited regulatory authority resources or conflicting priorities often lead to delays in regulatory approvals.

We may be required to generate additional data after a drug's approval because a regulatory authority may have concerns that impact the benefit/risk profile of the drug. For our marketed drugs, new data or meta-analyses have the potential to drive changes in the approval status or labelling. In addition, recent years have seen an increase in post-marketing regulatory requirements and commitments, an increased call for third-party access to regulatory and clinical trial data packages for independent analysis and interpretation, and broader data transparency. Such transparency, while important, could lead to inappropriate or incorrect data analyses which may damage the integrity of our products and our Company's reputation.

Delays in regulatory reviews and approvals could delay our ability to market our products and may adversely affect our revenue. In addition, post-approval requirements, including additional clinical trials, could result in increased costs, and may impact the labelling and approval status of currently marketed products.

With the UK planning to leave the EU by the end of March 2019, intense work is ongoing to manage Brexit related changes, identify scenarios for the many uncertainties still to be resolved, and determine the new UK requirements moving forward. This includes transferring licences and authorisations for EU markets currently held in the UK to an EU member state and building capability to test medicines in the EU for which such testing is currently undertaken in the UK. UK licences also need to be separated out from centrally approved products in the EU. These actions are required to ensure appropriate regulatory requirements can be met both in the EU and UK post 29 March 2019. Based on our corporate planning assumptions for a no deal Brexit, with no transition period, the Company is taking steps to protect product supply both in the UK and EU. Changes in regulatory reviews and approvals, and safety surveillance will certainly have implications on resources, ways of working and costs.

Failure to obtain, defend and enforce effective IP protection and IP challenges by third parties

A pharmaceutical product may be protected from being copied for a limited period of time under certain patent rights and/or related IP rights, such as Regulatory Data Protection or Orphan Drug status. Typically, products protected by such rights generate significantly higher revenues than those not protected. Our ability to obtain, maintain, defend and enforce patents and other IP rights in relation to our products is an important element in protecting and recouping our investment in R&D and creating long-term value for the business. Some countries in which we operate do not offer robust IP protection. This may be because IP laws are still developing, the scope of those laws is limited or the political environment does not support such legislation. We also recognise increasing use of compulsory licensing in some countries in which we operate.

We may also face challenges early in the patent application process and throughout a patent's life. The grounds for these challenges could be the validity of a patent and/or its effective scope and are based on ever-evolving legal precedents. We are experiencing increased challenges in the US and elsewhere in the world and there can be no guarantee of success for either party in patent proceedings and litigation.

We also bear the risk that our products may be found to infringe patents owned or licensed by third parties, including research-based and generic pharmaceutical companies and individuals. These third parties may seek remedies for patent infringement, including injunctions (for example, preventing the marketing of one of our products) and damages (for example, research-based competitors are alleging infringement of their patents and are seeking damages in relation to our marketing of *Imfinzi* and *Calquence*).

Details of material patent proceedings and litigation matters can be found in Note 29 to the Financial Statements from page 194.

Limitations on the availability of patent protection, the ability to obtain related IP rights or the use of compulsory licensing in certain countries in which we operate, as well as our ability to defend and enforce our patents, could allow for earlier entry of generic or biosimilar competitor products. This could have a material adverse effect on the pricing and sales of our products and, consequently, could materially adversely affect our revenues.

Third parties may be awarded remedies for alleged infringement of their IP, for example injunctions and damages for alleged patent infringement. In the US, courts may order enhanced (ie up to treble) damages for alleged wilful infringement of patents. From time to time we may acquire licences, discontinue activities and/or modify processes to avoid claims of patent infringement. These steps could entail significant costs and our revenue and margins could be materially adversely affected.

More information about protecting our IP, the risk of patent litigation and the early loss of IP rights is contained in the Intellectual Property section on page 35, the Competitive pressures including expiry or loss of IP rights and generic competition risk on page 222 and Note 29 to the Financial Statements from page 194.

Commercialisation risks	Impact

Competitive pressures including expiry or loss of IP rights, and generic competition

A pharmaceutical product competes with other products marketed by research-based pharmaceutical companies and with generic or biosimilar drugs marketed by generic drug manufacturers.

Generic versions of products, including biosimilars, are often sold at lower prices than branded products, as the manufacturer does not have to recoup the significant cost of R&D investment and market development. Expiry or loss of IP rights can materially adversely affect our revenues and financial condition due to the launch of cheaper generic copies of the product in the country where the rights have expired or been lost (see the table in the Patent Expiries of Key Marketed Products section from page 217). For example, in 2018 our US Product Sales of *Crestor* fell to $170 million (2017: $373 million) following the launch of generics.

Additionally, the expiry or loss of patents covering other innovator companies' products may also lead to increased competition and pricing pressure for our own, still-patented products in the same product class due to the availability of lower priced generic products in that product class.

Generic manufacturers may also take advantage of the failure of certain countries to properly enforce Regulatory Data Protection or other related IP rights and may launch generics during this protected period. This is a particular risk in some Emerging Markets where appropriate patent protection or other related IP rights may be difficult to obtain or enforce.

The biosimilars market has experienced notable growth since 2017, with approval of several monoclonal antibody biosimilars in the US and Europe. This trend is expected to continue. Increased regulatory and legal activity related to the launch and approval of these therapeutics is anticipated. Regulatory authorities in other territories continue to implement or consider abbreviated approval processes for biosimilars, allowing quicker entry to market for such products and earlier than anticipated competition for patented biologics.

As well as facing generic competition upon expiry or loss of IP rights, we also face the risk that generic drug manufacturers seek to market generic versions of our products prior to expiries of our patents and/or the Regulatory Exclusivity periods. For example, we are currently facing challenges from numerous generic drug manufacturers regarding our patents relating to key products, including *Symbicort*, *Brilinta*, *Faslodex* and *Farxiga*.

IP rights protecting our products may be challenged by external parties. We expect our most valuable products to receive the greatest number of challenges. Despite our efforts to establish and defend robust patent protection for our products, we bear the risk that courts may decide that our IP rights are invalid and/or that third parties do not infringe our asserted IP rights.

Where we assert our IP rights but are ultimately unsuccessful, third parties may seek damages, alleging, for example, that they have been inappropriately restrained from entering the market. In such cases, we bear the risk that we incur liabilities to those third parties.

Details of material patent litigation matters can be found in Note 29 to the Financial Statements from page 194.

If we are not successful in obtaining, maintaining, defending or enforcing our exclusive rights to market our products, particularly in the US where we achieve our highest Product Sales, our revenue and margins could be materially adversely affected. In addition, unsuccessful assertion of our IP rights may lead to damages or other liabilities to third parties that could materially adversely affect our financial performance.

Approval of competitive products for the same or similar indication as one of our products may result in immediate and significant decreases in our revenues.

Unfavourable resolution of current and potential future patent litigation may require us to make significant provisions in our accounts relating to legal proceedings and/or could materially adversely affect our financial condition or results of operations.

Commercialisation risks	Impact

Price controls and reductions

Most of our key markets have experienced the implementation of various cost control or reimbursement mechanisms for pharmaceutical products.

In the US, there is significant pricing pressure 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. These mechanisms can be used by payers to limit the use of branded products and put pressure on manufacturers to reduce net prices. In addition, patients are seeing changes in the design of their health plan benefits and may experience variation in how their plans cover their medications, including increases in the out-of-pocket payments for their branded medications. Patient out-of-pocket spending is generally in the form of a co-payment or co-insurance, but there is a growing trend towards high deductible health plans that require that patients pay the full list price of their drugs and services until they meet certain out-of-pocket thresholds. The US political landscape continues to consider a range of legislative and regulatory proposals to address the high costs of prescription drugs as well as reforms to the US healthcare system. We face uncertainties due to federal legislative and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the ACA. Additionally, there may be modifications to Medicare and other government programmes, price transparency requirements, and policies aimed at reducing drug list prices. For more information, please see Pricing of medicines in the Marketplace section from page 11. It is difficult to predict what specific proposals could be enacted and to determine the implications for the healthcare system and pharmaceutical industry. However, lowering drug costs remains a key campaign promise of the current administration and proposals that would significantly modify existing laws and regulations, including coverage and reimbursement of drugs in government programmes and policies relating to drug pricing, could affect private health insurance, coverage and reimbursement in Medicare, Medicaid and the health insurance exchange marketplaces, and other facets of the US healthcare market, with potentially significant impacts on the pharmaceutical industry.

Ongoing scrutiny of the US pharmaceutical industry, focused largely on pricing, is placing increased emphasis on the value of medications. This scrutiny will likely continue across many stakeholders, including policymakers and legislators.

In the US, consolidation among distributors, retail pharmacy chains and other purchasing organisations, including integration across the supply chain, creates concentration of credit risk and increasing potential for large integrated entities to exert more power in negotiations with AstraZeneca, which could result in margin erosion.

In Europe, the industry continues to be exposed to various *ad hoc* cost-containment measures and reference pricing mechanisms, which impact prices. There is a trend towards increasing transparency and comparison of prices among EU Member States which may eventually lead to a change in the overall pricing and reimbursement landscape. There is also a continued push across the EU to harmonise the Health Technology Assessment (HTA) review process. This could lead to an environment in the EU where medicines undergo duplicate HTA evaluations, both at an EU level and a country level, as it is unlikely organisations such as GBA in Germany or HAS in France would make changes to their systems.

In Emerging Markets, governments are increasingly controlling pricing in the self-pay sector and favouring locally manufactured drugs. In addition, the emergence of price referencing has been seen in some markets combined with a call from authorities to provide greater global price transparency.

Concurrently, many markets are adopting the use of HTA to provide a rigorous evaluation of the clinical efficacy of a product at, or post, launch. HTA evaluations are also increasingly being used to assess the clinical effect, as well as cost-effectiveness, of products in a particular health system. This comes as payers and policymakers attempt to increase efficiencies in the use and choice of pharmaceutical products.

A summary of the principal aspects of price regulation and how pricing pressures are affecting our business in our most important markets is set out in Pricing of medicines in the Marketplace section from page 11 and on the next page in the following risk factor.

Due to these pricing pressures, there will continue to be downward pressure on prices globally that will challenge the profitability levels of products in particular markets.

Any future replacement, modification or repeal of the ACA, or any significant spending reductions or cost controls affecting Medicare, Medicaid or other publicly funded or subsidised health programmes in the US, could adversely affect our business and financial results. The significant uncertainty about the future of the ACA, entitlement reform and healthcare laws in general in the US could have a material adverse effect on our results of operations, financial condition or business.

