AstraZeneca

What science can do

AstraZeneca Annual Report and Form 20-F Information 2017

Welcome

We are a global, science-led biopharmaceutical business and in this Annual Report we report on the progress we made in 2017 in pushing the boundaries of science to deliver life-changing medicines.

Science *can*

Expand treatment options

Oncology | From page 48

Understand disease

Cardiovascular & Metabolic Diseases | From page 52

Transform outcomes

Respiratory | From page 56

Front cover and inside front cover image:
Upstream intervention in the inflammatory cascade.

When lungs are stressed by allergens, pathogens or irritants, epithelial cells produce cytokines that trigger multiple downstream inflammatory pathways in the lungs. AstraZeneca is researching antibodies that bind to these upstream epithelial cytokines to prevent a range of inflammatory responses.

Important information for readers of this Annual Report
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, please see the Financial Review on page 66.

Definitions
The Glossary and the Market definitions table from page 235 are intended to provide a useful guide to terms and AstraZeneca's definitions of markets, as well as to acronyms and abbreviations, used in this Annual Report.

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.

Cautionary statement regarding forward-looking statements
A cautionary statement regarding forward-looking statements and other essential information relating to this Annual Report can be found on page 240.

Directors' Report
The following sections make up the Directors' Report, which has been prepared in accordance with the requirements of the Companies Act 2006:

- Chairman's Statement
- Chief Executive Officer's Review
- Business Review
- Therapy Area Review
- Financial Review: Financial risk management
- Corporate Governance: including the Audit Committee Report and Corporate Governance Report
- Directors' Responsibility Statement
- Development Pipeline
- Sustainability: supplementary information
- Shareholder Information

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
- Marketplace
- Business model and life-cycle of a medicine
- Strategy and Key Performance Indicators
- Business Review
- Therapy Area Review
- Risk Overview
- Financial Review

Contents

Financial highlights

Total Revenue*
down 2% to $22,465 million at actual rate of exchange (down 2% at CER), comprising Product Sales of $20,152 million and Externalisation Revenue of $2,313 million

2017	**$22,465m**
2016	$23,002m
2015	$24,708m

$22.5bn

Net cash flow from operating activities
down 14% at actual rate of exchange to $3,578 million

2017	**$3,578m**
2016	$4,145m
2015	$3,324m

$3.6bn

Reported operating profit
down 25% at actual rate of exchange to $3,677 million (down 28% at CER)

2017	**$3,677m**
2016	$4,902m
2015	$4,114m

$3.7bn

Core operating profit
up 2% at actual rate of exchange to $6,855 million (unchanged at CER)

2017	**$6,855m**
2016	$6,721m
2015	$6,902m

$6.9bn

Reported EPS
for the full year down 14% at actual rate of exchange to $2.37 (down 15% at CER)

2017	**$2.37**
2016	$2.77
2015	$2.23

$2.37

Core EPS
for the full year down 1% at actual rate of exchange to $4.28 (down 2% at CER)

2017	**$4.28**
2016	$4.31
2015	$4.26

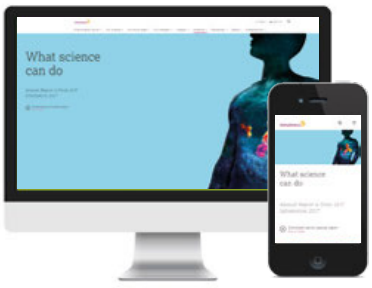
$4.28

Financial Review from page 66.

* As detailed on page 140, 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/annualreport2017

AstraZeneca at a glance

A global biopharmaceutical 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 and Key Performance Indicators from page 17.

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

11
new molecular entities (NMEs) in Phase III/ pivotal Phase II or under regulatory review covering 19 indications

Broad R&D platform in three main areas

Achieve Scientific Leadership from page 23 and Therapy Area Review from page 46.

Oncology
Our ambition is to eliminate cancer as a cause of death through scientific discovery and collaborations. We seek to achieve this by means of exploiting the power of four scientific platforms

Cardiovascular & Metabolic Diseases
We are following the science to transform how cardiovascular, renal and metabolic diseases are understood, interact and impact one another

Respiratory
We aim to transform the treatment of respiratory disease with our growing portfolio of medicines and scientific research targeting disease modification

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

Portfolio of specialty and primary care products (Product Sales)

Oncology

$4,024m
20% of total
2016: $3,383m
2015: $2,825m

Tagrisso sales up 126% (126% at CER) and approved in more than 60 markets

Iressa sales of $528 million, up 3% (3% at CER); *Lynparza* sales of $297 million, up 36% (35% at CER)

Imfinzi launched in the US in May and sales of $19 million; *Calquence* launched in the US in October and sales of $3 million

Cardiovascular & Metabolic Diseases

$7,266m
36% of total
2016: $8,116m
2015: $9,489m

Brilinta sales of $1,079 million, up 29% (29% at CER) and *Forxiga* sales of $1,074 million, up 29% (28% at CER)

Sales of *Onglyza* were down by 15% (16% at CER) to $611 million

Legacy sales: *Crestor* down 30% (30% at CER) to $2,365 million

Respiratory

$4,706m
23% of total
2016: $4,753m
2015: $4,987m

Symbicort sales of $2,803 million, down 6% (6% at CER)

Sales of *Pulmicort* up 11% (12% at CER) at $1,176 million

Fasenra approved in the US in November

Other Disease Areas

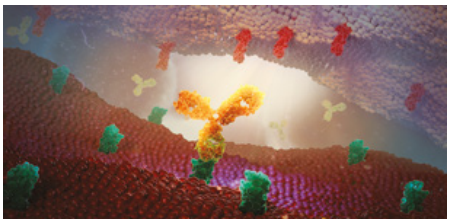
$4,156m
21% of total
2016: $5,067m
2015: $6,340m

Nexium sales down 4% (3% at CER) to $1,952 million

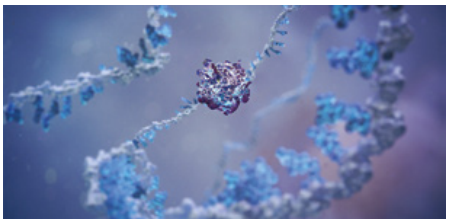
Sales of *Synagis* up 1% (1% at CER) to $687 million

Seroquel XR sales of $332 million, down 55% (55% at CER)

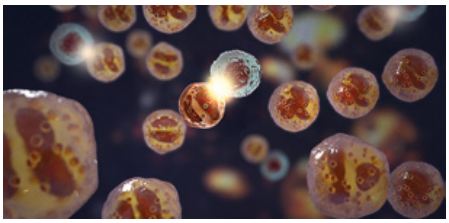
FluMist/Fluenz sales of $78 million, down 25% (28% at CER)



Oncology. See page 48



Cardiovascular & Metabolic Diseases. See page 52



Respiratory. See page 56

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

US	Emerging Markets	Europe	Established Rest of World
$6,169m	$6,149m	$4,753m	$3,081m
31% of total	30% of total	24% of total	15% of total
2016: $7,365m	2016: $5,794m	2016: $5,064m	2016: $3,096m
2015: $9,474m	2015: $5,822m	2015: $5,323m	2015: $3,022m

Commercial Highlights:

Growth Platforms grew by 5% (6% at CER) in 2017 and represented 68% of Total Revenue

Return to Growth from page 26.

US	Emerging Markets	Europe	Established Rest of World
Emerging Markets: Sales growth of 6% (8% at CER), in line with long-term ambitions. China sales in the year grew by 12% (15% at CER), supported by the launches of new medicines	New CVMD: Sales growth of 9% (9% at CER). Strong performances from *Farxiga* and *Brilinta*, with sales exceeding $1 billion in 2017 Respiratory: Sales declined by 1% (1% at CER). Sales of *Symbicort* declined by 6% (6% at CER) and *Pulmicort* sales rose by 11% (12% at CER)	Japan: 1% growth in sales (4% at CER), underpinned by the growth of *Tagrisso* and *Forxiga*, partly mitigated by the impact of the entry of generic competition to *Crestor* in the second half of the year	New Oncology: Sales growth of 98% (98% at CER). Sales of *Tagrisso* reached $955 million to become AstraZeneca's largest-selling Oncology medicine

Our talented employees:

Committed to achieving our Purpose in a sustainable way and upholding our Values by fostering a strong AstraZeneca culture

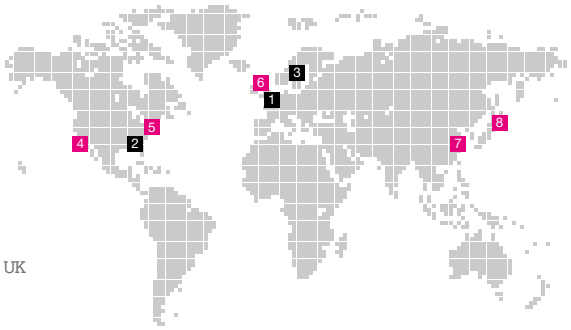
Be a Great Place to Work from page 34.

61,100
employees
2016: 59,700
2015: 61,500

100%
of employees trained in new Code of Ethics

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



CDP A LIST 2017 CLIMATE
CDP A LIST 2017 WATER
MEMBER OF Dow Jones Sustainability Indices In Collaboration with RobecoSAM

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 66.

Distributions to shareholders	Dividends	Proceeds from issue of shares	Total
	$3,519m	$(43)m	$3,476m
	2016: $3,561m	2016: $(47)m	2016: $3,514m
	2015: $3,486m	2015: $(43)m	2015: $3,443m

Dividend per Ordinary Share for 2017	1st interim dividend	2nd interim dividend	Total
	$0.90	$1.90	$2.80
	Pence: 68.9	Pence: 133.6	Pence: 202.5
	SEK: 7.40	SEK: 14.97	SEK: 22.37
	Payment date: 11 September 2017	Payment date: 19 March 2018	2016: $2.80
			2015: $2.80

Chairman's Statement

Your Board of Directors is focused on ensuring that AstraZeneca returns to growth.

"I share Pascal's excitement about AstraZeneca's prospects as a science-led innovator..."

One of the Board's basic responsibilities is to set our strategy and monitor progress towards meeting our objectives, so that we bring our science to patients, create value for society, and reward you, our shareholders.

Executing our strategy

In 2017, we made encouraging progress across all our therapy areas, as well as in commercial execution and cost discipline. After a number of years of falling revenue, I am pleased we were able to report a growth in Product Sales in the final quarter of 2017. We are now positioned for Product Sales growth from 2018.

I firmly believe that the significant progress we have made against each of our three strategic pillars vindicates the strategy we set in 2013. As a Board, we have reviewed and confirmed that strategy each year. We also regularly review the supporting business performance reports, including pipeline updates and the results of key clinical trials.

Continued global uncertainty

The progress made by AstraZeneca in executing its strategy is all the more impressive given the continued challenges we face. These include strong competition from both branded and generic medicines around the world. Pricing and reimbursement also remains challenging in many markets – including the US and Europe.

In Europe, there is the added uncertainty of Brexit, the UK's announcement under Article 50 of its intention to leave the EU, which has potential implications for both the UK and the remaining EU27. We are engaging with stakeholders and taking actions to mitigate potential risks arising from all possible outcomes.

Medicines for the long term

The long-term prospects for the pharmaceutical sector, however, remain encouraging. AstraZeneca too is focused on the long term and we are committed to operating in a way that recognises the interconnection between business growth, the needs of society and the limitations of the planet. Our listing, for another year, in the Dow Jones Sustainability World and European Indices bears testament to our continued achievements in this regard. We are also one of only 25 companies to be recognised by investor benchmarking organisation, CDP, for both our climate change and water stewardship programmes.

Returns to shareholders and outlook

In 2017, and against this background, Reported earnings per share (EPS) of $2.37 represented a decline of 14% (15% at CER). The performance was driven by a decline in Total Revenue and increased SG&A costs, partly offset by a net tax benefit, continued progress on R&D cost control and an increase in Other Operating Income and Expense. Core EPS declined by 1% (2% at CER) to $4.28. Given this performance, the Board has declared a second interim dividend of $1.90 per share (133.6 pence, 14.97 SEK) bringing the dividend per share for the full year to $2.80 (202.5 pence, 22.37 SEK). At the same time, the Board reaffirmed its continued commitment to our progressive dividend policy.

I share Pascal's excitement about AstraZeneca's prospects as a science-led innovator and its ability to deliver value for patients and shareholders.

Leif Johansson
Chairman

CVMD:
Stem cell differentiating into heart muscle (cardiac regeneration)

Chief Executive Officer's Review

While Total Revenue declined over the year, it rose in the last quarter of 2017, a sign of how we are steadily turning a corner.

"2017 represented a defining year for AstraZeneca. 2018 will be equally important..."

After experiencing the falling revenues of recent years, as some of our best-selling medicines lost exclusivity, our revenues improved over the course of 2017. Strong commercial execution helped us bring our science to more patients, making the most of our exciting pipeline. We made encouraging progress in all main therapy areas and delivered strong growth in China, our second largest market.

Strategic progress

In my Review for 2017, I would therefore like to pay tribute to our achievements and look more closely at five medicines we launched during the year that bring both very real benefits to patients and underpin our future growth. I also want to consider some of the challenges we face as we work to realise the full potential of our medicines and ensure we deliver our science to patients around the world.

The strategy we set ourselves in 2013 was based on three pillars. We wanted to:

> Achieve Scientific Leadership
> Return to Growth
> Be a Great Place to Work

Achieving scientific leadership

In the five years since then, we have launched 13 new molecular entities (NMEs), including four alone in 2017. And, in 2017, we brought those medicines to more people with 19 major regional approvals – a new AstraZeneca record. It is an indicator of our scientific leadership in our three chosen therapy areas that we published 82 manuscripts in 'high-impact' scientific publications compared to 75 in 2016, and just seven in 2010. We are well on our way to meeting our longer-term goals of delivering one or more NMEs annually and sustainably delivering two NMEs annually by 2020.

Returning to growth

Between 2011 and 2017, Product Sales in Established Markets of our very successful older products that have lost exclusivity reduced by more than $13 billion (after taking into account currency movements). We expect to lose a further $1 billion of Product Sales in 2018, in particular through the loss of exclusivity for *Crestor* in Europe and Japan. Overall, Total Revenue declined by 2% in 2017. As shown in the table overleaf, Product Sales declined by 5% from $21,319 million to $20,152 million, including a decline in *Crestor* sales of $1,036 million and *Seroquel XR* sales of $403 million.

But now, a new AstraZeneca is emerging from those headwinds, helped by our Growth Platforms, which gathered momentum during the year and grew by 5% (6% at CER). They now represent 68% of Total Revenue.

As well as launching five medicines last year, we continued to unlock more uses for existing treatments, including for *Lynparza* and *Tagrisso*. In addition, *Brilinta*/*Brilique* and *Farxiga*/*Forxiga*, by bringing benefits to millions of patients, each exceeded $1 billion in annual sales for the first time.

Externalisation Revenue in 2017 increased by 37% (38% at CER) to $2,313 million. Particularly significant was our global strategic oncology collaboration with MSD to co-develop and co-commercialise *Lynparza* for multiple cancer types. We will also jointly with MSD develop and seek to commercialise our MEK inhibitor selumetinib, currently being developed for multiple indications, including thyroid cancer.

Chief Executive Officer's Review *continued*

19

19 NME and major LCM regional approvals

68%

Five Growth Platforms represent 68% of Total Revenue

5

Five significant launches from each of our three therapy areas

"Our future depends, however, not only on the number of projects but the quality of our science…"

Global Product Sales by therapy area

	2017			2016			2015		
	Sales $m	**Actual growth %**	**CER growth %**	Sales $m	Actual growth %	CER growth %	Sales $m	Actual growth %	CER growth %
Oncology	**4,024**	**19**	**19**	3,383	20	20	2,825	(7)	7
Cardiovascular & Metabolic Diseases	**7,266**	**(10)**	**(10)**	8,116	(14)	(13)	9,489	(3)	4
Respiratory	**4,706**	**(1)**	**(1)**	4,753	(5)	(3)	4,987	(2)	7
Other Disease Areas	**4,156**	**(18)**	**(17)**	5,067	(20)	(19)	6,340	(23)	(16)
Total	**20,152**	**(5)**	**(5)**	21,319	(10)	(8)	23,641	(9)	(1)

Being a great place to work

As I talk to our employees around the world, whether in our labs, offices or on the road with our sales teams, I am constantly reminded that our achievements are only made possible by a skilled and talented team who live our Values and are true to our Purpose.

It is they who are transforming AstraZeneca: exploring new ways of working; improving productivity; and embracing new technology. The culture we are creating is aimed at releasing the talents of our people and enabling science to thrive. We know there is more we can do but we are simplifying how we work; improving diversity to reflect the world and societies in which we work; and increasing our focus on sustainability. Like the Chairman, I am particularly pleased to see the external recognition we are receiving for our sustainability activities. We also have cause to celebrate the start of our Healthy Lung Asia Programme, the third anniversary of our Healthy Heart Africa Programme and the seventh year of our Young Health Programme – a global disease prevention programme.

People at AstraZeneca know that scientific progress is best made when we take smart risks in following the science. We also know that sometimes means we experience setbacks. For example, in July, the initial 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 progression-free survival (PFS). The study for overall survival (OS) continues. Following the Phase III programme results, we decided to discontinue the development of tralokinumab, an antibody in severe, uncontrolled asthma. Earlier in the year, we received a second Complete Response Letter from the FDA for ZS-9, a potential new medicine for hyperkalaemia, an important area of unmet medical need, and we continue to work towards its approval. Overall, however, the number of successes far outweighed the disappointments.

Delivering for patients

By way of example, five significant launches from each of our three main therapy areas in 2017 showed how our rebuilt pipeline is starting to deliver our science to patients.

Imfinzi (durvalumab) received accelerated approval from the FDA in May for the treatment of advanced bladder cancer. It was a significant moment both for patients who had limited treatment options and for us as it was our first immuno-oncology (IO) approval. *Imfinzi* is the cornerstone of our extensive IO programme, in development across many tumour types, both as monotherapy and with other medicines. Later in May, we announced positive top-line results for the Phase III PACIFIC trial as *Imfinzi* demonstrated superior PFS in patients with locally-advanced, unresectable NSCLC.

In October, the FDA granted accelerated approval of ***Calquence*** (acalabrutinib) as a treatment for relapsed or refractory mantle cell lymphoma (MCL). This represented another landmark for us as it was our first approval in blood cancer and was approved less than five months after its regulatory submission. With a development programme including more than 35 clinical trials in multiple blood cancers, the promise of *Calquence* is significant.

In February, the FDA approved ***Qtern*** (*Forxiga* 10mg and *Onglyza* 5mg fixed-dose combination) as an adjunct to diet and exercise to improve glycaemic control in adults with Type 2 diabetes who have inadequate control with *Forxiga* (10mg) or who are already treated with *Forxiga* and *Onglyza*.

Finally, in our Respiratory therapy area, ***Bevespi Aerosphere*** (glycopyrrolate and formoterol fumarate) was launched in the US for COPD, using, for the first time, our *Aerosphere* delivery technology that uses a pressurised metered-dose inhaler (pMDI).

Fasenra (benralizumab) was approved in November in the US for patients with severe asthma with an eosinophilic phenotype and is our first approved respiratory biologic medicine. It is a new anti-eosinophilic monoclonal antibody which has demonstrated efficacy versus placebo in pivotal clinical trials and is the first respiratory biologic with an eight-week maintenance dosing regimen.

Sustainable delivery

If our launches are delivering benefits to patients now, our pipeline is intended to ensure we deliver those benefits sustainably in the years to come. During 2017, we made 18 NME or life-cycle management regulatory submissions in major markets and approved nine Phase III investment decisions. These will provide plenty of news in 2018 as we await regulatory decisions and data read outs from clinical trials. Looking further ahead, we approved 14 NME Phase II starts or progressions in 2017 which will shape our future in the years to come.

Our future depends, however, not only on the number of projects in our pipeline but the quality of our science. In that regard, we are relentless in our search for the best science – whether it is in our own labs or those of others with whom we collaborate. For example, we are harnessing the power of genomics through global collaborations and scientific innovation with the aim of transforming drug discovery and development. Additionally, by focusing on quality rather than quantity, our IMED Biotech Unit has seen a four-fold increase in productivity, while costs have remained broadly unchanged.

A great team

Great science needs great people, and great people need great teams if they are going to deliver their best work. I am therefore grateful to all my colleagues at AstraZeneca for their tremendous efforts in 2017. These efforts made it a defining year and continued to transform the organisation. I would also like to welcome three new members to the Senior Executive Team who joined during the year. Leon Wang joined us in January with responsibility for our International Region. Iskra Reic joined in April with responsibility for Europe and David Fredrickson took over from Jamie Freedman in charge of the Oncology Business Unit in October. I welcome the skills, experience and diversity they bring to our discussions. All three were internal appointments and speak to the strength of our pipeline of talent.

Looking ahead

2017 saw two more of our medicines each exceed $1 billion in annual sales, five significant launches and more potential uses found for existing medicines. We remain committed to our progressive dividend policy. Our strategy is working, propelled by a strong pipeline, good sales performance and continued cost discipline.

2017 represented a defining year for AstraZeneca. 2018 will be equally important as we seek to deliver the full potential of our medicines and ensure we deliver our science to patients around the world.

I am excited about AstraZeneca's prospects as a science-led innovator as I believe we will deliver value for patients and shareholders in the long term.

Pascal Soriot
Chief Executive Officer

***Imfinzi* PACIFIC trial**

Lung cancer accounts for about one quarter of all cancer deaths, more than any other cancer. With the emergence of new targeted small molecules and immunotherapies, significant progress is being made in the treatment of patients for whom the disease has already spread through the body (metastatic). But for patients with an earlier stage disease, known as locally advanced unresectable non-small cell lung cancer (NSCLC), treatment options have been limited and clinical outcomes remain poor.

Aiming to provide solutions to those unmet medical needs, we have initiated a broad immuno-oncology development programme in NSCLC, using the immune system to treat the cancer, both in the locally advanced and metastatic settings. For patients with locally advanced NSCLC, where the tumour cannot be surgically removed, the current standard of care is concurrent chemoradiation therapy (CRT), followed by a period of active surveillance during which patients are monitored closely for progression. Although most patients with locally advanced disease initially respond to CRT, the vast majority will advance to metastatic disease within 12 months. In the Phase III PACIFIC clinical trial, *Imfinzi* demonstrated a statistically significant and clinically meaningful improvement in progression-free survival following CRT, and reduced the rate of distant metastasis formation. No other Phase III trial has demonstrated these results in more than two decades.

Marketplace

Despite global economic, political and social challenges, the pharmaceutical industry is expected to enjoy long-term growth. This is due to favourable demographic trends and significant unmet medical needs.

"Pricing and reimbursement remain challenging in many markets."

The global context

> Global cyclical economic upswing continues, however:
  – Political and economic uncertainty resulting from the UK Brexit vote and US election of Donald Trump persists
  – Global recovery vulnerable and may not be sustainable

The October 2017 World Economic Outlook of the International Monetary Fund (IMF) highlighted that the global cyclical upswing that had begun during 2016 was continuing to gather strength, with accelerating growth in Europe, Japan, China and the United States.

However, both political and economic uncertainty continues following the Brexit vote in the UK and the election of Donald Trump to president of the US. The IMF goes on to suggest that the global recovery might not be sustainable and is also vulnerable to serious risks.

The pharmaceutical sector

> Demand for healthcare continues to increase, but challenges remain
> US is the largest global market, with 45% of global sales
> Strong growth in 2017, primarily from emerging markets
> Emerging market growth predicted to remain strong to 2021

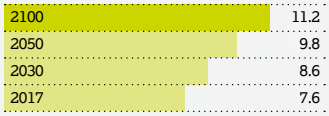
Against this uncertain background, however, the demand for healthcare continues to increase. While this is a favourable trend for long-term industry growth, challenges remain. These include expiring patents, competition from and growing use of generic medicines, obtaining regulatory approval, securing reimbursement for new medicines, improving R&D productivity, and attaining pricing and sales sufficient to generate revenue and sustain the cycle of innovation.

As shown in the table overleaf, global pharmaceutical sales grew by 2.9% in 2017. Established Markets saw average revenue decline of 2.7% and Emerging Markets revenue grew at 7.7%. The US, Japan, China, Germany and France are the world's top five pharmaceutical markets. In 2017, the US had 45.5% of global sales (2016: 45.9%; 2015: 46.0%).

Looking ahead, and as shown on the page opposite, expanding patient populations and continuing unmet medical need are expected to contribute to growth in pharmaceutical sales. The table on estimated pharmaceutical sales and market growth to 2021 overleaf also illustrates that we expect the developing markets, including Africa, Middle East, CIS, Indian subcontinent, South East and East Asia, and Latin America, to continue to fuel pharmaceutical growth.

Expanding patient populations

Estimated world population (UN, bn)



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

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

Unmet medical need

Prevalence of NCDs

40m

The prevalence of non-communicable diseases (NCDs), such as cancer and cardiovascular, metabolic and respiratory diseases, is increasing worldwide. NCDs are often associated with ageing populations and lifestyle choices, including smoking, diet and lack of exercise. The WHO estimates that NCDs kill 40 million people each year and disproportionately affect low- and middle-income countries where nearly three quarters of these deaths occur.

Oncology

Estimated annual cancer cases (m)

8.8m
Cancer is a leading cause of death worldwide and accounted for 8.8 million deaths in 2015.

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

CVMD

17.5m
More than 17.5 million people worldwide die from cardiovascular (CV) disease every year.

$3.76tn
From 2011 to 2025, the cumulative economic losses in low- and middle-income countries from CV disease are projected to be $3.76 trillion.

$2.5tn
The total economic burden of CV disease in upper middle-income countries through 2025 is estimated to be $2.52 trillion.

Respiratory

315m
Some 315 million adults in the world have asthma, with prevalence expected to rise. It causes some 346,000 deaths annually. Severe asthma accounts for ~10% of patients but ~50% of the economic burden of asthma.

329m
Globally, some 329 million people have chronic obstructive pulmonary disease (COPD), and this number is expected to rise. At initial diagnosis, ~31% of COPD patients have severe or very severe forms of this disease.

New approaches in the treatment of asthma
AstraZeneca is developing a therapy aimed at producing long-term benefit in asthma by addressing imbalances in the immune system that may be an underlying cause of the disease.

Rather than simply treating symptoms by relaxing airway constriction and dampening inflammation in the lung, this therapy aims to target toll-like receptor 9 in dendritic cells in the lung.

This could potentially change the way immune cells communicate with each other and restore a healthy balance to the immune system.

Global pharmaceutical sales

World ($bn)

2017	**996**
2016	968
2015	906

$996bn (2.9%)

US ($bn)

2017	**453**
2016	444
2015	416

$453bn (2.2%)

Europe ($bn)

2017	**214**
2016	209
2015	197

$214bn (2.8%)

Established ROW ($bn)

2017	**112**
2016	115
2015	109

$112bn (-2.7%)

Emerging Markets ($bn)

2017	**216**
2016	201
2015	183

$216bn (7.7%)

Data based on world market sales using AstraZeneca market definitions as set out in the Market definitions on page 235. Source: IQVIA, IQVIA Midas Quantum Q3 2017 (including US data). Reported values and growth are based at CER. Value figures are rounded to the nearest billion and growth percentages are rounded to the nearest tenth.

Estimated pharmaceutical sales and market growth – 2021

	North America	EU	Other Europe (Non-EU countries)
	$596bn	**$237bn**	**$23bn**
	4.3%	2.8%	8.5%

	Japan	Oceania	South East Asia and East Asia
	$80bn	**$16bn**	**$207bn**
	-1.4%	0.9%	6.0%

	Latin America	Africa	CIS
	$83bn	**$26bn**	**$28bn**
	6.2%	6.4%	8.0%

	Middle East	Indian subcontinent
	$25bn	**$41bn**
	4.2%	10.1%

Estimated pharmaceutical sales – 2021. 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 2016 to 2021. Source: IQVIA.

The pharmaceutical sector: opportunities and challenges

Advances in science and technology

Scientific innovation is critical to addressing unmet medical need and the delivery of new medicines will rely on a more advanced understanding of disease and the use of new technology and approaches. These include precision medicines, genomics and digital healthcare. Scientific and technological breakthroughs in small molecules and in biologics are also helping accelerate innovation. Innovation might also be accelerated through the use of large volumes of biological data from disease biology and genomics. Such advances have resulted in increased numbers of FDA Priority Reviews and Breakthrough Designations.

The cost of developing new medicines continues to rise with global R&D investment expected to reach more than $160 billion in 2017. 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 46 novel drugs in 2017 compared with 22 in 2016 and 45 in 2015. Nevertheless, the risk of any products failing at the development or launch stages, or not securing regulatory approvals continues.

Our strategic response

> Continue to focus on innovative science in our chosen therapy areas – secured 19 approvals of NMEs or major LCM projects in major markets in 2017.
> Work to develop a diverse range of drug modalities such as modified RNA, antisense oligonucleotides and bi-specific monoclonal antibodies (mAbs).
> Maintain scientific work on pioneering technologies including genome editing with CRISPR/Cas9, and machine learning and artificial intelligence.
> Our Precision Medicine and Genomics team is strengthening our ability to match targeted medicines to patients who need them most.
> Partner with academia, governments, industry and scientific organisations to allow us to access the best and most advanced science and technology.
> Commitment to science is reflected in our co-location near bio-science clusters in Cambridge, UK; Gaithersburg, MD, US; and Gothenburg, Sweden.
> Keep up our track record of high-impact publications with 82 in 2017 – compared with 75 in 2016.

For more information, please see Risk from page 210 and Achieve Scientific Leadership from page 23.

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. In the US, for example, the 21st Century Cures Act of 2016 and the FDA Reauthorization Act of 2017 focus on accelerating the discovery, development and delivery of innovative new treatments for patients, and modernising the US regulatory environment.

