

What science can do

AstraZeneca Annual Report and Form 20-F Information 2016



We are a global, science-led biopharmaceutical business and in this Annual Report we report on the progress we made in 2016 in pushing the boundaries of science to deliver life-changing medicines.

AstraZeneca.
What science can do.

- > From page 4, **Pascal Soriot**, our Chief Executive Officer, reviews the progress we made during the year in delivering our strategy.
- > From page 8, we outline our strategy, our business model and the marketplace in which we operate, our measures of success and the risks to delivering our strategy.
- > From page 23, we review our therapy areas, business and resources.
- > From page 62, our Chief Financial Officer, **Marc Dunoyer**, reviews our financial performance.
- > From page 82, **Leif Johansson**, our Chairman, reviews how our governance and approach to remuneration support delivery of our strategy.

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 64.

Definitions

The Glossary and the Market definitions table from page 239 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 243.

Directors' Report

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

- > Chief Executive Officer's Review
- > Therapy Area Review
- > Business Review
- > Resources Review: including Employees
- > 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
- > Corporate 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
- > Chief Executive Officer's Review
- > Strategy: including Risk overview
- > Therapy Area Review
- > Business Review
- > Resources Review
- > Financial Review

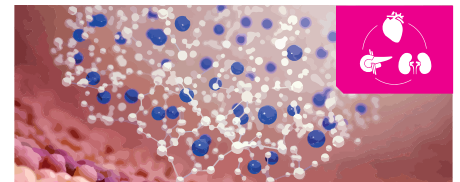
Learn about our main therapy areas:



Oncology

Our ambition is to eliminate cancer as a cause of death through scientific discovery and collaborations.

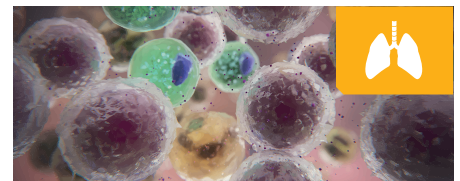
See page 25



Cardiovascular & Metabolic Disease

We address multiple risk factors to reduce cardiovascular morbidity, mortality and organ damage.

See page 30



Respiratory

We aim to transform the treatment of respiratory disease with our growing portfolio of medicines.

See page 35

Front cover

Treatment for hyperkalaemia

Current treatments for hyperkalaemia, a potentially life-threatening condition associated with chronic kidney disease and chronic heart failure, are poorly tolerated by patients. AstraZeneca is developing a treatment which traps potassium in the gut and removes it from the body.

Financial highlights

Total Revenue*

down 7% to \$23,002 million at actual rate of exchange (down 5% at CER)

2016	\$23,002m
2015	\$24,708m
2014	\$26,547m

\$23bn

Reported operating profit

up 19% at actual rate of exchange to \$4,902 million (up 9% at CER)

2016	\$4,902m
2015	\$4,114m
2014	\$2,137m

\$4.9bn

Reported EPS

for the full year up 24% at actual rate of exchange to \$2.77 (up 9% at CER)

2016	\$2.77
2015	\$2.23
2014	\$0.98

\$2.77

 [Financial Review from page 62](#)

* As detailed on page 142, Total Revenue consists of Product Sales and Externalisation Revenue.

Net cash flow from operating activities

up 25% at actual rate of exchange to \$4,145 million

2016	\$4,145m
2015	\$3,324m
2014	\$7,058m

\$4.1bn

Core operating profit

down 3% at actual rate of exchange to \$6,721 million (down 7% at CER)

2016	\$6,721m
2015	\$6,902m
2014	\$6,937m


\$6.7bn

Core EPS

for the full year up 1% at actual rate of exchange to \$4.31 (down 5% at CER)

2016	\$4.31
2015	\$4.26
2014	\$4.28

\$4.31

 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/annualreport2016

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AstraZeneca at a glance

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

Our strategic priorities reflect how we are working to achieve our Purpose of pushing the boundaries of science to deliver life-changing medicines:



1 Achieve scientific leadership



2 Return to growth



3 Be a great place to work

A science-led, innovation strategy

Distinctive R&D capabilities: small molecule and biologic medicine, including immunotherapies and protein engineering, as well as devices, biomarkers and translational science

Strategy and key performance indicators from page 16

12 new molecular entities (NMEs) in Phase III/pivotal Phase II or under regulatory review

12

2016		12
2015		15
2014		13
2013		11

Broad R&D platform in three main therapy areas

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 our combination-focused pipeline that exploits the power of four scientific platforms

Cardiovascular & Metabolic Disease

> We push the boundaries of science to create life-changing medicines for patients that reduce morbidity, mortality and organ damage by addressing multiple risk factors

Respiratory

> We aim to transform the treatment of respiratory disease with our growing portfolio of inhaled and biologic medicines along with scientific research targeting disease modification

Portfolio of specialty and primary care products

Oncology	Cardiovascular & Metabolic Disease	Respiratory	Other Disease Areas
<p>\$3,383m Product Sales</p> <p>2015: \$2,825m 2014: \$3,027m</p>	<p>\$8,116m Product Sales</p> <p>2015: \$9,489m 2014: \$9,802m</p>	<p>\$4,753m Product Sales</p> <p>2015: \$4,987m 2014: \$5,063m</p>	<p>\$5,067m Product Sales</p> <p>2015: \$6,340m 2014: \$8,203m</p>
<p>> Oncology sales represented 16% of Total Product Sales</p> <p>> <i>Lynparza</i> (sales of \$218 million) available in 31 countries by end 2016</p> <p>> <i>Iressa</i> sales of \$513 million, down 6% (5% at CER), as we prioritised <i>Tagrisso</i></p>	<p>> CVMD sales represented 38% of Total Product Sales</p> <p>> Sales of <i>Onglyza</i> in the US declined 10% to \$376 million, as we prioritised <i>Farxiga</i></p> <p>> In the US, <i>Crestor</i> sales declined 57% to \$1,223 million, reflecting entry of generic <i>Crestor</i></p>	<p>> Respiratory sales represented 22% of Total Product Sales</p> <p>> <i>Pulmicort</i> sales of \$1,061 million, up 5% (8% at CER)</p> <p>> <i>Bevespi Aerosphere</i> inhalation aerosol launched in the US in January 2017</p>	<p>> Other sales represented 24% of Total Product Sales</p> <p>> <i>Nexium</i> sales of \$2,032 million, down 19% (18% at CER) and <i>Seroquel XR</i> sales of \$735 million, down 28% (27% at CER) following loss of exclusivity</p>

Therapy Area Review from page 23 and Achieve scientific leadership from page 45

Global commercial presence, with strength in Emerging Markets

US	Europe	Established Rest of World	Emerging Markets
\$7,365m Product Sales 2015: \$9,474m 2014: \$10,120m	\$5,064m Product Sales 2015: \$5,323m 2014: \$6,638m	\$3,096m Product Sales 2015: \$3,022m 2014: \$3,510m	\$5,794m Product Sales 2015: \$5,822m 2014: \$5,827m

Commercial Highlights: Growth Platforms grew by 4% (5% at CER) in 2016

- > Emerging Markets: Stable (growth of 6% at CER), supported by China, up 4% (10% at CER) to \$2,636 million
- > Diabetes: Growth of 9% (11% at CER), as *Farxiga/Forxiga* became our largest-selling Diabetes medicine
- > Japan: Sales up 8% (decline of 3% at CER), reflecting exchange rate impact and a biennial price reduction
- > *Brilinta/Brilique* sales grew by 36% (39% at CER)
- > Respiratory: A decline of 5% (3% at CER), reflecting US pricing pressure for *Symbicort*
- > New Oncology: Strong sales with *Tagrisso* delivering sales of \$423 million in its first full year

Return to growth from page 48

Our talented employees are committed to achieving our Purpose in a sustainable way and our Values foster a strong AstraZeneca culture

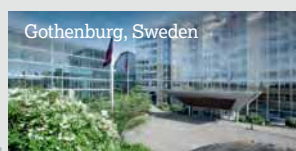
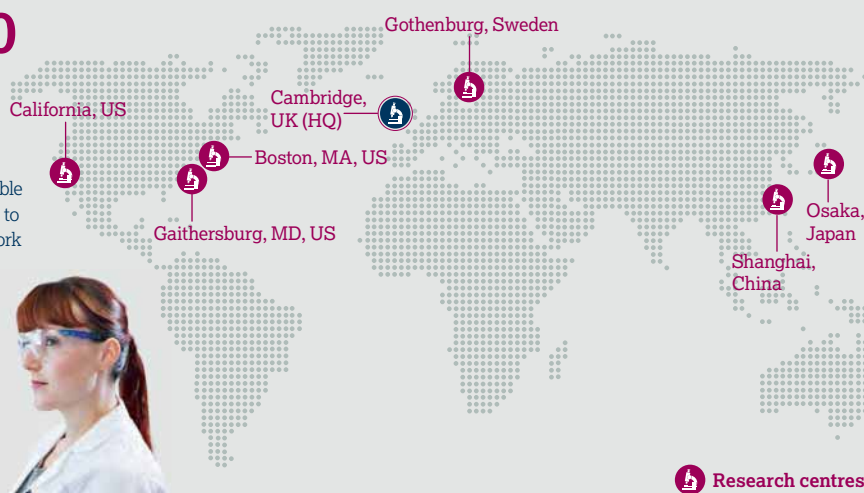
59,700

Employees

92%

of employees feel able to bring our Values to life in their daily work

Be a great place to work from page 52 and Employees from page 54



Our capital-allocation priorities strike a balance between the interests of the business, our financial creditors and shareholders, and support our progressive dividend policy

Distributions to shareholders \$m

	2016	2015	2014
Dividends	3,561	3,486	3,521
Proceeds from issue of shares	(47)	(43)	(279)
Total	3,514	3,443	3,242

Dividend per Ordinary Share \$

	2016	2015	2014
Dividend per Ordinary Share	2.80	2.80	2.80

Dividend per Ordinary Share for 2016

	\$	Pence	SEK	Payment date
First interim dividend	0.90	68.7	7.81	12 September 2016
Second interim dividend	1.90	150.2	16.57	20 March 2017
Total	2.80	218.9	24.38	

Financial Review from page 62

Chief Executive Officer's Review



While challenges still lie ahead, a new AstraZeneca is emerging and its shape is the result of the strategy we announced in March 2013. It is an AstraZeneca built on a pipeline-driven transformation and a focus on three main therapy areas.