We expect that consolidation and integration of drug distributors, retail pharmacy chains, private insurers, managed care organisations and other purchasing organisations may continue to have an effect on pharmaceutical manufacturers, including us.

The potential duplication of HTA evaluations could result in a delay to times of reimbursement and patient access.

The continued disparities in EU and US pricing systems could lead to marked price differentials between regions, which, by way of the implementation of existing or new reference pricing mechanisms, increases the pricing pressure affecting the industry. The importation of pharmaceutical products from countries where prices are low due to government price controls, or other market dynamics, to countries where prices for those products are higher, is already prevalent and may increase. Strengthened collaboration by governments may accelerate the development of further cost-containment policies (such as joint procurement). Increased and simplified access to national and regional prices in markets and the publication of these prices in centralised databases have facilitated the uptake and efficiency of price referencing across the world.

Commercialisation risks	Impact

Economic, regulatory and political pressures

Operating in over 100 countries, we are subject to political, socio-economic and financial factors (including foreign exchange movements) both globally and in individual countries.

A sustained global economic downturn may further exacerbate pressure from governments and other healthcare payers on medicine prices and volumes of sales in response to pressures on budgets, and may cause a slowdown or a decline in growth in some markets. Those most severely impacted by the economic downturn may seek alternative ways to settle their debts through, for example, the issuance of government bonds which might trade at a discount to the face value of the debt. Other customers may cease to trade, which may result in losses from writing off debts, or a reduction in demand for products.

We are highly dependent on being able to access a sustainable flow of liquid funds due to the high fixed costs of operating our business and the long and uncertain development cycles of our products. In a sustained economic downturn, financial institutions with whom we deal may cease to trade and there can be no guarantee that we will be able to access monies owed to us without a protracted, expensive and uncertain process, if at all.

The majority of our cash investments are managed centrally and are invested in collateralised bank deposits, fixed income securities in government, financial and non-financial securities, and AAA credit-rated institutional money market funds. Money market funds are backed by institutions in the US, EU or elsewhere, which, in turn, invest in other funds, including sovereign funds. This means our credit exposure is a mix of US, EU and rest of the world sovereign default risk, financial institution and non-financial institution default risk.

A number of our existing or future commercial or other agreements, such as borrowings, derivative financial instruments and commercial contracts, utilise or may utilise LIBOR or other similar rates as benchmark reference rates. LIBOR and other benchmark reference rates are the subject of ongoing national and international regulatory reform, the result of which could see them partially or fully replaced by alternative reference rates, with potential adjustments or renegotiations being necessary to our agreements in respect of the commercial terms or mechanisms to set the reference rate. Whilst different alternative reference rates could develop for different currencies and for different agreements, for example borrowings and derivative financial instruments, there is a risk that we fail to renegotiate our agreements. Any combination of these could have an adverse effect on the cost, cash flows, value, return on and trading market of (as appropriate) our borrowings, derivative financial instruments, commercial and other agreements, and could increase our administrative burden if the transition to alternative rates is required or necessary by regulation or market practice.

Deterioration of, or failure to improve, socio-economic conditions, and situations and/or resulting events, depending on their severity, could adversely affect our supply and/or distribution chain in the affected countries and the ability of customers or ultimate payers to purchase our medicines. This could adversely affect our business or results of operations.

While we have adopted cash management and treasury policies to manage the risk of not being able to access a sustainable flow of liquid funds (see the Financial risk management policies section of the Financial Review from page 86), we cannot be certain that these will be as effective as they are intended to be, in particular in the event of a global liquidity crisis. In addition, open positions where we are owed money and investments we have made in financial and non-financial institutions or money market funds cannot be guaranteed to be recoverable. Additionally, if we need access to external sources of financing to sustain and/or grow our business, such as the debt or equity capital financial markets, this may not be available on commercially acceptable terms, if at all, in the event of a severe and/or sustained economic downturn. This may, for instance, be the case in the event of any default by the Company on its debt obligations, which may materially adversely affect our ability to secure debt funding in the future or our financial condition in general. Further information on debt funding arrangements is contained in the Financial risk management policies section of the Financial Review from page 86.

In addition, as set out in the next section, the UK's exit from the EU due to take place on 29 March 2019 could adversely impact the operation of the financial system and the ability of financial institutions to perform certain activities and services upon which we rely.

Uncertainty and volatility in relation to the UK's planned exit from the EU

On 23 June 2016, the UK held a referendum on the UK's continuing membership of the EU, the outcome of which was a decision for the UK to leave the EU (Brexit). On 29 March 2017, the UK Government formally notified the EU under Article 50 of the UK's intention to leave the EU. This notification began the process of negotiation that will likely determine the future terms of the UK's relationship with the EU. Absent a negotiated agreement, the UK will leave the EU on 29 March 2019 and relevant EU law and agreements will cease to apply.

It is still too early to judge the full impact of Brexit. While a draft Withdrawal Agreement has been agreed between the UK government and the European Commission, it is unclear whether this will be ratified by the UK parliament in its current form, amended, or if the UK will leave the EU without a deal. In the absence of a ratified agreement, it is unclear what trading relationships the UK will have with the EU and other significant trading partners after 29 March 2019 given the range of political and legal options currently available including, for example, a no deal exit from the EU, extension or recission of the Article 50 notice and a second referendum. Brexit and implementation of the resulting changes could materially and adversely affect the tax, tax treaty, currency, operational, legal and regulatory regimes as well as the macro-economic environment in which the Group operates. Since the referendum, global markets and foreign exchange rates have experienced increased volatility, including a decline in the value of pound sterling as compared to the euro and US dollar. Upon leaving the EU, among other things, the UK could lose access to the single EU market, travel between the UK and EU countries could be restricted and border checks or other regulatory constraints may impede the free movement of goods. Our workforce, and in turn our ability to recruit and retain talent, could be impacted by any restrictions on the movement of persons as 3.9% of our employees in the UK are citizens of EU countries other than the UK. We could face new and greater costs and challenges if UK regulations and policies that govern our business diverge from those of the EU, or if there is any other new or increased friction in our trading environment.

Until the Brexit negotiation process is completed, it is difficult to anticipate the potential impact on our market share, sales, profitability and results of operations. For example, it is possible in the immediate aftermath of the UK leaving the EU that the capacity at major ports both in the UK and the EU is materially reduced for an indeterminate period of time. This could adversely affect our ability to transport medicines and raw materials/intermediates to the EU and *vice versa* with a consequential adverse impact.

The longer-term effects of Brexit are difficult to predict but could include further financial instability and slower economic growth or economic downturn in the UK in particular, but also in Europe and the global economy. Any restrictions on the movement of persons, deterioration in market access or trading terms, delay or restrictions to the movement of goods or increased cost and burdens in the form of new or diverging rules and regulations may have a significant adverse impact on our operations, profitability and business model. Further, uncertainty around the form and timing of any withdrawal agreement and the form and timing of any post-withdrawal trading arrangements (whether with the EU or third parties) could increase volatility and lead to adverse effects on the economy of the UK, other parts of Europe and the rest of the world, which in turn could have an adverse economic impact on our operations.

Commercialisation risks	Impact

Failures or delays in the quality and execution of our commercial strategies

Commercial success of our products and markets, including the development of growth markets, is a critical factor in sustaining or increasing global Product Sales and replacing lost Product Sales due to patent expiry. The successful launch of a new pharmaceutical product involves substantial investment in sales and marketing activities, launch stocks and other items. We may ultimately be unable to achieve commercial success for various reasons, including difficulties in manufacturing sufficient quantities of the product candidate for development or commercialisation in a timely manner, the impact of price control measures imposed by governments and healthcare authorities, the outcome of negotiations with third-party payers, erosion of IP rights, including infringement by third parties, failure to show a differentiated product profile and changes in prescribing habits.

The commercialisation of biologics is often more complex than for small molecule pharmaceutical products, primarily due to differences in the mode of administration, technical aspects of the product, and rapidly changing distribution and reimbursement environments.

We face particular challenges in Emerging Markets, including:

- More volatile economic conditions and/or political environments.
- Competition from multinational and local companies with existing market presence.
- Difficulties enforcing and protecting IP.
- Inadequate protection against crime (including counterfeiting, corruption and fraud).
- The need to impose developed market compliance standards.
- The need to meet a more diverse range of national regulatory, clinical, manufacturing and distribution requirements.
- Potential inadvertent breaches of local and international law and the need to manage sanctions and other restrictions that may be imposed in each jurisdiction.
- Recruitment of appropriately skilled and experienced personnel.
- Difficulty in identifying the most effective sales and marketing channels and routes to market.
- Intervention by local or national governments, or regulators, restricting market access and/or introducing adverse price controls.
- Difficulty in managing local partnerships such as co-promotion and co-marketing, in terms of performance, and adherence to AstraZeneca's compliance standards which are often higher than the market norm.
- Difficulties in cash repatriation due to strict foreign currency controls, risk of material currency devaluation and lack of hard currency reserves in some Emerging Markets.
- Complexity derived from direct exports to countries where we do not have a legal entity.

We may also seek to acquire complementary businesses or enter into other strategic transactions. The integration of an acquired business could involve incurring significant debt and unknown or contingent liabilities, as well as having a negative effect on our reported results of operations from acquisition-related charges, amortisation of expenses related to intangibles and charges for the implementation of long-term assets. The integration of new businesses with our own could result in operational complexities.

We may also experience difficulties in integrating geographically separated organisations, systems and facilities, and personnel with different organisational cultures. Disputes or difficulties in our relationship with our collaborators or partners may also arise, often due to conflicting priorities or conflicts of interest between parties.

Failure to execute our commercial strategies could materially adversely impact our business or results of operations.

If a new product does not succeed as anticipated or its rate of sales growth is slower than anticipated, there is a risk that we may be unable to fully recoup the costs incurred in launching it, which could materially adversely affect our business or results of operations.

Due to the complexity of the commercialisation process for biologics, the methods of distributing and marketing biologics could materially adversely impact our revenues from the sales of biologic medicines, such as *Synagis* and *FluMist/Fluenz*.

The failure to exploit potential opportunities appropriately in Emerging Markets or materialisation of the risks and challenges of doing business in such markets, including inadequate protection against crime (including counterfeiting, corruption and fraud) or inadvertent breaches of local and international law may materially adversely affect our reputation, business or results of operations.