In Japan, the PMDA has adopted a new conditional early approval system to speed patient access to medicines addressing unmet medical needs requiring the conduct of confirmatory clinical studies. In China, recent proposed changes in regulations focus on improving the ability of pharmaceutical companies to deliver innovative medicines to the marketplace in a more timely manner and providing treatments for diseases where there is an unmet medical need.

Furthermore, 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 exit from the EU, and the relocation of the EMA from London to Amsterdam in the Netherlands (and the likely disruption this will cause to regulatory processes). The impact of the implementation of the EU Clinical Trials Regulation on UK-based clinical trials needs to be assessed in the context of Brexit outcomes. The EMA has just over a year to prepare for the move and take up operations in Amsterdam on 30 March 2019 at the latest.

In the area of biosimilar development, regulatory requirements for the registration of biosimilar products continue to evolve and become better defined. However, significant areas of regulatory policy are still evolving. Among these are transparency of data regarding 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. We believe that transparency enhances the scientific understanding of how our medicines work and is in the medical interest of our patients.

For more information about biosimilars, please see Loss of exclusivity and genericisation on page 12.

Our strategic response

> Engage in responsible testing, manufacturing and marketing in compliance with regulations.
> Maintain effective working relationships with health authorities worldwide, including the FDA in the US, the EMA in the EU, the PMDA in Japan, and the CFDA in China.
> Continue to monitor the situation in the EU, as well as the broader global regulatory landscape, to ensure that we meet current and future drug approval requirements.
> Consistent with a long-standing commitment to making information about our clinical research publicly available, we continue to work with regulators and other stakeholders to ensure the appropriate level of data transparency.
> Continue to collaborate with industry, academia and government bodies to drive innovation, streamline regulatory processes, and define and clarify approval requirements for innovative drug and biologic products.

Marketplace
continued

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.

These efforts are all the more relevant given the shift in the industry over the last decade from primary care to a specialty care focus. Specialty drugs are used for the treatment of complex, chronic, or rare conditions such as cancers and hepatitis C. 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. These higher drug costs have heightened the desire and need for payers to manage their expenditure and drug utilisation.

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, in other markets, there has been a trend towards rigorous and consistent application of pricing regulations, including reference pricing. For example, in Saudi Arabia prices are set according to the lowest of a basket of reference market prices.

We are also experiencing pressure on pricing in the US from a number of quarters. For example, political leadership is considering drug pricing controls and transparency measures at the national and local levels. Changes to the Affordable Care Act (ACA) and ongoing efforts to reform the healthcare system continue to create uncertainty in the market. While policymakers in the US have advocated for repeal and replacement of the ACA, full repeal appears unlikely. Thus, the administration has taken steps to significantly change ACA regulations, including repealing the individual mandate provision of the ACA which requires citizens to have insurance or pay a penalty. Changes to ACA regulations may have downstream implications for coverage and access. With respect to healthcare reform more broadly, modifications to Medicare and other government programmes including changes aimed at reducing drug prices, such as importation schemes, are possible. Further, the healthcare industry may be used as a means to offset government spending. US federal agencies continue to propose and implement policies and programmes with the goal of expanding access and coverage, reducing costs, increasing transparency, transforming the delivery system, and improving quality and patient outcomes.

For more information about pricing and price controls in the US and other major markets, please see Return to Growth from page 26 and Risk from page 210.

Our strategic response

- Internal pricing policy based on four principles: value, sustainability, access and flexibility.
- Aim to enable our Emerging Markets to deliver better and broader patient access through innovative and targeted equitable pricing strategies and practices.
- Partner with industry, government and academia to find ways to bring new medicines to market more quickly and efficiently, as well as foster an environment that facilitates medical and scientific innovation.
- Engage with policymakers to support improvements in access, coverage, care delivery, quality of care and patient care outcomes.
- Consider innovative outcomes contracts with payers as a mechanism to pay for value.
- Evaluate the use of real-world evidence to further bolster the evidence base around therapeutic and economic value.

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 2017, generics constituted 84.9% of the market by volume (2016: 84.4%).

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. Similar to 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.

For more information, please see Intellectual Property from page 32.

Our strategic response

- Investment in innovative research and development, both internally and with partners, to advance novel therapeutics through the pipeline.
- A strong patent strategy – from building robust patent estates that protect our pipeline and products to defending and enforcing our patent rights.

Trust

The pharmaceutical industry faces 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 governmental and regulatory authorities. To address these challenges, companies are seeking to strengthen a culture of ethics and integrity, adopt higher governance standards and improve relationships with employees, shareholders and other stakeholders.

Numerous 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 DOJ and SEC under the Foreign Corrupt Practices Act are continuing across the industry, as are investigations by the UK Serious Fraud Office under the UK Bribery Act. During 2017, there were also Congressional hearings in the US related to pricing while, in the UK, the Competition and Markets Authority has been investigating allegations of excessive charging.

Sustainability programmes, particularly focused on access to healthcare, seek to build trust in pharmaceutical companies as providers of medicines for the long term.

More generally, if we want to be trusted by our stakeholders, we need to operate in a way that meets their expectations, thereby maintaining and building our reputation with them.

The reputation of the sector can be undermined by counterfeit medicines which can fail to provide effective treatment and sometimes cause direct harm to patients. They represent a global challenge and companies work with health authorities, industry bodies and law enforcement agencies to bring those involved to justice.

Our strategic response

> Furthering ethics and transparency, and broadening access to healthcare are two of our sustainability priorities.
> Launched an updated Code of Ethics built on a refusal to tolerate bribery or any other form of corruption.
> Enhanced programme to protect patients from dangers of illegally traded medicines.

For more information about ethics, please see Ethical sales and marketing from page 40.

Competition

Our competitors include large, research-based pharmaceutical companies (similar to AstraZeneca) that discover, develop and sell innovative, patent-protected prescription medicines and vaccines, smaller biotechnology and vaccine businesses, and companies that produce generic medicines. However, the pharmaceutical market is highly competitive. For example, our Diabetes and Respiratory franchises continue to see pricing pressure. 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, they tackle 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, business development deals (including licensing and collaborations) and competition for business development opportunities have continued.

The speed of technological change, including digital health, and the development of artificial intelligence also threatens to disrupt existing technologies and undermine current business models.

Our strategic response

> To be a 'pure-play', global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of unmet medical need in three therapy areas.
> Establishing priorities that reflect our focus on innovative science, emerging drug platforms and new technologies.

For more information, please see Strategy and Key Performance Indicators from page 17 and Risk from page 210.

"Scientific innovation is critical to addressing unmet medical need."

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 biopharmaceutical business which has:

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

Nucleotide therapies: antiMRNA

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 want to be valued and trusted by our stakeholders as a source of great medicines over the long term.

Our sustainability priorities – broadening access to healthcare, furthering ethics and transparency, and protecting the environment – underpin our business model and support the delivery of our business strategy.

Business Review from page 22.

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 product 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 35.

61,100
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 23.

$5.8bn
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 31.

>600
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 26.

>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 32.

>100
countries where we obtain patent protection

A robust supply chain
We need a supply of high-quality medicines, whether from one of the 31 Operations sites in 18 countries in which we manufacture or the $13 billion we spend on the purchase of goods, services and active pharmaceutical ingredients (APIs).

See Operations from page 30 and Supply chain management on page 42.

$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 66.

$4bn
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 66.

Strategy and Key Performance Indicators

Strategy

We announced our strategy for returning to growth in 2013. We moved on from the first phase in our journey, focused on rebuilding our pipeline, in 2015. The second stage is crucial as we drive our Growth Platforms forward, continue to launch new medicines and make them available to patients. As we look ahead to 2020 and beyond, continued investment in our pipeline will keep us on track to return to sustainable growth in line with our targets.

In 2017, our strategic priorities were focused under the following three pillars:

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.

Progress

The following pages present our Key Performance Indicators (KPIs) for 2017. 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 105.

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:

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 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 2017, as well as what is in the pipeline.

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

For more information:
Business Review from page 22;
Therapy Area Review from page 46;
Risk from page 210.

Messenger RNA being read by a ribosome to produce signalling proteins

Strategy and Key Performance Indicators *continued*

Strategic priorities

Achieve Scientific Leadership

Focus on innovative science in three main therapy areas
Focus on Oncology, Cardiovascular & Metabolic Diseases, 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 2017, 11 NMEs were in Phase III or under regulatory review, covering 19 indications.

Four NMEs were approved in 2017. Having met the targets for 2016 we had set ourselves in 2013, we are now on target to meet our longer-term goals of delivering one or more NMEs annually and 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.

Key Performance Indicators

NME Phase II starts/progressions

14

2017	**14**
2016	16[1]
2015	11

[1] 15 for determining annual bonus.
See page 112.

Phase III investment decisions

9

2017	**9**
2016	7
2015	6

NME or LCM project regulatory submissions in major markets

18

2017	**18[1]**
2016	14[2]
2015	12

[1] 13 for determining annual bonus.
[2] 13 for determining annual bonus.
See page 112.

NME and major LCM regional approvals

19

2017	**19**
2016	11
2015	6

Clinical-stage strategic transactions

7

2017	**7**
2016	10
2015	10

Achieve Scientific Leadership from page 23;
Therapy Area Review from page 46;
Development Pipeline from page 202.

"We delivered four new molecular entities (NMEs) in 2017 and are on target to meet our goals of delivering one or more NMEs annually and sustainable delivery of 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.

New CVMD – From 2017, New CVMD Growth Platform combined our broad and innovative Diabetes franchise, our cardiovascular medicine, *Brilinta/ Brilique*, and any new launches within renal disease treatment.

Japan – Strengthen our Oncology franchise and work to maximise the success of our Diabetes medicines and established medicines: *Symbicort*, *Nexium* and *Crestor*.

New Oncology – Aim to deliver six new cancer medicines to patients by 2020. We have delivered four New Oncology medicines to date: *Lynparza*, *Tagrisso*, *Imfinzi* and *Calquence* that make a meaningful difference to patients. New Oncology also includes *Iressa* (US).

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

$6,149m
Product Sales

2017	**$6,149m**
2016	$5,794m
2015	$5,822m

Actual growth	CER growth
2017 +6%	2017 +8%
2016 0%	2016 +6%
2015 0%	2015 +12%

Respiratory

$4,706m
Product Sales

2017	**$4,706m**
2016	$4,753m
2015	$4,987m

Actual growth	CER growth
2017 -1%	2017 -1%
2016 -5%	2016 -3%
2015 -2%	2015 +7%

New CVMD

$3,567m
Product Sales

2017	**$3,567m**
2016	$3,266m
2015	$2,843m

Actual growth	CER growth
2017 +9%	2017 +9%
2016 +15%	2016 +17%
2015 +17%	2015 +21%

Japan

$2,208m
Product Sales

2017	**$2,208m**
2016	$2,184m
2015	$2,020m

Actual growth	CER growth
2017 +1%	2017 +4%
2016 +8%	2016 -3%
2015 -9%	2015 +4%

New Oncology

$1,313m
Product Sales

2017	**$1,313m**
2016	$664m
2015	$119m

Actual growth	CER growth
2017 +98%	2017 +98%
2016 n/a	2016 n/a
2015 n/a	2015 n/a

Return to Growth from page 26;
Therapy Area Review from page 46;
Geographical Review from page 221.

"Our Growth Platforms grew by 5% in 2017 (6% at CER) and now represent 68% of Total Revenue."

Strategy and Key Performance Indicators *continued*

Strategic priorities | Key Performance Indicators

Be a Great Place to Work

Evolve our culture

Work to improve our employees' identification with our Purpose and Values and promote greater understanding of, and belief in, our strategy.

Invest in and implement tailored leadership development programmes.

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

Accelerate efforts to attract diverse, top talent with new capabilities.

Be a Great Place to Work from page 34.

Employee belief in our strategy

88%

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

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

70%

Employees who would recommend AstraZeneca as a great place to work

81%

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

Do business sustainably

Secure our future

Deliver our business strategy in a way that delivers wider benefits to society and the planet.

Focus on:

- increasing access to healthcare for more people
- furthering ethics and transparency in everything we do
- environmental protection.

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

Sustainability from page 38.

Dow Jones Sustainability Index rating

84%

Maintained listing in the Dow Jones Sustainability World and Europe Indices comprising the top 10% of the largest 2,500 companies. The decline to 84% places us within two percentage points of the industry's best score.

Access to healthcare: Healthy Heart Africa programme

5.7m
people

Healthy Heart Africa is a signature access to healthcare programme providing screenings, diagnosis and treatment of hypertension to nearly six million people since launching.

Environmental protection: Operational carbon footprint[1]

1,659 kt CO_2e

[1] Operational carbon footprint is emissions from all Scope 1, 2 and selected Scope 3 sources. See page 227.

Our 2017 operational carbon footprint met our target of progressing our Science Based Targets and represents a 7% reduction from our 2015 baseline.

Note: We will review the Be a Great Place to Work and Do business sustainably key performance indicators in 2018 to evaluate appropriate representation of the strategy. We will continue to make updates on current indicators publicly available.

"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.

Total Revenue[1]

$22,465m

2017	**$22,465m**
2016	$23,002m
2015	$24,708m

Actual growth	CER growth
2017 -2%	2017 -2%
2016 -7%	2016 -5%
2015 -7%	2015 +1%

[1] As detailed on page 70, Total Revenue consists of Product Sales and Externalisation Revenue.

Net cash flow from operating activities

$3,578m

2017	**$3,578m**
2016	$4,145m
2015	$3,324m

Actual growth
2017 -14%
2016 +25%
2015 -53%

Reported EPS

$2.37

2017	**$2.37**
2016	$2.77
2015	$2.23

Actual growth	CER growth
2017 -14%	2017 -15%
2016 +24%	2016 +9%
2015 +128%	2015 +137%

Core EPS

$4.28

2017	**$4.28**
2016	$4.31
2015	$4.26

Actual growth	CER growth
2017 -1%	2017 -2%
2016 +1%	2016 -5%
2015 0%	2015 +7%

Dividend per share[1]

$2.80

2017	**$2.80**
2016	$2.80
2015	$2.80

[1] First and second interim dividend for the year.

Financial Review from page 66.

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

Business Review

The first phase in AstraZeneca's strategy focused on strengthening and accelerating our product pipeline. In the second phase, our focus has been on driving our Growth Platforms and launching new products. This effort is driven by a business that is organised to deliver our return to sustainable growth.

Minute pieces of tumour DNA circulating in the bloodstream

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

As outlined below, our operating model includes our R&D, Commercial and Operations functions, together with our therapy areas.

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 66.

We are working to create a lean and simple organisation, focused on driving distinctive science in our main therapy areas.

Research & Development (R&D)

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

Phase I and II – discovery and early-stage development

IMED
The Innovative Medicines and Early Development (IMED) Biotech Unit focuses on scientific advances in small molecules, oligonucleotides and emerging drug platforms.

MedImmune
MedImmune is responsible for global biologics R&D.

Phase III (late-stage development) and life-cycle management

Both IMED and MedImmune are responsible for delivering projects to our Global Medicines Development (GMD) unit for late-stage development.

Commercial

We group our sales and marketing functions into regions: North America (US and Canada); Europe; and International (China, Hong Kong, Asia Area, Australia & New Zealand, Russia & Eurasia, Middle East & Africa, Latin America and Brazil). Japan is categorised separately and is one of our Growth Platforms.

Operations

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

Therapy areas

Our Global Product and Portfolio Strategy group (GPPS) leads our therapy area activities for two of our three main therapy areas – CVMD and Respiratory, as well as our portfolio of medicines in Other Disease Areas. GPPS also serves as the bridge between our R&D and Commercial functions and works to provide strategic direction from early-stage research to commercialisation.

GPPS works closely with healthcare providers, regulatory authorities and those who pay for our medicines, seeking to ensure those medicines help to fulfil unmet medical needs and provide economic as well as therapeutic benefits.

In addition to this Group-wide role, our Oncology Business Unit, formed in April 2017, has direct responsibility for sales, marketing and medical affairs activities in the US and in a number of European markets, including France, Germany, Italy, Spain and the UK. Responsibility for Oncology in other markets remains with the Commercial functions.

See Therapy Area Review from page 46.

1. Achieve Scientific Leadership

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

Overview

- 19 approvals of NMEs or major LCM projects in major markets
  - 9 Oncology approvals for *Imfinzi*, *Calquence*, *Faslodex*, *Lynparza* and *Tagrisso*
  - 6 CVMD approvals for *Bydureon*, *Bydureon BCise*, *Forxiga* and *Qtern*
  - 1 Respiratory approval for *Fasenra*
  - 3 Other approvals for *Duzallo*, *Kyntheum/Siliq*
- 18 NME or major LCM regulatory submissions in major markets
- 9 Phase III NME investment decisions
- 14 Phase II starts
- Accelerated reviews included
  - 3 Breakthrough Therapy Designations
  - 2 Orphan Drug Designations
  - 2 Accelerated approvals
  - 6 Priority Review Designations
- 10 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 biotech-style 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 82 manuscripts (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 1,054 in total. This represents a twelve-fold improvement since our drive to publish in 'high-impact' journals began in 2010.

Early science

We want to push the boundaries of science to strengthen our early-stage product portfolio. That means exploring novel biology and using more diverse drug platforms. For example, our partnership with Moderna is exploring the use of modified ribonucleic acid (RNA) for cardiac regeneration in patients undergoing coronary artery bypass graft surgery (AZD8601). With Ionis Therapeutics, we are investigating an antisense oligonucleotide in immuno-oncology (AZD9150), in combination with *Imfinzi*. Also in 2017, we formed partnerships with APT Therapeutics to access their therapeutic protein platform; with Pieris to develop novel inhaled drugs; and with Bicycle Therapeutics, in support of both our Respiratory and New CVMD Growth Platforms, to develop a new class of therapeutics based on its proprietary bicyclic peptide product platforms.

We also identify collaborations that allow us to out-license our own technology platforms. For instance, we continued to expand the utilisation of our antibody-drug conjugates (ADC) technology platform through an agreement with GamaMabs Pharma to produce an ADC as a potential cancer therapy.

Working collaboratively and fostering open innovation

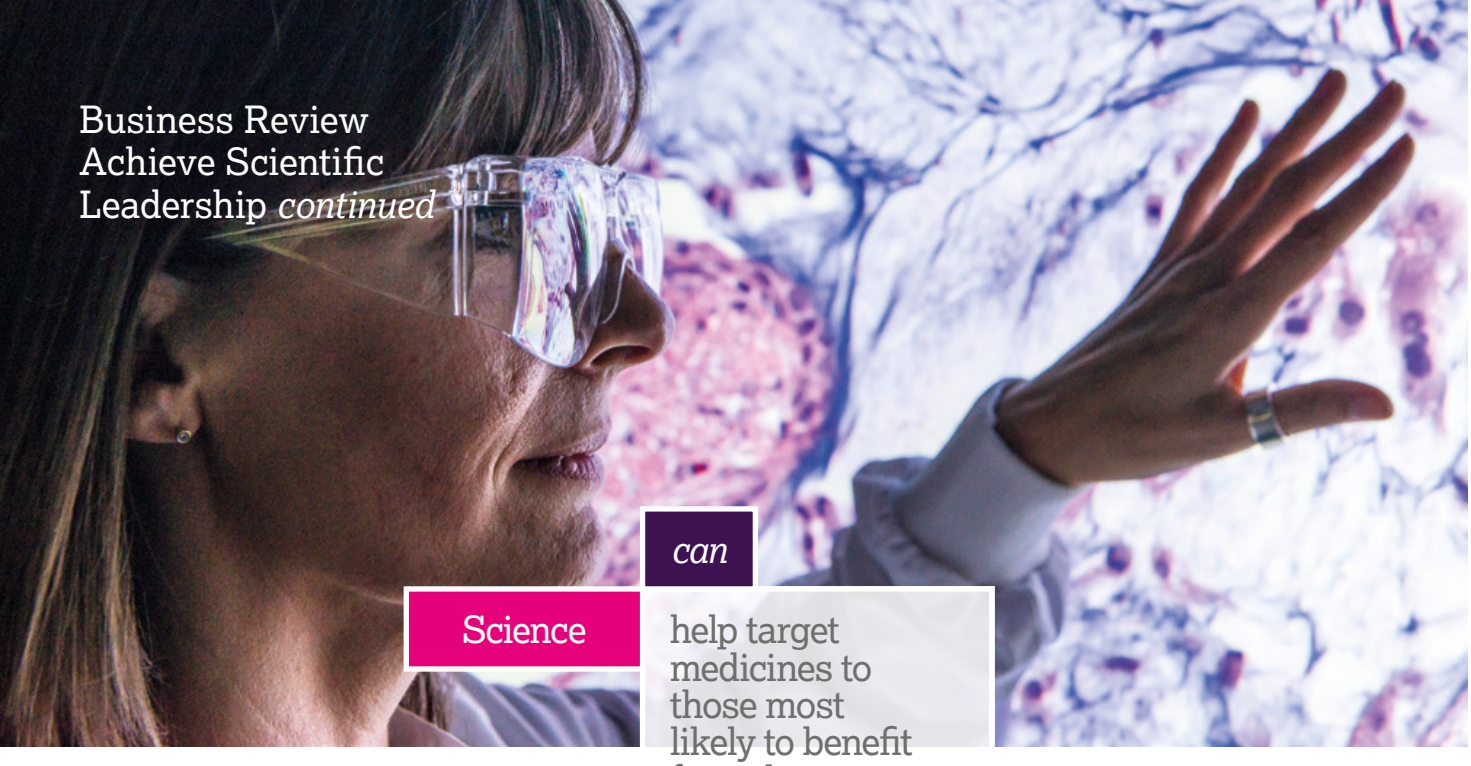
Our collaborative approach to science was exemplified in 2017 by our partnerships with Imperial College, Crick Institute, and the MRC Laboratory of Molecular Biology to further our understanding of the underlying biology of disease. Additionally, since the start of our joint blue-skies programme with the MRC Laboratory of Molecular Biology in 2014, we have funded 22 research projects. We have also continued to pioneer new approaches to open innovation, enabling our scientists to share their ideas more freely and collaborate on projects with external scientists. The IMED Open Innovation portal allows external researchers to access the full range of open innovation programmes. By the end of 2017, our teams had reviewed more than 500 proposals for new drug projects. Of these, 32 have progressed as far as clinical trials, while more than 294 are at pre-clinical trial stage.

During 2017, MedImmune continued to support its internal development efforts with collaborations. These included a research collaboration with Michigan Medicine to identify potential new therapies for the prevention and treatment of diabetes, obesity and related metabolic disorders. We also announced a collaboration with Washington University School of Medicine to advance next generation personalised cancer immunotherapy with neoantigen vaccines. We also renewed our collaboration with a subsidiary of the French National Institute of Health and Medical Research conducting research into translational biology and new disease mechanisms across a range of therapeutic areas.

Precision medicine and genomics

Precision medicine, our new name for personalised healthcare, reflects the broad range of cutting-edge diagnostic technologies we use, including molecular diagnostics, tissue diagnostics, next-generation sequencing and point-of-care diagnostics. Building on our historical focus on Oncology, we now cover all three main therapy areas. Today, 90% of our clinical pipeline follows a precision medicine approach – 10 percentage points more than in 2016. We are industry leading in this field with 19 diagnostic tests launched, linked to four of our medicines (*Iressa*, *Lynparza*, *Tagrisso* and *Imfinzi*) and one linked to a drug we have just externalised (*Zurampic*); joint first for the number of FDA approvals of precision medicines; and the highest number of biomarker-related publications in scientific journals since 2014.

In 2017, we delivered four diagnostic tests. These included one diagnostic to detect PD-L1 protein expression on both tumour and immune cells for *Imfinzi* (bladder cancer); one blood-based laboratory assay for BRCA genes for *Lynparza* (ovarian cancer); one point of care diagnostic for uric acid in blood that can be used for *Zurampic* (gout) and one tumour tissue next-generation sequencing diagnostic for *Tagrisso* (NSCLC). In Respiratory disease, we are now developing our first point-of-care test for eosinophilic respiratory disease with ChemBio Diagnostics. In total, we invested over $185 million in strategic partnerships with leading diagnostic companies in 2017, including Ventana (Roche Tissue Diagnostics), Illumina, Roche Molecular Systems and Myriad Genetics. We have an in-house Centre for Genomics Research which analyses genomes and enables us to identify more effectively novel genetic causes of diseases and integrate this knowledge across our entire drug discovery and development platform. We are also partnering with experts in genomics to enhance our expertise in this field.



Science *can* help target medicines to those most likely to benefit from them

Transformative approaches to drug discovery and development

Within our early science units, we are exploring emerging technologies to accelerate the design and testing of tomorrow's medicines. Since 2013, many of the discoveries and recommendations made by the IMED Futures programmes have been integrated into the way we operate today. Machine learning and artificial intelligence are helping us to transform our medicinal chemistry, and informatics are converting 'big data' into valuable knowledge. For example, our in-house gene-editing group has identified novel targets and drug combinations using CRISPR screens, and the teams published papers in 2017 that have advanced these technologies. Critical to improving target validation is the development of better predictive models of disease. We are collaborating with experts in organ-on-a-chip design, technology and biology from biotech and academia such as TissUse, Nortis and Emulate and, in 2017, five organ-chips were under development with our collaborators. In development, the 'iDecide' suite of digital platforms is enabling the Digital Experimental Cancer Medicine Team at The Christie in Manchester, UK to put into practice technology which will help to increase the access to real-time clinical data.

Late-stage development

During 2017, GMD delivered clinical trial data and submissions that resulted in 19 approvals for new medicines in the US, EU, China and Japan. As shown in the table opposite, our pipeline includes 144 projects, of which 132 are in the clinical phase of development, and we are making significant progress in advancing our late-stage programmes through regulatory approval with 18 NME or major LCM regulatory submissions during 2017.

***Imfinzi* diagnostic test**

Imfinzi's diagnostic test in bladder cancer, which was essential to the approval of the medicine, uses a novel patient selection approach by establishing PD-L1 status via immune cell or tumour cell staining. It not only provides clinicians with information that may guide immunotherapy decisions in 2nd line bladder cancer, but also enables AstraZeneca and diagnostic partner Ventana to drive up testing rates before *Imfinzi*'s launch in 1st line bladder cancer.

At the end of the year, we had 11 NME projects in pivotal studies or under regulatory review (covering 19 indications), compared with 12 at the end of 2016.

Also in 2017, 12 NMEs progressed to their next phase of development and 10 projects were discontinued: six for poorer than anticipated safety and efficacy results; and four 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 initial results of the MYSTIC trial showed that *Imfinzi* in combination with tremelimumab for 1st line NSCLC did not meet the primary endpoint of progression-free survival – please see Oncology from page 48 for more information. Also, the Phase III programme for tralokinumab did not achieve the desired outcomes of significantly reducing exacerbation rates for patients with severe, uncontrolled asthma or in reducing the use of oral corticosteroids. See Respiratory from page 56 for more information.

Accelerating the pipeline

GMD is prioritising its investment in specific programmes in order 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 2017, including key oncology trial outcomes for *Tagrisso* in 1st line EGFR-mutated NSCLC (FLAURA) and for *Imfinzi* in stage 3, locally-advanced unresectable NSCLC (PACIFIC), and we expect a continued flow of new data throughout 2018. Our teams have also been quick to turn positive clinical trial data into regulatory submissions. In 2017, we made submissions in the US, EU and Japan for both *Imfinzi* and *Tagrisso* for the indications noted above and, in the US, we made a submission and received approval for our first haematological cancer drug, *Calquence*, for relapsed/refractory mantle cell lymphoma. Furthermore, *Lynparza* was submitted in the US, EU and Japan for use by patients with platinum-sensitive recurrent ovarian cancer regardless of BRCA-mutation status, and has already received US approval. We also received approval in the US and EU for our first respiratory biologic treatment, *Fasenra*, for severe asthma, and in the EU for combination use of *Forxiga* and *Bydureon* for the treatment of Type 2 diabetes.

In 2017, we presented scientific rationale that resulted in nine regulatory designations for Breakthrough Therapy or Priority Review for new medicines which offer the potential to address unmet medical need in certain diseases, and we also secured Orphan Drug status for the development of three medicines to treat very rare diseases. For more information on our pipeline and regulatory designations made during 2017, please see the Therapy Area Review from page 46 and the Development Pipeline from page 202.

Development pipeline overview (as at 31 December 2017)

Phase I 50

> 50 projects in Phase I, including:
  – 34 NMEs
  – 16 oncology combination projects

Phase II 37

> 37 projects in Phase II, including:
  – 20 NMEs
  – 7 significant additional indications for projects that have reached Phase III
  – 10 oncology combination projects

Late-stage development* 23

> 23 projects in late-stage development, either in Phase III/pivotal Phase II studies or under regulatory review:
  – 11 NMEs not yet approved in any market
  – 8 projects exploring additional indications for these NMEs
  – 4 NMEs already approved or launched in the EU, China, Japan and/or the US

* NMEs and significant additional indications.

Life-cycle management projects* 34

> 34 LCM projects*

* Only includes material projects where first indication is launched in all markets.

We also work in partnership 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

GMD also drives 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* to extend treatment into breast cancer; we received US approval for a new auto-injector *Bydureon BCise* for Type 2 diabetes; and we secured US approval for *Faslodex* for earlier treatment of patients with advanced breast cancer.

To ensure we can deliver as many new medicines programmes as we can with our budgets and resources, we continuously seek opportunities to enhance our ways of working and, during 2017, we adopted new operating models – for example within our clinical supply chain – to drive further efficiencies and cost effectiveness.

R&D resources

We have approximately 8,400 employees in our R&D organisation, working in various sites around the world. We have three strategic R&D centres: Gaithersburg, MD, US; Gothenburg, Sweden; and Cambridge, UK.