A transitional phase

The first phase in our journey ended in 2015 and was focused on rebuilding our pipeline. 2016 was a crucial year in the second stage of our journey, as we manage a transitional period of patent expiries, drive our Growth Platforms and roll out our new medicines.

While now largely behind us, the impact of the loss of exclusivity on some of our most important medicines has been significant and will continue in 2017. Between 2011 and 2016, Product Sales in Established Markets of brands that have lost exclusivity, including *Crestor*, a statin, *Nexium*, a proton pump inhibitor and *Seroquel*, an anti-psychotic, have reduced from \$20 billion to \$6 billion. Unfavourable currency movements account for \$2 billion of this \$14 billion reduction. This decline represents a significant 'headwind', but we have made significant progress rebuilding our Company for the future and preparing for a new period of growth driven by our pipeline delivery.

In parallel to managing our legacy brands decline, we have launched a significant number of new medicines and increased revenues from our recently launched medicines. For example, *Tagrisso* was only launched in November 2015 and became our biggest lung cancer medicine during the

“2017 should be a turning point in our journey as we bring new medicines to patients across the globe.”

year with \$423 million in Product Sales in its first full year. In diabetes, *Farxiga/Forxiga* is a global leader in the SGLT2 class of diabetes treatments with a 35% volume share. Product Sales of *Brilinta/Brilique* reached \$839 million and in many countries it is the leading medicine for patients discharged with acute coronary syndrome.

While AstraZeneca benefits from realising the potential of the new medicines emerging from our pipeline, we never forget that the main beneficiaries of our life-changing medicines are patients. For instance, since its launch at the end of 2014, we have treated nearly 5,000 cancer patients with *Lynparza* and launched it in 31 countries with seven ongoing reviews.

Investing for the future

As we look ahead to 2017 and beyond, continued investment in our pipeline keeps us on track to return to sustainable growth in line with our targets. Examples of how we are investing for the future for the benefit of patients appear throughout this Annual Report. However, none is more significant than our investment in Cambridge, UK, as illustrated on page 7. Cambridge, along with Gaithersburg, MD, US and Gothenburg in Sweden, is one of our three strategic R&D centres and it also became our global corporate headquarters in May 2016. Our activities there demonstrate our focus on science, collaborative way of working and commitment to sustainability.

Achieve scientific leadership

The panel to the right provides an overview of how we performed against each of our three strategic priorities in 2016. At the heart of our plans to achieve scientific leadership is our focus on three therapy areas.

2016 Strategic priorities overview



Achieve scientific leadership

- > 11 approvals of NMEs or major LCM projects in major markets
 - Oncology: *Tagrisso* – lung cancer (EU, JP) and ctDNA blood test (US, JP)
 - CVMD: *Brilinta/Brilique* – post myocardial infarction (EU) and acute coronary syndromes and post myocardial infarction (JP); *Qtern* – Type 2 diabetes (EU)
 - Respiratory: *Bevespi Aerosphere* (PT003) – COPD (US)
 - Other: *Zurampic* – gout (EU); *Zavicefta* – serious infections (EU); Pandemic Live Attenuated Influenza Vaccine – pandemic influenza (EU)
- > 7 Phase III NME investment decisions
- > 14 NME or major LCM regulatory submissions in major markets: *Faslodex* – breast cancer (US, EU, JP); *Tagrisso* – lung cancer (CN); *Tagrisso* – lung cancer (AURA3 study for full approval) (US, EU); durvalumab – bladder cancer (US); DURATION-8 (exenatide+dapagliflozin) (EU); benralizumab – severe asthma (US, EU); lesinurad+allopurinol FDC – gout (US); three further submissions made await regulatory acceptance
- > 10 accelerated reviews included
 - Breakthrough Therapy Designation: durvalumab – bladder cancer (US)
 - Orphan Drug Designation: acalabrutinib – blood cancers (EU); selumetinib – thyroid cancer (US); inebilizumab (MEDI-551) – neuromyelitis optica (US)
 - Fast Track Designation: *Lynparza* – ovarian cancer (2nd line) (US), prostate cancer (2nd line) (US); MEDI8852 – hospitalised influenza (US); AZD3293 – Alzheimer's disease (US)
 - Priority Review Designation: *Tagrisso* (CN); durvalumab – bladder cancer (US)
- > 22 projects discontinued

Some of the most exciting science being undertaken at the moment is in Oncology as we explore the potential for novel therapies. As you can see, 2016 was a significant year for our Oncology team: we had four regional approvals, seven expedited reviews and seven regulatory submissions for our medicines. Looking ahead, we have the potential to deliver our third Oncology medicine in 2017 – halfway to our 2020 target in just four years.

Of course, pushing the boundaries of science means we sometimes encounter setbacks. Thus, in 2016, for example, we voluntarily withdrew the marketing authorisation application submitted to the EMA for cediranib in advanced ovarian cancer. However, there remain ongoing studies to investigate cediranib as a combination partner with *Lynparza* and other compounds. In addition, three of our Oncology trials failed to meet their primary endpoints. Another development showed our Values in action. In pushing the boundaries of science with clinical trials of durvalumab for head and neck squamous cell carcinoma, we observed bleeding events. Following the precautionary principle, we put patients first and placed a voluntary hold on the enrolment of new patients. This was followed by a partial clinical hold from the FDA. However, by following the science, we provided a comprehensive analysis about the events that had been observed and the FDA's hold was subsequently lifted.

In 2016, our Cardiovascular & Metabolic Disease team saw three approvals, four regulatory submissions and two *Brilinta* trials which failed to meet their primary endpoints. We received a complete response letter from the FDA for ZS-9 for the treatment of hyperkalaemia and subsequently made a resubmission. In diabetes, positive results from our DURATION-8 trials demonstrated the efficacy of *Farxiga* and *Bydureon* in combination for the treatment of Type 2 diabetes and should help us maximise the value of our Diabetes portfolio.

During the year, *Bevespi Aerosphere* was approved in the US and launched in early 2017. Our Respiratory team also made three regulatory submissions, including two in respect of benralizumab for treating severe, uncontrolled asthma. We believe benralizumab, which would be our first Respiratory biologic, will become an



Return to growth

- > 7% decrease in Total Revenue to \$23,002 million at actual rate of exchange; comprising Product Sales of \$21,319 million (down 10%) and Externalisation Revenue of \$1,683 million (up 58%)
 - At CER, Total Revenue declined by 5%
- > 4% increase in Growth Platforms revenue (5% at CER) contributing 63% of Total Revenue
 - Emerging Markets: Stable (growth of 6% at CER) to \$5,794 million, supported by China, up 4% (10% at CER) to \$2,636 million
 - Diabetes: Growth of 9% (11% at CER), as *Farxiga/Forxiga* became our largest-selling Diabetes medicine
 - Japan: Sales up 8% (down 3% at CER) to \$2,184 million, reflecting exchange rate impact and a biennial price reduction
 - *Brilinta/Brilique* sales grew by 36% (39% at CER) to \$839 million
 - Respiratory: A decline of 5% (3% at CER) to \$4,753 million, reflecting US pricing pressure for *Symbicort*
 - New Oncology: Strong sales of \$664 million, with *Tagrisso* delivering sales of \$423 million in its first full year
- > US revenue was down 22% to \$7,365 million; Europe down 5% to \$5,064 million; and Established ROW rose by 2% to \$3,096 million (all at actual rate of exchange)



Be a great place to work

- > Decline in scores in our employee survey (Pulse) reflects impact of reshaping the business
- > Second in Pharmaceuticals, Biotechnology and Life Sciences industry group of Dow Jones Sustainability Index
- > Biggest riser in the Access to Medicine Index since the last survey, moving to 7th place in 2016 from 15th in 2014

Chief Executive Officer's Review continued

important medicine for patients with severe asthma and potentially COPD, as well as an important growth driver for our Company, broadening and deepening our offering in the Respiratory market.

Business development and collaboration are at the heart of the way AstraZeneca operates. It is particularly evident in our work in Other Disease Areas. For example, we enter into collaborations to maximise the potential of key products that fall outside our main therapy areas and bring them to patients quicker. Examples in 2016 include our development and commercialisation agreements with LEO Pharma for brodalumab for psoriasis and tralokinumab for dermatitis, and with Allergan for MEDI2070 for inflammatory diseases. In Alzheimer's disease, together with our partner Lilly, we obtained a Fast Track Designation for the BACE inhibitor and have entered a second collaboration with them to co-develop MEDI1814. We are also partnering some of our in-line products that we believe still have growth potential but which cannot receive promotional support as we focus our resources on our main therapy areas. An example is the agreement we reached with China Medical System Holdings for the promotion of *Plendil* in China: our partner will manage the commercialisation and both companies will share the benefits. Finally, we have been divesting smaller non-core products that will be better managed by companies that can focus on them. The value unlocked through these deals is reinvested in our pipeline, creating more long-term value through our main therapy areas.

Prioritised and accelerated pipeline

Since we announced our science-led strategy in 2013, we set ourselves some ambitious pipeline targets for the end of 2016. For example, we aimed for nine to 10 new molecular entities (NMEs) in Phase III or registration: by the end of 2016, there were 12 such projects. We also set ourselves the target of eight to 10 new medicines and major line extension regulatory approvals in 2015 to 2016 and achieved a total of eight. This is a significant improvement compared to our historical pipeline performance.