Integration processes relating to strategic transactions may also result in business disruption, diversion of management resources, the loss of key employees and other issues, such as a failure to integrate IT and other systems.

Incurrence of significant debt or liabilities due to the integration of an acquired business could cause deterioration in our credit rating and result in increased borrowing costs and interest expense. We may issue additional shares to pay for acquired businesses, which would result in the dilution of the rights of our then existing shareholders.

Supply chain and business execution risks	Impact

Failure to maintain supply of compliant, quality products

We may experience difficulties, delays and interruptions in the manufacturing and supply of our products for various reasons, including:

- Demand significantly in excess of forecast demand, which may lead to supply shortages (this is particularly challenging before launch).
- Supply chain disruptions, including those due to natural or man-made disasters at one of our facilities, at a critical supplier or vendor, or during transit.
- Delays in construction of new facilities or the expansion of existing facilities, including those intended to support future demand for our products (particularly as the complexities associated with biologics facilities, especially for drug substances, increase the probability of delay).
- The inability to supply products due to a product quality failure or regulatory compliance action such as licence withdrawal, product recall or product seizure.
- Other manufacturing or distribution problems, including changes in manufacturing production sites, limits to manufacturing capacity due to regulatory requirements, changes in the types of products produced, or physical limitations or other business interruptions that could impact continuous and adequate supply.

As with the rest of the pharmaceutical industry, we work in a heavily regulated environment. It is necessary for us to meet all regulations, including compliance with Good Manufacturing Practices (GMP) and Good Distribution Practices (GDP) and comparable regulatory dossier conditions of approval in other countries in which our products are licensed, manufactured or sold. Regulatory agencies periodically inspect our manufacturing facilities to evaluate compliance with applicable requirements and may identify potential deficiencies.

We increasingly rely on third parties for the timely supply of goods, such as raw materials (for example, the API in some of our medicines and drug substances and/or finished drug products for some of our biologic medicines), equipment, formulated drugs and packaging, critical product components and services, all of which are key to our operations. Many of these goods are difficult to substitute in a timely manner or at all. We expect that external capacity for biologics drug substance production will remain constrained for the next few years and, accordingly, may not be readily available for supplementary production in the event that we experience an unforeseen need for such capacity.

Difficulties with manufacturing and supply, forecasting, distribution or third-party suppliers may result in product shortages, which may lead to lost Product Sales and materially adversely affect our reputation and revenues. Even slight variations in components or any part of the manufacturing process may lead to a product that is non-compliant and does not meet quality standards. This could lead to recalls, spoilage, product shortage, regulatory action and/or reputational harm.

Failure to comply with all manufacturing regulations can result in negative regulatory inspection findings leading to manufacturing cessation, product seizure, debarment or recalls which could have a material adverse effect on our business, financial condition and results of operations.

Illegal trade in our products

The illegal trade in pharmaceutical products is widely recognised by industry, non-governmental organisations and governmental authorities to be increasing. Illegal trade includes counterfeiting, theft and illegal diversion (that is, when our products are found in a market where we did not send them and where they are not approved or not permitted/allowed to be sold). There is a risk to public health when illegally traded products enter the supply chain, as well as associated financial risk. Authorities and the public expect us to help reduce opportunities for illegal trade in our products through securing our supply chains, surveillance, investigation and supporting legal action against those found to be engaged in illegal trade.

Public loss of confidence in the integrity of pharmaceutical products as a result of illegal trade could materially adversely affect our reputation and financial performance. In addition, undue or misplaced concern about this issue may cause some patients to stop taking their medicines, with consequential risks to their health. Authorities may take action, financial or otherwise, if they believe we are liable for breaches in our own supply chains.

There is also a direct financial loss when, for example, counterfeit and/or illegally diverted products replace sales of genuine products in a market or genuine products are recalled following discovery of counterfeit products.

Reliance on third-party goods and services

AstraZeneca spends approximately $10 billion each year with trade suppliers. The spend supports the length of our value chain from discovery to manufacture and commercialisation of our medicines.

Many of our business-critical operations, including certain R&D processes, IT systems, HR, finance, tax and accounting services have been outsourced to third-party providers. We are therefore heavily reliant on these third parties not just to deliver timely and high quality services, but also to comply with applicable laws and regulations and adhere to our ethical business expectations of third-party providers.

The failure of outsource providers to deliver timely services, and to the required level of quality, or the failure of outsource providers to co-operate with each other, could materially adversely affect our financial condition or results of operations. Moreover, the failure of these third parties to operate in an ethical manner could adversely impact our reputation, both internally and externally, or even result in non-compliance with applicable laws and regulations.

Our business and financial results could also be materially adversely affected by disruptions caused by our failure to successfully manage either the integration of outsourced services or the transition process of insourcing services from third parties.

Supply chain and business execution risks	Impact

Failure of information security, data protection and cybercrime

We are dependent on effective IT systems. These systems support key business functions such as our R&D, manufacturing, supply chain and sales capabilities. They provide an important means of safeguarding and communicating data, including critical or sensitive information, the confidentiality and integrity of which we rely on. We also rely on the effectiveness of our internal policies, controls and procedures to protect the confidentiality, integrity and availability of information held on our IT systems, as well as the effectiveness of our due diligence of, and ongoing oversight over, third-party vendors who hold or have access to our data. In addition, we must ensure that the personal data which we, or third-party vendors operating on our behalf, hold and process is protected in a manner that complies with the GDPR which entered into force in May 2018.

Examples of sensitive information that we protect include clinical trial records (patient names and treatments), personal information (employee bank details, home address), IP related to manufacturing process and compliance, key research science techniques, AstraZeneca property (ie, from theft) and privileged access (rights to perform IT tasks).

The size and complexity of our IT systems and cloud utilisation, and those of our third-party vendors (including outsource and Software as a Service (SaaS) providers) with whom we contract, have significantly increased over the past decade. Such systems are potentially vulnerable to service interruptions and security breaches from attacks by malicious third parties, or from intentional or inadvertent actions by our employees or vendors.

Significant changes in the business footprint and the implementation of the IT strategy, including the creation and use of captive offshore Global Technology Centres, could lead to temporary loss of capability.

We increasingly use the internet, digital content, social media, mobile applications, the internet of things (IoT), and other forms of new technology to communicate internally and externally. The accessibility and instantaneous nature of interactions with such media may facilitate or exacerbate the risk of unauthorised data loss from within AstraZeneca. It may also lead to false or misleading statements being made about AstraZeneca, which may damage our reputation, brand image or goodwill. As existing social media platforms expand and evolve, and new social media platforms emerge, it becomes increasingly challenging to identify new points of entry and to put structures in place to secure and protect sensitive information.

The GDPR and similar privacy legislation being passed in various jurisdictions globally introduce the obligation to report data protection breaches, whether intentional or inadvertent, to regulators and affected individuals within expedited timeframes. Such expedited reporting, often before the nature and impact of a data breach can be fully understood, could potentially cause reputational damage and a loss of public trust that ultimately may be disproportionate to the extent of the breach.

Any significant disruption to these IT systems (including breaches of data security or cybersecurity, failure to integrate new and existing IT systems) or failure to comply with additional requirements under the GDPR and other applicable laws, could harm our reputation and materially adversely affect our financial condition or results of operations.

While we invest heavily in the protection of our data and IT, we may be unable to prevent breakdowns or breaches in our systems or failures of our cybersecurity policies, controls or procedures. Any such breakdown, breach or failure could result in disclosure of confidential or other sensitive information, damage to our reputation, regulatory penalties, or sanctions, financial losses and/or other costs.

The inability to effectively back up and restore data could lead to permanent loss of data that could in turn result in non-compliance with applicable laws and regulations, and otherwise harm our business.

We and our vendors could be susceptible to third-party or internal attacks on our information security systems. Such attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organised criminal groups, 'hacktivists', nation states, employees and others. From time to time we experience intrusions, including as a result of computer-related malware. We may be unable to ward off such attacks which could have an adverse effect on our business.

Although we maintain cybersecurity insurance, there can be no assurance that our insurance coverage limits will protect against any future claim or that such insurance proceeds will be paid to us in a timely manner.

Inappropriate use of certain media vehicles could lead to the unauthorised or unintentional public disclosure of sensitive information (such as personally identifiable information on employees, healthcare professionals or patients, such as those enrolled in our clinical trials), which may damage our reputation, adversely affect our business or results of operations and expose us to legal risks and/or additional legal obligations. Similarly, the involuntary public disclosure of commercially sensitive information, or an information loss, could adversely affect our business or results of operations. In addition, negative posts or comments about us (or, for example, the safety of our products) on social media websites or other digital channels could harm our reputation, brand image or goodwill.

Failure of critical processes

Unexpected events and/or events beyond our control could result in the failure of critical processes within the Company or at third parties on whom we are reliant. The business faces threats to business continuity from many directions. Examples of material threats include:

> Disruption to our business or the global markets if there is instability in a particular geographic region, including as a result of war, terrorism, pandemics, armed conflicts, riots, unstable governments, civil insurrection or social unrest.
> Natural disasters in areas of the world prone to extreme weather events and earthquakes.
> Cyber threats similar to those detailed in the Failure of information security, data protection and cybercrime section above.

Failure of critical processes may result in an inability to research, manufacture or supply products to patients. AstraZeneca has developed a Business Resilience framework which is designed to mitigate such risks. However, there is no guarantee that these measures will be sufficient to prevent business interruption. This may expose the Company to litigation and/or regulatory action which may result in fines, loss of revenue and adversely affect the Company's financial results.

Any expected gains from productivity initiatives are uncertain

We continue to implement various productivity initiatives and restructuring programmes with the aim of enhancing the long-term efficiency of the business. However, anticipated cost savings and other benefits from these programmes are based on estimates and the actual savings may vary significantly or may not be achieved at all. In particular, these cost-reduction measures are often based on current conditions and cannot always take into account any future changes to the pharmaceutical industry or our operations, including new business developments or wage or price increases.

Our failure to successfully implement these planned cost-reduction measures, either through the successful implementation of employee relations processes (including consultation, engagement, talent management, recruitment and retention), or the possibility that these efforts do not generate the level of cost savings we anticipate, could materially adversely affect our business or results of operations.

Supply chain and business execution risks	Impact

Failure to attract and retain key personnel, and engage successfully with our employees

We rely heavily on recruiting and retaining talented employees with a diverse range of skills and capabilities to meet our strategic objectives.