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. More than 2,000 staff are already in the City and they will begin to move into the new strategic R&D centre from the end of 2018. The site will be fully operational from 2019. This is later than originally planned and reflects the additional innovation introduced into the development programme, combined with its scale and ambition. The overall investment in the project will be higher than initially planned and now stands at more than £500 million ($700 million), reflecting increased investment in new technologies and equipment (for example genomics, screening lab) as part of our ongoing investment in R&D in the UK.

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 Warsaw, Poland that focuses on late-stage development.

In 2017, R&D expenditure was $5,757 million (2016: $5,890 million; 2015: $5,997 million), including core R&D costs of $5,412 million (2016: $5,631 million; 2015: $5,603 million). In addition, we spent $404 million on acquiring product rights (such as in-licensing) (2016: $821 million; 2015: $1,341 million). We also invested $201 million on the implementation of our R&D restructuring strategy (2016: $178 million; 2015: $258 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

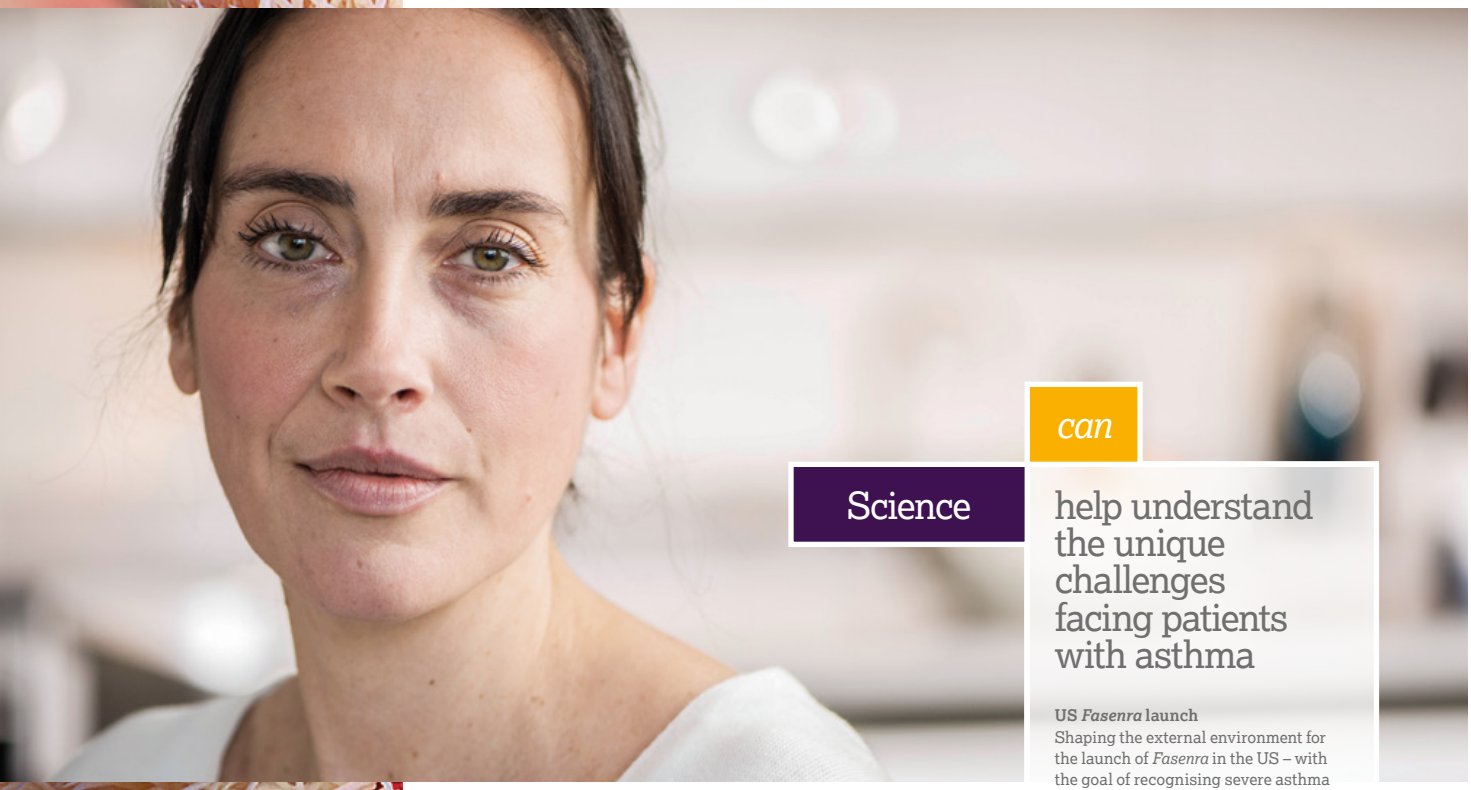
	2017	2016	2015
Discovery and early-stage development	**36%**	36%	39%
Late-stage development	**64%**	64%	61%

$5.8bn

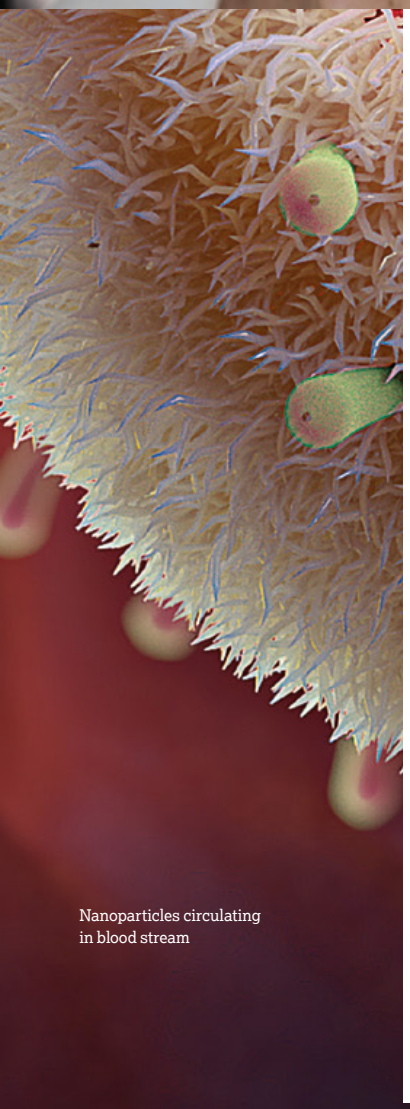
$5,757 million invested in our science

82

82 manuscripts published in 'high-impact' scientific publications – a record number



US *Fasenra* launch
Shaping the external environment for the launch of *Fasenra* in the US – with the goal of recognising severe asthma as a public health issue and highlighting the unique challenges facing patients with severe asthma, a cross-functional team engaged with decision makers and influencers, including state and federal policymakers, patients, providers, professional societies and advocacy groups. The result was the updating of how these stakeholders understand, acknowledge, and communicate around asthma as a heterogenous disease requiring an individualised treatment approach. This helped ensure that external stakeholders understand severe asthma and appreciate the need for personalised treatment plans with more advanced treatment options including *Fasenra*.



Nanoparticles circulating in blood stream

2. Return to Growth

We seek to return to growth by focusing 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

> 2% decrease in Total Revenue to $22,465 million at actual rate of exchange (2% at CER); comprising Product Sales of $20,152 million (down 5%; 5% at CER) and Externalisation Revenue of $2,313 million (up 37%; 38% at CER)
> 5% increase in Growth Platforms revenue (6% at CER), contributing 68% of Total Revenue
  – Emerging Markets: Sales growth of 6% (8% at CER) to $6,149 million. China sales in the year grew by 12% (15% at CER), supported by the launches of new medicines
  – Respiratory: Sales declined by 1% (1% at CER). *Symbicort* sales declined by 6% (6% at CER) and *Pulmicort* sales rose by 11% (12% at CER)
  – New CVMD: Sales growth of 9% (9% at CER). Strong performances from *Farxiga* and *Brilinta*, with sales exceeding $1 billion in 2017
  – Japan: 1% growth in sales (4% at CER), underpinned by the growth of *Tagrisso* and *Forxiga*, partly mitigated by the impact of the entry of generic competition to *Crestor* in the second half of the year
  – New Oncology: Sales growth of 98% (98% at CER). Sales of *Tagrisso* reached $955 million to become AstraZeneca's largest-selling Oncology medicine
> US revenue was down by 16% to $6,169 million; Europe down by 6% (7% at CER) to $4,753 million; and Established ROW was static (up 1% at CER) to $3,081 million

Our plans for growth

Our Commercial teams, which comprised around 34,600 employees at the end of 2017, 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 and market our products largely to primary care and specialty care physicians.

Even as we continue to be impacted by the loss of exclusivity on some of our leading medicines, we have delivered increasing revenues from our growth brands and launches. This return to growth is being underpinned by the Growth Platforms. In 2017, continued declines in revenue, for example from the loss of exclusivity in 2016 of *Crestor* and *Seroquel XR*, were substantially offset by the strong performance of certain products from our Emerging Markets, New CVMD and New Oncology Growth Platforms, including *Farxiga*, *Brilinta* and *Tagrisso.* As our strategy has progressed, so our Growth Platforms have evolved, as shown in Strategy and Key Performance Indicators from page 17. Respiratory was joined by New Oncology from January 2015 and, from January 2017, New CVMD replaced Diabetes and *Brilinta*/*Brilique*. Our two remaining Growth Platforms, Emerging Markets and Japan, reflect the importance of these markets to growing future revenues. Overall, our Growth Platforms grew by 5% at actual exchange rates (6% at CER) in 2017 and now represent 68% of all Total Revenue.

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.

More information on our performance around the world in 2017 can be found in the Geographical Review from page 221.

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. Nevertheless, and as outlined in Marketplace from page 8, we are acutely aware of the economic challenges faced by payers and remain committed to delivering value. 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.

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 2017, Product Sales in the US decreased by 16% to $6,169 million (2016: $7,365 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 50% of the patient's out-of-pocket costs during the 'coverage gap' portion of their benefit design. As part of the ACA, we also pay a portion of an overall industry Patient Protection and Affordable Care Act Branded Prescription Drug Fee.

In 2017, 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 $119 million (2016: $471 million; 2015: $786 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 2017, 84.9% of prescriptions dispensed in the US were generic, compared with 84.4% in 2016. 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. Proposed changes under consideration include varying approaches to price controls on medicines (including price transparency) as well as potential reforms to government regulated programmes (such as Medicare Part B, Medicare Part D, Medicaid or other provisions under the ACA). Repeal of the Medicare Part D non-interference clause that currently prohibits the government from negotiating directly with manufacturers on drug prices as well as allowing the importation of medicines into the US from other countries have been considered as a mechanism to reduce drug costs. 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's 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 4.5 million patients across the US and Puerto Rico over the past 10 years.

For more information, see Community Investment on page 45.

Europe

The total European pharmaceutical market was worth $214 billion in 2017. We are the fourteenth largest prescription-based pharmaceutical company in Europe (see Market definitions on page 235) with a 2.2% market share of pharmaceutical sales by value.

In 2017, our Product Sales in Europe decreased by 6% at actual rate of exchange (7% at CER) to $4,753 million (2016: $5,064 million). Key drivers of the decline, leaving aside the impact of divestments such as the anaesthetics portfolio, *Seloken* and *Zomig*, were continued competition from *Symbicort* analogues, ongoing volume erosion of *Pulmicort*, *Seroquel XR* and *Nexium* following loss of exclusivity, and the continued impact of early generic entry in certain markets for *Crestor* and *Faslodex*, which we expect to continue in 2018. 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 significant progress of certain products across our Growth Platforms, in particular with *Forxiga*, *Xigduo*, *Brilinta*, *Lynparza* and *Tagrisso*.

Following the presentation of the PACIFIC trial at ESMO in 2017, we have overseen a mobilisation of medical teams across Europe to be able to offer early access to *Imfinzi* for patients with unresectable stage 3 NSCLC.

The PACIFIC Early Access Programme (EAP) went live in September 2017 with the first patient included in October 2017. The PACIFIC EAP is now open in 16 EU countries with additional countries planned to be active. This is a great example of our ability to put the patient first and to offer life-changing medicine to patients in need.

Established Rest of World (ROW)*

In 2017, Product Sales in Japan increased by 1% at actual rate of exchange (increased 4% at CER) to $2,208 million (2016: $2,184 million), as a result of the strong growth from the brands in our Growth Platforms and *Nexium*. Particularly strong performances from *Tagrisso* and the Diabetes franchise helped to drive this volume growth, offsetting generic competition. *Crestor*, for example, is now facing significant generic competition. In September 2017, a *Crestor* authorised generic entered the market and in December 2017 we saw more than 20 generic companies enter the statin market with generic rosuvastatin. We now hold ninth position in the ranking of pharmaceutical companies by sales of medicines in Japan. Despite the mandated biennial government price cuts and increased intervention from the government to rapidly increase the volume share of generic products, Japan remains an attractive market for innovative pharmaceuticals. These price cuts are likely to continue as are experimental decisions by regulators based on cost effectiveness assessments.

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 63% funded by private payers and 37% with public plans.

Our sales in Australia and New Zealand declined by 5% at actual rate of exchange (7% at CER) in 2017. This was primarily due to the continued erosion of *Crestor*, *Nexium* and *Seroquel* by generic medicines and price reductions on established brands. Sales declined less in 2017 than in 2016 as the pace of generic erosion has moderated 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 15% at actual rate of exchange (10% at CER), 100% (actual and CER) and 27% at actual rate of exchange (25% at CER) respectively.

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

Expansion in Emerging Markets

Emerging Markets, as defined in Market definitions on page 235, comprise various countries with dynamic, growing economies. As outlined in Marketplace from page 8, these countries represent a major growth opportunity for the pharmaceutical industry due to high unmet medical needs 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 Diabetes, Respiratory, Oncology and CV portfolios. To educate physicians about our broad portfolio, we are selectively investing in sales capabilities where opportunities from unmet medical needs exist. We are also expanding our reach through multi-channel marketing and external partnerships.

With revenues of $6,149 million, AstraZeneca was the sixth largest multinational pharmaceutical company, as measured by prescription sales, and the second fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2017.

In China, AstraZeneca is the second largest pharmaceutical company by value in the hospital sector, as measured by sales. Sales in China in 2017 increased by 12% at actual rate of exchange (15% at CER) to $2,955 million (2016: $2,636 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 market expansion programmes in core therapy areas. In addition, five products including *Brilinta*, *Onglyza* and *Faslodex* were listed in the updated National Reimbursed Drug List (NRDL) and we launched two key products (*Tagrisso* and *Forxiga*) during 2017. 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. The industry-wide growth rate is expected to be a moderate single digit percentage, following the recent update 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.

Science *can* help more patients in China

China market development
Our business in China is able to expand only by meeting the needs of an increasing number of patients. In order to do this, we partner with stakeholders at the local, provincial and national level and we recognise that our ability to grow our business is directly related to even more patients being able to access quality healthcare.

One important way we do this is through our China Commercial Innovation Centre, where, with our partners, we develop ways to integrate technology into all parts of healthcare delivery, increasing the chance that the right treatment is delivered to the right patient at the right time. For example, by working with different stakeholders, our online nebulisation centres across certain parts of China are now up and running and their availability is updated in real time. Therefore, patients who need to access treatment have all the information they need to access care wherever they may need it.

Access to 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, Karte Zdorovia in Russia and FazBem in Brazil.

We also run donation programmes, such as in Cambodia, where we celebrated the ninth year of our partnership with Americares in support of the Cambodia Breast Cancer Initiative. In 2017, it provided approximately 700 screenings, more than 8,000 education sessions, and diagnosed 59 cases of breast cancer.

For more information on product donations, see Community investment on page 45.

Other programmes are focused on developing healthcare system infrastructure. For example, Phakamisa supports the South African 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 and lung disease through the promotion of primary prevention, early detection and access to affordable medicines. Launched in September 2017, Healthy Lung Asia is a region-wide initiative, with programmes being tailored and developed in nine countries across Asia in collaboration with local partners. The overall objective of Healthy Lung Asia is to raise the profile of respiratory disease with policy makers and build health system capacity to support future access. It started with programmes in Vietnam and Indonesia.

For more information, see page 39.

Healthy Heart Africa (HHA) was launched in Kenya in October 2014 in collaboration with the Ministry of Health in support of its commitment to combat NCDs. Following the success of HHA in Kenya, we developed a partnership with the Federal Ministry of Health in Ethiopia in 2016 to integrate HHA programming into the Ethiopian healthcare system, in support of the Government National Strategic Action Plan for NCDs. HHA aims to reach 10 million people with high blood pressure across Africa by 2025, supporting WHO's global target of a 25% reduction in hypertension prevalence by 2025, and on page 40 you can see the progress we have made.

For more information on Broadening access to healthcare as one of our sustainability priorities, please see page 39.

Strategic partnership with MSD
In July 2017, AstraZeneca announced a strategic collaboration with MSD to maximise the potential of *Lynparza* as a monotherapy and as the backbone for oncology combinations, as well as explore the potential of selumetinib, an inhibitor of MEK, part of the mitogen-activated protein kinase (MAPK) pathway. The collaboration was driven by our commitment to following the science: PARP inhibition is increasingly recognised as a foundation for mono and combination therapies. For example, blocking PD-L1 can potentiate the effect of PARP inhibition in tumour suppression and MEK inhibitors can make a tumour more responsive to immunotherapy. The collaboration enables us to work hand-in-hand with another leading oncology company and one of the key players in immuno-oncology to accelerate new and existing ideas. The increased resources and focus bring potential benefit to more patients in need faster than we can do alone. Together, we are building an even broader clinical programme and we are working hard to deliver it as quickly as possible.

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 biopharmaceutical 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.

In 2017, we hosted 56 independent inspections from 21 regulatory authorities. We reviewed observations from these inspections together with the outcomes of internal audits and, where necessary, implemented improvement actions.

Following the second CRL received at ZS Pharma for ZS-9, the site has completed manufacturing process validation and the NDA was refiled with the FDA in December. For further details please see the CVMD section from page 52.

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 (PT&D)

The integration of PT&D into our Operations organisation since 2016 has driven greater collaboration between our technical groups and manufacturing sites, allowing substantial manufacturing and scientific expertise and leadership to inform decisions for the discovery, development and commercialisation of small molecule portfolios.

We are actively working on over 150 drug projects across our R&D and Commercial portfolios, streamlining over 400 innovation ideas from concept to business case, and supporting more than 250 AstraZeneca clinical studies worldwide. We also support over 100 in-line brands and small molecule marketed products through our new global Manufacturing Science and Technology organisation and manufacturing site Centers of Excellence.

Our continued innovation in science and technology allows us to enable and differentiate products including *Lynparza*, *Qtern*, *Bevespi*, *Calquence*, *Brilinta* and potential new products such as PT010 as they are introduced into the marketplace and ultimately into the hands of patients globally. In 2017, we also launched the Turbo+ programme, our digital Integrated Patient Solution for *Symbicort Turbuhaler*.

For more information, please see Respiratory on page 56.

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, Brazil, Argentina and Algeria. 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 API 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; Boulder and Longmont, CO), 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 2017, we launched our first two new biologics medicines, *Imfinzi* and *Fasenra*, using our large-scale drug substance manufacturing facility in Frederick, MD, US. We continue to develop additional manufacturing capacity for both drug substance and drug product production. Our new small-scale/high-titre drug substance manufacturing facility, also in Frederick, began producing clinical supply material in 2017. Our recently acquired facility in Longmont, CO, US has been integrated into our Colorado Biologics operations to provide cold chain logistics support to our Boulder, CO, US drug substance manufacturing facility. In Sweden, we expect our new biologics drug product manufacturing facility to be available for clinical trial programmes by the end of 2018.

For small molecules we are constructing a new small-scale development and launch facility alongside our existing manufacturing facility in Wuxi, China. This investment will support the acceleration of delivery of our new innovative medicines to patients in China. Completion of this high-potential facility, expected in 2018, will complete our ability to execute in China across the whole life-cycle of a medicine from discovery to commercialisation.

At the end of 2017, approximately 12,600 people were employed at 31 Operations sites in 18 countries.

For more information on Supply chain management, please see page 42.

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 biopharmaceutical 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 600 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 2017.

Over the past three years, we have completed more than 250 major or strategically important business development transactions, including some 54 in 2017. Of these transactions, 17 were related to pre-clinical assets or programmes and nine to precision medicine and biomarkers. Twenty transactions helped expand our biologics capabilities.

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: (a) collaborations that help us access therapy area expertise and (b) 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.

Examples of collaborations entered into in 2017 that help us access therapy area expertise or generate sustainable and ongoing income include:

- our partnership with MSD regarding *Lynparza* and selumetinib in Oncology
- our collaboration with Sanofi Pasteur for MEDI8897
- our agreement with TerSera for *Zoladex* in the US and Canada.

In each case, we are optimising the long-term value of each medicine through the collaboration.

Examples of collaborations that help us increase our reach to a greater number of patients include the strategic partnership with Circassia regarding the promotion of *Tudorza* and the development and commercialisation of *Duaklir* in the US. *Tudorza* and *Duaklir* are important components of AstraZeneca's Respiratory franchise globally and this collaboration will support their commercialisation in the US for the benefit of millions of COPD patients. It also further sharpens our focus on *Symbicort*, *Bevespi Aerosphere*, *Fasenra* and other respiratory development programmes.

Alongside these externalisation opportunities, 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 2017, we sold to Aspen our remaining rights in the anaesthetic portfolio, we divested commercial rights to *Seloken/Seloken ZOK* in Europe to Recordati and divested to Grünenthal the global, ex-Japan, rights to *Zomig*. 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. Thirteen transactions that contribute to Externalisation Revenue and a further 10 divestments or out-licences were completed in 2017.

More information on our partnering activity in 2017 can be found in the Financial Review from page 66 and Notes 1 and 2 to the Financial Statements from page 145.

31

We have 31 Operations sites in 18 countries

250

Completed more than 250 major or strategically important business transactions in the last three years

600

We have more than 600 collaborations worldwide

"Our industry's principal economic safeguard is a well-functioning system of patent and related protection."

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 duration 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 28 to the Financial Statements from page 182. For more information on the risks relating to patent litigation and early loss and expiry of patents, please see Risk from page 210.

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 (PTE) 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 208 and 209 sets out certain patent expiry dates and sales for our key marketed products.

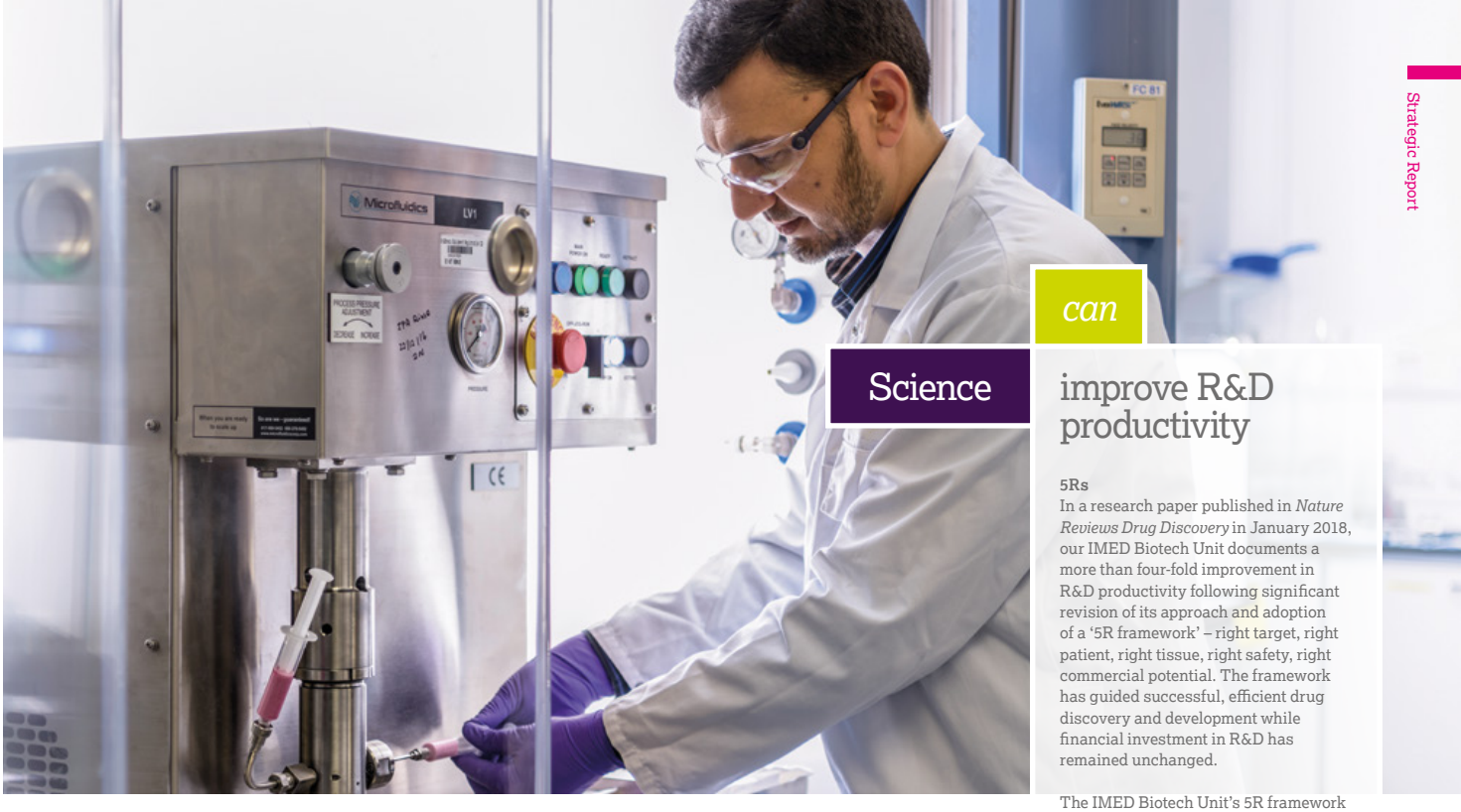
Other exclusivities

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 IP 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' marketing exclusivity.

In the US, new chemical entities (NCEs) are entitled to a period of five years' 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.



Science *can* improve R&D productivity

5Rs
In a research paper published in *Nature Reviews Drug Discovery* in January 2018, our IMED Biotech Unit documents a more than four-fold improvement in R&D productivity following significant revision of its approach and adoption of a '5R framework' – right target, right patient, right tissue, right safety, right commercial potential. The framework has guided successful, efficient drug discovery and development while financial investment in R&D has remained unchanged.

The IMED Biotech Unit's 5R framework focuses on quality rather than quantity at all stages of drug discovery and development. Hence, the number of projects in discovery has decreased while their likelihood of success has increased. Other key factors include investment in state-of-the-art technologies, such as CRISPR (see page 126), and next-generation sequencing, to produce better quality drug candidates for development, as well as a change in culture to focus on the science. As a result, its success rate in discovering new compounds, which then progress through the pipeline to completion of Phase III clinical trials, increased from 4% in the period 2005-2010 to 19% in the period 2012-2016. This places R&D productivity well above the pharmaceutical industry average of 6% for small molecules in the period 2013-2015.

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

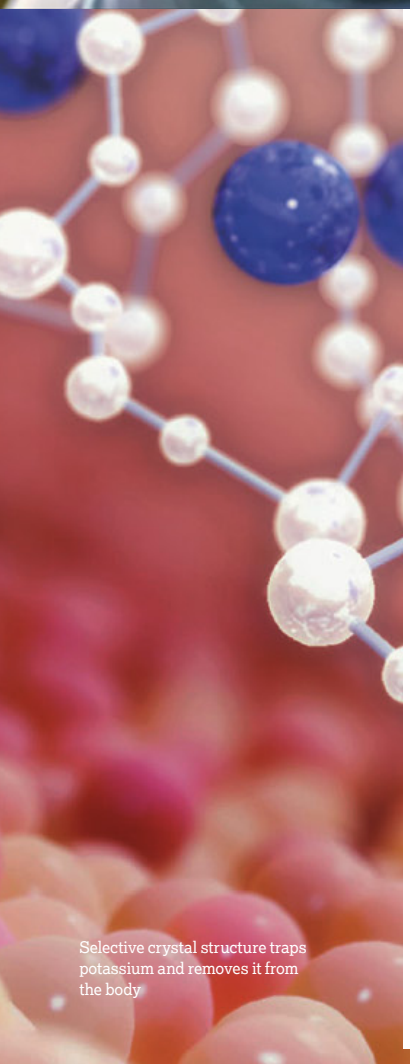
In 2017, we embarked on the second phase of our IT journey, taking what we successfully delivered in our three-year transformation to the next level. The foundation of our future focus is based on improved cost efficiency, systems performance and better support for the business priorities. Our focus for the next three years is to optimise and enable accelerated revenue growth and profitability through digitisation and innovation.

Leveraging the operating model implemented during the transformation, we will build on business productivity and ensure targeted outcomes that accelerate drug developments, help us bring products to market faster and support tools required for specialised medicines. We will also harness our internal capabilities to develop robust strategies on data and analytics, software engineering and cloud technology – all of which will support the business and its various transformation programmes.

Protecting our IT systems, IP and confidential information against cyber attacks is a key concern. Our IT organisation seeks continuous improvement of our IT protection by developing and implementing robust, effective and agile risk-based approaches to protect our resources and keep pace with the rapidly evolving cyber security risk landscape. To help guard against cyber threats, we have adopted a comprehensive cyber security process and policy, which we regularly review and update. We monitor our systems and data with sophisticated technology to identify and address potential weaknesses in the management of cyber security risk. Over 54,000 employees have also completed internal cyber awareness training in 2017. We recognise that cyber security is a rapidly evolving landscape and attacks display ever-increasing levels of sophistication. The risk of a cyber security event cannot be discounted despite these preventative actions.

For more details, please see Risk from page 210.

At the end of 2017, our IT organisation comprised approximately 3,715 people across our sites in the UK, Sweden, the US, and our global technology centres in India (Chennai) and Mexico (Guadalajara).



Selective crystal structure traps potassium and removes it from the body

"To foster innovation, we seek to ensure that our employees reflect the diversity of the communities in which we operate."