We also made substantial progress in reshaping our research and early development efforts to help us to produce a steady stream of new products that will

support our long-term growth: we believed we had the potential for 12 to 16 Phase II starts in 2015 to 2016. In fact, we achieved 25. Looking ahead, we believe we have the potential for an unprecedented number of submissions in the next 24 months, with around half in our Oncology therapy area. To ensure we can deliver this potential, in April we announced plans to sharpen further the prioritisation of investments in our main therapy areas, particularly Oncology. We also want to increase partnering in relation to projects in our inflammation, infection and neuroscience disease areas. The 10 strategic transactions we undertook in 2016 bear witness to the progress we have made in that regard. We also took action to align costs to our changing business shape and streamline our operations.

Return to growth

Our Return to growth is underpinned by our Growth Platforms, shown in the panel. As our strategy has progressed, so our Growth Platforms have evolved – New Oncology (new products) was added and, from January 2017, New CVMD combined our Diabetes and *Brilinta/Brilique* Platforms. As the treatment of diabetes becomes more focused on cardiovascular risk reduction based on recent data, we believe there are clear synergies managing diabetes and *Brilinta/Brilique* together.

The panel shows how our Growth Platforms performed in 2016. Despite increasing competition, pricing pressures and geopolitical instability, they grew by 4% at actual exchange rates (5% at CER) and now represent 63% of all revenues. Emerging Markets are particularly important in achieving our goals. This importance was recognised towards the end of the year with the appointment of Leon Wang, our Country President in China, as Executive Vice-President of Asia Pacific and a member of the Senior Executive Team.

Be a great place to work

None of the progress we are making in achieving our strategic objectives would be possible without our people; we want to ensure AstraZeneca is a great place to work and I am very grateful to each and every employee for all their efforts throughout the year.

Employee opinion surveys help us measure satisfaction and engagement and how we are doing in our aim to be a great place to work. Our most recent survey, carried out in December 2016, showed a decline compared to our very high 2015 score, although results are in line with the 'global pharma norm'. This decline might not be unexpected given the challenges of the strategic journey on which we are embarked and the restructuring we undertook in 2016 as we continued losing sales to patent expiries. Nevertheless, we are focused on improving performance in those areas employees tell us are important drivers of employee engagement. These include people development and line manager communication.

One area in which we made significant progress during 2016, and which the Chairman reports on in more detail in his Statement on page 82, was external recognition for our commitment to sustainability – whether that be in the Dow Jones Sustainability Index or Access to Medicine Index, or in the recognition of our science-based environmental targets. During the year, the Executive team also reviewed and refreshed our sustainability strategy.

Looking ahead

Our financial results for 2016 were in line with expectations and reflected our ongoing transition. We brought a sharper strategic focus to our three main therapy areas, boosting pipeline productivity further. Our underlying business is growing as the new AstraZeneca emerges, driven by competitive franchises and Emerging Markets.

2017 should be a turning point in our journey as we bring new medicines to patients across the globe. It is an exciting time as we approach the inflection point for our anticipated return to long-term growth, built on the foundations of a science-led pipeline.



Pascal Soriot
Chief Executive Officer



Investing for the future: Led by science in Cambridge

As we navigate the transitional phase in our strategy, locating our new R&D centre and corporate headquarters in Cambridge demonstrates our strategy in practice – a Company led by science and committed to sustainable development, where patients benefit from our collaborative approach.

We announced our move to Cambridge in 2013. In doing so, we join MedImmune who have been in the city for 25 years. We begin the staged occupation of our new state-of-the-art building (illustrated above and right) in 2018 and already have some 2,000 staff actively engaged in Cambridge's scientific, academic, clinical and business life. They are realising the value of being located at a world-leading academic and life science hub.

As a global science-led business, we have:

- > provided new life science businesses with access to more than 60 mentors from across AstraZeneca, including support for the University of Cambridge Judge Business School's 'Accelerate' programme



- > shaped the laboratory spaces at our R&D centre collaboratively, involving our scientists in the design and commissioning process, including an on-site teaching lab for science outreach.

As a scientific partner, we have:

- > initiated over 130 collaborations with Cambridge organisations, including over 100 with the University of Cambridge
- > collaborated with Microsoft to develop a new cancer treatment modelling system
- > established the CRUK MedImmune Alliance Laboratory to provide capabilities to discover novel biologics and diagnostics
- > established a world-class mass spectroscopy capability with the Laboratory of Molecular Biology and the University of Cambridge
- > developed the AstraZeneca Medical Research Council UK Centre for Lead Discovery.

Being committed to protecting the environment, we are:

- > working towards a Building Research Establishment 'excellent' rating for sustainability performance for our R&D centre in addition to delivering a low carbon emission facility
- > building the largest ground source heat pump system in Europe and a combined heat and power station to meet on-site energy needs.

To inspire the next generation of scientists, we:

- > have three schemes to support more than 80 PhD scholarships and eight clinical lectureships
- > partner with the Cambridge Science Centre to ensure life science education activities reach underserved communities in the wider Cambridgeshire area
- > have an active community support scheme, involving more than 160 staff volunteers, focused around science-based educational events for young people.



Key facts

130

Over 130 collaborations
in Cambridge



2,000

Around 2,000 employees
in Cambridge



Watch the video at
www.astrazeneca.com

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 make money, the resources we need and how we add value across the entire life-cycle of a medicine.

Why AstraZeneca?

We are an integrated, science-led biopharmaceutical Company with a strategic focus on three main therapy areas built around our differentiated:

- > pipeline
- > skills and capabilities
- > quality of science
- > commercial expertise
- > intellectual property

What do we do?

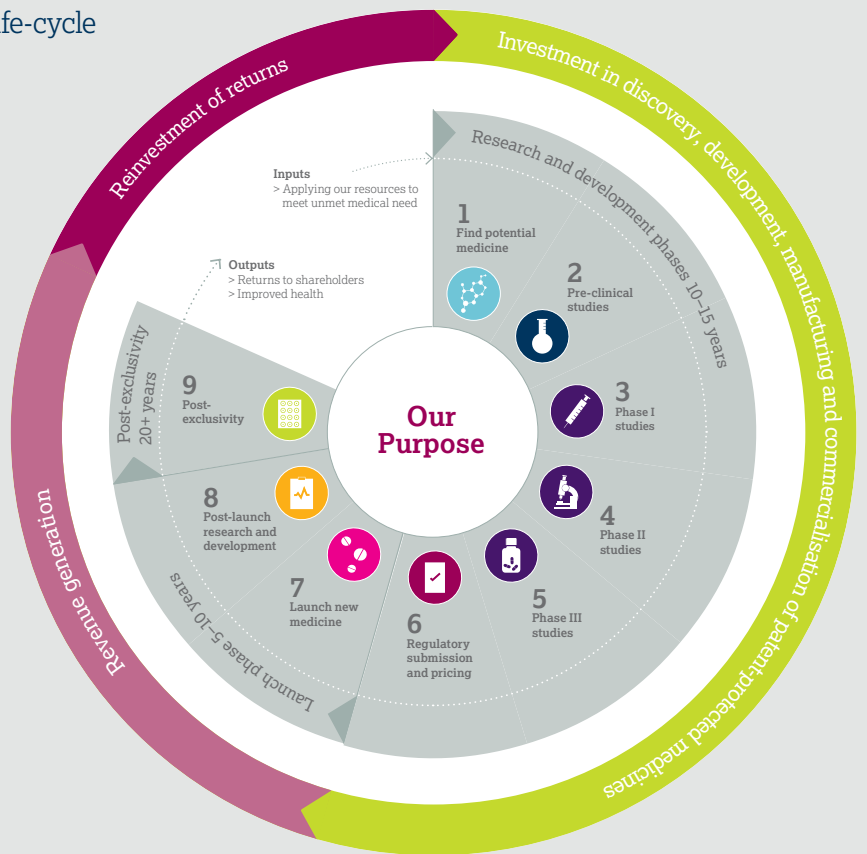
Our business activities span the entire life-cycle of a medicine.

How do we make money?

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 sales of our mature products and Growth Platform launches, as well as from our externalisation activities and divestments.
 Our focus is on creating products that facilitate future revenue generation.

Reinvestment
 We reinvest in developing the next generation of innovative medicines and in our Growth Platforms that provide the platform for future sustainable revenues in the face of potential losses of revenue from the loss of key product patents.



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.**

Life-cycle of a medicine

Research and development phases 10–15 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 5–10 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.

Sustainability

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.

We want to be valued and trusted by our stakeholders as a source of great medicines over the long term. Our sustainability commitments, which are driven by our Purpose and Values, underpin our business model and support the delivery of our business strategy.

 [Business Review from page 42](#)



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.

59,700 employees

See Employees from page 54

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.

\$5.9bn invested in our science

See Achieve scientific leadership from page 45 and R&D resources on page 59

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.

>100 countries in which we are active

See Return to growth from page 48

Intellectual property

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.

>100 countries where we obtain patent protection

See Intellectual Property from page 57

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 (API).

\$13bn spent with suppliers

See Manufacturing from page 58 and Working with suppliers from page 52

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.

600 collaborations worldwide

See Partnering from page 23

Financial strength

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

\$4.1bn net cash flow from operating activities

See Financial Review from page 62

How do we add value?

Financial value



Revenue from the sale of our medicines generates cash flow, which helps us:

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

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

See Financial Review from page 62

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.

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 need.

Overview

- > Global pharmaceutical sales grew by 6.9% in 2016
- > The sector remains highly competitive
- > Patient populations are expanding and ageing
- > Non-communicable diseases (NCDs) kill 39 million people each year
- > The costs of developing a new medicine continue to rise
- > Priority Reviews and Breakthrough Therapies are becoming more prevalent
- > A highly regulated sector reflects the demand for safe, effective and high quality medicines
- > Pricing and reimbursement continue to be challenging
- > Patents are expiring on some of the biggest-selling drugs ever produced
- > The sector faces challenges in building and maintaining trust
- > Changes in political landscape, such as Brexit and the US election results

The global context

The October 2016 World Economic Outlook of the International Monetary Fund (IMF) highlighted the precarious nature of the recovery eight years after the global financial crisis. It raised the spectre that persistent stagnation, particularly in advanced economies, could further fuel populist calls for restrictions on trade and immigration. The IMF went on to observe that such restrictions would hamper productivity, growth and innovation. In China, a shift from investment and industry towards consumption and services was expected to slow growth in the short term while building the foundations for a more sustainable long-term expansion. Japan's economy would be hampered by a shrinking population.