We face intense competition for well-qualified individuals, as the supply of people with specific skills and significant leadership potential or in specific geographic regions may be limited, and in the UK the added uncertainty created by Brexit could impact the hiring and retention of staff in some business-critical areas.

The successful delivery of our business objectives is dependent on high levels of engagement, commitment and motivation of the workforce. In January 2019, we announced organisational changes to support continued scientific innovation and commercial success as we enter the next phase in our strategic development. Such changes may increase levels of employee uncertainty leading to lower levels of engagement.

The inability to attract and retain highly-skilled personnel may weaken our succession plans for critical positions in the medium term, may materially adversely affect the implementation of our strategic objectives and could ultimately impact our business or results of operations.

Failure to engage effectively with our employees could lead to business disruption in our day-to-day operations, reduce levels of productivity and/or increase levels of voluntary turnover, all of which could ultimately materially adversely affect our business or results of operations.

Legal, regulatory and compliance risks	Impact

Failure to adhere to applicable laws, rules and regulations

Our many business operations are subject to a wide range of laws, rules and regulations from governmental and non-governmental bodies around the world.

Any failure to comply with these applicable laws, rules and regulations may result in us being investigated by relevant agencies and authorities and/or in legal proceedings being filed against us. Such investigations or proceedings could result in us becoming subject to civil or criminal sanctions and/or being forced to pay fines or damages. Relevant authorities have wide-ranging administrative powers to deal with any failure to comply with continuing regulatory oversight and this could affect us, whether such failure is our own or that of our contractors or external partners. Moreover, such laws, rules and regulations are subject to change.

Material examples of statutes, rules and regulations impacting business operations include:

- Compliance with Good Manufacturing Practice.
- Local, national and international environmental and occupational health and safety laws and regulations.
- Trade control laws governing our imports and exports including nationally and internationally recognised trade agreements, embargoes, trade and economic sanctions and anti-boycott requirements.
- Competition laws and regulations, including challenges from competition authorities and private damages actions.
- Rules and regulations established to promote ethical supply chain management.
- Financial regulations including, but not limited to, external financial reporting, taxation and money laundering.
- Employment practices.
- Disclosure of payments to healthcare professionals under the Sunshine Act and EFPIA legislation.
- Appropriate disclosure of community support, patient group support and product donations.
- Compliance with human rights and appropriate environmental practices of third-party contractors around the world including with, but not limited to, the conflict minerals rule in the US, and the UK Modern Slavery Act.

We have environmental and/or occupational health and safety-related liabilities at some current, formerly owned, leased and third-party sites. For more information on the most significant of these and for details on other significant litigation matters, please refer to Note 29 to the Financial Statements from page 194.

Failure to comply with applicable laws, rules and regulations; manage our liabilities; or to adequately anticipate or proactively manage emerging policy and legal developments could materially adversely affect our licence to operate or results of operations; adversely affect our reputation; cause harm to people or the environment; and/or lead to fines or other penalties.

For example, once a product has been approved for marketing by the regulatory authorities, it is subject to continuing control and regulation, such as the manner of its manufacture, distribution, marketing and safety surveillance. If regulatory issues concerning compliance with environmental, current Good Manufacturing Practice or safety monitoring regulations for pharmaceutical products (often referred to as pharmacovigilance) arise, this could lead to product recalls, loss of product approvals and seizures, and interruption of production, which could create product shortages and delays in new product approvals, and negatively impact patient access. As another example, violation of laws, rules, regulations or policies in countries subject to trade and economic sanctions could lead to loss of import or export privileges, civil or criminal penalties for us or our employees, or potential reputational harm, which could have a material adverse effect on our results of operations, financial condition or business.

Safety and efficacy of marketed products is questioned

Our ability to accurately assess, prior to launch, the eventual safety or efficacy of a new product once in broader clinical use can only be based on data available at that time, which is inherently limited due to relatively short periods of product testing and relatively small clinical study patient samples.

Any unforeseen safety concerns or adverse events relating to our products or failure to comply with laws, rules and regulations relating to provision of appropriate warnings concerning the dangers and risks of our products that result in injuries could expose us to large product liability damages claims, settlements and awards, particularly in the US. Adverse publicity relating to the safety of a product or of other competing products may increase the risk of product liability claims.

Details of material product liability litigation matters can be found in Note 29 to the Financial Statements from page 194.

Serious safety concerns or adverse events relating to our products could lead to product recalls, seizures, loss of product approvals, declining sales and interruption of supply and could materially adversely impact patient access, our reputation and financial revenues.

Significant product liability claims could also arise which could be costly, divert management attention, or damage our reputation and demand for our products.

Unfavourable resolution of such current and similar future product liability claims could subject us to enhanced damages, consumer fraud and/or other claims, including civil and criminal governmental actions, require us to make significant provisions in our accounts relating to legal proceedings, and could materially adversely affect our financial condition or results of operations, particularly where such circumstances are not covered by insurance. For more information, see the limited third party insurance coverage risk on page 230.

Legal, regulatory and compliance risks	Impact

Adverse outcome of litigation and/or governmental investigations

We may be subject to various product liability, consumer, commercial, anti-trust, environmental, employment or tax litigation or other legal proceedings and governmental investigations. Litigation, particularly in the US, is inherently unpredictable and unexpectedly high awards for damages can result from an adverse verdict. In many cases, plaintiffs may claim enhanced damages in extremely high amounts. In particular, the marketing, promotional, clinical and pricing practices of pharmaceutical manufacturers, as well as the manner in which manufacturers interact with purchasers, prescribers and patients, are subject to extensive regulation, litigation and governmental investigation. Many companies, including AstraZeneca, have been subject to claims related to these practices asserted by federal and state governmental authorities and private payers and consumers, which have resulted in substantial expense and other significant consequences. Note 29 to the Financial Statements from page 194 describes the material legal proceedings in which we are currently involved.

Governmental investigations, for example under the US Foreign Corrupt Practices Act or federal or state False Claims Acts or other types of 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, including enhanced damages, require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business or results of operations.

Failure to adhere to increasingly stringent anti-bribery and anti-corruption legislation

There remains an increased global focus on the implementation and enforcement of anti-bribery and anti-corruption legislation.

Two relevant pieces of legislation include the UK Bribery Act and the US Foreign Corrupt Practices Act, and many other countries where we operate are also enforcing their own laws more aggressively and/or adopting tougher new measures. There has also been an increase in co-operation and co-ordination between regulators across countries with respect to investigation and enforcement.

We have been the subject of anti-corruption investigations and there can be no assurance that we will not, from time to time, be subject to informal enquiries and formal investigations from governmental agencies. In the context of our business, governmental officials interact with us in various roles that are important to our operations, such as in the capacity of a regulator, partner or healthcare payer, reimburser or prescriber, amongst others. To the extent we are the subject of any such pending and material matters, details are included in Note 29 to the Financial Statements from page 194.

Despite taking measures to prevent breaches of applicable anti-bribery and anti-corruption laws by our personnel and associated third parties, breaches may still occur, potentially resulting in the imposition of significant penalties, such as fines, the requirement to comply with monitoring or self-reporting obligations, or debarment or exclusion from government sales or reimbursement programmes, any of which could materially adversely affect our reputation, business or results of operations.

Economic and financial risks	Impact

Failure to achieve strategic plans or meet targets and expectations

From time to time, we communicate our business strategy or our targets or expectations regarding our future financial or other performance (for example, the expectations described in Future prospects in the Financial Review on page 86). All such statements are of a forward-looking nature and are based on assumptions and judgements we make, all of which are subject to significant inherent risks and uncertainties, including those that we are unaware of and/or that are beyond our control.

There can be no guarantee that our financial targets or expectations will materialise on the expected timeline or at all. Actual results may deviate materially and adversely from any such target or expectation, including if one or more of the assumptions or judgements underlying any such target or expectation proves to be incorrect in whole or in part.

Any failure to successfully implement our business strategy, whether determined by internal or external risk factors, may frustrate the achievement of our financial or other targets or expectations and, in turn, materially damage our brand and materially adversely affect our business, financial position or results of operations.

Failure in financial control or the occurrence of fraud

Effective internal controls are necessary for us to provide reliable financial reports and are designed to prevent and detect fraud. Lapses in controls and procedures could undermine the ability to prevent fraud or provide accurate disclosure of financial information on a timely basis. Testing of our internal controls can provide only reasonable assurance with respect to the preparation and fair presentation of financial statements and may not prevent or detect misstatements or fraud.

Significant resources may be required to remediate any lapse or deficiency in internal controls.

Any such deficiency may also trigger investigations by a number of organisations, for example, the SEC, the DOJ or the UK Serious Fraud Office and may result in fines being levied against Group individual directors or officers.

Serious fraud may lead to potential prosecution or even imprisonment of senior management.

Economic and financial risks	Impact

Unexpected deterioration in the Group's financial position

A wide range of financial risks could result in a material deterioration in the Group's financial position.

As a global business, currency fluctuations can significantly affect our results of operations, which are reported in US dollars. Approximately 33% of our global 2018 Product Sales were in the US, which is expected to remain our largest single market for the foreseeable future. Product Sales in other countries are predominantly in currencies other than the US dollar, including Chinese renminbi, the euro, Japanese yen and pound sterling.

Our consolidated balance sheet contains significant investments in intangible assets, including goodwill. The nature of the pharmaceutical business is high risk and requires that we invest in a large number of projects in an effort to develop a successful portfolio of approved products. Our ability to realise value on these significant investments is often contingent upon, among other things, regulatory approvals, market acceptance, competition and legal developments. As such, in the course of our many acquisitions and R&D activities, we expect that some of our intangible assets will become impaired and be written off at some time in the future.

Inherent variability of biologics manufacturing increases the risk of write-offs of these product batches. Due to the value of the materials used, the carrying amount of biologic products is much higher than that of small molecule products. As we continue to grow our biologics business, we also increase the risk of potential impairment charges.

The costs associated with product liability litigation have increased the cost of, and narrowed the coverage afforded by, pharmaceutical companies' product liability insurance. To contain insurance costs, as of February 2006, we adjusted our product liability coverage profile, accepting uninsured exposure above $100 million. In addition, where claims are made under insurance policies, insurers may reserve the right to deny coverage on various grounds. For example, product liability litigation cases relating to *Farxiga* and *Nexium* in the US are not covered by third-party product liability insurance. See Note 29 to the Financial Statements from page 194 for details.