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 release 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
- Employee retention remains challenging in specific areas of the business
- Maintained listing in Pharmaceuticals, Biotechnology and Life Sciences industry group of Dow Jones Sustainability Index
- Launched Code of Ethics based on our Values
- Continued progress towards our target to source 100% renewable power by 2025
- Launched Healthy Lung Asia to raise profile of respiratory disease and build health system capacity

Employees

To achieve our strategic priorities, we continue to acquire, 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 committed to hiring and promoting talent ethically and in compliance with applicable laws. Our current Global People Policy sets out how we will meet our commitment to promoting and maintaining a culture of diversity and equal opportunity, in which individual success depends solely on personal ability and contribution. 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. The Global People Policy 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. More information on our Global Policy framework can be found on page 40, our Code of Ethics on page 98 and our Global Policies can be found on our website, www.astrazeneca.com/sustainability.

To help deliver our strategic priorities, we are identifying and recruiting emerging talent, as well as investing in internships and recruitment opportunities globally. For example, we conduct a global programme to hire recent graduates for our pharmaceutical technical development, procurement, quality, engineering, IT, supply chain, and biometrics and information sciences functions. We also have 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 therapeutic area.

Hiring over recent years means that employees with less than two years' service now represent 31% of our global workforce (up from 20% in 2012). This provides a greater balance in terms of refreshing talent and retaining organisational experience. 2017 saw an increase in hiring to support our strategic objectives. Our data indicates that these recent hires are performing strongly, although in some areas of the business retention of this population is challenging. During 2017, we hired 11,000 permanent employees. Voluntary employee turnover remained stable at 9.7% in 2017.

The voluntary employee turnover rate among our high performers increased in 2017 to 7.1% (from 6.1% in 2016), while the voluntary employee turnover of recent hires decreased to 12.2% (from 12.7% in 2016). 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 in the referendum in June 2016 could have an impact on hiring and retaining staff in some business-critical areas. Consequently, we are considering ways in which we might support existing staff who might be impacted and, through our hiring process, ways of supporting potential staff.

Develop a strong and diverse pipeline of leaders

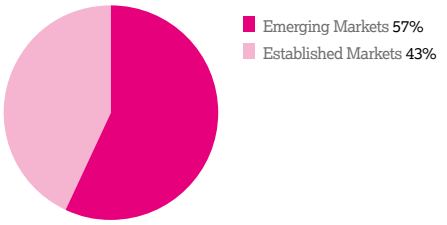
To foster innovation, we seek to harness different perspectives, talents and ideas as well as ensuring that our employees reflect the diversity of the communities in which we operate.

As part of our commitment to diversity and inclusion 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, in some parts of the business, the creation of a People Manager objective to ensure all recruitment includes diverse applicant slates and diverse interview panels.

Our commitments include a goal to increase the number of women on our leadership teams. As shown in the gender diversity figure on page 37, women comprise 50.1% of our global workforce. There are currently five women on our Board (42% of the total). 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 44.4% in 2017 (from 43.2% in 2016), which exceeded our scorecard target of 43.5% 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 2017, AstraZeneca was ranked 15th in the FTSE 100 for Women on Boards and 9th for Women on Executive Committees and Direct Reports. Our progress has been recognised externally with Bahija Jallal (Executive Vice-President, MedImmune) being named 2017 Woman of the Year by the Healthcare Businesswomen's Association.

In 2017, we extended our Women as Leaders experience to support the accelerated development of high-potential women in AstraZeneca. In addition, we have developed women's networks in most countries, held a womens' summit in the UK, US and Sweden, and continued to support mentoring relationships, for example introducing mentoring by senior females for emerging talent in Operations.

Sales and Marketing workforce composition (%)



In 2017, 88% of vacancies across the top three levels of our organisation were filled internally, reflecting our long-term commitment to develop high-quality leaders. 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 2017, 13.4% of leadership roles that report to our senior leadership team have a country of origin that is an Emerging Market or Japan (an increase from 5% in 2012, but below our 2017 target of 16%).

Diversity is integrated across our new Code of Ethics and associated workforce policy. In addition to the two diversity metrics tracked in the AstraZeneca scorecard, on an 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.

Drive a vibrant, high-performing culture

Continuing our emphasis on high performance, in 2017 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 87% of the population (60% in 2016). We encourage participation in various employee share plans, some of which are described in the Directors' Remuneration Report from page 105, and also in Note 27 to the Financial Statements, from page 179.

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

Employee opinion surveys help us measure employee satisfaction and engagement, and progress in our aim of being a great place to work. Our most recent survey, carried out in December 2017, showed an improvement compared to the survey at the start of the year in scores for all 11 items common to both surveys. Importantly, we saw good progress in employee understanding and belief in our strategy, perception of AstraZeneca as a great place to work and questions related to personal development. Despite progress in the latest survey, there remains further opportunity for improvement around leadership communication.

Generate a passion for people development

We encourage employees to take ownership of their own development and encourage 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 18,500 applications from internal candidates through this platform in 2017.

As part of our ambition to transform the learning culture in AstraZeneca, we have implemented a best-practice cloud-based global learning management system that will provide a platform to ensure development opportunities are available to all employees.

In 2017, we launched 'Leading People', a social online learning platform, with over 4,000 managers enrolling on the course. We saw a significant increase in the score in a number of key Pulse survey items among this cohort, in particular those around engagement and personal development. This work was recognised with a significant external award. Furthermore, in 2017, we also launched a pilot for over 200 employees for the related programme 'Leading Self', which will be rolled out to all employees globally in 2018.

Human rights

Our Global People Policy 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.

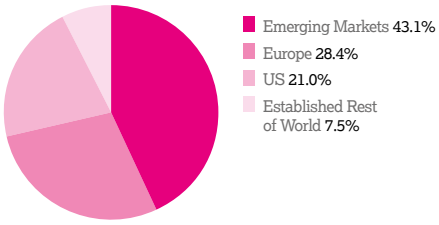
We support the principles set out in the United Nations Universal Declaration of Human Rights and the International Labour Organization's (ILO) standards on child labour and minimum wages. We are also members of the United Nations Global Compact on Human Rights.

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, please see page 227.

A global business

Employees by reporting region (%)



All numbers as at 31 December 2017.

61,100
employees

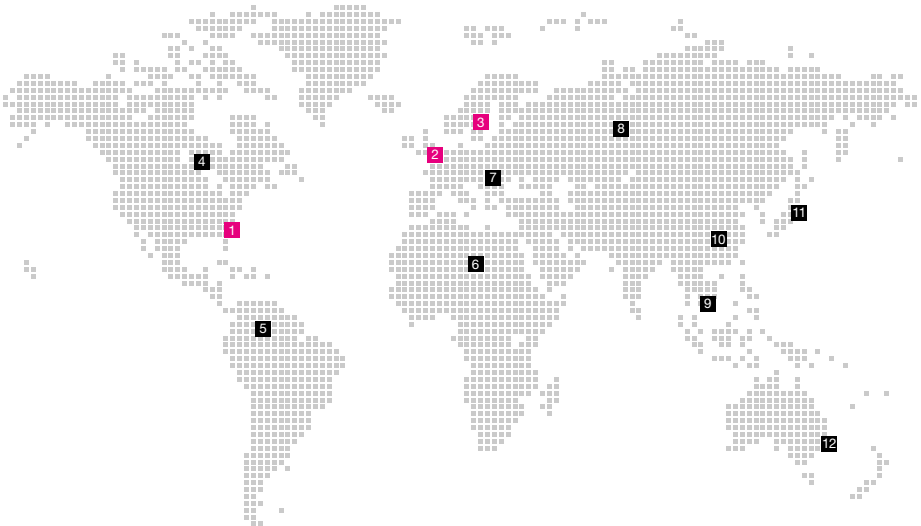
Co-locating around three strategic R&D centres

1. Gaithersburg, MD, US
2,900

2. Cambridge, UK
2,200

3. Gothenburg, Sweden
2,200

By geographical area



1. US
12,800
(21.0%)

2. UK
6,600
(10.7%)

3. Sweden
5,800
(9.4%)

4. Canada
700
(1.2%)

5. Central and South America
3,000
(4.9%)

6. Middle East and Africa
1,600
(2.6%)

7. Other Europe
7,500
(12.4%)

8. Russia
1,300
(2.1%)

9. Other Asia Pacific
6,300
(10.3%)

10. China
11,600
(19.0%)

11. Japan
2,900
(4.7%)

12. Australia and New Zealand
1,000
(1.6%)

In 2017, we signed up to the 'Fair Wage' database and will use this data to measure and monitor performance and issue directions on the Living Wage.

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, as at 31 December 2017, 2,200 employees were working in Cambridge and, of these employees, 560 have relocated from other sites in the UK. In addition to the 750 employees hired in 2015 and 2016, we hired a further 350 permanent employees in Cambridge in 2017. We are using interim infrastructure in and around Cambridge to house these employees until our new site 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 our move to Cambridge, please see R&D resources on page 25.

For more information on our restructuring programme, please see the Financial Review from page 66.

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.

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 Global Safety, Health and Environment Policy located 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 assured by Bureau Veritas.

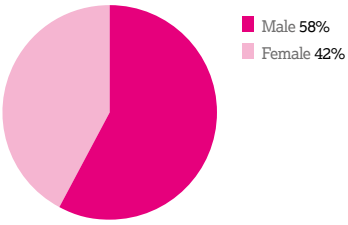
For more information, please see page 227.

As shown below, we made progress against our strategic targets in 2017, achieving a 17% reduction in the reportable injury rate and a 28% reduction in vehicle collision rate from the 2015 baseline. 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 67% of our sites.

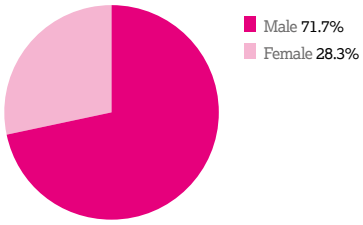
In 2017, we carried out several activities and initiatives focused on delivery of improvements in key risk areas, including driver safety (our highest risk for significant injury and fatalities), behavioural safety, ergonomics, fall prevention and industrial hygiene. We also increased focus on learning from incidents.

Gender diversity

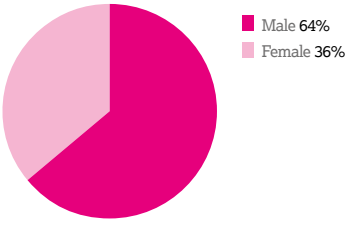
Board of Directors of the Company



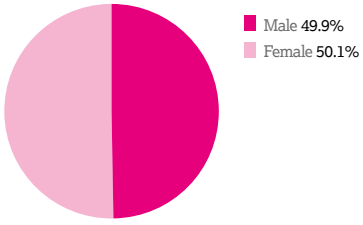
Directors of the Company's subsidiaries*



SET*



AstraZeneca employees



* For the purposes of section 414C(8)(c)(ii) of the Companies Act 2006, 'Senior Managers' are the SET, the directors of all of the subsidiaries of the Company and other individuals holding named positions within those subsidiaries.

Safety

Vehicle collisions

Year	Collisions per million km	Target
2017	**2.97**	**3.76**
2016†	3.60	4.00
2015 baseline 4.13		

Reportable injuries

Year	Reportable injury rate per million hours worked	Target
2017	**1.44**	**1.56**
2016†	1.52	1.64
2015 baseline 1.73		

† 2016 data re-stated.

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

We have three priority areas aligned with our Purpose and business strategy that allow us to have the most impact on benefiting our patients, our business, broader society and the planet. We determined these priorities, along with a set of foundational areas, through a structured sustainability materiality assessment that engaged external and internal stakeholders. We measure our progress towards our objectives through annual and long-term targets.

Learn more in our 2017 Sustainability Report available on our website, www.astrazeneca.com/sustainability.

Priority areas and objectives

1. Broadening access to healthcare

Through collaboration and innovation we strive to expand access to our medicines.

See from page 39.

- Commitment 1: Promote awareness and prevention of non-communicable diseases (NCDs) to reduce their global burden and cost
- Commitment 2: Build capacity to help improve the underlying healthcare infrastructure and remove barriers to accessing medical treatment
- Commitment 3: Make our medicines available and more affordable to people on a commercially and socially sustainable basis

2. Furthering ethics and transparency

We commit to maintaining integrity in everything we do.

See from page 40.

- Commitment 1: Working to consistent global standards of ethical sales and marketing practices in all our markets
- Commitment 2: Working only with suppliers who have standards consistent with our own
- Commitment 3: Working on continued transparency with our data in clinical trials
- Commitment 4: Applying sound bioethics to all our work
- Commitment 5: Maintaining a strong focus on patient safety

3. Protecting the environment

We follow the science to protect the planet.

See from page 43.

- Commitment 1: Managing our impact on the environment, across all our activities, with a particular focus on greenhouse gas emissions, waste and water use
- Commitment 2: Ensuring the environmental safety of our products

Our focus on these three areas does not diminish our commitment to the foundational areas of our sustainability agenda.

See from page 35 and page 40.

- Ensuring that diversity in its broadest sense is reflected in our leadership and people strategies
- Embedding a consistent approach to human rights across our worldwide activities
- Promoting the safety, health and wellbeing of all our people worldwide
- Building a robust talent pipeline to support our future growth
- Investing in community growth

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: Codes of Business Conduct, Labour Practice Indicators, Climate Strategy, Policy Influence and Health Outcome Contribution

CDP

CDP DRIVING SUSTAINABLE ECONOMIES

- Climate A List – Among the top 5% of companies participating in CDP's climate change programme in recognition of our strategy and actions to reduce emissions and mitigate climate change
- Water A List – Among the top 10% of companies participating in CDP's water stewardship programme for our commitment to transparency around environmental risks and demonstration of pursuing best practice
- We are one of only 25 companies worldwide to be included on the A List for both climate and water in 2017. We are one of only 13 companies worldwide on both A lists for two consecutive years

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, please see Sustainability: supplementary information on page 227 and the letter of assurance on the Sustainability pages on our website, www.astrazeneca.com.

Science *can* help people with respiratory disease in Asia

Healthy Lung Asia
The overall objective of Healthy Lung Asia is to raise the profile of respiratory disease with policy makers and build health system capacity to support future access to healthcare. Our three-pillar approach includes:

- Partnerships and awareness: Convene national taskforces to raise awareness of/address health system changes needed to improve outcomes.
- Understanding and skills: Develop medical education materials with a clear objective of spreading evidence-based practice at scale.
- Capacity and access: Holistic, partnership-driven interventions in selected countries to resolve issues of infrastructure, education or access.

So far, we have signed three Memoranda of Understanding, including with Vietnam and Indonesia, formed 14 partnerships, educated some 2,000 GPs, screened more than 10,000 patients, and committed to create more than 500 respiratory centres.

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. Beginning in 2017, every member of the SET is accountable for a specific sustainability initiative.

Our Sustainability Advisory Board (SAB), is comprised of five SET members and four external sustainability experts. It met once in 2017 to guide strategic direction, recommend opportunities and provide external insight and feedback. Throughout the year, we engaged with employees and external stakeholders including investors, Ministries of Health, NGOs, patients and suppliers.

1. Broadening access to healthcare

Marketplace on page 8 demonstrates the burden of NCDs with 40 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 26, 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. We are also developing health systems infrastructure by building capacity to help improve the underlying healthcare infrastructure and access to medical treatment.

To address local needs, our programmes are typically governed by their respective commercial market leaders. Due diligence 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 please see page 227.

Young Health Programme

We also promote awareness and prevention of NCDs to reduce their burden and cost. To that end, we continue to develop our Young Health Programme (YHP), a global disease prevention programme with a focus on youth. Through YHP, we invest in on-the-ground programmes, advocacy, and research and evidence generation to address this global health issue. 2017 was the seventh year of our commitment to YHP and, during the year, we reached nearly 427,000 young people with health information on NCDs and risk behaviours and trained more than 2,800 peer educators. We launched a new three-year programme in Brazil and renewed multi-year commitments in Germany and Portugal. We also worked collaboratively with our advocacy partners, NCD Child and Rise Up Together, to ensure youth health needs were represented at the World Health Assembly, the UN and in national advocacy efforts.

Understanding our impact was a primary focus of activities in 2017, with publication of our first Social Return on Investment analysis. We looked at four YHP markets and calculated a social return of between approximately $6 and $9 for every dollar invested.

For more information on YHP, please see page 201.

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

Learn more in our 2017 Sustainability Report, on www.astrazeneca.com/sustainability.

Science *can* help people with hypertension in Africa

Healthy Heart Africa
Since launching in Kenya in October 2014 and in Ethiopia in 2016, Healthy Heart Africa (HHA) has:

- Conducted 5.7 million blood pressure screenings in the community and in healthcare facilities.
- Trained over 5,000 healthcare workers, including doctors, nurses, community health volunteers and pharmacists to provide education and awareness, screening and treatment services for hypertension.
- Activated 675 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 one million people living with high blood pressure.

Following the announcement of our innovative public-private partnership with the US President's Emergency Plan for AIDS Relief (PEPFAR) in September 2016, we are working to optimise the HIV/hypertension integration and have extended our relationship with our implementing partner for a further 12 months. Together, we screened some 300,000 people over the year and observed an indicative growth in male engagement. In Ethiopia, we moved beyond the pilot phase and screened some 470,000 people in the course of 2017.

2. Ethics and transparency

Code of Ethics and policy framework

We are committed to employing high ethical standards when carrying out all aspects of our business globally. In 2017, we launched a Code of Ethics (the Code) which replaced our Code of Conduct. The Code is based on our company 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 2017, 100% of all active employees completed the annual training on the new Code of Ethics.

The new Code includes four high-level Global Policies covering Science, Interactions, Workplace and Sustainability. During 2018, these new, high-level Global Policies will continue to be complemented by underlying Standards and will replace the current suite of 12 existing 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 97, 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, and audit professionals in Internal Audit Services, in partnership with external audit experts, also conduct compliance audits on selected marketing companies. Our reporting in this area is assured by Bureau Veritas.

For more information, please see page 227.

Approximately 34,600 employees are engaged in our Commercial activities and, in 2017, we identified six confirmed breaches of external sales and marketing regulations or codes (2016: six). There were 1,431 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 (2016: 1,729). We removed a total of 176 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 477 others and provided further guidance or coaching on our policies to 1,157 more. The most serious breaches were raised with 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. This commitment was conveyed in the 2017 annual Code training and is reinforced through anti-bribery/anti-corruption training materials made available to employees and relevant 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 with only 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.

Transparency reporting

AstraZeneca is committed to the highest standards of conduct in all our operations, including transparency in how we partner with physicians and medical institutions. 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.

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 current Global Bioethics Policy sets out our global standards in key areas. These standards 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 these 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, including reports of non-compliance with the Bioethics Policy, and advises on whatever actions are necessary. BAG met five times in 2017 and, in this period, there were no cases of non-compliance with the Bioethics Policy. BAG also considers emerging trends and scientific advances that may have an impact, supporting the development of policy in relevant areas. Ethical discussions in 2017 included the potential impacts of advances in precision genome editing, consenting and privacy issues arising from the use of human biological samples, and the implications of research into human-animal chimaeras.

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 2017, we conducted a range of clinical trials across regions as shown in the charts to 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.

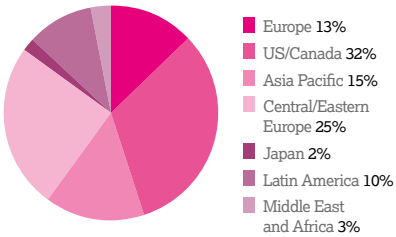
All our clinical studies are designed and finally interpreted in-house. Some are conducted by CROs on our behalf and we require these organisations to comply with our global standards.

As of 15 December 2017, we shared anonymised individual patient-level data from 149 studies with 25 research teams and responded to 74 requests from external researchers using our portal, http://astrazenecagroup-dt.pharmacm.com to request our clinical data and reports to support additional research. In 2017, we continued our commitment to be more transparent by expanding patient access to trial results summaries. We therefore participated in the launch of a new industry-wide portal at www.trialsummaries.com where we provide lay summaries in easy-to-understand language and translate these to the local language for all sites where a study is conducted. In 2017, we published trial results summaries for 34 AstraZeneca studies. This initiative led to the Clinical Trial Transparency Office receiving the 2017 Communication Award from TOPRA, a membership organisation for individuals working in healthcare regulatory affairs, for our patient-focused approach to delivering against the new EU Clinical Trial Regulations several years earlier than required.

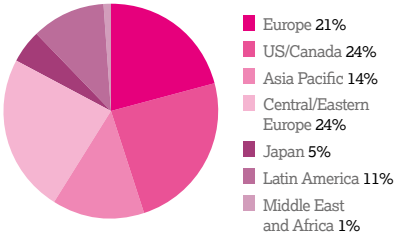
For more information, please see our website, www.astrazeneca.com, or our clinical trials website, www.astrazenecaclinicaltrials.com.

Clinical trials by region (%)

Small molecule studies (50%)



Biologics studies (35%)



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 a new safety signal management platform to provide consolidated risk oversight for all our products in use. The platform supports comprehensive awareness of the signals, intelligent analysis of their impact, and enables appropriate measures to reduce risks to patients.

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 2017, one research proposal that includes use of cells derived from hFT has been approved, resulting in two projects being in progress as at 31 December. In addition, three projects using three different hESC lines or derived cells have been approved.

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. Internally, our Council for Science and Animal Welfare (C-SAW) leads initiatives on the 3Rs, openness about our use of animals, and builds a culture of care in the way we conduct our research. For example, C-SAW runs a global awards scheme and also promotes global learning and continuing professional development opportunities for employees working with animals. C-SAW acts as 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.

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 2017, animals were used for in-house studies 131,615 times (2016: 193,451). In addition, animals were used on our behalf for CRO studies 28,545 times, (2016: 25,651). 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 improve the quality of our animal studies.

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. With most of our API manufacturing outsourced, we need an uninterrupted supply of high-quality raw materials. We therefore place great importance on our global procurement policies and 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.

We also seek to manage reputational risk. Our ethical standards are integral to our procurement and partnering activities and we continuously 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 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 7,198 assessments in 2017, taking our total number of assessments to 25,493 since we established this process in May 2014. Of the 2017 assessments, 1,888 were in the Asia Pacific region, 2,227 in Europe and 2,038 in the Americas. The remaining 1,045 assessments relate to global suppliers and those based in the Middle East and Africa.

Renewable energy
In 2017, we began using sustainable heat pump technology at our Gothenburg, Sweden site. This technology is highly efficient and electrifies some of the site's heat demand, with the estimated potential to replace up to 60% of the site's natural gas consumption, thereby reducing the site's CO_2 footprint. Coupled with the site transitioning to renewable electricity in 2016, the investment is estimated to save approximately 2,500 tonnes of CO_2 equivalent per year.

In 2017, we conducted 41 audits on high-risk suppliers, seeking to ensure that they employ appropriate practices and controls. Ten percent of these suppliers met our expectations, with a further 90% implementing improvement plans to address minor instances of non-compliance. Through our due diligence process, we rejected 12 suppliers because of reputational concerns.

3. Protecting the environment

We follow the science to protect the planet by managing our impact on the environment across all our operations. Our current Global Safety, Health and Environment (SHE) Policy 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, internal auditing and an annual management review. We are on track to deliver our 2016 to 2025 environment targets.

Managing our impact on natural resources

Our 2017 natural resource targets (against a 2015 baseline) included:

- reducing operational greenhouse gas footprint as approved by the Science Based Target initiative
- reducing energy consumption by 2% to 1,761,081 MWh
- reducing waste generation by 4% to 29,328 tonnes
- reducing water use by 4% to 4.16 million m^3.

The table overleaf provides data on our global greenhouse gas emissions, energy use, waste production and water consumption for 2017. 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. The data quoted in this Annual Report are generated from the revised data. 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 2017, approximately $19 million (2016: $25 million) was committed to resource efficiency projects at our manufacturing and R&D sites, and a further $20 million has been committed for 2018.

100%

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

Greenhouse gas reduction

We are working to reduce our greenhouse gas 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 Avoid-Reduce-Substitute. During 2017, 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, reduced energy consumption at our sites, and procurement of electricity from certified renewable sources increasing to represent 63% of total electricity imports. Our total Scope 1 and Scope 2 emissions have been reduced by 29% 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, reduced business air travel, and improved accounting of our Scope 3 footprint that will lead to future efficiency improvements.

Our pMDI inhaler therapies rely on hydrofluoroalkane (HFA) propellants, which affects our Scope 3 greenhouse gas footprint. While HFAs have no ozone depletion potential and a third or less of the global warming potential than the chlorofluorocarbons they replace, they are still potent greenhouse gases. During 2017, we continued to explore practical opportunities to reduce the climate impact of these devices during production and use while continuing to fulfil patient needs, including the launch of a new pMDI device that uses an HFA propellant with less than half the global warming impact of our legacy portfolio. Including emissions from patient use of our inhaler therapies, our operational greenhouse gas footprint totalled 1,658,548 metric tonnes in 2017, a reduction of 7% from our 2015 baseline.

For more information on carbon reporting, please see Sustainability: supplementary information on page 227.

Energy use

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. In 2017, we targeted a 3% reduction in total energy consumption from our 2015 baseline. In 2017, our energy use was 1,742 GWh, a reduction of 3%. We have made further progress on our target to source 100% renewable power by 2025. In 2017, we procured certified zero emission power equivalent to 63% of total consumption and generated a further 11,874 MWh of renewable energy on our sites.

Waste management

Waste management is another key aspect of our commitment to minimise environmental impact. In 2017, we targeted a 4% reduction in waste generation from our 2015 baseline. In 2017, our total waste was 31,222 metric tonnes, a 2% increase on 2015. Although large waste reduction projects came online in 2017, bringing savings of equivalent to 2.5% of our total waste footprint, our waste reduction target has been missed due to increasing activity across our site network. While waste prevention is an essential goal, we seek to maximise treatment by material recycling and avoiding landfill disposal when prevention is impractical.

Water use reduction

We recognise the need to use water responsibly and, where possible, to minimise water use in our facilities. In 2017, we targeted a 4% reduction from our 2015 water use. In 2017, our water footprint was 3.89 million m^3, a 10% reduction. Water reduction and reuse projects throughout our site network have improved the efficiency of water use across our operations. During 2017, our major sites and those in water-stressed areas maintained or completed 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.

Ensuring the environmental safety of our products

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 active pharmaceutical ingredient (API) production and formulation processes, devices and packaging through distribution, patient use and final disposal. We aim to lead our industry in understanding and mitigating the effects of pharmaceuticals in the environment (PIE).

As part of our progress towards our 2025 environmental targets, our 2017 product environmental safety targets included:

- Safe API discharges for AstraZeneca sites (100%) and globally managed first tier suppliers (>90%). Target met – safe API discharges confirmed.
- Management of PIE through our 'ecopharmacovigilance' programme. Target met – programme delivered.

Pharmaceuticals in the environment

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.

We also conduct collaborative research to understand the fate, behaviour and impact of pharmaceuticals on the environment. In 2017, we co-authored 14 peer-reviewed publications to enhance our knowledge of the risks associated with this emerging issue.

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.

Operational greenhouse gas footprint emissions (tonnes CO_2e)

1,658,548 tonnes CO_2e

Energy consumption (MWh)

1,742,325 MWh

% certified renewable
2017 27%
2016 25%
2015 6%

Waste production (tonnes)

31,222 tonnes

Water use (million m^3)

3.89 million m^3

STEM learning and careers
Bahija Jallal, President, MedImmune and Executive Vice-President, AstraZeneca, works with a student on the MDBio Mobile eXploration lab, America's largest, most advanced mobile laboratory. MXLab is custom-designed to expand new technology and laboratory science experiences to pique students' interest in science, technology, engineering and mathematics (STEM) learning and careers.

Dr Jallal was the Healthcare Businesswomen's Association (HBA) 2017 Woman of the Year.