More generally, both political and economic uncertainty followed the Brexit vote in the UK and the election of Donald Trump to president of the US. Instability in a number of other European countries has been exacerbated by refugees fleeing civil war and unrest in the Middle East and from further afield.

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.

2bn



By 2050, the world's population aged 60 years and older is expected to total some 2 billion.

\$154bn

Global investment in pharmaceutical R&D expected to reach an estimated \$154 billion in 2016, an 11% increase from \$139 billion in 2012.

Marketplace continued

Global pharmaceutical sales

World \$bn

2016	967
2015	905
2014	826

\$967bn (6.9%)

US \$bn

2016	446
2015	416
2014	369

\$446bn (7.1%)

Europe \$bn

2016	201
2015	190
2014	179

\$201bn (5.6%)

Established ROW \$bn

2016	120
2015	115
2014	110

\$120bn (5.1%)

Emerging Markets \$bn

2016	200
2015	184
2014	168

\$200bn (9.1%)

Data based on world market sales using AstraZeneca market definitions as set out in the Market definitions on page 239. Source: IMS Health, IMS Midas Quantum Q3 2016 (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.

Expanding patient populations

The number of people accessing healthcare is increasing, as is healthcare spending, particularly by the elderly. For example, WHO estimates that, by 2050, the world's population aged 60 years and older is expected to total some two billion, up from 900 million in 2015 and that, by then, 80% of all older people will live in low- and middle-income countries. As the diagram on page 14 shows, we expect developing markets to continue to fuel pharmaceutical growth.

Unmet medical need

The prevalence of 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. Many NCDs require long-term management. WHO estimates that NCDs kill 39 million people each year and disproportionately affect low- and middle-income countries where nearly three-quarters of these deaths occur. For example, more than 60% of the world's total new annual cancer cases occur in Africa, Asia, and Central and South America. These regions account for 70% of the world's cancer deaths.

The pharmaceutical sector: opportunities and challenges

As shown in the table on the left, global pharmaceutical sales grew by 6.9% in 2016. Established Markets saw average revenue growth of 6.4% and Emerging Markets revenue grew at 9.1%. The US, Japan, China, Germany and France are the world's top five pharmaceutical markets. In 2016, the US had 44.7% of global sales (2015: 46.0%; 2014: 44.7%).

Science and technology

Innovation is critical to addressing unmet medical need. The delivery of new medicines will rely on a more advanced understanding of disease and the use of new technology and approaches, including personalised healthcare (PHC) and predictive science.

Technological breakthroughs in the design and testing of novel compounds present fresh opportunities for using small molecules as the basis for new medicines. The use of large molecules, or biologics, has also become an important source of innovation. Biologics are among the most commercially successful new products. By 2020, biologics, excluding vaccines, are expected to account for 27% of the global pharmaceutical market, having risen from 14% in 2006. As such, most pharmaceutical companies now pursue R&D in both small molecules and biologics.

Priority Reviews and Breakthrough Therapies are becoming more prevalent. Between the inception of the Breakthrough Therapy Designation programme in October 2012 and the end of 2016, the FDA granted more than 150 such requests (out of more than 450 applications), and one-third of these have already resulted in product approvals.

The cost of developing new medicines continues to rise. Global R&D investment is expected to reach \$154 billion in 2016. While the growth rate of R&D spend has slowed in recent years, pharmaceutical companies continue to deliver new medicines. In 2016, the FDA approved 22 novel drugs compared with 45 in 2015 and 41 in 2014.

To ensure sustainable returns on R&D investment, the industry is working to increase its success rate in developing commercially viable new drugs while achieving a lower, more flexible cost base. Regulators and payers, however, are demanding greater evidence of comparative effectiveness of medicines. This increases development times and costs.

Fortunately, innovative technology is helping accelerate product approvals. A greater emphasis on Proof of Concept is also helping to improve productivity and reduce costs by showing the potential efficacy of drugs earlier in the development process.

Regulatory requirements


A highly regulated biopharmaceutical industry reflects the public's expectation of safe, effective and high-quality medicines. Meeting this expectation requires responsible testing, manufacturing and marketing. It also relies on maintaining 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. Increasingly, regulation and governmental policy are being introduced to stimulate innovation in drug development. In the US, for example, the 21st Century Cures Act, signed into law on 13 December 2016, focuses on accelerating the discovery, development and delivery of promising new treatments for patients. Similarly, the Prescription Drug User Fee Act reauthorisation legislation that is required to be considered by the US Congress in 2017 is anticipated to contain proposals aimed at accelerating innovation and modernising the US regulatory environment. Additionally, the growing complexity and globalisation of clinical studies have led to an increase in public-private consortia. Such consortia, which include industry, academia and government bodies, aim to drive innovation, streamline regulatory processes, and define and clarify approval requirements for innovative drug and biologic products.

Regulatory health authorities continue to implement programmes intended to address unmet medical need and to speed up patient access to transformative medicines. This is demonstrated by the Breakthrough Therapy programme employed by the FDA and the EMA's initiative to implement 'adaptive pathways' to improve timely patient access to new medicines. In Japan, the SAKIGAKE Designation System has been introduced to designate innovative medicines that hold the promise for a significant advance over currently available therapy. Once designated, the PMDA collaborates with sponsors to accelerate the development and approval of these promising unapproved medicines for serious and life-threatening diseases. The lengthy review process in China extends new medicine approval periods to as long as five years. This challenges the ability of pharmaceutical companies to deliver innovative medicines and treat unmet medical need in China. However, recent developments, including

the in-progress review of China's Drug Administration Law and Drug Registration Regulation are likely to help address this issue over the next few years.

Greater transparency and public access to regulatory submissions that support approval of new medicines continue to be an area of interest. A recent example involves the EMA policy 0070 on publication of clinical data for medicinal products for human use, which provides guidance for the publication of clinical reports that underpin the EMA's decision making. Paediatric development continues to present challenges to the industry as differences between study requirements and timeframes may vary significantly among health authorities. However, there have been efforts to provide incentives to stimulate paediatric research. An example is the EMA's initiative offering free-of-charge meetings focused on paediatric studies early in drug development. In addition, the industry has appreciated the opportunity afforded by the US paediatric rare disease voucher programme to encourage paediatric drug development. International harmonisation is being advanced in this area through the revision of the ICH E11 paediatric guideline, which has facilitated discussion between regulators and the industry on topics of mutual interest.

Regulatory requirements for the registration of biosimilar products continue to develop and become better defined, as exemplified by the publication of a new pathway for China and the approvals of more biosimilar products in the US. 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.

 For more information about biosimilars, please see Patent expiries and genericisation on page 15

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.

In the US, the Affordable Care Act (ACA) has directly affected the healthcare system by reshaping the market through various policies and approaches designed to expand insurance coverage, reduce costs, transform the delivery system, and improve healthcare and patient coverage. We, along with other pharmaceutical companies, have continued to work with policymakers and regulators to increase access, improve outcomes and to support an environment that fosters medical and scientific innovation and value.

The new political leadership in the US has proposed to repeal and replace the ACA and has taken initial steps to that end. While it is unclear if some or all of the ACA might be repealed or what the scope of replacement might entail if implemented, it is possible that proposals could require the healthcare industry to offset the cost of replacement. This may include changes to the pharmaceutical industry excise tax, Medicaid reform by, for example, granting the states greater flexibility in designing and funding their Medicaid programmes, including the choice of a block grant or *per capita* allotment of federal funds, and/or repeal the marketplace exchanges that were established under the ACA. These changes, whether directly or indirectly targeted at drugs or the pharmaceutical industry, could impact pharmaceutical coverage and patient access to healthcare under insurance plans and government programmes and could, accordingly, significantly affect the pharmaceutical industry.

 Further details on the impact of the ACA on our business are contained in Return to growth on page 48

Marketplace continued

“We expect developing markets to continue to boost pharmaceutical growth.”

Political leadership in the US has also continued to focus on drug pricing. Various drug pricing proposals have included measures relating to the repeal of the Medicare Part D non-interference clause that currently prohibits the government from negotiating directly with manufacturers on drug prices and US drug importation policies. In addition, lawmakers and policymakers at both the federal and state level have developed drug pricing transparency proposals 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. While the implementation timeline and details of such proposals are not clear, significant changes to laws and regulations regarding drug pricing could have a significant impact on the pharmaceutical industry.

Romania and Italy. In France, price negotiations are particularly challenging due to budgetary pressures. In Germany, Europe’s largest pharmaceutical market, manufacturers must now prove the added benefit of their drug over existing alternatives if they are to avoid relegation to an unfavourable price reference or face non-pricing barriers to market access.

In China, pricing practices remain a priority for regulators. New national regulations and provincial and hospital tenders continue to put increasing pricing pressures on pharmaceutical companies. In Russia and selected Middle East markets, governments are encouraging local manufacturing by offering more favourable pricing legislation. In Japan, mandated biennial cuts are likely to continue as are experimental decisions by regulators based on cost effectiveness assessments. In Latin America, pricing is increasingly controlled by governments as, for example, in Colombia and Brazil with price referencing regulations.

84.7%

Generics constituted 84.7% of prescriptions dispensed in the US.