The integrated nature of our worldwide operations can produce conflicting claims from revenue authorities as to the profits to be taxed in individual countries. The majority of the jurisdictions in which we operate have double tax treaties with other foreign jurisdictions, which provide a framework for mitigating the incidence of double taxation on our revenues and capital gains.

The Group's worldwide operations are taxed under laws in the jurisdictions in which they operate. International standards governing the global tax environment regularly change. The Organisation for Economic Co-operation and Development (OECD) has proposed a number of changes under the Base Erosion and Profit Shifting (BEPS) Action Plans which are now being progressively implemented by tax authorities around the world.

Our defined benefit pension obligations are largely backed by assets invested across the broad investment market. Our most significant obligations relate to defined benefit pension funds in the UK, Sweden and the US. The largest obligation is in the UK.

Movements in the exchange rates used to translate foreign currencies into US dollars may materially adversely affect our financial condition or results of operations. Some of our subsidiaries import and export goods and services in currencies other than their own functional currency, and so the financial results of such subsidiaries could be affected by currency fluctuations arising between the transaction and settlement dates. In addition, there are foreign exchange differences arising on the translation of investments in subsidiaries.

We have significant investments in goodwill and intangible assets as a result of our acquisitions of various businesses and our purchases of certain assets, such as product development and marketing rights. Impairment losses may materially adversely affect our financial condition or results of operations. Details of the carrying values of goodwill and intangible assets, and the estimates and assumptions we make in our impairment testing, are included in Notes 8 and 9 to the Financial Statements from page 168.

Financial liabilities arising due to product liability or other litigation, in respect of which we do not have insurance coverage, or if an insurer's denial of coverage is ultimately upheld, could require us to make significant provisions relating to legal proceedings and could materially adversely affect our financial condition or results of operations.

For more information, please see the Adverse outcome of litigation and/or governmental investigations risk on page 229.

The resolution of tax disputes regarding the profits to be taxed in individual territories can result in a reallocation of profits between jurisdictions and an increase or decrease in related tax costs, and has the potential to affect our cash flows, EPS and post-tax earnings. Claims, regardless of their merits or their outcome, are costly, divert management attention and may adversely affect our reputation.

If any double tax treaties are withdrawn or amended, especially in a territory where a member of the AstraZeneca Group is involved in a taxation dispute with a tax authority in relation to cross-border transactions, such withdrawal or amendment could materially adversely affect our financial condition or results of operations, as could a negative outcome of a tax dispute or a failure by tax authorities to agree through competent authority proceedings. Changes to the application of double tax treaties, as a result of the parent company of the Group no longer being an EU entity following Brexit, could also result in adverse consequences such as those described above. See the Financial risk management policies section of the Financial Review on page 86 for tax risk management policies and Note 29 to the Financial Statements from page 194 for details of current tax disputes.

Changes in tax regimes, such as those relating to the US federal tax regime which were effective from 1 January 2018, could result in a material impact on the Group's cash tax liabilities and tax charge, resulting in either an increase or a reduction in financial results depending upon the nature of the change. We represent views to the OECD, governments and tax authorities through public consultations to ensure international institutions and governments understand the business implications of proposed law changes. Specific OECD BEPS recommendations that we expect to impact the Group include changes to patent box regimes, restrictions of interest deductibility and revised transfer pricing guidelines.

Sustained falls in asset values could reduce pension fund solvency levels, which may result in requirements for additional cash, restricting the cash available for our business. Changes to funding regulations for defined benefit pensions may also result in a requirement for additional cash contributions by the Group. If the present value of the liabilities increases due to a sustained low interest rate environment, an increase in expectations of future inflation, or an improvement in member longevity (above that already assumed), this could also reduce pension fund solvency ratios. The likely increase in the IAS 19 accounting deficit generated by any of these factors may cause the credit rating agencies to review our credit rating, with the potential to negatively affect our ability to raise debt and the price of new debt issuances. See Note 21 to the Financial Statements from page 178 for further details of the Group's pension obligations.

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:

> Key Performance Indicators – Be a Great Place to Work, page 22
> Key Performance Indicators – Do business sustainably, page 22
> Emerging market healthcare, page 32
> Develop a strong and diverse pipeline of leaders, page 40
> Human rights, page 41
> Managing change, page 41
> Employee relations, page 41
> Safety, health and wellbeing, page 41
> Sustainability, page 42
> Sustainability strategy, page 42
> Sustainability governance, page 43
> Broadening access to healthcare, page 43
> Ethics and transparency, page 43
> Protecting the environment, page 46
> Community investment, page 48
> Young Health Programme, page 48
> Donation programmes, page 48
> Greenhouse gas (GHG) reporting, page 231

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's scope of work, methodology, overall opinion, and limitations and exclusions, is available on our website, www.astrazeneca.com.

Greenhouse gas (GHG) reporting

We have reported on all of the emission sources required under the Quoted Companies Greenhouse Gas 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 (IEA), USEPA eGRID, US Green-e and the Association of Issuing Bodies (AIB) databases and for all other fuels and emission sources from the 2006 IPCC Guidelines for National Greenhouse Gas Inventories.

Bureau Veritas has undertaken a limited assurance on the 2018 GHG emissions data. The assurance statement, including scope, methodology, overall opinion, and limitations and exclusions, is available on our website, www.astrazeneca.com.

Global greenhouse gas emissions data for the period 1 January 2018 to 31 December 2018[1]

	Tonnes CO_2e		
	2018	2017	2016
Emissions from: Scope 1: Combustion of fuel and operation of facilities[2]	**301,055**	291,694	309,685
Scope 2 (Market-based): Electricity (net of market instruments), heat, steam and cooling purchased for own use[3]	**158,987**	178,614	218,770
Scope 2 (Location-based): Electricity, heat, steam and cooling purchased for own use[3]	**294,906**	273,681	288,210
Company's chosen intensity measurement: Scope 1 + Scope 2 (Market-based) emissions reported above normalised to million US dollar revenue	**20.8**	20.9	23.0
Scope 3 in our Operational Footprint: Supply chain emissions: Upstream emissions from personal air travel, goods transport, waste incineration, and first tier active pharmaceutical ingredients and formulation & packaging suppliers (>90% of category spend, energy only, one year in arrears); Downstream emissions from HFA propellants released during patient use of our inhaled medicines	**1,309,069**	1,234,739	1,155,504
2016-2025 Strategy 'Operational Footprint' KPI: Scope 1 + Scope 2 (Market-based) + our Operational Footprint Scope 3 sources. Baseline year is 2015	**1,769,110**	1,705,047	1,683,959
Scope 3 Total: Emissions from all 15 Greenhouse Gas Protocol Scope 3 Categories[4]	**5,819,517**	5,830,380	5,813,138
2016-2025 Strategy Scope 3 intensity measurement KPI: Scope 3 emissions from all 15 Greenhouse Gas Protocol Scope 3 Categories normalised to million US dollar revenue. Baseline year is 2015 (one year in arrears)	**263**	260	253

1 Regular review of the data is carried out to ensure accuracy and consistency. This has led to changes in the data from previous years. The majority of adjustments made are not material individually, except for business air travel (new data supplier, leading to restated baseline) and product use phase (recalculated using improved life-cycle emissions data). The data quoted in this Annual Report are generated from the revised data.

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.

3 GHGs from imported electricity are calculated using the GHG Protocol Scope 2 Guidance (January 2015) requiring the 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.

4 In previous years, this data has been reported one year in arrears. GHG accounting has been updated to align the 2016 and 2017 reporting with the actual year's emissions data. For 2018 reporting, a significant proportion has been estimated and will be refined in future external reports.

Shareholder Information

The principal markets for trading in AstraZeneca shares are the London Stock Exchange, Nasdaq Stockholm and 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 the New York Stock Exchange are in the form of American Depositary Shares (ADSs), evidenced by American Depositary Receipts (ADRs) issued by the Company's ADR depositary, Citibank, N.A. Two ADSs are equivalent to one Ordinary Share. Before 27 July 2015 the ratio was one ADS per one Ordinary Share.

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
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SE-101 23 Stockholm
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ADR depositary

Citibank Shareholder Services
PO Box 43077
Providence
RI 02940-3077
USA
Tel (toll free in the US): +1 (888) 697 8018
Tel (outside the US): +1 (781) 575 4555
citibank@shareholders-online.com

Annual general meeting (AGM)

The 2019 AGM will be held on 26 April 2019. The meeting place will be in London, UK. Shareholders holding Ordinary Shares directly are entitled to attend and vote at the meeting or may submit a proxy voting instruction in advance, by following the instructions in the notice of AGM.

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 2019 are shown in the financial calendar on page 233. 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. Further information on dividends declared can be found in the Shareholder Information section of AstraZeneca's website at www.astrazeneca.com.

Shareholders holding Ordinary Shares directly may opt for dividends to be paid straight to their bank or building society account, rather than being paid by cheque. To elect for this swift and secure method of payment, contact the Ordinary Share registrar, visit www.shareview.co.uk or fill in the mandate form that will be sent to you with your next dividend cheque. If you hold shares listed in Stockholm, you should contact your personal broker or, if you hold a VP account, contact the bank that services your VP account. If you hold ADRs directly you should contact Shareholder Services on the number provided. If you hold your shares through a nominee, you should direct any queries relating to your shareholding and dividend payments to the nominee provider.

Shareholder communications

Copies of shareholder communications and annual reports are available on AstraZeneca's website at www.astrazeneca.com. If you hold Ordinary Shares directly, currently receive hard copies of shareholder communications and/or the annual report and would rather receive these documents electronically, you can manage your communication preferences at www.shareview.co.uk or by contacting the Ordinary Share registrar. If your record on the Ordinary Share register has been duplicated you may receive multiple copies of shareholder communications; if this is the case please contact the Ordinary Share registrar so that this can be rectified.

Holders of shares listed in Stockholm should contact Computershare AB, PO Box 610, SE-182 16 Danderyd, Sweden (Tel: +46 (0)8 588 04 200) and holders of ADRs should contact the ADR depositary or their personal broker with queries relating to shareholder communications.

Shareview

Holders of Ordinary Shares may create a portfolio at www.shareview.co.uk to view and manage their AstraZeneca shareholding. Shareview is a free and secure online service provided by the Ordinary Share registrar that allows users to, among other things, update personal details, manage communication preferences, view dividend information and manage direct dividend payments.