Community investment

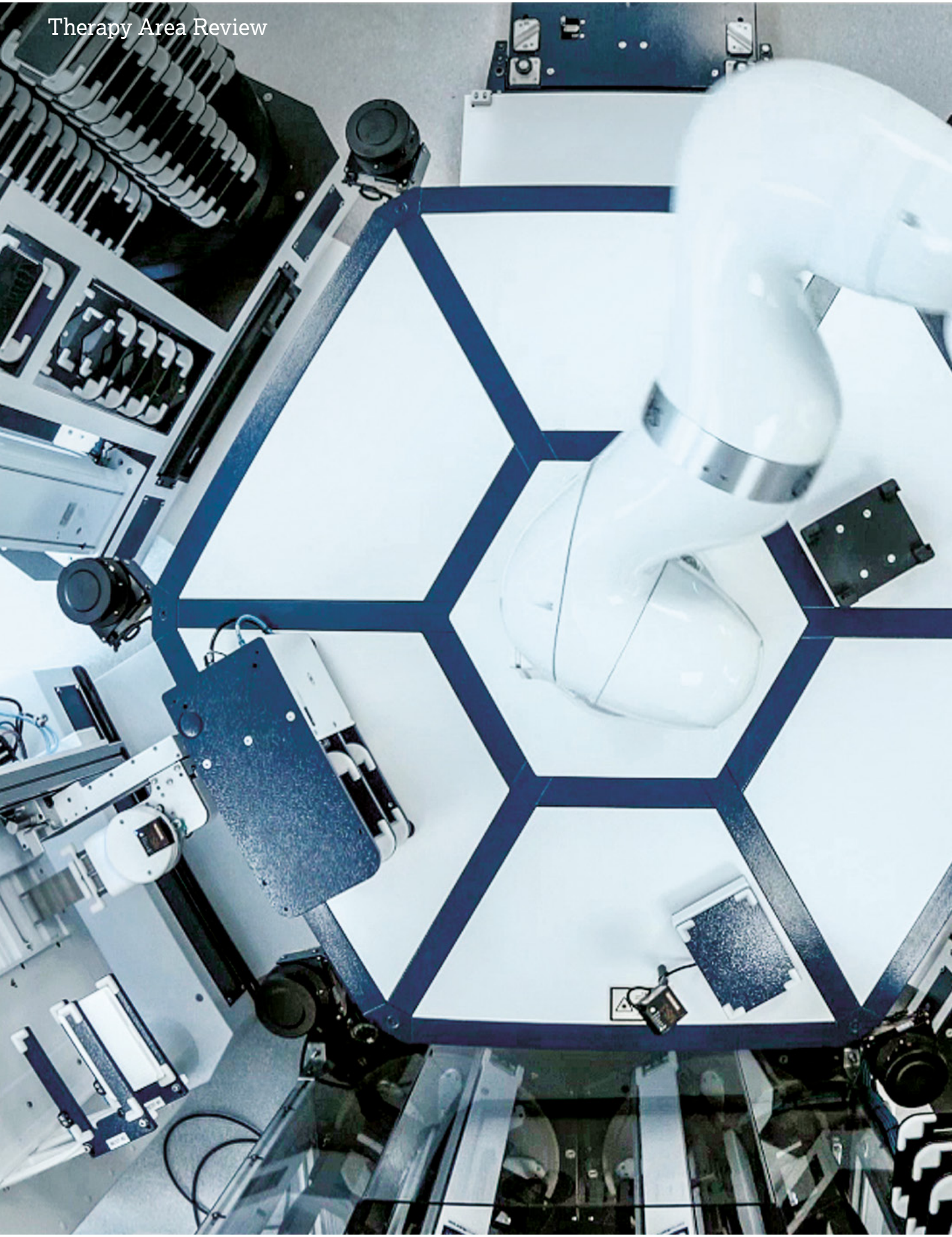
Wherever we work in the world, we aim to make a positive impact on our communities. Our Community Investment Contributions Standard outlines our global areas of focus and provides guidance to ensure a consistent, transparent and ethical approach around the world, based on local need. Our global community investment activities are focused on healthcare in the community and supporting science education. They include financial and non-financial community sponsorships, partnerships and charitable donations. In 2017, we gave more than $25 million (2016: $39 million) through our community investment activities to more than 900 non-profit organisations in 61 countries, which includes more than $4 million (2016: $20 million) for product donations that were given in support of public health needs and disaster relief. In addition to these community investments, we also donated more than $401 million (2016: $468 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 on our patient assistance programmes, please see from page 28, and on our Young Health Programme, a global disease prevention programme with a focus on youth, please see pages 39 and 201.

Our global disaster relief partners are the British Red Cross, Americares, Direct Relief International and Health Partners International of Canada. In 2017, we funded the deployment of the British Red Cross Mass Sanitation Unit to Northern Uganda where it provided more than 13,000 refugees with access to a safe latrine and reached more than 19,000 refugees with hygiene promotion activities. We also responded to appeals for the South Asian Floods and support for the Atlantic Hurricane Season.

In 2017, we donated products across multiple therapeutic areas to 17 countries to respond to public health needs and disaster relief. This includes pre-positioning products in partner warehouses to allow for quick deployment which was a critical part of our partner's response efforts during the Atlantic Hurricane Season.

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 volunteering. In 2017, our employees volunteered more than 29,000 hours on community projects in countries around the world.

Non-Financial Reporting Regulations
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. Information required by these Regulations is included in Business model and life-cycle of a medicine from page 14, Strategy and Key Performance Indicators from page 17, and the Business Review from page 34.



Science *can*

Expand treatment options

Oncology | From page 48

Understand disease

Cardiovascular & Metabolic Diseases | From page 52

Transform outcomes

Respiratory | From page 56

Develop best-in-class therapies

Other Disease Areas | From page 60

Smarter, faster and cheaper drug discovery
The world's most advanced drug discovery robot is working alongside our scientists to help make drug discovery smarter, faster and cheaper. Designed to work three times more quickly than previous drug discovery robots, NiCoLA-B can test up to 300,000 compounds a day and is also more scientist-friendly, flexible and responsive.

For more information, see www.astrazeneca.com/meet-NiCoLA-B.

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 49, 53, 57 and 61 and the Development Pipeline table from page 202. For information on Patent Expiries of our Key Marketed Products, please see from page 208.

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 28 to the Financial Statements from page 182.

Details of relevant risks are set out in Risk from page 210.

Oncology

Our ambition is to eliminate cancer as a cause of death through scientific discovery and collaborations. We seek to achieve this by means of exploiting the power of four scientific platforms.

Cancer is the second leading cause of death globally, claiming more than eight million lives every year. R&D continues to push boundaries in how we understand and fight cancer, but there is still more to do. At AstraZeneca, we are committed to advancing the science of oncology to deliver life-changing medicines to people most in need.

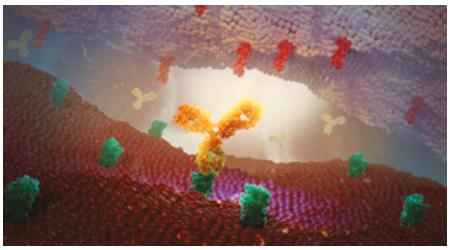
Our strategic priorities

In Oncology, our vision is to push the boundaries of science to respond to unmet medical need and ultimately redefine the cancer treatment paradigm. We are doing this through scientific innovation, accelerated clinical programmes and collaboration.
We have a deep-rooted heritage in Oncology and offer a growing line of new medicines that has the potential to transform patients' lives and AstraZeneca's future. At least six oncology medicines are expected to be launched between 2014 and 2020, of which *Lynparza*, *Tagrisso*, *Imfinzi* and *Calquence* are already benefiting patients.

In 2015, we decided that all new Oncology launches would form a new Growth Platform, under the designation of New Oncology.

Our broad pipeline of next-generation medicines is aimed at expanding our treatment options for solid tumours and haematological cancers, using four key scientific platforms:

- **Immuno-oncology (IO):** 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. Example: *Imfinzi*.
- **Tumour drivers and resistance mechanisms:** Potent inhibition of genetic disease drivers is a clinically validated approach to shrink tumours and improve progression-free survival and overall survival. 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. Examples: *Tagrisso*, *Calquence*.



Antibody that blocks inhibitory signals from the tumour to cells of the immune system resulting in enhanced anti-tumour immunity.

- **DNA damage response:** Exploiting mechanisms that selectively damage tumour cell DNA is another clinically validated approach to shrink tumours and improve progression-free and overall survival. Our market-leading programmes in DNA Damage Response focus on multiple ways to identify and exploit vulnerabilities to kill the tumour cells, while minimising toxicity to the patient. Example: *Lynparza*.
- **Antibody-drug conjugates (ADC):** The use of ADCs is a clinically validated, highly potent approach that selectively targets cancer cells. We seek to combine innovative antibody engineering capabilities with cytotoxic drug molecules to attack and kill the tumour while minimising toxicity to the patient. Example: moxetumomab.

At the heart of our Oncology strategy is a powerful combinations portfolio that leverages our four scientific platforms to simultaneously attack multiple mechanisms of tumour progression. In a very competitive and fast-moving environment, AstraZeneca has a broad development programme focused on first-in-class or best-in-disease opportunities across multiple tumour types.

Our 2017 commercial focus

In total, our marketed oncology medicines generated Product Sales of $4 billion worldwide in 2017. Sales from our New Oncology Growth Platform, totalled $1.3 billion in 2017, an increase of 98% at actual rate of exchange (98% at CER) over 2016 ($0.7 billion).

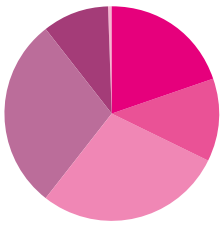
Faslodex 500mg is approved in more than 80 countries, including the EU, the US and Japan. In 2017, *Faslodex* received 1st line label

Therapy area world market

(MAT/Q3/17)

$96.2bn

Annual worldwide market value



- Chemotherapy $19.2bn
- Hormonal therapies $12.0bn
- Monoclonal antibodies (mAbs) $27.5bn
- Small molecule tyrosine kinase inhibitors (TKIs) $27.8bn
- Immune checkpoint inhibitors $9.7bn
- Other Oncology Therapies $0.05bn

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

extension for use as the treatment of oestrogen receptor positive, locally advanced or metastatic breast cancer in postmenopausal women not previously treated with endocrine therapy in Japan, Russia, the EU and the US. The approvals were based on positive results from the Phase III FALCON clinical trial comparing the efficacy and safety of *Faslodex* with *Arimidex* in the 1st line advanced breast cancer setting (hormone-naïve patients), which was presented in 2016.

In November 2017, the FDA approved a new indication for *Faslodex*, expanding the indication to include use with abemaciclib for the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer in women with disease progression. This approval, based upon the MONARCH2 study, further expands the growing body of evidence for using *Faslodex* in combination as a treatment for advanced breast cancer, as illustrated by the FDA-approved combination with palbociclib in March 2016. *Iressa* was the first epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) to be approved for the treatment of advanced epidermal growth factor receptor (EGFR) mutation non-small cell lung cancer (NSCLC) and, as of 31 December 2017, had been approved in 90 countries. *Iressa* received approval in the US in July 2015.

Zoladex continues to be a significant asset in our on-market portfolio and a driver of our prostate cancer and breast cancer portfolios.

Oncology – pipeline progressions

Regional approvals	> *Imfinzi* 2nd line bladder cancer (US) > *Calquence* 2nd line mantle cell lymphoma (US) > *Faslodex* 1st line breast cancer (FALCON) (US, JP, EU) > *Lynparza* 2nd line ovarian cancer + (SOLO-2) (US, JP*); breast cancer (OlympiAD) (US*) > *Tagrisso* 2nd line lung cancer + (AURA3) (US, EU) > *Tagrisso* 2nd line lung cancer + (AURA17) (CN)
Expedited review	> Breakthrough Therapy Designation: *Calquence* blood cancers (US); *Imfinzi* 1st line lung cancer stage 3 (PACIFIC) (US); *Tagrisso* 1st line lung cancer (FLAURA) (US) > Orphan Drug Designation: *Lynparza* breast cancer (OlympiAD) (JP); *Lynparza* ovarian cancer (JP) > Priority Review Designation: *Calquence* blood cancers (US); *Imfinzi* lung cancer stage 3 (PACIFIC) (EU, JP); *Lynparza* 2nd line ovarian cancer (US); *Lynparza* breast cancer (OlympiAD) (US, JP); *Tagrisso* 1st line lung cancer (FLAURA) (US) > Accelerated approval: *Calquence* non-hodgkin's lymphoma (US); *Imfinzi* 2nd line bladder cancer (US)
Regulatory submissions	> *Calquence* mantle cell lymphoma (US) > *Imfinzi* lung cancer stage 3 (PACIFIC) (EU, US, JP) > *Lynparza* 2nd line ovarian cancer + (SOLO-2) (EU, US, JP) > *Lynparza* breast cancer (OlympiAD) (JP, US) > *Tagrisso* 1st line lung cancer (FLAURA) (US, EU, JP)
Phase III investment decisions	> *Imfinzi* non-muscle invasive bladder cancer > *Imfinzi* + tremelimumab + chemotherapy 1st line lung cancer > *Imfinzi* + chemo-radiation therapy lung cancer stage III > *Imfinzi* + epacadostat + chemo-radiation therapy lung cancer > *Lynparza* + *Imfinzi* + *Avastin* ovarian cancer > *Tagrisso* lung cancer stage 3 > *Forxiga* HF with a preserved ejection fraction*
Phase II starts/ progressions	AZD4635 + *Imfinzi* lung cancer; AZD8186 + abiraterone for castration-resistant prostate cancer; *Imfinzi* + AZD9150 head and neck squamous-cell carcinoma; *Imfinzi* + oleclumab (MEDI9447) solid tumours; *Imfinzi* + monalizumab solid tumours; *Imfinzi* + *Darzalex* for relapsed refractory multiple myeloma; *Imfinzi* + MEDI0457 head and neck squamous-cell carcinoma
Strategic transactions completed	A global strategic oncology collaboration was established with MSD to co-develop and co-commercialise *Lynparza* for multiple cancer types. We will also jointly seek to develop and commercialise 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. Licensing agreement for rights to *Zoladex* in the US and Canada with TerSera
Setbacks and terminated projects	The MYSTIC trial did not meet its primary endpoint of improving PFS compared to standard of care (SoC) in PD-L1 >25% in patients with 1st line NSCLC. In addition, *Imfinzi* monotherapy would not have met a pre-specified threshold of PFS benefit over SoC. With respect to safety, the *Imfinzi* plus tremelimumab profile was consistent with expectations based on prior clinical data. The MYSTIC trial continues as planned to assess the additional primary endpoints of overall survival for *Imfinzi* monotherapy and for the *Imfinzi* + tremelimumab combination. Discontinued: MEDI-573 for IGF metastatic breast cancer

* Approved in January 2018.

Lynparza is an oral poly ADP ribose polymerase (PARP) inhibitor available in more than 30 countries for the treatment of adult patients with BRCA-mutated high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer. In August 2017, the FDA granted approval for new use of the tablet formulation of *Lynparza* as a maintenance treatment for patients with recurrent, epithelial ovarian, fallopian tube or primary peritoneal adult cancer who are in response to platinum-based chemotherapy, regardless of BRCA status based on results from two randomised trials, SOLO-2 and Study 19.

On 12 January 2018, based on data from the randomised, open-label, Phase III OlympiAD trial, the FDA approved *Lynparza* for use in patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2- metastatic breast cancer who have been previously treated with chemotherapy in the neoadjuvant, adjuvant or metastatic

Our marketed products

- *Arimidex* (anastrozole)
- *Casodex/Cosudex* (bicalutamide)
- *Calquence* (acalabrutinib)
- *Faslodex* (fulvestrant)
- *Imfinzi* (durvalumab)
- *Iressa* (gefitinib)
- *Lynparza* (olaparib)
- *Nolvadex* (tamoxifen citrate)
- *Tagrisso* (osimertinib)
- *Zoladex* (goserelin acetate implant)

Full product information on page 208.

$4bn

Product Sales of $4,024 million, up 19% (19% at CER)

setting. This new approval for *Lynparza* makes it the first and only PARP inhibitor approved in metastatic breast cancer, and the only PARP inhibitor approved beyond ovarian cancer. *Tagrisso* is the first approved EGFR-TKI indicated for patients with metastatic EGFR T790M mutation-positive NSCLC. After receiving accelerated approval in several countries in 2015-2016, *Tagrisso* was granted full approval based on the Phase III AURA3 confirmatory trial in the US and EU in early 2017, and is now approved in more than 60 countries worldwide, including the US, EU, Japan and China, for patients with EGFR T790M mutation-positive advanced NSCLC. *Imfinzi* is a human mAb directed against PD-L1 and our first IO product on market. In May 2017, *Imfinzi* received its first accelerated approval in the US in previously treated patients with advanced bladder cancer.

Calquence is a selective inhibitor of Bruton tyrosine kinase (BTK). In October 2017, the medicine was granted accelerated approval by the FDA for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

Details of material patent litigation relating to *Calquence*, *Faslodex*, *Imfinzi* and *Tagrisso* are included in Note 28 to the Financial Statements from page 182.

In the pipeline

Our Oncology pipeline continues to progress. It now includes 32 NMEs in development. In October 2017, AstraZeneca received a sixth Breakthrough Therapy Designation for an oncology medicine from the FDA since 2014. During the year, we also expanded several of our projects to incorporate novel combinations and various types of cancer. Some of our key projects from each of our platforms are outlined below.

Immuno-oncology franchise

- *Imfinzi* is also being explored as a monotherapy and in combination with tremelimumab, an anti-cytotoxic T-lymphocyte-associated protein 4 antibody, across multiple tumour types and lines of therapy. This includes Phase III registrational trials in various stages of NSCLC, small-cell lung cancer, metastatic urothelial cancer, head and neck squamous cell carcinoma (HNSCC), and hepatocellular carcinoma (HCC). Our IO development programme also includes additional Phase I/II studies in a broad range of haematologic and solid tumours and an extensive range of combinations, including with small molecules, other biologics and chemotherapies.
- In May 2017, *Imfinzi* met a primary endpoint of statistically-significant and clinically-meaningful progression-free survival (PFS) in 'all-comer' patients with locally-advanced, unresectable (Stage 3) NSCLC whose disease has not progressed following chemo-radiation therapy in a planned interim analysis of the PACIFIC Phase III trial. The full data were presented at the European Society for Medical Oncology congress in September 2017. *Imfinzi* is the first medicine to show superior PFS in this setting. In July 2017, Breakthrough Therapy Designation was granted by the FDA for *Imfinzi* in this indication and it included Priority Review status in the US. The therapy is currently under regulatory review in the EU and US.
- In June 2017, the first patient was dosed with *Imfinzi* in POSEIDON, a Phase III 1st line NSCLC study of *Imfinzi* and *Imfinzi* + tremelimumab combined with chemotherapy. In November 2017, the first patient was also dosed in HIMALAYA, a Phase III study designed to assess *Imfinzi* and *Imfinzi* + tremelimumab in the treatment of patients with no prior systemic therapy for unresectable HCC.
- In July 2017, the Phase III MYSTIC trial, a 1st line NSCLC study of *Imfinzi* and *Imfinzi* + tremelimumab, failed to meet one of its primary endpoints – improving PFS – when comparing against the standard of care in patients whose tumours express PD-L1 on 25% or more of their cancer cells. The study is ongoing for its two other primary endpoints, overall survival (OS) in each of the monotherapy arm and the combination therapy arm.
- Other IO agents in early development include: MEDI9447, targeting ecto-5'-nucleotidase (CD73); AZD9150, an antisense oligonucleotide that downregulates STAT3 expression in the tumour microenvironment; AZD5069, a chemokine receptor 2 inhibitor; MEDI9197, a small molecule agonist targeting toll-like receptor 7/8; MEDI0562, a humanised agonistic mAb that targets OX40; MEDI1873, targeting glucocorticoid-induced tumour necrosis factor receptor-ligand; MEDI0457, a DNA vaccine against human papilloma virus 16/18; NKG2A, a checkpoint receptor inhibiting the anti-cancer functions of NK and cytotoxic T-cells; MEDI0680, an anti-programmed cell death protein 1 (PD1) mAb blocking interactions with PD1 and its ligands; and AZD4635, an adenosine 2A receptor inhibitor. These agents are in Phase I/II development for a range of solid tumours and have the potential for combination with other molecules in the portfolio, including *Imfinzi*.

Tumour drivers and resistance mechanisms franchise

- *Tagrisso* is a highly selective, irreversible inhibitor of the activating sensitising EGFR mutation and the resistance mutation T790M. The product is being investigated in Phase III studies in the adjuvant setting for the treatment of patients with EGFRm NSCLC and in the advanced setting as a 1st line treatment of EGFRm NSCLC and as a ≥2nd line treatment of EGFRm T790M NSCLC. Additionally, studies in combination with other small molecules are under investigation.
- In July 2017, AstraZeneca announced positive results from the Phase III FLAURA trial comparing the efficacy and safety of *Tagrisso* with current 1st line EGFR-TKIs in previously untreated patients with EGFRm NSCLC. The results were subsequently presented at the European Society for Medical Oncology congress in September 2017. In October 2017, the FDA granted Breakthrough Therapy Designation for *Tagrisso* for the 1st line treatment of patients with metastatic EGFRm NSCLC. The therapy is currently under regulatory review in the US, EU and Japan.
- *Calquence* is a BTK inhibitor in Phase III development in B-cell malignancies and solid tumours. In August 2017, the FDA granted Breakthrough Therapy Designation for *Calquence* for the treatment of patients with MCL who have received at least one prior therapy.
- Selumetinib is a mitogen-activated protein kinase inhibitor in Phase III development for adjuvant differentiated thyroid cancer. Selumetinib's development programme also includes trials in neurofibromatosis type 1 and solid tumours.
- Savolitinib is a selective inhibitor of c-MET (mesenchymal epithelial transition factor) receptor tyrosine kinase, an enzyme which has been shown to function abnormally in many types of solid tumours. It is in Phase III trials in papillary renal cell cancer in patients with a genetic aberration in the c-MET pathway and in Phase II trials in combination with *Tagrisso* and *Iressa* in EGFR mutated lung cancer with c-MET amplification.

Science *can* bring benefits to more patients

OlympiAD
With over three years' experience in ovarian cancer, *Lynparza*, the first poly-ADP ribose polymerase (PARP) inhibitor, represents the proof that targeting the DNA Damage Response pathway works beyond the laboratory. Following the initial approval of this new class of medicine, in June 2017, we presented the full results from the Phase III OlympiAD trial, the first positive randomised trial to evaluate the efficacy and safety of a PARP inhibitor beyond ovarian cancer. The OlympiAD results also marked the first time a targeted therapy showed benefit over the current standard of care for patients with germline BRCA-mutated HER2- metastatic breast cancer. On 12 January 2018, the FDA granted approval to *Lynparza* in this indication. *Lynparza* has the broadest clinical trial programme of any PARP inhibitor, and this milestone demonstrates how AstraZeneca followed the science to expand the potential of *Lynparza* to benefit many patients in multiple settings.

- Cediranib is an orally administered multi-vascular endothelial growth factor receptor (VEGFR) inhibitor which is currently being tested in combination with *Lynparza* in Phase III trials in patients with platinum-sensitive relapsed ovarian cancer and platinum-resistant/refractory ovarian cancer.
- AZD5363 is a protein kinase B inhibitor in Phase II development for breast and prostate cancer.
- Vistusertib is an inhibitor of the mammalian target of rapamycin serine/threonine kinase (TORC1, TORC2) and is in Phase II development for the treatment of solid and haematological tumours.
- AZD9496 is a selective oestrogen receptor down-regulator in Phase I development for the treatment of breast cancer.
- Other agents in early development include: AZD5991, an MCL1 inhibitor; AZD4753, a CDK9 inhibitor; AZD5153, a bromodomain 4 inhibitor; AZD4785, an antisense oligonucleotide targeting KRas; and AZD8186 an inhibitor of PI3 kinase β and δ.

DNA damage response franchise

- *Lynparza* is being evaluated in a broad range of Phase III trials, including BRCAm adjuvant and metastatic breast cancer, gBRCAm pancreatic cancer, gBRCAm ovarian cancer and prostate cancer.
- In February 2017, AstraZeneca announced positive results of OlympiAD, a Phase III randomised, open-label, multicentre study assessing the efficacy and safety of *Lynparza* tablets compared to 'physician's choice' chemotherapy in patients with HER2- metastatic breast cancer with germline BRCA1 or BRCA2 mutations, which are predicted or suspected to be deleterious. The results were subsequently presented at the American Society of Clinical Oncology congress in June 2017 and submitted to Health Authorities for regulatory review in the US, EU and Japan.
- AZD1775 is a Wee1 inhibitor in Phase II development for ovarian and other solid tumours in combination with *Lynparza*. It is also being evaluated in combination with chemotherapy and as monotherapy.
- AZD6738 is an ATR inhibitor in Phase II development in combination with *Lynparza* in 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.
- Phase I clinical studies are progressing for the ATM inhibitor, AZD0156 (for the treatment of gastric and colorectal cancers) and the aurora B kinase inhibitor, AZD2811 in acute myeloid leukaemia and solid tumours. An ATM inhibitor designed to cross the blood brain barrier, AZD1390 is in Phase I development for the treatment of gliobastoma multiforme in combination with radiation.

Antibody-drug conjugates franchise

- Moxetumomab pasudotox, an anti-CD22 recombinant immunotoxin, is being investigated in a Phase III study for adult patients with hairy cell leukaemia who have relapsed after, or not responded to, standard therapy. In November 2017, AstraZeneca announced moxetumomab had met the primary endpoint of this study.
- MEDI4276 is an HER2 bispecific ADC, which entered clinical development for a range of solid tumours.
- MEDI3726 is a PSMA ADC and MEDI7247 is an ADC against an undisclosed target.

Key Oncology collaborations and transactions

In 2017, collaborations between AstraZeneca and various partners have continued to mature, with new data presented at medical congresses. We also concluded three new major agreements.

In February 2017, AstraZeneca entered into an agreement with TerSera for the commercial rights to *Zoladex* in the US and Canada. *Zoladex* is an injectable luteinising hormone-releasing hormone agonist, used to treat prostate cancer, breast cancer and certain benign gynaecological disorders.

In July 2017, AstraZeneca and MSD announced that they had entered into a global strategic oncology collaboration to co-develop and co-commercialise *Lynparza* for multiple cancer types. The companies will develop and commercialise *Lynparza* jointly, both as monotherapy and in combination with other potential medicines. Independently, the companies will develop and commercialise *Lynparza* in combination with their respective PD-L1 and PD-1 medicines, *Imfinzi* and pembrolizumab. The companies will also jointly develop and commercialise AstraZeneca's selumetinib, an oral, potent, selective inhibitor of MEK, part of the mitogen-activated protein kinase pathway, currently being developed for multiple indications, including thyroid cancer.

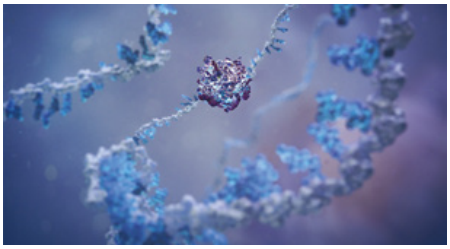
On 31 October 2017, AstraZeneca and Incyte announced the expansion of their clinical collaboration. As part of the agreement, the companies will evaluate the efficacy and safety of epacadostat, Incyte's investigational selective IDO1 enzyme inhibitor, in combination with *Imfinzi*, a human mAb directed against PD-L1, compared to *Imfinzi* alone. The exclusive collaboration for the study population allows for the two companies to conduct a Phase III trial in patients with locally-advanced (Stage 3), unresectable NSCLC whose disease has not progressed following platinum-based chemotherapy concurrent with radiation therapy.

Cardiovascular & Metabolic Diseases

AstraZeneca is following the science to transform how cardiovascular, renal and metabolic diseases are understood, interact and impact one another.

Our strategic priorities

Cardiovascular (CV) disease remains the number one cause of death globally and constitutes a burden on patients' overall health and wellbeing, as well as on society and healthcare systems. However, science is now uncovering commonalities between CV, renal and metabolic diseases (CVMD), explaining why reducing CV risk is so complex. We know there is clinical overlap between these diseases and their associated complications, yet, in many cases, each condition is managed in isolation.



Messenger RNA being read by a ribosome to produce signalling proteins.

Recognising that these conditions often co-exist, we are seeking to address unmet medical need by better understanding how our portfolio of medicines might be used to help tackle multiple risk factors or co-morbidities across CVMD, and whether combinations of these medicines might offer benefits for patients. As we begin to recognise the common underlying mechanisms behind CV, renal and metabolic diseases, we can use this knowledge to redefine the way these diseases are understood, how patients are treated, and how we can ultimately reduce CV risk.

A distinctive strategy

To address this 'extended' CVMD risk, we are focusing our efforts on the commonalities between diseases and their underlying mechanisms. We have a three-pronged science-driven strategy:

1. Today, we are delivering life-changing results in the core CV disease areas as we know them and their complications, with medicines already being used or in late-stage development:

- Metabolic disease: *Forxiga*, *Bydureon*, *Onglyza*
- Heart failure (HF): *Forxiga*
- Renal: ZS-9, roxadustat, *Forxiga*
- Atherosclerosis: *Brilinta*, *Epanova*, *Crestor.*

2. 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.

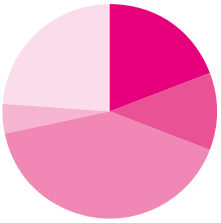
We have more than 25 potential medicines and medicine combinations in our pipeline, including small molecules and biologics, to address cardiac regeneration and conditions such as chronic kidney disease (CKD), acute coronary syndromes (ACS), HF and nonalcoholic steatohepatitis (NASH).

Our approach

We believe this strategy makes us different. For example, we are pioneering a new approach in the field of cardiac regeneration, while investing in rigorous clinical programmes evaluating the use of our medicines in large patient populations in both Established and Emerging Markets. These include global randomised clinical trials that are as close as possible to clinical practice, as well as real-world evidence research.

Therapy area world market
(MAT/Q3/17)

$186.4bn
Annual worldwide market value



- High blood pressure $36.2bn
- Abnormal levels of blood cholesterol $21.3bn
- Diabetes $76.2bn
- Thrombosis $8.5bn
- Other $44.1bn

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

We continue to strengthen our commitment to following the science through strategic partnerships, collaborations and new clinical studies.

We also develop programmes that seek to improve access to healthcare by providing education about these diseases. For example, Early Action in Diabetes is collecting and sharing better practices in policymaking from more than 35 countries, outlining how policymakers, payers and other decision-makers can best prevent, diagnose and control diabetes. Our Healthy Heart Africa Programme seeks to tackle hypertension and the increasing burden of CV disease in Africa. For more information on Healthy Heart Africa, see pages 29 and 40.

Cardiovascular disease
Our 2017 focus

Brilinta/Brilique 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 over 100 countries, and is included in 12 major ACS treatment guidelines globally.

Cardiovascular & Metabolic Diseases – pipeline progressions

Regional approvals	> *Bydureon* Type 2 diabetes (DURATION-8) (US, EU) > *Bydureon BCise* Type 2 diabetes (US) > *Bydureon* Type 2 diabetes (DURATION-7) (EU) > *Forxiga* Type 2 diabetes (CN) > *Qtern* (saxagliptin + dapagliflozin FDC) Type 2 diabetes (US)
Expedited review	> Priority Review Designation: roxadustat CKD (CN)
Regulatory submissions	> *Bydureon* Type 2 diabetes (DURATION-7) (US, EU) > *Bydureon* weekly autoinjector Type 2 diabetes (EU) > roxadustat anaemia in CKD (CN)
Phase III investment decisions	> *Brilinta* paediatric programme
Phase II starts/ progressions	verinurad for CKD; AZD5718 FLAP coronary artery disease; MEDI0382 GLP-1/glucagon dual agonist Type 2 diabetes; MEDI5884 cholesterol modulation
Strategic transactions completed	Licensing agreement for rights to *Seloken* in Europe with Recordati
Setbacks and terminated projects	Discontinued: MEDI4166 (PCSK9/GLP-1) for diabetes/CV; AZD4076 (miR103/107) for NASH; MEDI8111 for trauma/bleeding

In its indication for the long-term prevention of CV death, heart attack and stroke for patients with a history of heart attack, *Brilinta* 60mg is approved in over 60 countries.