In Europe, governments continue to implement and expand price control measures for medicines, including mandatory discounts, clawbacks and price referencing rules. These measures are decreasing drug prices, particularly in the challenged economies of Greece,

For more information about price controls, reductions and US healthcare reform, and price regulation, please see the Business Review, Return to growth from page 48 and Risk from page 214

Estimated pharmaceutical sales and market growth – 2020

Region	Estimated pharmaceutical sales – 2020 (at CER)	Estimated pharmaceutical market growth – 2015 to 2020 (Compound annual growth rate)
North America	\$640bn	7.0%
EU	\$240bn	3.2%
Other Europe (Non-EU countries)	\$23bn	8.7%
Japan	\$92bn	0.6%
Oceania	\$15bn	4.8%
South East and East Asia	\$202bn	6.5%
Latin America	\$78bn	2.3%
Africa	\$28bn	8.1%
CIS	\$23bn	6.7%
Middle East	\$25bn	6.6%
Indian subcontinent	\$38bn	12.1%

● Estimated pharmaceutical sales – 2020. Ex-manufacturer prices at CER. Source: IMS Health.
 ● Estimated pharmaceutical market growth – 2015 to 2020. Compound annual growth rate. Source: IMS Health.

Patent expiries and genericisation

Patent protection for pharmaceutical products is finite. Patents are expiring on some of the biggest-selling drugs ever produced and this means that payers, physicians and patients are gaining 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 2016, generics constituted 84.7% of the market by volume (2015: 84.0%).

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.

Building trust

The pharmaceutical industry faces challenges in building and maintaining trust, particularly with governments and regulators. This reflects the past decade's legal disputes between pharmaceutical companies and governmental and regulatory authorities. To address this challenge, companies are strengthening a culture of ethics and integrity, adopting higher governance standards and improving relationships with employees, shareholders and other stakeholders.

During 2016, there were also pharmaceutical industry investigations and Congressional hearings in the US related to pricing while, in the UK, the Competition and Markets Authority has been investigating allegations of excessive charging and fining companies for unfair prices.

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. Investigations by the DOJ and SEC under the Foreign Corrupt Practices Act are continuing as are investigations by the UK Serious Fraud Office under the UK Bribery Act. Information about material legal proceedings can be found in Note 28 to the Financial Statements from page 185.

Strategic responses

Our industry remains highly competitive. It includes large, research-based pharmaceutical companies (such as 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 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.

While many of 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. A number of companies are focused on improving R&D productivity and operational efficiency. Other companies have looked to geographic expansion, especially in Emerging Markets and Japan.

Across the industry, business development deals (including licensing and collaborations), and competition for business development opportunities, while down over 2015, continued in 2016. For example, one report estimates that the value of mergers and acquisitions announced in the healthcare sector during the year amounted to more than \$270 million, compared with almost \$400 million in 2015.


As outlined in AstraZeneca at a glance from page 2 and our Business model from page 8, our strategic response to the pharmaceutical marketplace is 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 diseases in three main therapy areas. The strategic priorities that follow on from this response are outlined in the next section.

Strategy and key performance indicators

We are focused on returning to growth through a science-led innovation strategy. Our strategic priorities, and the indicators against which we measure our success, are based on investing in three therapy areas, building a strong and balanced portfolio of primary care and specialty care medicines, and accelerating key R&D programmes. They also include targeted business development and leveraging our global commercial presence.

Achieve scientific leadership

Strategic priorities	Key performance indicators																				
<p>Focus on innovative science in three therapy areas Focus on Oncology, Cardiovascular & Metabolic Disease, and Respiratory. We are also selectively active in Autoimmunity, Infection and Neuroscience.</p> <p>Work across small molecules and biologics, including immunotherapies and protein engineering, as well as devices, biomarkers and translational science.</p> <p>Prioritise and accelerate our pipeline Accelerate and invest in key R&D programmes. At the end of 2016, 12 NMEs were in Phase III or under regulatory review compared with our March 2013 target of nine to 10.</p> <p>Against the targets we had set ourselves since 2013, by the end of 2016, we had made 25 Phase II starts (2015 to 2016 target: 12 to 16); 14 NME and major line extension regulatory submissions (2015 to 2016 target: 14 to 16); and eight NME and major line extension regulatory approvals (2015 to 2016 target: eight to 10).</p> <p>Strengthen our early-stage pipeline through novel science and technology.</p> <p>Transform our innovation and culture model Focus on novel science, such as immune-mediated therapy combinations and PHC.</p> <p>Co-location near bioscience clusters at three strategic centres in Cambridge, UK; Gaithersburg, Maryland US; and Gothenburg, Sweden helps to leverage our capabilities and foster collaboration with leading scientists and research organisations.</p> <p>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.</p> <p>Collaborate strategically to broaden and accelerate the development of key pipeline assets (externalisation) and divest non-core assets to realise value.</p>	<p>Phase III investment decisions</p> <p>7</p> <table border="1" data-bbox="448 943 774 1032"> <tr><td>2016</td><td>7</td></tr> <tr><td>2015</td><td>6</td></tr> <tr><td>2014</td><td>9</td></tr> </table> <p>savolitinib (papillary renal cell carcinoma); durvalumab+tremelimumab (hepatocellular carcinoma); <i>Forxiga</i> (heart failure); <i>Forxiga</i> (chronic kidney disease); AZD3293 (BACE) Alzheimer’s disease; two further decisions made through strategic partnering.</p>	2016	7	2015	6	2014	9	<p>NME or LCM project regulatory submissions in major markets</p> <p>14</p> <table border="1" data-bbox="799 943 1125 1032"> <tr><td>2016</td><td>14¹</td></tr> <tr><td>2015</td><td>12</td></tr> <tr><td>2014</td><td>6</td></tr> </table> <p><i>Faslodex</i> – breast cancer (US, EU, JP); <i>Tagrisso</i> – lung cancer (CN); <i>Tagrisso</i> – lung cancer (AURA3 study for full approval) (US, EU); durvalumab – bladder cancer (US); DURATION-8 (exenatide+dapagliflozin) (EU); benralizumab – severe asthma (US, EU); lesinurad+allopurinol FDC – gout (US); three further submissions made await regulatory acceptance.</p> <p>¹ 13 for determining Annual Bonus. See page 108</p>	2016	14 ¹	2015	12	2014	6	<p>Clinical-stage strategic transactions</p> <p>10</p> <table border="1" data-bbox="1150 943 1476 1032"> <tr><td>2016</td><td>10</td></tr> <tr><td>2015</td><td>10</td></tr> <tr><td>2014</td><td>3</td></tr> </table> <p>Includes alliances, collaborations and acquisitions to enhance our portfolio and pipeline in our main therapy areas; externalisation activity to maximise the value of our assets; and divestments of non-priority medicines.</p>	2016	10	2015	10	2014	3
2016	7																				
2015	6																				
2014	9																				
2016	14 ¹																				
2015	12																				
2014	6																				
2016	10																				
2015	10																				
2014	3																				
	<p>NME Phase II starts/progressions</p> <p>16</p> <table border="1" data-bbox="448 1536 774 1626"> <tr><td>2016</td><td>16¹</td></tr> <tr><td>2015</td><td>11</td></tr> <tr><td>2014</td><td>13</td></tr> </table> <p><i>Vidaza</i> and durvalumab for the treatment of acute myeloid leukaemia and CC486+durvalumab for myelodysplastic syndromes (with Celgene); MEDI0680+durvalumab for solid tumours; MEDI0562 (humanised OX40); AZD6738+Lynparza for gastric cancer; AZD1775 (Wee1); daratumumab+durvalumab for multiple myeloma; in collaboration with Incyte, epacadostat (IDO)+durvalumab for solid tumours; MEDI4166 (PCSK9/GLP-1); MEDI0382; AZD4076; abediterol (AZD0548) (LABA); AZD1419 (Inhaled TLR9); MEDI2070 (IL-23); MEDI13902 (pseudomonas bispecific (Psl-PcrV)); MEDI8897 (RSV).</p> <p>¹ 15 for determining Annual Bonus. See page 108</p>	2016	16 ¹	2015	11	2014	13	<p>NME and major LCM regional approvals</p> <p>11</p> <table border="1" data-bbox="799 1536 1125 1626"> <tr><td>2016</td><td>11</td></tr> <tr><td>2015</td><td>6</td></tr> <tr><td>2014</td><td>12</td></tr> </table> <p><i>Tagrisso</i> – lung cancer (EU, JP) and ctDNA blood test (US, JP); <i>Brilinta</i> <i>Brilique</i> – post myocardial infarction (EU) and acute coronary syndromes and post myocardial infarction (JP); <i>Otern</i> – Type 2 diabetes (EU); <i>Bevespi Aerosphere</i> (PT003) – COPD (US); <i>Zurampic</i> – gout (EU); <i>Zavicefta</i> – serious infections (EU); Pandemic Live Attenuated Influenza Vaccine – pandemic influenza (EU).</p>	2016	11	2015	6	2014	12							
2016	16 ¹																				
2015	11																				
2014	13																				
2016	11																				
2015	6																				
2014	12																				

 Therapy Area Review from page 23  Achieve scientific leadership from page 45  Development Pipeline from page 204