ShareGift

Shareholders that hold only a small number of shares, the value of which makes it uneconomical to sell them, may wish to consider donating them to charity through ShareGift, an independent charity share donation scheme (registered charity number 1052686). Further information about ShareGift can be found on its website at www.sharegift.org or by calling +44 (0)20 7930 3737.

The Unclaimed Assets Register

AstraZeneca provides information to the Unclaimed Assets Register (UAR) relating to unclaimed dividends paid on Ordinary Shares. The UAR database provides a facility to search for financial assets that may have been forgotten and can be contacted on +44 (0)333 000 0182 or uarenquiries@uk.experian.com.

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 AstraZeneca's 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.

Investor Relations

www.astrazeneca.com/investors
irteam@astrazeneca.com
Tel (UK): +44 (0)20 3749 5824
Tel (toll free in the US): +1 866 381 7277

Financial calendar

Event	Provisional date
Second interim dividend for 2018	
Ex-dividend date	28 February 2019
Record date	1 March 2019
Payment date	27 March 2019
Announcement of first quarter results for 2019	26 April 2019
Annual general meeting (AGM)	26 April 2019
Announcement of second quarter and half-year results for 2019	25 July 2019
First interim dividend for 2019	
Ex-dividend date	8 August 2019
Record date	9 August 2019
Payment date	9 September 2019
Announcement of third quarter results for 2019	24 October 2019
Financial year end	31 December 2019

History and development of the Company

AstraZeneca PLC was incorporated in England and Wales on 17 June 1992 under the Companies Act 1985. It is a public limited company domiciled in the UK. The Company's registered number is 2723534 and its registered office is at 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA, UK (Tel: +44 (0)20 3749 5000). From February 1993 until April 1999, the Company was called Zeneca Group PLC. On 6 April 1999, the Company changed its name to AstraZeneca PLC.

The Company was formed when the pharmaceutical, agrochemical and specialty chemical businesses of Imperial Chemical Industries PLC were demerged in 1993. In 1999, the Company sold the specialty chemical business. Also in 1999, the Company merged with Astra of Sweden. In 2000, it demerged the agrochemical business and merged it with the similar business of Novartis to form a new company called Syngenta AG. In 2007, the Group acquired MedImmune, a biologics and vaccines business based in the US.

In 1999, in connection with the merger between Astra and Zeneca, the Company's share capital was redenominated in US dollars. On 6 April 1999, Zeneca shares were cancelled and US dollar shares issued, credited as fully paid on the basis of one dollar share for each Zeneca share then held. This was achieved by a reduction of capital under section 135 of the Companies Act 1985. Upon the reduction of capital becoming effective, all issued and unissued Zeneca shares were cancelled and the sum arising as a result of the share cancellation credited to a special reserve, which was converted into US dollars at the rate of exchange prevailing on the record date. This US dollar reserve was then applied in paying up, at par, newly created US dollar shares.

At the same time as the US dollar shares were issued, the Company issued 50,000 Redeemable Preference Shares for cash, at par. The Redeemable Preference Shares carry limited class voting rights, no dividend rights and are 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 Redeemable Preference Shares.

A total of 826 million Ordinary Shares were issued to Astra shareholders who accepted the merger offer before the final closing date, 21 May 1999. The Company received acceptances from Astra shareholders representing 99.6% of Astra's shares and the remaining 0.4% was acquired in 2000, for cash.

Issued share capital, shareholdings and share prices

At 31 December 2018, the Company had 83,588 registered holders of 1,267,039,436 Ordinary Shares. There were 105,266 holders of Ordinary Shares held under the Euroclear Services Agreement, representing 10.1% of the issued share capital of the Company and 1,818 registered holders of ADSs, representing 20.1% of the issued share capital of the Company.

Ordinary Shares in issue

	2018	2017	2016	2015	2014
Ordinary Shares in issue – millions					
At year end	**1,267**	1,266	1,265	1,264	1,263
Weighted average for year	**1,267**	1,266	1,265	1,264	1,262
Stock market price per Ordinary Share (London Stock Exchange)					
Highest (pence)	**6317.0**	5508.0	5220.0	4863.0	4823.5
Lowest (pence)	**4712.5**	4194.0	3774.0	3903.5	3549.5
At year end (pence)	**5873.0**	5121.0	4437.5	4616.5	4555.5

Analysis of shareholdings as a percentage of issued share capital at 31 December

Number of Ordinary Shares[1]	**2018 %**	2017 %	2016 %	2015 %	2014 %
1 – 250	**0.4**	0.5	0.5	0.5	0.5
251 – 500	**0.5**	0.5	0.5	0.6	0.6
501 – 1,000	**0.5**	0.6	0.6	0.7	0.7
1,001 – 5,000	**0.8**	0.8	0.8	0.9	1.0
5,001 – 10,000	**0.2**	0.2	0.2	0.2	0.2
10,001 – 50,000	**1.0**	1.0	0.9	0.9	1.0
50,001 – 1,000,000	**12.1**	11.9	12.3	13.0	13.3
Over 1,000,000	**84.5**	84.5	84.2	83.2	82.7

[1] Includes Euroclear and ADR holdings.

Shareholder Information
continued

Reported high and low share prices during the year

		Ordinary Shares London Stock Exchange[1]		Ordinary Shares Nasdaq Stockholm[2]		ADRs New York Stock Exchange[3]	
		High (pence)	Low (pence)	High (SEK)	Low (SEK)	High (USD)	Low (USD)
2018	– December	6211.0	5720.0	722.0	661.8	39.87	36.86
	– November	6317.0	5732.0	754.8	692.4	41.49	37.85
	– October	6078.0	5546.0	725.0	665.5	40.08	37.15
	– September	5963.0	5572.0	702.1	659.6	39.72	37.07
	– August	6107.0	5795.0	721.8	680.7	39.61	37.96
	– July	5865.0	5182.0	685.3	608.2	39.13	34.76
	– Quarter 4	6317.0	5546.0	754.8	661.8	41.49	36.86
	– Quarter 3	6107.0	5182.0	721.8	608.2	39.72	34.76
	– Quarter 2	5478.0	4867.0	648.4	584.3	37.05	34.55
	– Quarter 1	5204.0	4712.5	587.3	531.7	36.63	32.97
2017	– Quarter 4	5180.0	4705.0	581.0	541.0	34.78	32.09
	– Quarter 3	5192.0	4325.0	578.0	466.2	34.16	28.88
	– Quarter 2	5508.0	4566.0	619.0	534.0	35.36	29.76
	– Quarter 1	4974.5	4194.0	558.0	470.6	31.80	26.72

[1] For shares listed on the London Stock Exchange, the reported high and low middle market closing quotations are derived from the Daily Official List.
[2] For shares listed on Nasdaq Stockholm, the high and low closing sales prices are as stated in the Official List.
[3] For ADRs listed on the New York Stock Exchange, the reported high and low sales prices are as reported by Dow Jones (ADR quotations).

US holdings

At 31 January 2019, the proportion of Ordinary Shares represented by ADSs was 20.0% of the issued share capital of the Company. At 31 January 2019, there were 83,479 registered holders of Ordinary Shares, of which 688 were based in the US and there were 1,813 record holders of ADRs, of which 1,785 were based in the US.

Major shareholdings

At 31 December 2018, 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:

Shareholder	Number of Ordinary Shares	Date of disclosure to Company[1]	**Number of Ordinary Shares disclosed as a percentage of issued share capital at 31 December 2018**
BlackRock, Inc.	100,885,181	4 December 2009	**7.96**
Investor AB	51,587,810	2 February 2012	**4.07**
The Capital Group Companies, Inc.	63,802,495	17 July 2018	**5.04**

[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.

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 2018 and 31 January 2019.

Changes in the percentage ownerships disclosed by major shareholders during the past three years are set out below. Major shareholders do not have different voting rights.

Shareholder	**31 January 2019**	31 January 2018	31 January 2017	31 January 2016
BlackRock, Inc.	**7.96**	7.97	7.97	7.98
Investor AB	**4.07**	4.07	4.08	4.08
The Capital Group Companies, Inc.	**5.04**	4.98	3.00	3.00

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' and officers' shareholdings

At 31 January 2019, the total amount of the Company's voting securities owned by Directors and officers of the Company was:

Title of class	Amount owned	Percentage of class
Ordinary Shares	**564,514**	**0.04**

Options to purchase securities from registrant or subsidiaries

(a) At 31 January 2019, options outstanding to subscribe for Ordinary Shares were:

Number of shares	Subscription price (pence)	Normal expiry date
1,689,933	**2280-4724**	**2019-2024**

The weighted average subscription price of options outstanding at 31 January 2019 was 3610 pence. All options were granted under Company employee share schemes.

(b) Included in paragraph (a) are options granted to officers of the Company as follows:

Number of shares	Subscription price (pence)	Normal expiry date
1,407	**3307-3597**	**2021**

(c) Details of Directors' option holdings are shown in the Remuneration Report on page 138. No options were held by Directors at 31 December 2018.

During the period 1 January 2019 to 31 January 2019, no Director was granted or exercised any options.

Related party transactions

During the period 1 January 2019 to 31 January 2019, 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 200).

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.

Rights, preferences and restrictions attaching to shares

As at 31 December 2018, the Company had 1,267,039,436 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 closing mid-point USD/GBP exchange rate on 31 December 2018 as published in the London edition of the Financial Times newspaper).

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.

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.

Shareholder Information
continued

Documents on display
The Articles and other documents concerning the Company which are referred to in this Annual Report may be inspected at the Company's registered office at 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA, UK.

Compliance requirements under Listing Rule 9.8.4
Other than as set out below, the Company has nothing to report under Listing Rule 9.8.4.

Item	Location of details in Annual Report
Details of any long-term incentive schemes	Note 28 of the Financial Statements and Directors' Remuneration Report
Shareholder waiver of dividends	Page 106 in the Corporate Governance Report

Property
Substantially all of our properties are held freehold, free of material encumbrances and are fit for their purpose. For more information please refer to Note 7 to the Group Financial Statements on page 167.

Tax information for shareholders
Taxation for US persons
The following summary of material UK and US federal income tax consequences of ownership of Ordinary Shares or ADRs held as capital assets by the US holders described below is based on current UK and US federal income tax law, including the US/UK double taxation convention relating to income and capital gains, which entered into force on 31 March 2003 (the Convention). This summary does not describe all of the tax consequences that may be relevant in light of the US holders' particular circumstances and tax consequences applicable to US holders subject to special rules (such as certain financial institutions, entities treated as partnerships for US federal income tax purposes, persons whose functional currency for US federal income tax purposes is not the US dollar, tax-exempt entities, persons that own directly, indirectly or constructively ADRs or Ordinary Shares representing 10% or more of our voting power or value, persons subject to alternative minimum tax, persons subject to the Medicare contribution tax on 'net investment income', or persons holding Ordinary Shares or ADRs in connection with a trade or business conducted outside of the US). US holders are urged to consult their tax advisers regarding the UK and US federal income tax consequences of the ownership and disposition of Ordinary Shares or ADRs in their particular circumstances.