In May 2017, a new formulation of *Brilique* 90mg, an orally-dispersable tablet (ODT), was approved by the EMA, making *Brilique* the first and only P2Y12 receptor inhibitor to be made available in ODT form in Europe.

In June 2017, the CFDA in China approved *Brilinta* 60mg tablets for patients with a history of heart attack. Subsequently, in July 2017, the Ministry of Human Resources and Social Security agreed to add *Brilinta* 90mg to the National Reimbursable Drugs List (NRDL), following which provincial reimbursement listing (PRDL) was achieved in all 31 provinces by the end of 2017.

In August 2017, a new sub-analysis of Phase III trial data (PEGASUS-TIMI 54) was presented at the Annual Congress of the European Society of Cardiology (ESC) in Barcelona, Spain, demonstrating a 29% risk reduction in CV death from treatment with *Brilinta* 60mg twice daily, versus placebo, in patients taking low-dose aspirin but still at high risk of an atherothrombotic event – the specific patient population defined in the European label for *Brilinta*.

At the same congress, the ESC published two major new Guidelines – for the management of ST-segment elevation patients, and for dual antiplatelet therapy (DAPT). These were significant not only for their recommendation of *Brilinta* 90mg as the preferred oral antiplatelet therapy over clopidogrel for 12 months DAPT post-ACS, but also for the first time, preferentially recommending *Brilinta* 60mg for >12 months DAPT in high-risk post-heart attack patients.

Our marketed products:

Cardiovascular disease
- *Atacand*[1]/*Atacand* HCT/*Atacand* Plus (candesartan cilexetil)
- *Brilinta/Brilique* (ticagrelor)
- *Crestor*[2] (rosuvastatin calcium)
- *Plendil*[3] (felodipine)
- *Seloken/Toprol-XL*[4] (metoprolol succinate)
- *Tenormin*[5] (atenolol)
- *Zestril*[6] (lisinopril dihydrate)

Metabolic diseases
- *Bydureon* (exenatide XR injectable suspension)
- *Byetta* (exenatide injection)
- *Farxiga/Forxiga* (dapagliflozin)
- *Kombiglyze* XR (saxagliptin and metformin HCl)
- *Komboglyze* (saxagliptin and metformin HCl)
- *Onglyza* (saxagliptin)
- *Qtern* (saxagliptin/dapagliflozin)
- *Symlin* (pramlintide acetate)
- *Xigduo* (dapagliflozin and metformin HCl)
- *Xigduo* XR (dapagliflozin and metformin HCl)

Full product information on page 208.

1 Licensed from Takeda Chemicals Industries Ltd.
2 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.
3 Divested China rights to China Medical Systems Holdings Ltd effective 29 February 2016.
4 Divested US rights to Aralez Pharmaceuticals Trading DAC effective 4 October 2016.
5 Divested US rights to *Tenormin* to Alvogen Pharma US Inc. effective 9 January 2015.
6 Licensed from Merck. Divested US rights to *Zestril* to Alvogen Pharma US Inc. effective 9 January 2015.

Therapy Area Review
Cardiovascular & Metabolic Diseases *continued*

In December 2017, we announced investment in THALES, a new randomised, placebo-controlled Phase III DAPT trial in stroke. This study forms part of PARTHENON, AstraZeneca's largest ever CV outcomes programme involving nearly 80,000 patients, within which THEMIS is the next major trial due to read out, studying the benefit of ticagrelor for the prevention of CV events among Type 2 diabetes patients.

Crestor is approved in over 115 countries for the treatment of dyslipidaemia and hypercholesterolaemia (elevated cholesterol). *Crestor* faces competition from generic products. The substance patent protecting *Crestor* in Japan expired in May 2017 followed by the launch of an authorised generic in September 2017 and subsequent generic entrants. The substance patent protecting *Crestor* in Europe expired on 30 June 2017 and the paediatric extension expired in December 2017.

In the pipeline

RhLCAT (MEDI6012) is an enzyme essential to high-density lipoproteins (HDL) maturation that is in Phase II development for reduction of CV events.

AZD8601 is an investigational modified mRNA-based therapy that encodes for vascular endothelial growth factor-A (VEGF-A) and is currently in Phase II for HF treatment.

AZD5718 is a target based on a genome-wide association study linking halotypes of FLAP gene. It is currently in Phase II with the first launch indication in ACS patients with treatment initiation within the first month from myocardial infarction.

Clinical studies

With *Epanova* (omega-3-carboxylic acids), we are evaluating patient groups where there is high unmet medical need. Therefore, AstraZeneca continues to advance its large-scale CV outcomes trial (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 CV outcomes trial of any prescription omega-3 and completed enrolment in April 2017, with approximately 13,000 patients. Results are anticipated in 2019.

Renal diseases

In the pipeline

We continue to develop roxadustat, a potential first-in-class oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI). We are collaborating on the development and commercialisation of roxadustat in the US, China and other markets not covered by an agreement between FibroGen and Astellas. In October 2017, our partner FibroGen announced that the CFDA had accepted the NDA for roxadustat, based on positive top-line China results announced in January 2017.

We continue to progress ZS-9 (sodium zirconium cyclosilicate), a treatment for hyperkalaemia. In March 2017, the FDA issued a second Complete Response Letter (CRL). The CRL was related to an inspection by the FDA of the dedicated manufacturing facility in Texas, US and did not require the generation of new clinical data. Subsequently, AstraZeneca completed the manufacturing process validation and submitted an NDA for ZS-9, with a decision expected in the first half of 2018. In the EU, we announced in February 2017 that the CHMP of the EMA had issued a positive opinion recommending the approval of ZS-9 for the treatment of hyperkalaemia. After a pause in advancing the opinion, in light of the CRL, the CHMP re-adopted its positive opinion in January 2018 with a decision expected in the first half of 2018. The CRL and the CHMP pause have extended our originally-anticipated timelines for launch, but the long-term potential of the therapy has not been impacted by these short-term delays.

Verinurad (RDEA3170) is a potent selective uric acid reabsorption inhibitor that has been in Phase II development as a urate-lowering therapy. A Phase II trial was initiated in June 2017 and will now progress the development of verinurad for CKD.

Clinical studies

Roxadustat is in Phase III development for the treatment of anemia in patients with CKD, on dialysis and not on dialysis with a programme consisting of 15 studies which are expected to enrol more than 10,000 patients worldwide. The initial data read-out for our sponsored trials, ROCKIES and OLYMPUS, is anticipated to align with the availability of pooled safety data in co-ordination with our partners, expected in 2018, and we expect to present data read-outs from both trials in 2018.

$7.3bn

Product Sales of $7,266 million, down 10% (10% at CER)

$1bn

Annual sales of *Brilinta/Brilique* and *Farxiga/Forxiga* each exceeded $1 billion

Metabolic diseases

Our 2017 focus

We are focused on redefining the approach to treating Type 2 diabetes and harnessing complementary mechanisms of action by refining our R&D efforts to include diverse populations and patients with significant co-morbidities, such as CV disease, obesity, NASH, and CKD. Our global clinical research programmes seek to advance understanding of the treatment effects of our diabetes medicines in broad patient populations, as well as explore combination products to help more patients achieve treatment success earlier in their disease.

In February 2017, the FDA approved once-daily *Qtern* tablets (*Forxiga* 10mg and *Onglyza* 5mg fixed-dose combination) as an adjunct to diet and exercise to improve glycaemic control in adults with Type 2 diabetes who have inadequate control with *Forxiga* (10mg) or who are already treated with *Forxiga* and *Onglyza*. We are committed to making *Qtern* available to patients and, after securing the appropriate access, *Qtern* was launched in the US at the beginning of January 2018.

In March 2017, we received marketing authorisation from the CFDA for *Forxiga* 5mg and 10mg once-daily oral tablets. *Forxiga* was the first SGLT2 inhibitor to be approved in China. This is an important milestone for patients with Type 2 diabetes in China given its prevalence – it now impacts some 114 million patients in China, representing almost one third of diabetes cases worldwide.

Science can improve patient outcomes

The DapaCare programme
We have initiated the extensive DapaCare clinical programme aimed at better understanding the CV and renal profile of *Forxiga* across a spectrum of people with established CV disease, CV risk factors and varying stages of renal disease, both with and without Type 2 diabetes. We aim to provide healthcare providers with evidence needed to improve patient outcomes. The DapaCare programme will enrol nearly 30,000 patients in randomised clinical trials, supported by a multinational real-world evidence study. The DapaCare clinical programme currently comprises:

- DECLARE, DAPA-HF, DAPA-CKD: Three large outcomes trials.
- DELIGHT: An exploratory Phase II/III study evaluating efficacy, safety and pharmacodynamics of dapagliflozin alone and in combination with saxagliptin in CKD patients with Type 2 diabetes and albuminuria.
- DAPA-MECH: Series set of mechanistic studies of the SGLT2 inhibitor class.
- CVD-REAL: The first wave primary study evaluated the risk of hospitalisation for HF and mortality in patients with Type 2 diabetes and assessed data from more than 300,000 patients across six countries, 87% of whom did not have a history of CV disease.

Also in March, we shared results of the landmark CVD-REAL study. This first large real-world evidence study of its kind showed that treatment with SGLT2 inhibitors, versus other Type 2 diabetes medicines, significantly reduced rates of hospitalisation due to HF and mortality.

At the annual American Diabetes Association scientific sessions in June 2017, we presented updated safety data on the risk-benefit profile of *Forxiga* and data from the DURATION-8 trial evaluating the efficacy and safety of *Forxiga* in combination with *Bydureon*, supporting the established clinical profiles of these medicines. In the updated safety analysis of *Forxiga*, data pooled from 30 Phase IIb/III clinical trials showed no new safety signals and the incidence of adverse events was generally similar to that in the control groups.

In August 2017, the EMA approved the incorporation of DURATION-8 data into the *Bydureon* and *Forxiga* European label.

In September 2017, during the annual meeting of the European Association for the Study of Diabetes, we presented the full results from the EXSCEL (EXenatide Study of Cardiovascular Event Lowering) trial. The trial demonstrated CV safety with *Bydureon* in patients with Type 2 diabetes at a wide range of CV risk. *Bydureon* did not increase the incidence of major adverse CV events, a composite endpoint of CV death, non-fatal heart attack (myocardial infarction) or non-fatal stroke, compared to placebo. While there were fewer CV events observed in the *Bydureon* arm of the trial, the primary efficacy objective did not meet statistical significance.

The 24-week data from the DEPICT-1 trial showed that *Forxiga*, when given as an oral adjunct to adjustable insulin in patients with inadequately-controlled Type 1 diabetes, demonstrated significant and clinically-relevant reductions from baseline in HbA1c, weight reductions, and lowered total daily insulin dose at 24 weeks compared to placebo at both the 5mg and 10mg dose.

In October 2017, the FDA approved *Bydureon BCise* injectable suspension, a new formulation of *Bydureon* in an improved once-weekly, single-dose autoinjector device for adults with Type 2 diabetes whose blood sugar remains uncontrolled on one or more oral medicines in addition to diet and exercise to improve glycaemic control. A regulatory application for the new autoinjector device was accepted by the EMA. Also in October 2017, in a separate sNDA, the FDA approved the inclusion of data from the DURATION-8 clinical trial into the *Farxiga* and *Bydureon* labels.

In the pipeline

MEDI0382 is a novel dual GLP1-glucagon peptide, which was discovered in our MedImmune laboratories and which was inspired by our scientists studying the molecular mechanisms that drive the beneficial effects of bariatric surgery. The molecule completed a first Phase II study earlier in the year and we have seen promising data. We are currently evaluating MEDI0382 in a larger global Phase II study to understand dose-response and in a number of clinical pharmacology studies.

Clinical studies

The DECLARE study, a large CV outcomes trial to assess the impact of *Forxiga* on CV risk/benefit, when added to a patient's current diabetes therapy, continued in 2017. The trial was fully enrolled in 2015 with approximately 17,000 adult patients with Type 2 diabetes and is expected to be completed in the second half of 2018.

Two further international, multicentre, parallel group, event-driven, randomised, double-blind, placebo-controlled *Forxiga* studies are underway. One, DAPA-HF, is evaluating its effect on the incidence of worsening HF or CV death for patients with chronic HF while the second, DAPA-CKD, is evaluating its effect on renal outcomes and CV mortality in patients with CKD.

Respiratory

We aim to transform the treatment of respiratory disease for patients with our growing portfolio of inhaled and biologic medicines along with scientific research targeting the underlying causes of disease.

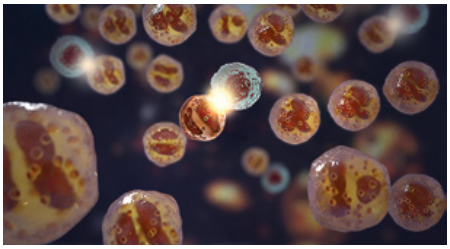
Breaking new ground with respiratory biologics

Building on our 40-year heritage in inhaled respiratory medicines, AstraZeneca is now positioned for leadership in respiratory biologics. The approval of *Fasenra* in the US, Europe and Japan is a positive step towards our ambition to transform care for severe asthma patients whose disease is driven by eosinophilic inflammation. *Fasenra* is a new anti-eosinophilic mAb which has demonstrated efficacy versus placebo in pivotal clinical trials and is the first approved respiratory biologic with an 8-week maintenance dosing regimen. Looking further ahead, the Phase IIb results for tezepelumab, published in the *New England Journal of Medicine* in September 2017, signalled its potential as 'the broadest and most promising biologic for the treatment of persistent uncontrolled asthma seen to date'*.

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

Our strategic priorities

Today, more than 600 million individuals have asthma or chronic obstructive pulmonary disease (COPD) and significant opportunities remain to expand care. About 250 million of asthma and COPD patients are in AstraZeneca's top 12 commercial markets (US, Australia, Brazil, Canada, China, France, Germany, Italy, Japan, Russia, Spain and the UK), but more than 175 million of those patients today do not receive any maintenance treatment. Despite currently-available treatments, therapeutic advances are needed to reduce the morbidity and mortality of these chronic diseases. AstraZeneca estimates that these advances will help to drive 8% growth in the global respiratory medicine market over the next decade, reaching $52 billion by 2027.



Esonophil prior to apoptosis. Natural killer cell being recruited by a biologic.

Respiratory is one of AstraZeneca's main therapy areas, and our medicines reached more than 18 million patients in 2017. 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:

- our strength in inhaled combination medicines including *Symbicort*, AstraZeneca's number one medicine in 2017 by Product Sales
- a leading biologics portfolio, initially for patients with severe respiratory disease
- a robust early pipeline where our goal is to achieve disease modification, early intervention and cure.

Asthma is one of the most common and chronic lung diseases worldwide and a serious global health problem, affecting airways in the lung. Inflammation and narrowing of the airways may cause wheezing, breathlessness, chest tightness and coughing. Combination therapy, given in a single-inhaler of an inhaled corticosteroid (ICS) with a long-acting beta2-agonist (LABA) such as *Symbicort*, is a cornerstone of treatment, helping to treat moderate-to-severe asthma. For patients with mild asthma, we are investigating the use of *Symbicort Turbuhaler*

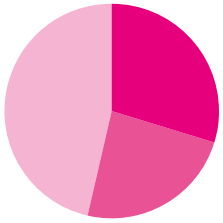
Respiratory – pipeline progressions

Regional approvals	> *Fasenra* (CALIMA, SIROCCO) severe asthma (US, EU*, JP*)
Expedited review	> None
Regulatory submissions	> *Fasenra* – severe asthma (JP) > *Bevespi Aerosphere* – COPD (EU)
Phase III investment decisions	> tezepelumab – asthma > Phase III investment decision
Phase II starts/ progressions	AZD8871 (MABA) for COPD; AZD7986 DPP1 COPD**; Phase II mild asthma study
Strategic transactions completed	None
Setbacks and terminated projects	tralokinumab STRATOS 1 and STRATOS 2 (asthma) trials failed to meet their primary endpoints, and the programme for asthma has been terminated. Also discontinued: *Symbicort* breath actuated inhaler development for asthma/COPD; AZD9412 (Inhaled βIFN) for asthma/COPD; AZD9898 for LTC4S asthma

* Approved in January 2018.
** Partnered with Insmed.

Therapy area world market
(MAT/Q3/17)

$67.3bn
Annual worldwide market value



- Asthma $20.2bn
- COPD $16.0bn
- Other $31.2bn

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

prescribed as an anti-inflammatory reliever as needed, recognising the variability and inflammatory nature of disease in these patients. This programme will demonstrate the impact of *Symbicort* as-needed on exacerbations and asthma control compared to standard of care in patients with mild asthma. Up to 10% of asthma patients have severe, uncontrolled asthma despite standard of care asthma controller medications. Such patients experience debilitating symptoms and face increased risk of hospitalisations, emergency room visits and even death, despite current treatments. Severe, uncontrolled asthma can lead to a dependence on oral corticosteroids (OCS), with systemic steroid exposure potentially leading to serious short- and long-term adverse effects, including weight gain, diabetes, osteoporosis, glaucoma, anxiety, depression, CV disease and immuno-suppression. There is also a significant physical and socioeconomic burden associated with severe, uncontrolled asthma with these patients accounting for 50% of asthma-related costs. For these difficult to treat patients, we are developing biologic medicines that address the underlying causes of their disease.

COPD is a chronic, progressive disease characterised by obstruction of airflow in the lungs that can result in debilitating bouts of breathlessness. Improving lung function, managing daily symptoms such as breathlessness, and reducing exacerbations are important to the management of COPD. Exacerbations are associated with mortality in COPD, with one study reporting that 50% of COPD patients will die within four years of their first hospital admission for a severe exacerbation. COPD is associated with significant economic burden, accounting for $32 billion of direct costs and $20 billion of indirect costs in the US, while in Europe, COPD accounts for 56% of the €39 billion cost of respiratory diseases. COPD remains underdiagnosed and often under-treated. AstraZeneca's current inhaled portfolio includes both ICS in combination with a long-acting bronchodilator and non-ICS-containing dual bronchodilator combinations to address patients with different needs across the spectrum of disease severity. AstraZeneca's current pipeline includes a triple combination of PT010 (budesonide/glycopyrronium/formoterol fumarate) in development for COPD patients.

Our 2017 focus

Inhaled combination medicines

We continue to invest in *Symbicort* which, in addition to being AstraZeneca's number one medicine in Product Sales in 2017, was also the number one ICS/LABA combination globally in volume terms in 2017. Pricing pressure was in line with expectations as prices rebase ahead of anticipated generic entries. This trend will continue to be offset by Emerging Market growth, led by demand for acute and maintenance care in China.

In January 2017, the FDA approved *Symbicort* Inhalation Aerosol 80/4.5 micrograms for the treatment of asthma in paediatric patients aged six to 12 years. The FDA approval was based on the CHASE (ChildHood Asthma Safety and Efficacy) clinical trial programme, which included the CHASE 3 Phase III trial. In addition, in January 2017, the FDA granted six months of paediatric exclusivity for *Symbicort* Inhalation Aerosol. *Symbicort* was already approved in the US to treat asthma in patients 12 years and older and for the maintenance treatment of airflow obstruction in COPD in adults.

Our marketed products:
- *Accolate* (zafirlukast)
- *Bevespi Aerosphere* (glycopyrrolate and formoterol fumarate)[1]
- *Bricanyl Respules* (terbutaline)[2]
- *Bricanyl Turbuhaler* (terbutaline)[3]
- *Daliresp/Daxas* (roflumilast)
- *Duaklir Genuair* (aclidinium/formoterol)[3]
- *Eklira Genuair/Tudorza Pressair* (aclidinium)[3]
- *Fasenra* (benralizumab)[4]
- *Oxis Turbuhaler* (formoterol)[3]
- *Pulmicort Turbuhaler/Pulmicort Flexhaler* (budesonide)[3]
- *Pulmicort Respules* (budesonide)[2]
- *Symbicort* pMDI (budesonide/formoterol)[5]
- *Symbicort Turbuhaler* (budesonide/formoterol)[3]
- *Tudorza Pressair* (aclidinium)[3]

Full product information on page 208.

[1] Inhalation aerosol.
[2] Inhalation solution.
[3] In a dry powder inhaler.
[4] Subcutaneous injection.
[5] Inhalation suspension.

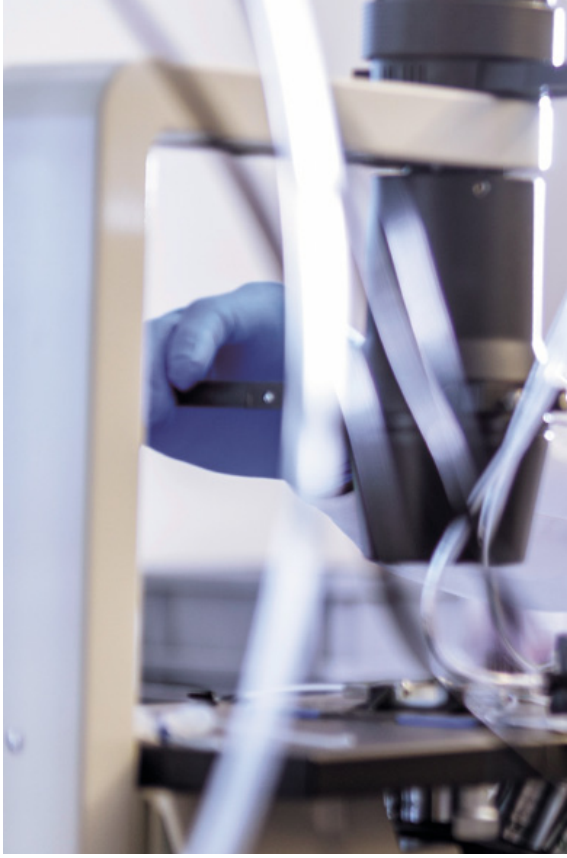
Therapy Area Review
Respiratory *continued*

$4.7bn

Product Sales of $4,706 million, down 1% (1% at CER)

18m

Respiratory medicines reached 18 million patients in 2017



In September 2017, the FDA approved *Symbicort* for the reduction of exacerbations in patients with COPD. The approval was based on data that evaluated COPD exacerbations as the primary endpoint in two Phase IIIb trials (RISE and Study 003), supported by data from two legacy Phase IIIa trials (SUN and SHINE). The RISE data was published in *Respiratory Medicine*. In November 2017, we announced clinical data from the Phase III SYGMA trials, which examined *Symbicort Turbuhaler* prescribed as an anti-inflammatory reliever as needed in patients with mild asthma. The primary objectives in severe-asthma exacerbation rates and asthma control were met.

In 2017, AstraZeneca launched the Turbu+ programme in eight countries. Turbu+ is our digital Integrated Patient Solution for *Symbicort Turbuhaler*, which helps patients with asthma and/or COPD to better manage their disease using a Bluetooth-enabled monitoring device and smartphone app.

AstraZeneca is advancing its portfolio of next-generation inhaled medicines which utilise *Aerosphere* Delivery Technology. In 2017, we launched *Bevespi Aerosphere*, our dual combination of glycopyrrolate/formoterol fumarate, in the US for the maintenance treatment of adults with COPD, and our regulatory submission for *Bevespi Aerosphere* in the EU was accepted. Our *Aerosphere* Delivery Technology provides consistent drug delivery in a pressurised metered-dose inhaler.

In April 2017, AstraZeneca entered a strategic collaboration with Circassia for the development and commercialisation in the US of two inhaled medicines, *Tudorza* (LAMA) and *Duaklir* (LAMA/LABA), for the treatment of COPD. Under the terms of the collaboration, Circassia was granted the rights to *Duaklir* in the US. Circassia is also leading the promotion of *Tudorza* in the US, with the option to gain full commercial rights in the future. In September 2017, we announced positive top-line results from the Phase III AMPLIFY trial for *Duaklir*, which met its primary endpoints and demonstrated a statistically-significant improvement in lung function in patients with moderate to very severe stable COPD, compared to each individual component (either aclidinium bromide or formoterol). We anticipate the US submission of an NDA in the first half of 2018.

In December 2017, we also announced positive top-line results from the Phase III ASCENT trial for *Tudorza*, which met its primary efficacy endpoint of demonstrating a statistically significant reduction in the annual rate of moderate or severe COPD exacerbations compared to placebo. The ASCENT trial also met the primary safety endpoint, demonstrating an increase in time to first major adverse cardiovascular event (MACE) compared to placebo. We plan to submit an sNDA for an expanded *Tudorza* label following these positive results.

Biologic medicines

AstraZeneca's first respiratory biologic, *Fasenra*, was approved for severe, eosinophilic asthma by the FDA in November 2017, as well as by the EC and the Japanese Ministry of Health, Labour and Welfare in January 2018. *Fasenra* distinctively targets and depletes eosinophils, the biological effector cells in approximately 50% of asthma patients that lead to frequent exacerbations, impaired lung function and asthma symptoms. *Fasenra* is the first respiratory biologic with an 8-week maintenance dosing regimen. The approval of *Fasenra*, in the US and EU respectively, is based on results from the WINDWARD clinical trial programme, including two pivotal Phase III exacerbation trials, SIROCCO and CALIMA, reported in the *Lancet* in September 2016. The approvals were also based on the Phase III OCS-sparing trial, ZONDA, which was published in the *New England Journal of Medicine* in May 2017. ZONDA demonstrated a statistically-significant and clinically-meaningful reduction in daily maintenance, OCS use from baseline for patients with severe, uncontrolled OCS-dependent eosinophilic asthma receiving benralizumab compared with placebo.

In the pipeline

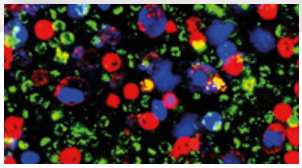
Inhaled combination medicines

AstraZeneca has made significant progress in delivering the ATHENA programme, our Phase III clinical trial programme for PT010, which includes more than 11 trials and 15,500 patients. The four key ATHENA trials are ETHOS, KRONOS, TELOS and SOPHOS. In January 2018, we announced top-line results from the KRONOS trial that PT010 demonstrated a statistically-significant improvement compared with dual combination therapies in six out of seven lung function primary endpoints, based on forced expiratory volume in one second (FEV1) assessments in patients with moderate to very severe COPD. In total, eight of the nine primary endpoints in the KRONOS trial were met, including two non-inferiority endpoints to qualify PT009 (budesonide/formoterol fumarate) as one of the comparators.

In February 2018, we announced results of the Phase III TELOS trial, which compared two doses of PT009 (budesonide/formoterol fumarate) to its individual components, PT005 (formoterol fumarate) and PT008 (budesonide), and to *Symbicort Turbuhaler* to assess lung

Science *can* help us understand how targeted therapies work in respiratory diseases

Cell imaging technology
As scientists in the field of respiratory research, we use cell imaging technology to illuminate what happens when a specific pathway is activated with an investigational medicine.



The illustration shows two different immune cell types, one red and one green. The red cells are eosinophils, which play a key pathogenic role in inflammation in asthma. The green cells are natural killer cells. The eosinophils have been treated such that they are now recognisable to the natural killer cells. The natural killer cells target the eosinophils which results in cell death (blue).

Severe asthma is a heterogeneous disease with complex biology. Cell imaging helps us to visualise the effects of our investigational drugs on inflammation and follow the science to develop medicines targeted to a particular inflammatory phenotype.

For more information, please see our website, www.astrazeneca.com/our-focus-areas/respiratory, Down the microscope.

function in patients with moderate to very severe COPD to qualify PT009 as active comparator in PT010 clinical programme. All primary endpoints were met, with the exception of the lung function primary endpoint comparing low dose PT009 to PT005.

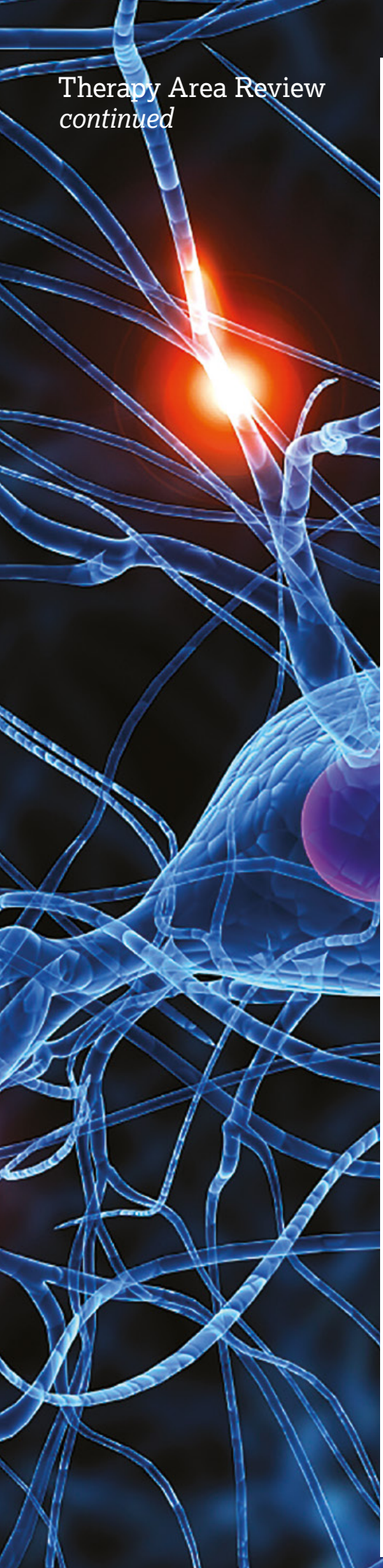
Biologic medicines

In addition to AstraZeneca's progress with *Fasenra* in severe asthma, AstraZeneca is investigating *Fasenra* for at-home use in an autoinjector device as well as for indications in other diseases. In the first half of 2018, we expect the results of our Phase III COPD trials, TERRANOVA and GALATHEA.