Return to growth

Strategic priorities	Key performance indicators																																												
<p>Focus on Growth Platforms <i>Brilinta/Brilique</i> – Work to deliver <i>Brilinta/Brilique</i>'s potential to reduce cardiovascular deaths through ongoing clinical studies.</p> <p>Diabetes – Work to maximise the potential of our broad and innovative non-insulin, anti-diabetic portfolio to transform patient care.</p> <p>From January 2017, New CVMD Growth Platform combines our Diabetes franchise, <i>Brilinta/Brilique</i> and any new launches.</p> <p>Respiratory – Work to maximise pipeline value, devices and medicines to fulfil unmet medical need and improve patient outcomes in asthma and COPD.</p> <p>New Oncology – Aim to deliver six new cancer medicines to patients by 2020. It became our sixth Growth Platform in January 2015 and includes <i>Lynparza</i>, <i>Iressa</i> (US) and <i>Tagrisso</i>.</p> <p>Japan – Strengthen our Oncology franchise and work to maximise the success of our Diabetes medicines and established brands: <i>Symbicort</i>, <i>Nexium</i> and <i>Crestor</i>.</p> <p>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 India. The ongoing transformation of our capabilities is supporting new products and improving access and affordability.</p> <p>Transform through specialty care, devices and biologics Biologics 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.</p>	<p>Brilinta/Brilique</p> <p>\$839m Product Sales</p> <table border="1"> <tr><td>2016</td><td>\$839m</td></tr> <tr><td>2015</td><td>\$619m</td></tr> <tr><td>2014</td><td>\$476m</td></tr> </table> <table> <tr><td>Actual growth</td><td>CER growth</td></tr> <tr><td>2016 +36%</td><td>2016 +39%</td></tr> <tr><td>2015 +30%</td><td>2015 +44%</td></tr> <tr><td>2014 +68%</td><td>2014 +70%</td></tr> </table>	2016	\$839m	2015	\$619m	2014	\$476m	Actual growth	CER growth	2016 +36%	2016 +39%	2015 +30%	2015 +44%	2014 +68%	2014 +70%	<p>Diabetes</p> <p>\$2,427m Product Sales</p> <table border="1"> <tr><td>2016</td><td>\$2,427m</td></tr> <tr><td>2015</td><td>\$2,224m</td></tr> <tr><td>2014</td><td>\$1,870m</td></tr> </table> <table> <tr><td>Actual growth</td><td>CER growth</td></tr> <tr><td>2016 +9%</td><td>2016 +11%</td></tr> <tr><td>2015 +19%</td><td>2015 +26%</td></tr> <tr><td>2014 +138%</td><td>2014 +139%</td></tr> </table>	2016	\$2,427m	2015	\$2,224m	2014	\$1,870m	Actual growth	CER growth	2016 +9%	2016 +11%	2015 +19%	2015 +26%	2014 +138%	2014 +139%	<p>Respiratory</p> <p>\$4,753m Product Sales</p> <table border="1"> <tr><td>2016</td><td>\$4,753m</td></tr> <tr><td>2015</td><td>\$4,987m</td></tr> <tr><td>2014</td><td>\$5,063m</td></tr> </table> <table> <tr><td>Actual growth</td><td>CER growth</td></tr> <tr><td>2016 -5%</td><td>2016 -3%</td></tr> <tr><td>2015 -2%</td><td>2015 +7%</td></tr> <tr><td>2014 +8%</td><td>2014 +10%</td></tr> </table>	2016	\$4,753m	2015	\$4,987m	2014	\$5,063m	Actual growth	CER growth	2016 -5%	2016 -3%	2015 -2%	2015 +7%	2014 +8%	2014 +10%
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	<p><i>Brilinta</i> delivered Product Sales of \$839 million. Continued progress was seen across the US and Europe with 45% and 12% growth (15% at CER) in the year respectively.</p>	<p>Diabetes Product Sales grew by 9% (11% at CER) despite intense competition in this space with a positive contribution from all Regions. Our focus in diabetes remains on the fastest-growing SGLT2 and GLP-1 classes.</p>	<p>2016 was a challenging year. Respiratory Product Sales declined by 5% (3% at CER), the main driver of this being <i>Symbicort</i>, which continued to grow volume share, however, Product Sales were down by 12% (10% at CER), reflecting developments in the US and Europe, offsetting the positive Emerging Markets and Established ROW growth.</p>																																										
	<p>New Oncology</p> <p>\$664m Product Sales</p> <table border="1"> <tr><td>2016</td><td>\$664m</td></tr> <tr><td>2015</td><td>\$119m</td></tr> <tr><td>2014</td><td>N/A</td></tr> </table> <table> <tr><td>Actual growth</td><td>CER growth</td></tr> <tr><td>2016 n/m</td><td>2016 n/m</td></tr> <tr><td>2015 N/A</td><td>2015 N/A</td></tr> <tr><td>2014 N/A</td><td>2014 N/A</td></tr> </table>	2016	\$664m	2015	\$119m	2014	N/A	Actual growth	CER growth	2016 n/m	2016 n/m	2015 N/A	2015 N/A	2014 N/A	2014 N/A	<p>Japan</p> <p>\$2,184m Product Sales</p> <table border="1"> <tr><td>2016</td><td>\$2,184m</td></tr> <tr><td>2015</td><td>\$2,020m</td></tr> <tr><td>2014</td><td>\$2,227m</td></tr> </table> <table> <tr><td>Actual growth</td><td>CER growth</td></tr> <tr><td>2016 +8%</td><td>2016 -3%</td></tr> <tr><td>2015 -9%</td><td>2015 +4%</td></tr> <tr><td>2014 -10%</td><td>2014 -3%</td></tr> </table>	2016	\$2,184m	2015	\$2,020m	2014	\$2,227m	Actual growth	CER growth	2016 +8%	2016 -3%	2015 -9%	2015 +4%	2014 -10%	2014 -3%	<p>Emerging Markets</p> <p>\$5,794m Product Sales</p> <table border="1"> <tr><td>2016</td><td>\$5,794m</td></tr> <tr><td>2015</td><td>\$5,822m</td></tr> <tr><td>2014</td><td>\$5,827m</td></tr> </table> <table> <tr><td>Actual growth</td><td>CER growth</td></tr> <tr><td>2016 0%</td><td>2016 +6%</td></tr> <tr><td>2015 0%</td><td>2015 +12%</td></tr> <tr><td>2014 +8%</td><td>2014 +12%</td></tr> </table>	2016	\$5,794m	2015	\$5,822m	2014	\$5,827m	Actual growth	CER growth	2016 0%	2016 +6%	2015 0%	2015 +12%	2014 +8%	2014 +12%
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	<p>New Oncology Product Sales of <i>Lynparza</i>, <i>Iressa</i> (US) and <i>Tagrisso</i> were \$664 million. <i>Tagrisso</i> continued to demonstrate strong uptake in the US, Europe and Japan with global Product Sales of \$423 million and 46 regulatory approvals. <i>Lynparza</i> Product Sales were \$218 million.</p>	<p>In Japan, Product Sales were up by 8% (down 3% at CER), reflecting exchange rate impact and the mandated biennial price cuts. We had volume growth of about 2%. Our three biggest medicines, <i>Crestor</i>, <i>Nexium</i> and <i>Symbicort</i>, continued to perform well, but <i>Crestor</i> Product Sales were impacted by inventory reductions at our local marketing partner.</p>	<p>Emerging Markets growth mainly driven by <i>Brilinta</i>, <i>Forxiga</i> and our Respiratory franchise. China represented just under half of the total Emerging Markets Product Sales in 2016.</p>																																										

 Return to growth from page 48

 Therapy Area Review from page 23

 Geographical Review from page 226

Strategy and key performance indicators continued

Be a great place to work

Strategic priorities	Key performance indicators																													
<p>Evolve our culture Work to improve our employees' identification with our Purpose and Values and promote greater understanding of and belief in our strategy.</p> <p>Invest in and implement tailored leadership development programmes.</p> <p>Simplify our business Develop simpler, more efficient processes and flatten our organisational structure to encourage accountability and improve decision making and communication.</p> <p>Attract and retain the best talent Accelerate efforts to attract diverse, top talent with new capabilities.</p>	<p>Employee belief in our strategy</p> <p>80%</p> <table border="1"> <tr><td>2016</td><td><div style="width: 80%;"></div></td><td>80%¹</td></tr> <tr><td>2015</td><td><div style="width: 89%;"></div></td><td>89%²</td></tr> <tr><td>2014</td><td><div style="width: 86%;"></div></td><td>86%³</td></tr> </table> <p>This is a key indicator of employee engagement. Decline reflects impact of reshaping the business.</p> <p>¹ Source: December 2016 Pulse survey across a sample of the organisation. ² Source: January 2016 Pulse survey across a sample of the organisation. ³ Source: Global FOCUS all-employee survey.</p>	2016	<div style="width: 80%;"></div>	80% ¹	2015	<div style="width: 89%;"></div>	89% ²	2014	<div style="width: 86%;"></div>	86% ³	<p>Organisational structure – percentage of employees within six management steps of the CEO</p> <p>82%</p> <table border="1"> <tr><td>2016</td><td><div style="width: 82%;"></div></td><td>82%</td></tr> <tr><td>2015</td><td><div style="width: 71%;"></div></td><td>71%</td></tr> <tr><td>2014</td><td><div style="width: 75%;"></div></td><td>75%</td></tr> </table> <p>This is a key indicator of our progress in organisational efficiency, through improved decision making, driving accountability to the right level and improving communication flow.</p>	2016	<div style="width: 82%;"></div>	82%	2015	<div style="width: 71%;"></div>	71%	2014	<div style="width: 75%;"></div>	75%	<p>Employees who would recommend AstraZeneca as a great place to work</p> <p>74%</p> <table border="1"> <tr><td>2016</td><td><div style="width: 74%;"></div></td><td>74%¹</td></tr> <tr><td>2015</td><td><div style="width: 83%;"></div></td><td>83%²</td></tr> <tr><td>2014</td><td><div style="width: 82%;"></div></td><td>82%³</td></tr> </table> <p>This is a key indicator of whether employees believe AstraZeneca is a great place to work. Decline reflects impact of reshaping the business.</p> <p>¹ Source: December 2016 Pulse survey across a sample of the organisation. ² Source: January 2016 Pulse survey across a sample of the organisation. ³ Source: Global FOCUS all-employee survey.</p>	2016	<div style="width: 74%;"></div>	74% ¹	2015	<div style="width: 83%;"></div>	83% ²	2014	<div style="width: 82%;"></div>	82% ³
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 Be a great place to work from page 52  Employees from page 54