This summary is based in part on representations of Citibank as depositary for ADRs and assumes that each obligation in the deposit agreement among the Company and the depositary and the holders from time to time of ADRs and any related agreements will be performed in accordance with its terms. The US Treasury has expressed concerns that parties to whom American depositary shares are released before shares are delivered to the depositary (pre-release), or intermediaries in the chain of ownership between holders and the issuer of the security underlying the American depositary shares, may be taking actions that are inconsistent with the claiming, by US holders of American depositary shares, of foreign tax credits for US federal income tax purposes. Such actions would also be inconsistent with the claiming of the reduced tax rates, described below, applicable to dividends received by certain non-corporate US holders. Accordingly, the availability of the reduced tax rates for dividends received by certain non-corporate US holders could be affected by actions that may be taken by parties to whom ADRs are pre-released.

For the purposes of this summary, the term 'US holder' means a beneficial owner of Ordinary Shares or ADRs that is, for US federal income tax purposes, a citizen or resident of the US, a corporation (or other entity taxable as a corporation) created or organised in or under the laws of the US, any state in the US or the District of Columbia, or an estate or trust, the income of which is subject to US federal income taxation regardless of its source.

This summary assumes that we are not, and will not become, a passive foreign investment company, as discussed below.

UK and US income taxation of dividends
The UK does not currently impose a withholding tax on dividends paid by a UK company, such as the Company.

For US federal income tax purposes, distributions paid by the Company to a US holder are included in gross income as foreign source ordinary dividend income to the extent paid out of the Company's current or accumulated earnings and profits, calculated in accordance with US federal income tax principles. The Company does not maintain calculations of its earnings and profits under US federal income tax principles and so it is expected that distributions generally will be reported to US holders as dividends. The amount of the dividend will be the US dollar amount received by the depositary for US holders of ADRs (or, in the case of Ordinary Shares, the US dollar value of the foreign currency payment, determined at the spot rate of the relevant foreign currency on the date the dividend is received by the US holders, regardless of whether the dividend is converted into US dollars), and it will not be eligible for the dividends received deduction generally available to US corporations. If the dividend is converted into US dollars on the date of receipt, US holders of Ordinary Shares generally should not be required to recognise foreign currency gains or losses in respect of the dividend income. They may have foreign currency gain or loss (taxable at the rates applicable to ordinary income) if the amount of such dividend is converted into US dollars after the date of its receipt.

Subject to applicable limitations and the discussion above regarding concerns expressed by the US Treasury, dividends received by certain non-corporate US holders of Ordinary Shares or ADRs may be taxable at favourable US federal income tax rates. US holders should consult their own tax advisers to determine whether they are subject to any special rules which may limit their ability to be taxed at these favourable rates.

Taxation on capital gains
Under present English law, individuals who are neither resident nor ordinarily resident in the UK, and companies which are not resident in the UK, will not be liable for UK tax on capital gains made on the disposal of their Ordinary Shares or ADRs, unless such Ordinary Shares or ADRs are held in connection with a trade, profession or vocation carried on in the UK through a branch or agency or other permanent establishment.

A US holder will generally recognise US source capital gains or losses for US federal income tax purposes on the sale or exchange of Ordinary Shares or ADRs in an amount equal to the difference between the US dollar amount realised and such holder's US dollar tax basis in the Ordinary Shares or ADRs. US holders should consult their own tax advisers about the treatment of capital gains, which may be taxed at lower rates than ordinary income for non-corporate US holders and capital losses, the deductibility of which may be subject to limitations.

Passive Foreign Investment Company (PFIC) rules

We believe that we were not a PFIC for US federal income tax purposes for the year ended 31 December 2018. However, since PFIC status depends on the composition of our income and assets, and the market value of our assets (including, among others, less than 25% owned equity investments), from time to time, there can be no assurance that we will not be considered a PFIC for any taxable year. If we were treated as a PFIC for any taxable year during which Ordinary Shares or ADRs were held, certain adverse tax consequences could apply to US holders.

Information reporting and backup withholding

Payments of dividends and sales proceeds that are made within the US or through certain US-related financial intermediaries may be subject to information reporting and backup withholding, unless: (i) the US holder is a corporation or other exempt recipient; or (ii) in the case of backup withholding, the US holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding. The amount of any backup withholding from a payment to a US holder will be allowed as a credit against the holder's US federal income tax liability and may entitle the holder to a refund, provided that the required information is timely supplied to the US Internal Revenue Service (IRS).

Certain US holders who are individuals (or certain specified entities), may be required to report information relating to securities issued by non-US persons (or foreign accounts through which the securities are held), generally on IRS Form 8938, subject to certain exceptions (including an exception for securities held in accounts maintained by US financial institutions). US holders should consult their tax advisers regarding their reporting obligations with respect to the Ordinary Shares or ADRs.

UK inheritance tax

Under the current Double Taxation (Estates) Convention (the Estate Tax Convention) between the US and the UK, Ordinary Shares or ADRs held by an individual shareholder who is domiciled for the purposes of the Estate Tax Convention in the US, and is not for the purposes of the Estate Tax Convention a national of the UK, will generally not be subject to UK inheritance tax on the individual's death or on a chargeable gift of the Ordinary Shares or ADRs during the individual's lifetime, provided that any applicable US federal gift or estate tax liability is paid, unless the Ordinary Shares or ADRs are part of the business property of a permanent establishment of the individual in the UK or, in the case of a shareholder who performs independent personal services, pertain to a fixed base situated in the UK. Where the Ordinary Shares or ADRs have been placed in trust by a settlor who, at the time of settlement, was a US domiciled shareholder, the Ordinary Shares or ADRs will generally not be subject to UK inheritance tax unless the settlor, at the time of settlement, was a UK national, or the Ordinary Shares or ADRs are part of the business property of a permanent establishment of the individual in the UK or, in the case of a shareholder who performs independent personal services, pertain to a fixed base situated in the UK. In the exceptional case where the Ordinary Shares or ADRs are subject to both UK inheritance tax and US federal gift or estate tax, the Estate Tax Convention generally provides for double taxation to be relieved by means of credit relief.

UK stamp duty reserve tax and stamp duty

A charge to UK stamp duty or UK stamp duty reserve tax (SDRT) may arise on the deposit of Ordinary Shares in connection with the creation of ADRs. The rate of stamp duty or SDRT will generally be 1.5% of the value of the consideration or, in some circumstances, the value of the Ordinary Shares. There is no 1.5% SDRT charge on the issue of Ordinary Shares (or, where it is integral to the raising of new capital, the transfer of Ordinary Shares) into the ADR arrangement.

No UK stamp duty will be payable on the acquisition or transfer of existing ADRs provided that any instrument of transfer or written agreement to transfer is executed outside the UK and remains at all times outside the UK. An agreement for the transfer of ADRs will not give rise to a liability for SDRT.

A transfer of, or an agreement to, transfer Ordinary Shares will generally be subject to UK stamp duty or SDRT at 0.5% of the amount or value of any consideration, provided, in the case of stamp duty, it is rounded up to the nearest £5.

Transfers of Ordinary Shares into CREST will generally not be subject to stamp duty or SDRT, unless such a transfer is made for a consideration in money or money's worth, in which case a liability to SDRT will arise, usually at the rate of 0.5% of the value of the consideration. Paperless transfers of Ordinary Shares within CREST are generally liable to SDRT at the rate of 0.5% of the value of the consideration. CREST is obliged to collect SDRT from the purchaser on relevant transactions settled within the system.

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 subsidiary, Zeneca Wilmington Inc.

Exchange rates

The following information relating to average and spot exchange rates used by AstraZeneca is provided for convenience:

	SEK/USD	USD/GBP
Average rates (statement of comprehensive income, statement of cash flows)		
2018	**8.6419**	**1.3405**
2017	8.5835	1.2835
2016	8.5286	1.3673
End of year spot rates (statement of financial position)		
2018	**8.9537**	**1.2743**
2017	8.2467	1.3468
2016	9.1162	1.2272

Trade Marks

AstraZeneca, the AstraZeneca logotype, and the AstraZeneca symbol are all trade marks of the Group.

The following brand names which appear in italics in this Annual Report are trade marks of the Group:

Trade mark			
Arimidex	*Diprivan*[2]	*Marcaine*[2]	*Seloken*
Atacand[1]	*Duzallo*	*Movantik*	*Seroquel*
Atacand HCT	*EMLA*[2]	*Moventig*	*Seroquel XR*
Atacand Plus[1]	*Farxiga*	*Naropin*[2]	*Symbicort*
BCise	*Fasenra*	*Nexium*	*Symbicort SMART*
Bevespi Aerosphere	*Faslodex*	*Onglyza*	*Symbicort Turbuhaler*
Brilinta	*Fluenz*	*Plendil*	*Symlin*
Brilique	*FluMist*	*Pressair*	*Synagis*[5]
Bydureon	*Forxiga*	*Prilosec*	*Tagrisso*
Byetta	*Genuair*	*Provisacor*	*Toprol-XL*
Calquence	*Imdur*[3]	*Pulmicort*	*Turbuhaler*
Carbocaine[2]	*Imfinzi*	*Pulmicort Flexhaler*	*Vimovo*[6]
Casodex	*Iressa*	*Pulmicort Respules*	*Xigduo*
Citanest[2]	*Kombiglyze*	*Pulmicort Turbuhaler*	*Xylocaine*[2]
Cosudex	*Komboglyze*	*Qtern*	*Zavicefta*[7]
Crestor	*Losec*	*Respules*	*Zoladex*
Daliresp	*Lokelma*	*Rhinocort*[4]	*Zomig*[8]
Daxas	*Lynparza*	*Rhinocort Aqua*[4]	*Zurampic*

1 AstraZeneca divested these trade marks in Europe to Cheplapharm effective 28 September 2018.
2 AstraZeneca divested these trade marks to Aspen group effective 1 November 2017.
3 AstraZeneca assigned this trade mark to Everest Future Limited effective 1 May 2016.
4 AstraZeneca assigned *Rhinocort* and *Rhinocort Aqua* to Cilag outside the US effective 5 December 2016.
5 AstraZeneca owns this trade mark in the US only. AbbVie owns it in the rest of the world.
6 AstraZeneca divested the global rights (excluding the US and Japan) for this trade mark to Grünenthal, effective 3 December 2018.
7 AstraZeneca assigned this trade mark to Pfizer Inc. effective 23 December 2016.
8 AstraZeneca assigned the rights to this trade mark outside Japan to Grünenthal effective 7 June 2017. In Japan, AstraZeneca divested this product to Sawai Pharmaceutical effective 3 October 2017.