AstraZeneca and our partner Amgen published landmark data in the *New England Journal of Medicine* from the PATHWAY Phase IIb trial of tezepelumab in patients with severe, uncontrolled asthma. Tezepelumab is a first-in-class anti-thymic stromal lymphopoietin (TSLP) mAb that blocks TSLP, an upstream driver of multiple downstream inflammatory pathways. Tezepelumab met its primary efficacy endpoint in PATHWAY with the data demonstrating significant annual asthma exacerbation rate reductions of 61%, 71% and 66% in the tezepelumab arms receiving either 70mg or 210mg every four weeks or 280mg every two weeks, respectively. Significant and clinically-meaningful reductions in exacerbation rates were observed independent of baseline blood eosinophil count or other type 2 (T2) inflammatory biomarkers. Due to its activity early in the inflammatory cascade, tezepelumab may be suitable for patients with both T2 and non-T2 driven asthma, including those ineligible for current biologic therapies which only target the T2 pathway. A pivotal Phase III trial (NAVIGATOR) for tezepelumab in severe asthma was initiated in November 2017.

The ALLEVIAD Phase IIa trial data showed that tezepelumab did not meet statistical significance on the primary endpoint (EASI 50) of the 12-week exploratory trial that evaluated tezepelumab in moderate to severe atopic dermatitis (AD) as add-on treatment to regular medium-to-high strength topical glucocorticosteroids. Numeric differences in favour of tezepelumab, however, were observed across a number of disease activity endpoints (EASI, IGA and SCORAD response) compared to placebo.

During the year, we announced the results of Phase III trials for tralokinumab, an investigational anti-IL-13 human immunoglobulin-G4 mAb that blocks binding and signalling of IL-13 to IL-3 receptors, a potential target in severe, uncontrolled asthma patients. STRATOS 1 and STRATOS 2 were Phase III trials designed to evaluate the efficacy and safety of tralokinumab in patients with severe, uncontrolled asthma, despite treatment with ICS plus LABA. In the STRATOS 1 trial, tralokinumab did not meet its primary endpoint of a significant reduction in the annual asthma exacerbation rate (AAER), although a clinically-relevant reduction in AAER was observed in a sub-population of patients with elevated FeNO (Fractional exhaled Nitric Oxide), a biomarker associated with increased IL-13 activity. The primary analysis population specified in the STRATOS 2 trial was subjects with elevated FeNO, but tralokinumab did not achieve a statistically-significant reduction in AAER. In the OCS-sparing trial, TROPOS, tralokinumab did not achieve a statistically-significant reduction in OCS use when added to the standard of care in patients dependent on OCS. AstraZeneca has discontinued the development of tralokinumab in severe asthma. Through a licence agreement signed in 2016, LEO Pharma is developing tralokinumab in adults with moderate-to-severe atopic dermatitis and Phase III trials are ongoing.



Other Disease Areas

In addition to our focus on the treatment of diseases in our three main therapy areas, we are also selectively active in the areas of autoimmunity, infection, neuroscience and gastroenterology, where we aim to develop best-in-class therapies and follow an opportunity-driven approach.

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 company stake in the most promising assets.

Autoimmunity

Systemic lupus erythematosus (SLE), or lupus, is an autoimmune disease that occurs when the immune system produces antibodies that attack healthy tissue, including skin, joints, kidney, the brain and blood vessels. SLE can cause a wide range of symptoms. Among these are pain, rashes, fatigue, swelling in joints, and fevers. SLE is associated with a greater risk of death from causes such as infection, nephritis and cardiovascular disease. Inflammation of the kidneys caused by SLE – known as lupus nephritis – can lead to significant morbidity and even death. Current treatment of SLE focuses on suppressing symptoms and controlling disease flares and, in the case of lupus nephritis, preventing renal failure.

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, life-threatening autoimmune disease of the central nervous system in which the body's immune system attacks healthy cells, most commonly in the optic nerves and spinal cord, resulting in severe damage. NMOSD may cause severe muscle weakness and paralysis, loss of vision, respiratory failure, problems with bowel and bladder function and neuropathic pain. There is currently no cure or approved medicine for this rare disease.

Psoriasis is a chronic disease in which the immune system causes skin cells to grow rapidly. Instead of being shed, the skin cells pile up, causing painful and itchy, red, scaly patches that can bleed. Approximately 100 million people worldwide suffer from psoriasis. Despite available treatment options for moderate-to-severe plaque psoriasis, many patients do not experience a resolution of underlying inflammation, clearing of symptoms or an improved quality of life.

In the pipeline

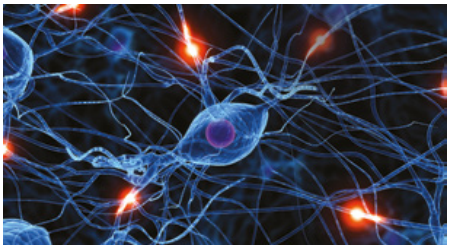
We are making important progress in advancing our pipeline and improving treatment options and clinical outcomes for patients with inflammatory and autoimmune diseases. Common molecular pathways are often shared across multiple autoimmune diseases, which provides opportunities to identify and work with approaches that could become treatments for more than one disease.

Anifrolumab is a developmental mAb that inhibits the activity of all type I interferons (IFN), which play a central role in lupus. A majority of patients with SLE show a high interferon gene signature, and increased levels of type I IFN have been shown to correlate with SLE disease activity and severity. During 2017, we completed enrolment in two Phase III trials, TULIP-SLE1 and TULIP-SLE2, of anifrolumab in patients with moderate-to-severe SLE. We also completed enrolment in a Phase II SLE study evaluating a subcutaneous route of administration of anifrolumab. Anifrolumab is also in Phase II development for lupus nephritis.

Other Disease Areas – pipeline progressions

Regional approvals	> *Duzallo* gout (US) > *Kyntheum* (brodalumab) psoriasis (EU; by partner) > *Siliq* (brodalumab) psoriasis (US; by partner) > *Nexium* paeds and sachet GERD (JP*)
Expedited review	> Orphan Drug Designation: inebilizumab (MEDI-551) – neuromyelitis optica (EU)
Regulatory submissions	> None
Phase III investment decisions	> None
Phase II starts/ progressions	None
Strategic transactions completed	Partnership with Sanofi for development and commercialisation of MEDI8897 (RSV antibody). Divestment to Aspen of the remaining rights in the anaesthetics portfolio and to Grünenthal of the rights to *Zomig* outside Japan
Setbacks and terminated projects	Discontinued: verinurad for hyperuricemia/gout; AZD3241 (MPO) for multiple system atrophy

* Approved in January 2018.



In March 2017, the EMA granted Orphan Drug Designation to inebilizumab (MEDI-551) for the treatment of NMOSD. Inebilizumab is currently in Phase II/III clinical development for NMOSD.

Brodalumab is a human mAb that targets the interleukin-17 (IL-17) receptor. During 2017, brodalumab (*Siliq* in the US and *Kyntheum* in Europe) received both FDA and EMA approvals 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 no longer respond to other systemic therapies.

Through collaboration agreements, Valeant holds the exclusive licence to develop and commercialise brodalumab globally, except in Japan and certain other Asian countries where rights are held by Kyowa Hakko Kirin through an agreement with Amgen, and in Europe, where LEO Pharma holds exclusive rights to develop and commercialise *Kyntheum* for psoriasis.

Infection

Seasonal influenza is a serious public health problem that causes severe illness and death in high-risk populations. In 2017, the US Advisory Committee on Immunization Practices, under the Centers for Disease Control and Prevention (CDC), continued its recommendation (issued in 2016) that *FluMist* Quadrivalent (LAIV) should not be used in the US for the 2017 to 2018 influenza season until further data is available. This recommendation was based on concerns regarding low effectiveness of the vaccine in the US in previous seasons. The vaccine remains licensed in the US, Canada and the EU and we remain committed to supporting *FluMist* Quadrivalent/*Fluenz* Tetra in the US and in the rest of the world. Our investigation into findings of lower than expected vaccine effectiveness informed our selection of a new A/H1N1 LAIV strain for the 2017 to 2018 flu season. The new A/H1N1 LAIV strain has demonstrated improved performance in laboratory assays and we are currently conducting a clinical study to further evaluate this strain. We continue to keep the US CDC updated on our progress.

FluMist Quadrivalent/*Fluenz* Tetra continues to be recommended for use in many countries outside the US based on their respective public health authorities' review of existing and recent vaccine effectiveness data. We also have an ongoing agreement with the WHO to donate and supply at reduced prices a portion of vaccine production in the event of an influenza pandemic.

Our marketed products:

Infection
> *Fluenz FluMist*/Tetra Quadrivalent[1,2] (live attenuated influenza vaccine)
> *Synagis*[3] (palivizumab)

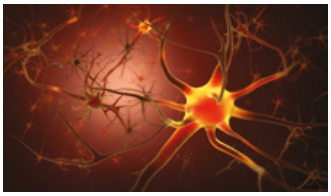
Neuroscience
> *Movantik/Moventig* (naloxegol)
> *Seroquel* IR (quetiapine fumarate)
> *Seroquel XR* (quetiapine fumarate)
> *Vimovo*[4] (naproxen and esomeprazole magnesium)

Gastrointestinal
> *Losec/Prilosec* (omeprazole)
> *Nexium* (esomeprazole magnesium)

Full product information on page 208.

[1] Intra-nasal.
[2] Daiichi Sankyo holds rights to *Fluenz* Tetra/*FluMist* Quadrivalent in Japan.
[3] US rights only. AbbVie holds rights to *Synagis* outside the US.
[4] Licensed from Pozen. Divested US rights to Horizon Pharma USA, Inc. effective 22 November 2013.

Therapy Area Review
Other Disease Areas
continued



$4.2bn

Product Sales of $4,156 million, down 18% (17% at CER)

MEDI8852, an investigational human mAb for the treatment of patients hospitalised with Type A strain influenza, received Fast Track Designation from the FDA in March 2016. The programme is on hold while a government or industry partner is sought to share late-stage development costs and commercialisation activities. Discussions with potential partners are ongoing.

Respiratory Synctial Virus (RSV) is a common seasonal virus and the most prevalent cause of lower respiratory tract infections among infants and young children. It is the leading cause of hospitalisations and admissions to paediatric intensive care units and leads to nearly 200,000 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 globally against RSV. *Synagis* is approved in more than 80 countries and we continue to work with our worldwide partner, AbbVie, to protect vulnerable infants.

MEDI8897 is a novel extended half-life mAb for the prevention of serious respiratory disease caused by RSV in infants. It is designed to require dosing only once per RSV season – a potential breakthrough in RSV prophylaxis. In March 2017, we formed an alliance with Sanofi to develop and commercialise MEDI8897 jointly. MEDI8897 is currently in a Phase IIb clinical trial in preterm infants who are ineligible for *Synagis*, the current standard of care medicine.

Neuroscience

Alzheimer's disease (AD) is the most common form of dementia worldwide and is a major health challenge facing the world today. We are progressing lanabecestat (AZD3293), our BACE inhibitor, in collaboration with Lilly for the potential treatment of AD. A second interim analysis in the Phase III AMARANTH trial was completed in July 2017, and the independent data monitoring committee recommended the trial proceed with no modifications. In addition, we initiated a new extension trial of the AMARANTH study to further evaluate the benefit of earlier intervention in the course of the disease.

Building on the current partnership for lanabecestat, we are also now co-developing with Lilly MEDI1814, an antibody selective for amyloid-beta 42 (Aβ42), which is currently in Phase I development as a potential disease-modifying treatment for AD.

Current commercialised AstraZeneca neuroscience brands include *Seroquel* IR and *XR* (atypical antipsychotics), which have lost exclusivity in all major markets. The largest market for *Seroquel XR* was the US, where we lost exclusivity in November 2016. Two licensed generics were launched at that time followed by four additional generic entrants in May 2017 and another two in November 2017. Three additional generics received final FDA approval but have not yet entered the US market.

In June 2017, AstraZeneca announced an agreement with Grünenthal for the global rights to *Zomig* (zolmitriptan) outside Japan, including the US, where the rights were previously licensed to Impax Pharmaceuticals. In October 2017, we entered into an agreement with Sawai Pharmaceuticals Company Ltd for the rights to *Zomig* in Japan.

In September 2017, AstraZeneca announced an agreement with Aspen, under which Aspen acquired the residual rights to our remaining anaesthetic medicines. This builds on the agreement with Aspen in June 2016, under which they gained the exclusive commercialisation rights to the medicines in markets outside the US. The agreement covered seven established medicines – *Diprivan* (general anaesthesia), *EMLA* (topical anaesthetic) and five local anaesthetics (*Xylocaine/Xylocard/Xyloproct, Marcaine, Naropin, Carbocaine* and *Citanest*).

In the pain space, we are continuing to explore ways of bringing *Movantik/Moventig* to patients who need to manage the side effect of opioid induced constipation. In August 2017, the FDA updated the indication of *Movantik* to include adult patients with chronic pain related to prior cancer or its treatment who do not require frequent opioid dosage escalation.

Gastrointestinal

In 2017, use of *Nexium* continued to grow in a limited number of markets such as China and Japan. Demand for *Nexium* in China is expected to continue to grow over the next several years, based on broader geographic expansion as well as anticipated label expansions, and has the potential to become a top-selling medicine in its class, as in Japan. Patent protection for *Nexium* remains in Japan. For the rest of the world, *Nexium* is subject to generic competition. *Nexium* sales continue to decline under generic pressure in the US and EU.

Risk Overview

We face a diverse range of risks and uncertainties. The Board defines those risks which have a potential to have a material impact on our business or results of operations as 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 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 210 to 220 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.

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 210 to 220.

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, 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 page 97.

Viability statement

In accordance with provision C.2.2 of the 2014 UK Corporate Governance Code, the Board has determined that a three-year period to 31 December 2020 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 considers a 10-year long-range projection but, given the inherent uncertainty involved, believes that the three-year statement presents readers of the 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. This analysis contemplates a severe downside scenario reflecting the Principal Risks including market pricing and access, delivery of pipeline, unexpected loss of patent protection and the need to meet pension fund obligations. 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 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 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 process is 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 committee to understand, assess, plan and implement operational actions that may be required. Some of these actions are being implemented based on assumptions rather than defined positions so that the Company is able to mitigate the risks arising from variable external outcomes. Currently, a number of areas for action have been identified including 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 upgrades. The Board reviews the potential impact of Brexit as an integral part of its Principal Risks (as outlined overleaf) rather than as a stand-alone risk. As the process of Brexit evolves, the Board will continue 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	
Meet quality, regulatory and ethical drug approval and disclosure requirements	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	
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	Increased number of patent litigation suits alleging patent infringement filed against AstraZeneca by research-based pharmaceutical competitors. Details of material patent litigation matters can be found in Note 28 to the Financial Statements from page 182
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	Global economic and political conditions placing downwards 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	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	

Risk category and Principal Risks	Context/potential impact	Management actions	Trend versus prior year
Supply chain and business execution *continued*			
Information technology and data security and privacy	Significant disruption to our IT systems, cyber security incidents including breaches of data security, or failure to prepare for emerging EU Global Data Privacy Regulations (GDPR), 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	> Cyber security framework and dashboard > Privacy office established to oversee compliance with EU GDPR 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 and introduction of new EU GDPR regulation effective May 2018
Delivery of gains from productivity initiatives	Inappropriately managed initiatives could lead to low employee engagement and reduced productivity, increased absence and attrition levels, or even industrial action. All could adversely impact the value of the initiative	> Appropriate project governance structure and oversight > Regular review of strategic initiatives by appropriate senior executive and Board level committees	↔
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. Failure to engage our employees could impact productivity and turnover. Both could adversely affect the achievement of our strategic objectives	> Targeted recruitment and retention strategies deployed > Support of staff impacted by Brexit > Development of our employees > Evolve our culture > Focus on simplification	↑ Increasingly competitive labour markets, with particular focus in specific locations and capability sets, and in the UK the added uncertainty created by Brexit, could impact the hiring and retention of staff in some business-critical areas
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

In 2017, our financial performance reflected the launch of several new medicines, the strong performance of our Growth Platforms and the continued impact from patent expiries; most notably for *Crestor* and *Seroquel XR* in the US.

Overall, Total Revenue declined by 2% (CER: 2%) to $22.5 billion. Strong acceleration in our New Oncology medicines (driven by *Tagrisso*), supported by continued good growth in Emerging Markets, particularly in China, resulted in a 5% increase (CER: 6%) in our Growth Platform sales. Within Growth Platforms, New CVMD grew by 9% to $3.6 billion, with both *Farxiga* and *Brilinta* each exceeding annual Product Sales of $1 billion. In 2017, we realised $2.3 billion in Externalisation Revenue, including $1.2 billion received as part of our collaboration with MSD on *Lynparza* and selumetinib, and $0.6 billion in additional Ongoing Externalisation Revenue. However, the continued effect of patent expiries, including those impacting *Crestor* and *Seroquel XR* in the US and *Symbicort* in Europe, and pricing pressures, resulted in a decline in Total Revenue.

Our continued focus on cost discipline delivered a decrease of 2% (CER: 1%) in Reported R&D costs and a decrease of 4% (CER: 3%) in Core R&D costs, despite the rapid progression of the pipeline. Reported SG&A costs increased by 9% (CER: 10%) reflecting the impact of favourable fair value adjustments to long-term liabilities in the comparative period, and Core SG&A costs declined by 4% (CER: 3%) with the benefit of efficiency savings being only partially offset by the selective investment in launches of new products.

Reported other operating income was $1.8 billion in the year and included income from various disposal transactions, including the sale of the remaining rights to the anaesthetics portfolio to Aspen and the sale of rights to *Seloken* in Europe to Recordati.

The Reported tax rate of (29)% benefited from a favourable net adjustment of $0.6 billion to deferred tax, reflecting the recently reduced US Federal Income tax rate and non-taxable remeasurement of acquistion-related liabilities. Additionally, there was a $0.5 billion benefit to the Reported and Core tax rates resulting from a number of factors, including the reduction in tax provisions. The Core tax rate for the year was 14%.

Reported operating profit declined by 25% (CER: 28%) to $3.7 billion and Core operating profit increased by 2% (CER: stable) to $6.9 billion in the year. Reported EPS was $2.37 and Core EPS was $4.28.

We generated a net cash inflow from operating activities of $3.6 billion in the year and we maintain a strong, investment-grade credit rating. During the year, we issued new bonds totalling $2 billion and repaid $1.75 billion of bonds maturing. We ended the year with total long-term debt of $15.6 billion and net debt of $12.7 billion.

Marc Dunoyer
Chief Financial Officer

Next-generation DNA sequencing: Specifically, the process in which the polymerase creates a complementary strand of the hybridised fragments at the beginning of cluster generation

Contents

The purpose of this Financial Review is to provide a balanced and comprehensive analysis of the financial performance of the business during 2017, 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 8, the Therapy Area Review from page 46 and the Geographical Review from page 221, and describes in detail the developments in both our products and the geographical regions in which we operate.

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 208.
- 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 euro, Japanese yen, pound sterling, Chinese renminbi and Swedish krona.
- Macro factors such as greater demand from an ageing population and increasing requirements of Emerging Markets.

Further details of the risks faced by the business are given in Risk Overview from page 63 and Risk from page 210.

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 whether and when it will generate future products.

The most significant features of our financial results in 2017 are:

- Total Revenue down 2% to $22,465 million (CER: 2%). Product Sales were down 5% (CER: 5%) reflecting the continued impact of generic versions of *Crestor* in the US and pricing pressure in the US on *Symbicort*. Product Sales of *Crestor* and *Symbicort* in the US declined by 70% and 12% respectively.
- Revenues from our Growth Platforms increased by 5% (CER: 6%) and constituted 68% of our Total Revenue, with
  - Emerging Markets up 6% (CER: 8%) supported by China, up by 12% (CER: 15%).
  - Japan up 1% (CER: 4%) to $2,208 million reflecting growth of *Tagrisso* and *Forxiga.*
  - Respiratory down 1% (CER: 1%) reflecting a 12% fall in US Product Sales of *Symbicort.*
  - New Oncology Product Sales of $1,313 million, up 98% (CER: 98%) primarily due to the growth of *Tagrisso*, which reached sales of $955 million.
  - New CVMD grew by 9% (CER: 9%) following strong performances by *Farxiga* and *Brilinta*, which both exceeded $1 billion of sales in the year.
- Reported operating profit was down 25% (CER: 28%) to $3,677 million (2016: $4,902 million), including a $109 million charge in 2017, with 2016 having benefited from a $1,158 million credit, on revaluation of contingent consideration arising from business acquisitions.
- Core operating profit was up 2% (stable at CER) to $6,855 million (2016: $6,721 million).
- Reported operating margin of 16.4% of Total Revenue was down 4.9 percentage points (CER: 5.8 percentage points). Core operating margin was 30.5% of Total Revenue (2016: 29.2%).
- Reported EPS was down 14% (CER: 15%) to $2.37. Core EPS was $4.28, down 1% (CER: 2%).
- Dividends paid amounted to $3,519 million (2016: $3,561 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 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 2017 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, results from Joint Ventures and Associates and charges for depreciation, amortisation and impairment. Reference should be made to the Reconciliation of Reported Profit Before Tax to EBITDA included on page 70 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 74 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 date of completion of an agreement or transaction). Ongoing Externalisation Revenue comprises, among other items, royalties, milestones and profit sharing income. Reference should be made to the reconciliation of Externalisation Revenue to Ongoing Externalisation Revenue included on page 70 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 2017 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 allows 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 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 2017 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. You should also refer to our Reported financial information in the 2017 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 2017

2017 Reported operating profit

	2017			2016	Percentage of Total Revenue		Reported 2017 compared with Reported 2016	
	Reported $m	CER growth $m	Growth due to exchange effects $m	Reported $m	Reported 2017 %	Reported 2016 %	Actual growth %	CER growth[1] %
Product Sales	**20,152**	**(1,053)**	**(114)**	21,319			**(5)**	**(5)**
Externalisation Revenue	**2,313**	**639**	**(9)**	1,683			**37**	**38**
Total Revenue	**22,465**	**(414)**	**(123)**	23,002			**(2)**	**(2)**
Cost of sales	**(4,318)**	**(277)**	**85**	(4,126)	**(19.2)**	(17.9)	**5**	**7**
Gross profit	**18,147**	**(691)**	**(38)**	18,876	**80.8**	82.1	**(4)**	**(4)**
Distribution costs	**(310)**	**10**	**6**	(326)	**(1.4)**	(1.5)	**(5)**	**(3)**
Research and development expense	**(5,757)**	**68**	**65**	(5,890)	**(25.6)**	(25.6)	**(2)**	**(1)**
Selling, general and administrative costs	**(10,233)**	**(964)**	**144**	(9,413)	**(45.5)**	(40.9)	**9**	**10**
Other operating income and expense	**1,830**	**177**	**(2)**	1,655	**8.1**	7.2	**11**	**11**
Operating profit	**3,677**	**(1,400)**	**175**	4,902	**16.4**	21.3	**(25)**	**(28)**
Net finance expense	**(1,395)**			(1,317)				
Share of after tax losses of joint ventures and associates	**(55)**			(33)				
Profit before tax	**2,227**			3,552				
Taxation	**641**			(146)				
Profit for the period	**2,868**			3,406				
Basic earnings per share ($)	**2.37**			2.77				

[1] As detailed on page 68, CER growth is calculated using prior year actual results adjusted for certain exchange effects including hedging.

2017 Reconciliation of Reported results to Core results

	2017 Reported $m	Restructuring costs $m	Intangible amortisation and impairments $m	Diabetes Alliance $m	Other[3] $m	2017 Core[1] $m	Core 2017 compared with Core 2016[1] Actual growth %	Core 2017 compared with Core 2016[1] CER growth %
Gross profit	**18,147**	**181**	**149**	**–**	**–**	**18,477**	**(3)**	**(3)**
Product Sales gross margin %[2]	***79.6***					***81.2***		
Total Revenue gross margin %	***80.8***					***82.2***		
Distribution costs	**(310)**	**–**	**–**	**–**	**–**	**(310)**	**(5)**	**(3)**
Research and development expense	**(5,757)**	**201**	**144**	**–**	**–**	**(5,412)**	**(4)**	**(3)**
Selling, general and administrative costs	**(10,233)**	**347**	**1,469**	**641**	**(77)**	**(7,853)**	**(4)**	**(3)**
Other operating income and expense	**1,830**	**78**	**45**	**–**	**–**	**1,953**	**14**	**14**
Operating profit	**3,677**	**807**	**1,807**	**641**	**(77)**	**6,855**	**2**	**–**
Operating margin as a % of Total Revenue	***16.4***					***30.5***		
Net finance expense	**(1,395)**	**–**	**–**	**313**	**432**	**(650)**		
Taxation	**641**	**(169)**	**(453)**	**(198)**	**(681)**	**(860)**		
Basic earnings per share ($)	**2.37**	**0.50**	**1.07**	**0.60**	**(0.26)**	**4.28**		

[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 72 for further details of other adjustments.

Financial Review
continued

Total Revenue
Total Revenue for the year was down 2% (CER: 2%) to $22,465 million, comprising Product Sales of $20,152 million, down 5% (CER: 5%) and Externalisation Revenue of $2,313 million, an increase of 37% (CER: 38%).

By Geography
US Product Sales were down 16% to $6,169 million, reflecting continued competition from multiple generic *Crestor* medicines that entered the US market in 2016 as well as lower Product Sales of *Nexium* and *Symbicort*. In Europe, Product Sales declined by 6% (CER: 7%) to $4,753 million, partly driven by pricing pressures on *Symbicort* and the initial impact from generic competition on *Crestor*. Established Markets remained stable (CER: up 1%) to $3,081 million including an increase of 1% in Japan (CER: 4%) to $2,208 million. *Crestor* Product Sales in Japan declined 6% (CER: 4%) to $489 million as generic competition entered the market in the year. Product Sales in Emerging Markets increased by 6% (CER: 8%) to $6,149 million in 2017, with growth in China of 12% (CER: 15%) to $2,955 million.

By Product
Our largest selling products in 2017 were *Symbicort* ($2,803 million), *Crestor* ($2,365 million), *Nexium* ($1,952 million) and *Pulmicort* ($1,176 million). Global Product Sales of *Crestor* declined in the year by 30% (CER: 30%), which primarily reflected the impact of generic competition. *Symbicort* global Product Sales declined by 6% (CER: 6%) including a reduction of 12% in the US due to the impact of a competitive environment on net pricing. *Nexium* Product Sales were down 4% (CER: 3%), including a 10% decrease in the US, reflecting continued lower demand and inventory de-stocking as a result of the loss of exclusivity from 2015. Strong underlying volume growth in Emerging Markets drove an 11% global Product Sales increase in *Pulmicort* (CER: 12%), with 71% of Product Sales of the medicine coming from that region in the year. There were also strong performances from *Farxiga* and *Brilinta* each exceeding $1 billion of sales in the year.

Reconciliation of Reported Profit Before Tax to EBITDA

	2017 $m	2016 $m	Actual growth %	CER growth %
Reported Profit Before Tax	**2,227**	3,552	**(37)**	**(38)**
Net Finance Expense	**1,395**	1,317	**6**	**(4)**
Share of after tax losses of joint ventures and associates	**55**	33	**66**	**66**
Depreciation, Amortisation and Impairment	**3,036**	2,357	**29**	**29**
EBITDA	**6,713**	7,259	**(8)**	**(10)**

Growth Platforms

	2017 Product Sales $m	2016 Product Sales $m	Actual growth %	CER growth %
Emerging Markets	**6,149**	5,794	**6**	**8**
Respiratory	**4,706**	4,753	**(1)**	**(1)**
New CVMD[1]	**3,567**	3,266	**9**	**9**
Japan	**2,208**	2,184	**1**	**4**
New Oncology[2]	**1,313**	664	**98**	**98**
Total Growth Platform Product Sales[3]	**15,231**	14,491	**5**	**6**

[1] New Cardiovascular & Metabolic Diseases, incorporating *Brilinta* and Diabetes.
[2] New Oncology comprises *Lynparza*, *Iressa* (US), *Tagrisso*, *Imfinzi* and *Calquence*.
[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

	2017 $m	2016 $m
Externalisation Revenue – Initial		
Lynparza/selumetinib (MSD)	**997**	–
Zoladex (TerSera)	**250**	–
MEDI8897 (Sanofi)	**127**	–
Global non-US anaesthetics portfolio (Aspen)	**–**	520
Plendil (CMS)	**–**	298
Toprol-XL (Aralez)	**–**	175
tralokinumab (LEO Pharma)	**–**	115
Other	**118**	219
Total Initial Externalisation Revenue	**1,492**	1,327
Ongoing Externalisation Revenue		
Lynparza/selumetinib (MSD) – option exercised	**250**	–
Global non-US anaesthetics portfolio (Aspen) – milestone	**150**	–
brodalumab (Valeant) – milestone	**130**	–
AZD3293 (Lilly) – milestone	**50**	100
Royalties	**108**	119
Other	**133**	137
Total Ongoing Externalisation Revenue	**821**	356
Total Externalisation Revenue	**2,313**	1,683

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 5% (CER: 6%), representing 68% 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 6% compared to 2016 (CER: 8%). Product Sales in China increased by 12% in 2017 (CER: 15%), representing 48% of Emerging Markets Product Sales in the year.

Product Sales of our Respiratory medicines declined by 1% (CER: 1%), reflecting pricing pressure in the US for *Symbicort.*

New CVMD grew by 9% with revenue of $3,567 million (2016: $3,266 million). Within New CVMD, sales of *Brilinta* in the year were $1,079 million, an increase of 29%. *Brilinta* sales in the US were up 46% to $509 million, as it remained the branded oral anti-platelet market leader.