Do business sustainably

Strategic priorities	Key performance indicators																													
<p>Deliver business success over the long term Deliver our business strategy in a way that delivers wider benefits to society and the planet.</p> <p>Focus on:</p> <ul style="list-style-type: none"> > maintaining ethics and transparency in everything we do > increasing access to healthcare for more people > minimising the environmental impact of our products and processes. <p>Align our work with the UN Sustainable Development Goals and work to integrate our commitments into day-to-day business activities.</p>	<p>Dow Jones Sustainability Index ranking</p> <p>86%</p> <table border="1"> <tr><td>2016</td><td><div style="width: 86%;"></div></td><td>86%</td></tr> <tr><td>2015</td><td><div style="width: 84%;"></div></td><td>84%</td></tr> <tr><td>2014</td><td><div style="width: 79%;"></div></td><td>79%</td></tr> </table> <p>Met the target of maintaining position in the Dow Jones Sustainability World and Europe Indexes comprising the top 10% of the largest 2,500 companies with a score of 86%.</p>	2016	<div style="width: 86%;"></div>	86%	2015	<div style="width: 84%;"></div>	84%	2014	<div style="width: 79%;"></div>	79%	<p>Screening, diagnosis and treatment of hypertension as part of Healthy Heart Africa programme</p> <p>2 million patients</p> <table border="1"> <tr><td>2016</td><td><div style="width: 2m;"></div></td><td>2m</td></tr> <tr><td>2015</td><td><div style="width: 1m;"></div></td><td>1m</td></tr> <tr><td>2014</td><td><div style="width: N/A;"></div></td><td>N/A</td></tr> </table> <p>Healthy Heart Africa was launched in October 2014. By the end of 2016, we had conducted over two million hypertension screenings in the community and healthcare facilities.</p>	2016	<div style="width: 2m;"></div>	2m	2015	<div style="width: 1m;"></div>	1m	2014	<div style="width: N/A;"></div>	N/A	<p>Operational carbon footprint¹</p> <p>1,657 kt CO₂e</p> <table border="1"> <tr><td>2016</td><td><div style="width: 1,657kt;"></div></td><td>1,657 kt CO₂e</td></tr> <tr><td>2015</td><td><div style="width: 1,743kt;"></div></td><td>1,743 kt CO₂e</td></tr> <tr><td>2014</td><td><div style="width: N/A;"></div></td><td>N/A</td></tr> </table> <p>Our 2016 operational carbon footprint met our target emission of 1,708 kt CO₂e and represents a 5% reduction from our 2015 baseline.</p> <p>¹ Operational carbon footprint is emissions from all Scope 1, 2, and selected Scope 3 sources. See page 231.</p>	2016	<div style="width: 1,657kt;"></div>	1,657 kt CO ₂ e	2015	<div style="width: 1,743kt;"></div>	1,743 kt CO ₂ e	2014	<div style="width: N/A;"></div>	N/A
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 Sustainability from page 43

Note: Confirmed breaches of external sales and marketing codes or regulations globally is no longer regarded as a KPI. However, this information is reported on page 52 of the Annual Report.

Achieve Group financial targets

Strategic priorities

Drive on-market value

Invest in R&D and on-market Growth Platforms to return to growth. Our aim is to deliver industry-leading productivity by restructuring to create scope for investment 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, operational cash balance and periodic share repurchases.

Key performance indicators

Total Revenue¹

\$23,002m

2016	\$23,002m
2015	\$24,708m
2014	\$26,547m

Actual growth	CER growth
2016 -7%	2016 -5%
2015 -7%	2015 +1%
2014 +3%	2014 +5%

Total Revenue comprised Product Sales of \$21,319 million (down by 10% at actual rate of exchange and 8% at CER) and Externalisation Revenue of \$1,683 million (up by 57% at actual rate of exchange and 59% at CER). Decline in Total Revenue at actual exchange rates reflected the particular weakness of key trading currencies against the US dollar.

¹ As detailed on page 142, Total Revenue consists of Product Sales and Externalisation Revenue.

Net cash flow from operating activities

\$4,145m

2016	\$4,145m
2015	\$3,324m
2014	\$7,058m

Actual growth
2016 +25%
2015 -53%
2014 -5%

Cash generated from operating activities improved cash management performance and one-off tax refunds.

Dividend per share¹

\$2.80

2016	\$2.80
2015	\$2.80
2014	\$2.80

Dividend is consistent with the progressive dividend policy pursuant to which the Board intends to maintain or grow the dividend each year.

¹ First and second interim dividend for the year.

Reported EPS

\$2.77

2016	\$2.77
2015	\$2.23
2014	\$0.98

Actual growth	CER growth
2016 +24%	2016 +9%
2015 +128%	2015 +137%
2014 -52%	2014 -34%

Reported EPS of \$2.77 represented growth of 24% (9% at CER). This included a gain of \$0.76 on the revaluation of acquisition-related liabilities.

Core EPS

\$4.31

2016	\$4.31
2015	\$4.26
2014	\$4.28

Actual growth	CER growth
2016 +1%	2016 -5%
2015 0%	2015 +7%
2014 -15%	2014 -8%

Core EPS increased by 1% (decreased 5% at CER), driven by the same rate of decline in Total Revenue at CER.

 Financial Review from page 62

Risk overview




Principal Risks

We face a diverse range of risks and uncertainties and this table provides insight into the Principal Risks that could have a materially adverse effect on the business or results of operations. We outline 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.

Risk category and Principal Risks	Context/potential impact
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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
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
Secure and protect product IP 	Discovering and developing medicines requires a significant investment of resources. For this to be a viable investment, through generation of sufficient revenues, new medicines must be safeguarded from being copied with a reasonable amount of certainty for a reasonable amount of time




Commercialisation

Externally driven demand, pricing, access and competitive pressures 	Operating in over 100 countries, we are subject to political, socio-economic 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
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


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
Information technology and data security and privacy 	Significant disruption to our IT systems, cybersecurity incidents including breaches of data security, or failure to integrate new systems, 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
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
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

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
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 or penalties, adversely affecting our financial results
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

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
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Strategy key

-  Achieve scientific leadership
-  Be a great place to work
-  Return to growth
-  Achieve Group financial targets

Trend key

-  Increasing risk
-  Decreasing risk
-  Unchanged

 Further information on our key risk management and assurance processes can be found in Risk from pages 214 to 225 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

Management actions	Trend versus prior year
<ul style="list-style-type: none"> > Prioritise and accelerate our pipeline > Strengthen pipeline through acquisitions, licensing and collaborations > Focus on innovative science in three main therapy areas 	 Increasing importance of pipeline contribution given loss of exclusivity on key brands
<ul style="list-style-type: none"> > Quality management systems incorporating monitoring, training and assurance activities > Collaborating with regulatory bodies and advocacy groups to monitor and respond to changes in the regulatory environment, including revised process, timelines and guidance 	 Unchanged
<ul style="list-style-type: none"> > Active management of IP rights 	 Unchanged
<ul style="list-style-type: none"> > 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
<ul style="list-style-type: none"> > Focus on Growth Platforms > Accelerate and risk share through business development and strategic collaborations and alliances 	 Loss of exclusivity on key brands increases challenge to achieve our short- to medium-term targets
<ul style="list-style-type: none"> > Business continuity and resilience initiatives, disaster and data recovery and emergency response plans > Establishment of new manufacturing facilities, creating capacity and technical capability to support new product launches, particularly biologics > Contingency plans including dual sourcing, multiple suppliers and stock levels > Quality management systems 	 Supply chain evolving to incorporate new supply chains and to support product launches
<ul style="list-style-type: none"> > Disaster and data recovery plans > Strategies to secure critical systems and processes 	 Several key transformational programmes involving large IT-related aspects
<ul style="list-style-type: none"> > Appropriate project governance structure and oversight > Regular review of strategic initiatives by appropriate senior executive and Board level committees 	 Ongoing restructuring projects
<ul style="list-style-type: none"> > Evolve our culture > Focus on simplification > Development of our employees 	 Ongoing restructuring projects
<ul style="list-style-type: none"> > 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
<ul style="list-style-type: none"> > Combined internal and external counsel management 	 Unchanged
<ul style="list-style-type: none"> > Strong ethical and compliance culture > Established compliance framework in place including annual Code of Conduct training for all employees > Focus on due diligence and oversight of third party engagements > Established new requirements on providing appropriate information about our products > Established sustainability framework in place including a refreshed sustainability strategy for 2016 	 Increasing government and regulatory scrutiny and evolving compliance challenges as complexity of business relationships increases
<ul style="list-style-type: none"> > 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

Risk overview continued

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 214 to 225. 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.

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 Senior Executive Team (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 Conduct can be found in the Corporate Governance Report from page 90](#)

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 2019 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 recognises the significant political uncertainty arising from Brexit, the US presidential election result and elections in other key markets. Risks to the sales and cost forecasts are identified at a market and SET function level. The plan is used to perform central net debt and headroom profile analysis. This analysis considers a severe but plausible downside scenario incorporating the Principal Risks such as market pricing and access, delivery of pipeline and loss of IP. The resilience of the Group to absorb further Principal Risk events such as regulatory/litigious fines and the need to meet pension fund obligations has also been analysed. The Group has adequate resilience against these and the other Principal Risks due to our diversified product portfolio; our global footprint; our robust supply infrastructure; our access to external financing, which includes committed facilities; and our ability to manage our cost base.

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 remain-or-leave referendum on the UK's membership within the EU, the outcome of which was a decision for the UK to exit from the EU (Brexit). A process of negotiation will likely determine the future terms of the UK's relationship with the EU, as well as whether the UK will be able to continue to benefit from the EU's free trade and similar arrangements. Until the Brexit negotiation process is initiated and 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 before, 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 Board reviews the potential impact of Brexit as an integral part of its Principal Risks (as outlined on page 20) rather than as a stand-alone risk. As the process of Brexit evolves, the Board will continue to assess its impact.

Therapy Area Overview and Pipeline

Our Therapy Area teams are focused on maximising the value of our pipeline for patients and shareholders alike. We adopt a dynamic approach to portfolio management and use business development to supplement our pipeline and our own efforts.