The following brand 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.
Epanova	Chrysalis Pharma AG
Fluimucil	Zambon S.p.A.
Linzess	Ironwood
Lumoxiti	Innate Pharma
Tudorza	Almirall, S.A.

The following brand names which appear in italics throughout this Annual Report are not owned by or licensed to the Group and are owned by the entities set out below:

Trade mark	Owner
Imbruvica	Depending on geography, the trade mark is owned by Pharmacyclics, Inc., Johnson & Johnson or Janssen Pharmaceutica NV.
Keytruda	MSD
messenger RNA Therapeutics	Moderna

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*	

* IQVIA, IQVIA Midas Quantum Q3 2018 data is 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 2018 of less than $1 million.

Established Markets means US, Europe and Established ROW.

North America means US and Canada.

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, Swaziland, 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

Glossary
continued

The following abbreviations and expressions have the following meanings when used in this Annual Report:

AbbVie – AbbVie Inc.

ACA (Affordable Care Act) – the US Patient Protection and Affordable Care Act which was signed into law on 23 March 2010 as amended by the Health Care and Education Reconciliation Act which was signed into law on 30 March 2010.

Acerta Pharma – Acerta Pharma B.V.

ACS – acute coronary syndromes.

Actavis – Actavis plc.

ADR – an American Depositary Receipt evidencing title to an ADS.

ADS – an American Depositary Share representing half an underlying Ordinary Share.

Aegerion – Aegerion Pharmaceuticals, Inc.

AGM – an Annual General Meeting of the Company.

AI – artificial intelligence.

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 2018.

API – active pharmaceutical ingredient.

Aralez – Aralez Pharmaceuticals Trading DAC.

Ardea – Ardea Biosciences, Inc.

Articles – the Articles of Association of the Company.

Aspen – Aspen Global Incorporated.

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 nonprofit 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.

ATM – Ataxia telangiectasia mutated.

Avillion – Avillion LLP.

AZIP – AstraZeneca Investment Plan.

BACE – beta secretase cleaving enzyme.

biologic(s) – a class of drugs that are produced in living cells.

biosimilars – a copy of a biologic that is sufficiently similar to meet regulatory requirements.

BMS – Bristol-Myers Squibb Company.

Board – the Board of Directors of the Company.

Bureau Veritas – Bureau Veritas UK Limited.

CDP – a not-for-profit that runs the global disclosure system for investors, companies, cities, states and regions to manage their environmental impacts.

Celgene – Celgene International Sàrl/Celgene Corporation.

CEO – the Chief Executive Officer of the Company.

CER – constant exchange rates.

CFO – the Chief Financial Officer of the Company.

Cheplapharm – Cheplapharm Arzneimittel GmbH.

CHMP – the Committee for Medicinal Products for Human Use.

Cilag – Cilag GmbH International.

Circassia – Circassia Pharmaceuticals plc.

CIS – Commonwealth of Independent States.

CKD – Chronic kidney disease.

CMS – China Medical System Holdings Ltd.

Code of Ethics – the Group's Code of Ethics.

Company or Parent Company – AstraZeneca PLC (formerly Zeneca Group PLC (Zeneca)).

COPD – chronic obstructive pulmonary diseases.

Covis – Covis Pharma B.V.

CREST – UK-based securities settlement system.

CRL – Complete Response Letter.

CROs – contract research organisations.

CRUK – Cancer Research UK.

CV – cardiovascular.

CVRM – Cardiovascular, Renal and Metabolism.

Daiichi Sankyo – Daiichi Sankyo, Inc.

Definiens – Definiens AG.

Director – a director of the Company.

DJSI – Dow Jones Sustainability Index.

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.

EC – European Commission.

EFPIA – European Federation of Pharmaceutical Industries and Associations.

EGFR – epidermal growth factor receptor.

EMA – European Medicines Agency.

Entasis – Entasis Therapeutics Ltd and Entasis Therapeutics Inc.

EPO – European Patent Office.

ERK – extracellular signal-regulated kinases.

ESMO – European Society for Medical Oncology.

ESPC – Early Stage Product Committee.

ESRD – end-stage renal disease.

EVP – Executive Vice-President.

EU – the European Union.

EU 5 – European Union Five (France, Germany, Italy, Spain and the UK).

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.

FDC – fixed-dose combination.

FibroGen – FibroGen, Inc.

FRC – Financial Reporting Council.

GAAP – Generally Accepted Accounting Principles.

GDPR – General Data Protection Regulation.

GINA – Global Initiative for Asthma.

GQCE – Generics Quality Consistency Evaluation.

Gilead – Gilead Sciences, Inc.

GMD – Global Medicines Development.

GPPS – Global Product and Portfolio Strategy.

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.

HF – heart failure.

HFA – hydrofluoroalkane.

HHA – Healthy Heart Africa programme.

HNSCC – head and neck squamous cell carcinoma.

HR – human resources.

HTA – health technology assessment.

IA – the Group's Internal Audit Services function.

IAS – International Accounting Standards.

IASB – International Accounting Standards Board.

ICS – inhaled corticosteroid.

IFPMA – International Federation of Pharmaceutical Manufacturers and Associations.

IFRS – International Financial Reporting Standards or International Financial Reporting Standard, as the context requires.

IMED – Innovative Medicines and Early Development.

Innate Pharma – Innate Pharma S.A.

IO – immuno-oncology.

IP – intellectual property.

IQVIA – IQVIA Solutions HQ Limited. For more information, see page 244.

Ironwood – Ironwood Pharmaceuticals, Inc.

IS – information services.

ISAs – International Standards on Auditing.

IT – information technology.

Johnson & Johnson – Johnson & Johnson.

KPI – key performance indicator.

krona or SEK – references to the currency of Sweden.

Kyowa Hakko Kirin – 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.

Lean – means enhancing value for customers with fewer resources.

LEO Pharma – LEO Pharma A/S.

Lilly – Eli Lilly and Company.

LSPC – Late Stage Product Committee.

LTI – long-term incentive, in the context of share plan remuneration arrangements.

Luye Pharma – Luye Pharma Group.

MAA – a marketing authorisation application, which is an application for authorisation to place medical products on the market. This is a specific term used in the EU and European Economic Area markets.

mAb – monoclonal antibody, a biologic that is specific, that is, it binds to and attacks one particular antigen.

major market – US, EU, Japan (JP) and China (CN).

MAT – moving annual total.

MedImmune – MedImmune, LLC (formerly MedImmune, Inc.).

MEK – part of the mitogen-activated protein kinase (MAPK) pathway.

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.

Nasdaq Stockholm – previously the Stockholm Stock Exchange.

NCD – non-communicable disease.

NDA – a new drug application to the FDA for approval to market a new medicine in the US.

New Medicines – *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Lumoxiti*, *Farxiga*, *Brilinta*, *Lokelma*, *Bevespi* and *Fasenra*.

NME – new molecular entity.

NMPA – National Medical Products Administration, formerly the China Food and Drug Administration (CFDA).

Novartis – Novartis Pharma AG.

Novo Nordisk – Novo Nordisk A/S.

NSAID – a non-steroidal anti-inflammatory drug.

NSCLC – non-small cell lung cancer.

NYSE – the New York Stock Exchange.

n/m – not meaningful.

OECD – the Organisation for Economic Co-operation and Development.

OIC – opioid-induced constipation.

Omthera – Omthera Pharmaceuticals, Inc.

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 which 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.

OTC – over-the-counter.

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.

Pfizer – Pfizer, 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 but it does not get 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.

Glossary
continued

PHC – personalised healthcare.

Pieris Pharmaceuticals – Pieris Pharmaceuticals, Inc.

PMDA – Pharmaceuticals and Medical Devices Agency of Japan.

pMDI – pressurised metered-dose inhaler.

pound sterling, £, GBP or pence – references to the currency of the UK.

Pozen – POZEN, Inc.

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.

PSP – AstraZeneca Performance Share Plan.

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.

R&D – research and development.

Recordati – Recordati S.p.A.

Redeemable Preference Share – a redeemable preference share of £1 each in the share capital of the Company.

Regulatory Data Protection (RDP) – see Intellectual Property from page 35.

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.

Sanofi – SANOFI S.A./Sanofi Pasteur, Inc.

Sarbanes-Oxley Act – the US Sarbanes-Oxley Act of 2002.

SDRT – UK stamp duty reserve tax.

SEC – the US Securities and Exchange Commission, the governmental agency that regulates the US securities industry and stock markets.

Seroquel – *Seroquel* IR and *Seroquel XR*.

SET – Senior Executive Team.

SG&A costs – selling, general and administrative costs.

SGLT-2 – sodium-glucose co-transporter 2.

SHE – Safety, Health and Environment.

Shionogi – Shionogi & Co. Ltd.

Shire – Shire plc.

SLE – systemic lupus erythematosus.

sNDA – supplemental New Drug Application.

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.

TerSera – TerSera Therapeutics LLC.

Teva – Teva Pharmaceuticals USA, Inc.

Total Revenue – the sum of Product Sales and Externalisation 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 April 2016 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.

Valeant – Valeant Holdings Ireland/Valeant Pharmaceutical International, Inc.

Viela Bio – Viela Bio, Inc.

WHO – World Health Organization, the United Nations' specialised agency for health.

YHP – Young Health Programme.

Zambon – Zambon S.p.A.

ZS Pharma – ZS Pharma, Inc.

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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 expressed or implied by these statements. 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, those factors identified in the Risk section from page 220 of this Annual Report. 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 2018 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 2018; such data is 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 52 countries contained in the IQVIA database, which amounted to approximately 88% (in value) of the countries audited by IQVIA.

AstraZeneca websites

Information on or accessible through our websites, including www.astrazeneca.com, www.astrazenecaclinicaltrials.com and www.medimmune.com, 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.

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