Our Diabetes Product Sales were 3% higher than in 2016 (CER: 2%), driven primarily by growth of 29% (CER: 28%) on *Farxiga* with global sales of $1,074 million as it continued to be our largest-selling Diabetes medicine and SGLT2-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 increased by 1% (CER: 4%) underpinned by the growth of *Tagrisso* and *Forxiga*, partly mitigated by the impact of the entry of generic competition to *Crestor* in the year.

Product Sales of New Oncology medicines were up to $1,313 million in 2017 (2016: $664 million), $955 million of which came from *Tagrisso* (2016: $423 million) which continues to be our leading medicine for the treatment of lung cancer and received regulatory approval in more than 60 countries by the end of 2017.

Externalisation Revenue

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

- 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, 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. Subsequent to deal completion, MSD exercised the first licence option resulting in additional Externalisation Revenue of $250 million.
- 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.
- 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 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 June 2016, AstraZeneca entered into a licence agreement with LEO Pharma for the global development and commercialisation of tralokinumab in dermatology indications. AstraZeneca will manufacture and supply tralokinumab to LEO Pharma. LEO Pharma has been granted an exclusive licence to the global dermatology rights to tralokinumab, which has completed Phase IIb for atopic dermatitis. LEO Pharma paid an upfront payment of $115 million for the exclusive licence. LEO Pharma will also pay up to $1 billion in commercially-related milestones and up to mid-teen tiered percentage royalties on Product Sales.
- 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. Further details of the new arrangement are included on page 72.

- 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.
- In April 2015, the Group signed a Collaboration and License Agreement with Celgene, a global leader in haematological cancers, to develop and commercialise *Imfinzi* across a range of blood cancers including non-hodgkin's lymphoma, myelodysplastic syndromes and multiple myeloma. Under the terms of the agreement, Celgene made an upfront payment of $450 million to AstraZeneca in relation to *Imfinzi*, which was recorded within Externalisation Revenue in 2015. Celgene lead on development across all clinical trials within the collaboration and took on all R&D costs until the end of 2015, after which they now take on 75% of these costs. Celgene will also be responsible for global commercialisation of approved treatments. AstraZeneca will manufacture and record all sales of *Imfinzi* and will pay a royalty to Celgene on worldwide sales in haematological indications. The royalty rate will start at 70% and will decrease to approximately half of the sales of *Imfinzi* in haematological indications over a period of four years.
- In March 2015, AstraZeneca announced a co-commercialisation agreement with Daiichi Sankyo, for *Movantik* in the US. The drug was launched on 31 March 2015. Under the agreement, Daiichi Sankyo paid a $200 million upfront fee, recognised as Externalisation Revenue in 2015, and will pay sales-related payments of up to $625 million. AstraZeneca will be responsible for manufacturing, will record all sales and will make sales-related commission payments to Daiichi Sankyo. Both companies will be jointly responsible for commercial activities.

As detailed in Risk from page 210, 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 4% to $18,147 million. Core gross profit declined by 3% to $18,477 million. Externalisation Revenue of $2,313 million included $1,247 million received as part of the *Lynparza* and selumetinib collaboration with MSD. This was outweighed by the adverse impact of product mix, the increase of the manufacturing capacity for new medicines and the inclusion of the profit share on the aforementioned collaboration.

Reported R&D expense in the year declined by 2% (CER: 1%) to $5,757 million, as the Group continued to focus on resource prioritisation and cost discipline. Core R&D costs declined by 4% (CER: 3%) to $5,412 million. The movement compared to prior year was in line with indications made in 2017.

Reported SG&A costs increased by 9% (CER: 10%) to $10,233 million. The large movement in Reported SG&A is influenced by a favourable $999 million fair value adjustment recorded in 2016 related to the acquisition of BMS's share of the Global Diabetes Alliance, based on revised milestone probabilities, and revenue and royalty forecasts. Core SG&A decreased by 4% (CER: 3%) to $7,853 million. The decrease in Core SG&A reflects the indications made in 2017 and incorporated the necessity to invest in the launch programme, given the productivity and success of the pipeline.

Reported other operating income and expense in the year was up 11% at $1,830 million which includes $555 million from the sale of the remaining rights to the anaesthetics portfolio to Aspen, $301 million from the sale of rights to *Seloken* in Europe to Recordati, milestone receipts of $175 million from the disposal of *Zavicefta* to Pfizer, $165 million on the sale of the global rights to *Zomig* outside Japan to Grünenthal and $161 million of gains from the sale of short-term investments. As these elements of our income arose from product divestments, where we no longer retain a significant element of continued interest, in accordance with our Externalisation Revenue definition and the requirements of IFRS, proceeds from these divestments are recorded as other operating income.

Reported operating profit declined by 25% (CER: 28%) to $3,677 million in the year. The Reported operating margin declined by 4.9 percentage points (CER: 5.8 percentage points) to 16.4% of Total Revenue. The decrease was primarily driven by the movement in Reported SG&A costs as detailed above.

Core operating profit increased by 2% (stable at CER) in the year to $6,855 million. The Core operating profit margin increased by 1% to 31% of Total Revenue.

Reported net finance expense increased by 6% (CER: decreased 4%) in the year to $1,395 million (2016: $1,317 million) primarily reflecting a foreign exchange impact relating to the classification of certain non-structural intra-group loans. Reported net finance expense declined by 4% at CER, reflecting reduced levels of discount unwind on acquisition-related liabilities resulting from the diabetes alliance with BMS. Excluding the discount unwind on acquisition-related liabilities and adverse foreign exchange impact, Core net finance expense declined by 2% (CER: 4%) in the year to $650 million.

Profit before tax amounted to $2,227 million in 2017 (2016: $3,552 million). Pre-tax adjustments to arrive at Core profit before tax amounted to $3,923 million in 2017 (2016: $2,475 million), comprising $3,178 million adjustments to operating profit (2016: $1,819 million) and $745 million to net finance expense (2016: $656 million). EBITDA declined by 8% (CER: 10%) to $6,713 million.

Excluded from Core results were:

- Restructuring costs totalling $807 million (2016: $1,107 million), incurred as we continued to enhance productivity through the implementation of our restructuring initiatives.
- Amortisation totalling $1,319 million (2016: $1,247 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 155.

- Intangible impairment charges of $488 million (2016: $44 million) excluding those related to IT. Further details relating to intangible asset impairments are included in Note 9 to the Financial Statements from page 155.
- Costs associated with our acquisition of BMS's share of our Global Diabetes Alliance in February 2014 amounting to $954 million (2016: credit of $238 million). As noted above, the 2016 net credit included a contingent consideration fair value decrease of $999 million reflecting lower than expected Diabetes portfolio revenues. The 2017 costs of $954 million included $426 million of amortisation charges, $313 million of interest charges relating to a discount unwind on contingent consideration arising on the acquisition and a fair value increase of $208 million.
- Net legal provisions and other charges of $355 million (2016: $315 million) include $305 million (2016: $267 million) discount unwind charges offset by $309 million (2016: $199 million) of net fair value adjustments relating to contingent consideration arising on our other business combinations as detailed in Note 18 to the Financial Statements from page 163. The net charge of $355 million also included legal charges relating to the Texas Attorney General and *Pulmicort Respules* proceedings. Further details of legal proceedings in which we are currently involved are contained within Note 28 to the Financial Statements from page 182.
- Also included in other charges are foreign exchange gains and losses of $125 million relating to the classification of certain non-structural intra-group loans and a one-off adjustment of $617 million reflecting adjustments to deferred tax in line with the recently reduced US federal income tax rate.

Reported EPS of $2.37 in the year represented a decline of 14% (CER: 15%). The performance was driven by a decline in Total Revenue and increased Reported SG&A costs, partly offset by a net tax benefit, continued progress on Reported R&D cost control and an increase in other operating income and expense. Core EPS in the year declined by 1% (CER: 2%) to $4.28.

The Reported tax credit for the year of $641 million (2016: charge of $146 million) consisted of a current tax charge of $378 million (2016: $370 million) and a credit arising from movements on deferred tax of $1,019 million (2016: $224 million). The current tax charge included a prior period current tax credit of $287 million (2016: $14 million).

The Reported tax rate for the year was (29)% (2016: 4%).

The Reported tax rate of (29)% in the year benefited from a favourable net adjustment of $617 million to deferred tax, reflecting the recently reduced US federal income tax rate and non-taxable remeasurements of acquisition-related liabilities. Additionally, there was a $472 million benefit to the Reported tax rate reflecting the favourable impact of UK Patent box profits, the recognition of previously unrecognised tax losses, and reductions in net tax provisions and provision to return adjustments arising on the expiry of statute of limitations or favourable progress of discussion with tax authorities. Absent these benefits, the Reported tax rate for the year would have been 22%.

The Core tax rate for the year was 14%. Excluding the $472 million benefit above, the Core tax rate would have been 22%.

The tax paid for the year was $454 million (20% of Reported profit before tax). The cash tax paid for the year was $1,095 million higher than the tax charge for the year as a result of certain items with no cash impact including $617 million deferred tax credit reflecting the reduction in US federal income tax rate, $402 million of other deferred tax credits, other net reductions 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.

Total comprehensive income increased by $1,879 million from the prior year, resulting in a net income of $3,507 million for 2017. The decrease in profit for the year of $538 million was more than offset by an increase of $2,417 million in other comprehensive income. The increase in other comprehensive income arose principally from foreign exchange gains arising on consolidation of $536 million (2016: losses of $1,050 million) and foreign exchange gains arising on designating borrowings in net investment hedges of $505 million (2016: loss of $591 million), partially offset by losses recorded on the remeasurement of our defined benefit pension liability of $242 million (2016: loss of $575 million), due to a decrease in the discount rate applied to our pension liabilities reflecting an increase in corporate bond yields and other reference interest rate instruments.

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 remains at $1.5 billion but this will be incurred by 2019, with benefits expected to be $1.3 billion in 2018 and $1.4 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 2017, 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 2020 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 2018. By the end of 2017, these programmes had incurred costs of $225 million with total expected costs rising to $300 million.

The aggregate restructuring charge incurred in 2017 across all our restructuring programmes was $807 million (2016: $1,107 million), including the ongoing integration of BMS 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 planning

Following the UK referendum outcome of a decision in June 2016 for the UK to leave the EU, the progress of current negotiations between the UK Government and the EU 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 its regulatory frameworks.

In response to this, the Company has taken the decision to implement certain actions to mitigate potential risk of disruption to the supply of medicines 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 upgrades. 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. However, until the Brexit negotiation process is completed, it is difficult to anticipate the overall potential impact on AstraZeneca's operations and hence the final expected costs to be incurred.

Cash flow and liquidity – for the year ended 31 December 2017

Summary cash flows

	2017 $m	2016 $m	2015 $m
Net debt brought forward at 1 January	**(10,657)**	(7,762)	(3,223)
Profit before tax	**2,227**	3,552	3,069
Sum of changes in interest, depreciation, amortisation, impairment, and share of after tax losses on joint ventures and associates	**4,486**	3,707	3,897
Movement in working capital and short-term provisions	**(50)**	926	(49)
Tax paid	**(454)**	(412)	(1,354)
Interest paid	**(698)**	(677)	(496)
Gains on disposal of intangible assets	**(1,518)**	(1,301)	(961)
Fair value movements on contingent consideration arising from business combinations	**109**	(1,158)	(432)
Non-cash and other movements	**(524)**	(492)	(350)
Net cash available from operating activities	**3,578**	4,145	3,324
Disposal/(purchase) of intangibles (net)	**1,082**	559	(330)
Non-contingent payments on business combinations	**(1,450)**	(2,564)	(2,446)
Payment of contingent consideration from business combinations	**(434)**	(293)	(579)
Other capital expenditure (net)	**(1,319)**	(1,405)	(1,326)
Investments	**(2,121)**	(3,703)	(4,681)
Dividends	**(3,519)**	(3,561)	(3,486)
Share proceeds	**43**	47	43
Distributions	**(3,476)**	(3,514)	(3,443)
Other movements	**(3)**	177	261
Net debt carried forward at 31 December	**(12,679)**	(10,657)	(7,762)

Net debt reconciliation

	2017 $m	2016 $m	2015 $m
Cash and cash equivalents	**3,324**	5,018	6,240
Other investments[1]	**1,300**	898	613
Net derivative financial instruments	**504**	235	438
Cash, investments and derivatives	**5,128**	6,151	7,291
Overdraft and short-term borrowings	**(845)**	(451)	(849)
Finance leases	**(5)**	(93)	(95)
Current instalments of loans	**(1,397)**	(1,769)	–
Loans due after one year	**(15,560)**	(14,495)	(14,109)
Loans and borrowings	**(17,807)**	(16,808)	(15,053)
Net debt	**(12,679)**	(10,657)	(7,762)

[1] Other investments in 2017 includes $70 million (2016: $14 million) of non-current Treasury investments.

Bonds issued in 2017 and 2016

	Repayment dates	Face value of bond $m	Net book value of bond at 31 December 2017 $m
Bonds issued in 2017:			
2.375% USD bond	2022	1,000	**992**
Floating rate USD notes	2022	250	**249**
3.125% USD bond	2027	750	**742**
Total 2017		2,000	**1,983**
Bonds issued in 2016:			
0.25% Euro bond	2021	566	**594**
0.75% Euro bond	2024	1,016	**1,067**
1.25% Euro bond	2028	897	**941**
Total 2016		2,479	**2,602**

Net cash generated from operating activities was $3,578 million in the year ended 31 December 2017, compared with $4,145 million in 2016. The 2016 operating cash inflows benefited from a $926 million improvement in working capital and short-term provisions that reflected improved cash management performance compared to prior years.

Net investment cash outflows were $2,121 million (2016: $3,703 million).

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. 2016 cash outflows included $2,383 million relating to the majority investment in Acerta Pharma. Investment cash outflows also include $434 million (2016: $293 million) of payments against contingent consideration arising on business combinations and $294 million (2016: $868 million) for the purchase of other intangible assets. The comparative period in 2016 included $561 million on the purchase of respiratory assets from Takeda.

Investment cash inflows include $1,376 million (2016: $1,427 million) from the sale of intangible assets, including $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. The comparative period in 2016 included $552 million for the disposal of our late-stage antibiotics assets, $330 million for the sale of our rights to *Rhinocort Aqua* outside the US and $250 million on the out-licence of MEDI-2070.

Net cash distributions to shareholders were $3,476 million (2016: $3,514 million), including dividends of $3,519 million (2016: $3,561 million). Proceeds from the issue of shares on the exercise of share options amounted to $43 million (2016: $47 million).

In June 2017, we issued $2.0 billion of bonds in the dollar debt capital markets with maturities of 5 and 10 years. We also repaid a $1.75 billion 5.9% bond, which matured in September 2017.

At 31 December 2017, outstanding gross debt (interest-bearing loans and borrowings) was $17,807 million (2016: $16,808 million). Of the gross debt outstanding at 31 December 2017, $2,247 million is due within one year (2016: $2,307 million). Net debt at 31 December 2017 was $12,679 million, compared to $10,657 million at the beginning of the year, as a result of the cash flows as described above.

Financial position – 31 December 2017

All data in this section is on a Reported basis.

Summary statement of financial position

	2017 $m	Movement $m	2016 $m	Movement $m	2015 $m
Property, plant and equipment	**7,615**	**767**	6,848	435	6,413
Goodwill and intangible assets	**38,013**	**(1,231)**	39,244	4,798	34,446
Inventories	**3,035**	**701**	2,334	191	2,143
Trade and other receivables	**5,856**	**382**	5,474	(2,055)	7,529
Trade and other payables	**(19,481)**	**493**	(19,974)	(854)	(19,120)
Provisions	**(1,468)**	**(50)**	(1,418)	(176)	(1,242)
Net income tax payable	**(826)**	**128**	(954)	142	(1,096)
Net deferred tax liabilities	**(1,806)**	**1,048**	(2,854)	(1,483)	(1,371)
Retirement benefit obligations	**(2,583)**	**(397)**	(2,186)	(212)	(1,974)
Non-current other investments (excluding Treasury investments of $70m in 2017 (2016: $14m))	**863**	**150**	713	255	458
Investment in associates and joint ventures	**103**	**4**	99	14	85
Net debt	**(12,679)**	**(2,022)**	(10,657)	(2,895)	(7,762)
Net assets	**16,642**	**(27)**	16,669	(1,840)	18,509

Business combinations

In 2016, we acquired a majority equity stake in Acerta Pharma. In 2015, we completed the acquisition of ZS Pharma. No business acquisitions were made in 2017. Further details of our business combinations are contained in Note 25 to the Financial Statements from page 173.

Property, plant and equipment

Property, plant and equipment increased by $767 million to $7,615 million. Additions of $1,311 million (2016: $1,449 million) were offset by depreciation of $624 million (2016: $609 million), impairments of $78 million (2016: $2 million), exchange adjustments of $352 million (2016: $329 million) and disposals and other movements of $194 million (2016: $74 million).

Goodwill and intangible assets

Our goodwill of $11,825 million (2016: $11,658 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 $26,188 million at 31 December 2017 (2016: $27,586 million). Intangible asset additions were $441 million in 2017 (2016: $8,205 million). 2016 additions included product rights acquired from the majority equity investment of Acerta Pharma of $7,307 million. Amortisation in the year was $1,829 million (2016: $1,701 million). Impairment charges in the year amounted to $491 million (2016: $45 million) including impairments on launched products *Byetta, FluMist* and *Movantik* as a consequence of revised market share assumptions and, for *FluMist,* the expected timing of renewed recommendation in the US market. Disposals of intangible assets totalled $307 million in the year (2016: $331 million).

Further details of our additions to intangible assets, and impairments recorded, are included in Note 9 to the Financial Statements from page 155.

Receivables, payables and provisions

Trade and other receivables increased by $382 million with trade receivables increasing by $219 million to $2,802 million principally as a result of higher invoiced sales in China. Non-current other receivables decreased by $54 million to $847 million.

Trade and other payables decreased by $493 million in 2017 to $19,481 million. The movement included a $1,450 million payment of deferred consideration on the majority investment in Acerta Pharma, partially offset by amounts deferred from the upfront receipt of $1.6 billion from MSD on the *Lynparza* and selumetinib collaboration to reflect future commitments and the effects of foreign exchange retranslation.

The increase in provisions of $50 million in 2017 included a $281 million increase to charges on legal provisions and reductions to severance provisions of $129 million. Further details of the charges made against provisions are contained in Notes 19 and 28 to the Financial Statements on page 164, and 182 to 188, respectively.

Contingent consideration

The majority of our business acquisitions in recent years 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.

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 $0.9 billion for future development, launch, and sales-related milestones and various other sales-related milestone payments, and sales-related royalty payments as detailed in Note 18 to the Financial Statements on page 163. 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'.

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 2017, we recorded an interest charge of $402 million on the discount unwind on contingent consideration arising on our business combinations, and a net fair value increase on contingent consideration of $109 million (which resulted in a charge to our income statement for the same amount) driven, principally, by revised forecasts for revenues for our Diabetes franchise. At 31 December 2017, our contingent consideration liability was $5,534 million (2016: $5,457 million) with the movements of the balance detailed in the table below.

Tax payable and receivable

Net income tax payable has decreased by $128 million to $826 million, principally due to the revision to the presentation of interest on tax contingencies, as described in the Group Accounting Policies section of the Financial Statements on page 139. The tax receivable balance of $524 million (2016: $426 million) comprises tax owing to us from certain governments expected to be received on settlements of transfer pricing audits and disputes of $275 million (see Note 28 to the Financial Statements from page 182) and cash tax timing differences of $249 million.

Net deferred tax liabilities decreased by $1,048 million in the year reflecting adjustments to deferred taxes in line with the recently reduced 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 148.

Contingent consideration arising on business combinations

	2017			2016		
	Acquisition of BMS's share of Diabetes Alliance $m	**Other business combinations $m**	**Total 2017 $m**	Acquisition of BMS's share of Diabetes Alliance $m	Other business combinations $m	Total 2016 $m
At 1 January	**4,240**	**1,217**	**5,457**	5,092	1,319	6,411
Settlements	**(284)**	**(150)**	**(434)**	(242)	(51)	(293)
Fair value adjustments	**208**	**(99)**	**109**	(999)	(159)	(1,158)
Discount unwind	**313**	**89**	**402**	389	108	497
At 31 December	**4,477**	**1,057**	**5,534**	4,240	1,217	5,457

Payments due by period

	Less than 1 year $m	**1-3 years $m**	**3-5 years $m**	**Over 5 years $m**	**2017 Total $m**	2016 Total $m
Bank loans and other borrowings[1]	**2,844**	**3,708**	**3,752**	**15,575**	**25,879**	24,889
Finance leases	**5**	**–**	**–**	**–**	**5**	95
Operating leases	**112**	**178**	**126**	**107**	**523**	441
Contracted capital expenditure	**570**	**–**	**–**	**–**	**570**	629
Total	**3,531**	**3,886**	**3,878**	**15,682**	**26,977**	26,054

[1] Bank loans and other borrowings include interest charges payable in the period, as detailed in Note 26 to the Financial Statements on page 175.

Retirement benefit obligations

Approximately 92% of our total retirement benefit obligations (or around 79% of net obligations) are concentrated in the UK, the US and Sweden. Net retirement benefit obligations increased by $397 million in 2017 (2016: increase of $212 million) to $2,583 million. Net re-measurement adjustments of $242 million primarily in the UK, Sweden and Germany arose principally from reductions in discount rate assumptions driven by falls in long-term bond yields. A negative $219 million impact of exchange rate movements also arose in the year as the US dollar weakened against pound sterling, euro and Swedish krona increasing liability obligations in US dollar terms. These adverse movements were mitigated by employer contributions to the pension scheme of $157 million. Benefits paid amounted to $581 million (2016: $500 million).

Over the course of 2017, the UK Actuarial Valuation (as at 31 March 2016) was finalised with the UK Trustee and was accepted by the pensions regulator. In recent years, we have undertaken several initiatives to reduce our net pension obligation exposure. For the UK defined benefit pension scheme, which is our largest defined benefit scheme, these initiatives have included agreeing funding principles for cash contributions to be paid into the UK pension scheme to target a level of assets in excess of the current expected cost of providing benefits, and, in 2010, amendments to the scheme to freeze pensionable pay at 30 June 2010 levels. Furthermore, liability management exercises have been carried out including the completion of a Pensions Increase Exchange exercise in 2017 and other exercises are planned.

In the US we realised a credit of $92 million from the closure of both the qualified and non-qualified US pension plans to future accrual in December 2017 and from a change in eligibility criteria for the US post-retirement welfare plan. The legacy defined benefit pension plan participants are eligible for defined contribution benefits from January 2018.

From January 2017, for the defined benefit plans in the UK, the US, Sweden and Germany, the Group moved to a multiple discount rate approach. This has resulted in separate discount rates being utilised to value defined benefit obligations, service cost and interest cost. The change has impacted on the measurement of the service and interest cost items in 2017.

Further details of our pension schemes are included in Note 20 to the Financial Statements from page 164.

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 139. We also have taxation contingencies. These are described in the Taxation section in the Critical accounting policies and estimates section on page 82 and in Note 28 to the Financial Statements from page 182.

Off-balance sheet transactions and commitments

We have no off-balance sheet arrangements and our derivative activities are non-speculative. The table on page 76 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 28 to the Financial Statements on page 182. As detailed in Note 28, 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 250 major or strategically important business development transactions over the past three years, two of which were accounted for as business acquisitions under IFRS 3 'Business Combinations', being the majority investment in Acerta Pharma in 2016 and the acquisition of ZS Pharma in 2015.

In addition to the business development transactions detailed under Externalisation Revenue from page 71 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 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 CVMD and Oncology. Utilising both companies' expertise, significant progress has also been made to 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 significance determination. 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

Dividends for 2017

	$	Pence	SEK	Payment date
First interim dividend	0.90	68.9	7.40	11 September 2017
Second interim dividend	1.90	133.6	14.97	19 March 2018
Total	2.80	202.5	22.37	

Capitalisation

The total number of shares in issue at 31 December 2017 was 1,266 million (2016: 1,265 million). 1.0 million Ordinary Shares were issued upon share option exercises for a total of $43 million. Shareholders' equity increased by $106 million to $14,960 million at the year end. Non-controlling interests were $1,682 million (2016: $1,815 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 (133.6 pence, 14.97 SEK) to be paid on 19 March 2018. This brings the full-year dividend to $2.80 (202.5 pence, 22.37 SEK). Against Core earnings per share the Group had a dividend cover ratio of 1.5 in 2017 (2016:1.5).

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 October 2012.

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.

As we experience a period of patent expiries:

- 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 2018: additional commentary

In 2018, the sum of Externalisation Revenue and Other operating income and expense is anticipated to reduce versus 2017. Core R&D costs in 2018 are expected to be in the range of a low single-digit percentage decline to stable. This expectation includes the favourable impact of development costs from the MSD collaboration. The Group maintains its focus on reducing operational and infrastructure costs. Total Core SG&A costs in 2018, however, are expected to increase by a low to mid single-digit percentage, wholly reflecting targeted support for launches and potential launches, including *Fasenra* in severe, uncontrolled asthma and *Imfinzi* in locally, unresectable lung cancer. A Core tax rate of 16 to 20% is expected for 2018.

These targets represent management's current estimates and are subject to change. Please see the Cautionary statement regarding forward-looking statements from page 240.

Financial risk management

Financial risk management policies

Insurance

Our risk management processes are described in Risk Overview from page 63. 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. Risks to which we pay particular attention include business interruption, directors' and officers' liability, and property damage. 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 and cash resources.

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.

Our capital and risk management objectives and policies are described in further detail in Note 26 to the Financial Statements from page 175 and in Risk Overview from page 63. Sensitivity analysis of the Group's exposure to exchange rate and interest rate movements is also detailed in Note 26 to the Financial Statements from page 175.

Critical accounting policies and estimates

Our Financial Statements are prepared in accordance with IFRSs 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 139. 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
- business combinations and contingent consideration
- impairment testing of goodwill and intangible assets
- litigation
- post-retirement 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 – a particular feature in the US. 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. Revenue is recognised when the significant risks and rewards of ownership have 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. 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 $8,468 million in 2017 (2016: $12,275 million) with the decrease driven by an overall reduction 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.

Gross to net Product Sales
US pharmaceuticals

	2017 $m	2016 $m	2015 $m
Gross Product Sales	**14,637**	19,640	23,641
Chargebacks	**(2,299)**	(3,449)	(2,985)
Regulatory – Medicaid and state programmes	**(1,462)**	(1,903)	(1,714)
Contractual – Managed-care and Medicare	**(3,598)**	(5,219)	(7,543)
Cash and other discounts	**(30)**	(358)	(472)
Customer returns	**(37)**	(130)	(333)
US Branded Pharmaceutical Fee	**3**	(145)	(174)
Other	**(1,045)**	(1,071)	(946)
Net Product Sales	**6,169**	7,365	9,474

Movement in provisions
US pharmaceuticals

	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

	Brought forward at 1 January 2015 $m	Provision for current year $m	Adjustment in respect of prior years $m	Returns and payments $m	Carried forward at 31 December 2015 $m
Chargebacks	457	3,019	(34)	(3,118)	324
Regulatory – Medicaid and state programmes	707	1,809	(95)	(1,644)	777
Contractual – Managed-care and Medicare	2,366	7,666	(123)	(7,703)	2,206
Cash and other discounts	33	464	8	(461)	44
Customer returns	318	349	(16)	(184)	467
US Branded Pharmaceutical Fee	245	206	(32)	(155)	264
Other	163	947	(1)	(923)	186
Total	4,289	14,460	(293)	(14,188)	4,268

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 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 pre-determined percentage.

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 can be measured reliably. 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 2017 net US pharmaceuticals revenue by 8.9% (2016: 6.0%; 2015: 3.1%). However, taking into account the adjustments affecting both the current and the prior year, 2016 revenue would have been increased by 1.4% and 2015 revenue would have been increased by 1.6%, 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 14, 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. The contracts 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 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 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 so cannot be anticipated.

Research and development

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. 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 25 to the Financial Statements from page 173.

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 recent 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 18 to the Financial Statements on page 163.

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.

Impairment testing of goodwill and intangible assets

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 154. The Group, including acquisitions, is considered a single operating segment for impairment purposes. No impairment of goodwill was identified.

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 on a fair value less cost to sell basis using discounted cash flow calculations. 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.

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 25 to the Financial Statements from page 173, 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 2017 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 155, including details of the estimates and assumptions we make in impairment testing of intangible assets.

Litigation

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 28 to the Financial Statements from page 182.

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.

Post-retirement benefits

We offer post-retirement benefit plans which cover many of our employees around the world. In keeping with local terms and conditions, most of these plans are defined contribution in nature, where the resulting income statement charge is fixed at a set level or is a set percentage of employees' pay. However, several plans, mainly in the UK (which has by far the largest single scheme), the US and Sweden are defined benefit plans where benefits are based on employees' length of service and final salary (typically averaged over one, three or five years). The UK and US defined benefit schemes were closed to new entrants in 2000. New employees in these countries are offered defined contribution schemes.

In applying IAS 19 'Employee Benefits', we recognise all actuarial gains and losses immediately through Other Comprehensive Income. 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 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 price inflation, and future salary and pension increases.

Further details of our accounting for post-retirement benefit plans are included in Note 28 to the Financial Statements from page 182.

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 to be probable, 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 28 to the Financial Statements from page 182.

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.

The Directors have concluded that our internal control over financial reporting is effective at 31 December 2017 and the assessment is set out in the Directors' Annual Report on Internal Controls over Financial Reporting on page 128. PwC has audited the effectiveness of our internal control over financial reporting at 31 December 2017 and their report is unqualified.

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
- Marketplace
- Business model and life-cycle of a medicine
- Strategy and 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
2 February 2018