Strategy

We have transformed our drugs portfolio by focusing on three main therapy areas: Oncology, Cardiovascular & Metabolic Disease (CVMD) and Respiratory, while selectively pursuing promising therapies in Autoimmunity, Infection and Neuroscience. Our sales in each of these areas in 2016 are shown in the table below.

We are building value by strengthening our in-line portfolios through commercial excellence, life-cycle management and expansion into new patient populations as well as by translating our late-stage pipeline into differentiated therapies for disease areas with high unmet medical need. We continue to pursue externalisation where it provides an opportunity to focus and enhance our portfolio as well as access capabilities we do not have internally.

We are seeking to expand our comprehensive Respiratory portfolio to meet the needs of asthma and COPD patients across the severity spectrum of these diseases. Building on an ICS/LABA foundation with *Symbicort*, we are evolving our mono- and fixed-dose combination therapies as well as optimising our delivery device platforms.

In CVMD, we are expanding our portfolio into the cardiovascular-renal area with late-stage assets such as ZS-9 and roxadustat, as well as investing to explore the potential benefits of our SGLT2 and GLP-1 franchises in chronic kidney disease (CKD) and heart failure (HF).

We have completed the transformation of our Oncology portfolio where we are balancing our efforts across four disease areas – lung, ovarian, breast and haematology – and investing in immuno-oncology (IO) which has the potential to benefit patients in multiple tumour types and different lines of therapy.

As we invest in our main therapy areas we continue to build upon our strong commercial and medical capabilities to ensure that our medicines reach the patients who need them most.

Development pipeline

As shown in the table overleaf, our pipeline includes 132 projects, of which 120 are in the clinical phase of development, and we are making significant progress in advancing our late-stage programmes through regulatory approval with 14 NME or major LCM regulatory submissions during 2016, and 11 major approvals. At the end of 2016, we had 12 NME projects in pivotal studies or under regulatory review compared with 15 at the end of 2015. 15 NMEs progressed to their next phase of development, 22 projects were discontinued in 2016, 17 for poorer than anticipated safety and efficacy results, four as a result of strategic shift in the environment or portfolio prioritisation, and one because of a change in regulatory requirements.

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 26, 31, 36 and 38 and the Development Pipeline table from page 204. For information on Patent Expiries of our Key Marketed Products, please see from page 211.

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 185.

Details of relevant risks are set out in Risk from page 214.

Partnering

As outlined in Strategy and key performance indicators from page 16, 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 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.

Global Product Sales by therapy area

	2016			2015			2014		
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %
Oncology	3,383	20	20	2,825	(7)	7	3,027	(5)	(2)
Cardiovascular & Metabolic Disease	8,116	(14)	(13)	9,489	(3)	4	9,802	11	12
Respiratory	4,753	(5)	(3)	4,987	(2)	17	5,063	8	10
Other Disease Areas	5,067	(20)	(19)	6,340	(23)	(16)	8,203	(9)	(7)
Total	21,319	(10)	(8)	23,641	(9)	(1)	26,095	1	3

Therapy Area Overview and Pipeline continued

Development pipeline overview (as at 31 December 2016)

Phase I	Phase II	Late-stage development*	Life-cycle management projects*
41	36	27	28
<p>> 41 projects in Phase I, including:</p> <ul style="list-style-type: none"> - 29 NMEs - 1 significant additional indication for projects that have reached Phase III - 11 oncology combination projects 	<p>> 36 projects in Phase II, including:</p> <ul style="list-style-type: none"> - 25 NMEs - 4 significant additional indications for projects that have reached Phase III - 7 oncology combination projects 	<p>> 27 projects in late-stage development, either in Phase III/pivotal Phase II studies or under regulatory review:</p> <ul style="list-style-type: none"> - 12 NMEs not yet approved in any market - 9 projects exploring additional indications for these NMEs, of which 5 are oncology combinations - 5 NMEs already approved or launched in the EU, China, Japan and/or the US - 1 confirmatory study for full approval of a launched NME <p>* NMEs and significant additional indications.</p>	<p>> 28 LCM projects</p> <p>* Only includes material projects where first indication is launched in all markets.</p>

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. Acquisitions completed during 2016 included the acquisition of Takeda's respiratory portfolio, in May, and the acquisition of a controlling equity position in Acerta Pharma, in February, both of which were signed in 2015.

Over the past three years, we have completed more than 270 major or strategically important business development transactions, including some 80 in 2016. Of these transactions, 55 were related to pre-clinical assets or programmes and 11 to PHC and biomarkers. 17 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 sit outside our main therapy areas.

Examples of collaborations that help us access therapy area expertise include:

- > in Alzheimer's disease through our partnership with Lilly for the BACE inhibitor
- > in dermatology through our agreements with Valeant and LEO Pharma for brodalumab and LEO Pharma for tralokinumab
- > in haematology through our collaboration with Celgene for durvalumab.

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 *Plendil*, an established cardiovascular medicine, and the anaesthetics portfolio. We partnered with Aspen on our anaesthetics portfolio, as a company with established expertise who can dedicate the right resources to

grow the business, while we retain a significant proportion of the value, which we also book as Externalisation Revenue.

Alongside these externalisation opportunities, we also divest medicines that 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 2016, we sold to Pfizer the commercialisation and development rights to our late-stage small molecule antibiotics business in most markets outside the US. The agreement reinforces our focus on developing transformational medicines in our three main therapy areas, while realising value through Pfizer's dedicated commercialisation and development capabilities in anti-infectives.

The resulting revenue from these activities supports our R&D investments in our main therapy areas. Ten transactions that contribute to Externalisation Revenue and a further nine divestments or out-licences were completed in 2016.

 [More information on our partnering activity in 2016 can be found in subsequent sections of this Therapy Area Review, Business Review from page 42, Financial Review from page 62 and Note 25 to the Financial Statements from page 173](#)

Tumour drivers and resistance: AstraZeneca is investigating a number of proteins and signalling molecules designed to impact tumour growth and resistance mechanisms.



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 our combination-focused pipeline that exploits the power of four scientific platforms.

Oncology continued

Following the science of oncology

More than eight million lives are lost every year to cancer. Even as R&D continues to push boundaries in how we understand and fight cancer, 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

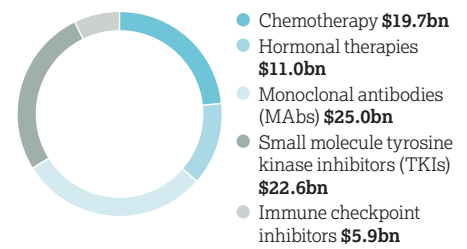
In Oncology, our vision is to respond to unmet medical need by redefining the cancer treatment paradigm. We are doing this through scientific innovation, accelerated clinical programmes and collaboration. We have a strong heritage – more than 40 years – in developing cancer drugs. By the end of 2016, several submissions were underway and we aim to deliver at least four new cancer therapies, in addition to *Lynparza* and *Tagrisso*, and 12 new line extensions by 2020. In 2015, we decided to consider all new Oncology launches, including *Lynparza*, *Iressa* (US) and *Tagrisso*, as our sixth Growth Platform, under the designation of New Oncology.

Our broad pipeline of next-generation medicines is focused on four main disease areas: breast, ovarian, lung and haematological cancers, using four key scientific approaches: immunotherapy, tumour drivers and resistance mechanisms, DNA damage response, and antibody-drug conjugates.

Therapy area world market (MAT/Q3/16)

\$84.2bn

Annual worldwide market value



Four key scientific platforms are driving our efforts to discover new cancer treatments:

- > **Immunotherapy:** Our ambition is to be a scientific leader in immunotherapy, a promising therapeutic approach that harnesses the patient’s own immune system to help fight cancer. We are working to understand how cancer evades the immune system and to identify approaches that enhance the immune system’s ability to fight cancer.
- > **Tumour drivers and resistance mechanisms:** Potent inhibition of genetic disease drivers is a clinically validated approach to shrink tumours and improve progression-free 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.
- > **DNA damage response:** Exploiting mechanisms that selectively damage tumour cell DNA is another clinically validated approach to shrink tumours and improve progression-free survival. Our programmes focus on identifying and exploiting vulnerabilities unique to tumour cells to kill the tumour cells while minimising toxicity to the patient.
- > **Antibody-drug conjugates:** The use of antibody-drug conjugates (ADC) 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.

Oncology – pipeline progressions

Regional approvals	<i>Tagrisso</i> – lung cancer (EU, JP) and ctDNA blood test (US, JP)*
Expedited review	Breakthrough Therapy Designation: durvalumab – bladder cancer (US) Orphan Drug Designation: acalabrutinib – blood cancers (EU); selumetinib – thyroid cancer (US) Fast Track Designation: <i>Lynparza</i> – ovarian cancer (2nd line) (US), prostate cancer (2nd line) (US) Priority Review Designation: <i>Tagrisso</i> (CN); durvalumab – bladder cancer (US)
Regulatory submissions	<i>Faslodex</i> – breast cancer (1st line) (US, EU, JP) <i>Tagrisso</i> – lung cancer (CN) <i>Tagrisso</i> – lung cancer (AURA3 study for full approval) (US, EU) Durvalumab – bladder cancer (US)
Phase III investment decisions	Savolitinib – papillary renal cell carcinoma Durvalumab+tremelimumab – hepatocellular carcinoma
Phase II starts/progressions	In collaboration with Celgene, the combination of <i>Vidaza</i> and durvalumab for the treatment of acute myeloid leukaemia and CC486+durvalumab for myelodysplastic syndromes; MEDI0680+durvalumab for solid tumours; MEDI0562 (humanised OX40) for solid tumours; AZD6738+ <i>Lynparza</i> for gastric cancer; AZD1775 (Wee1) for solid tumours; daratumumab+durvalumab for multiple myeloma; in collaboration with Incyte, epacadostat (IDO)+durvalumab for solid tumours
Strategic transactions completed	Acquisition of majority stake in Acerta Pharma providing access to acalabrutinib
Setbacks and terminated projects	FDA placed and subsequently lifted a partial clinical hold on the enrolment of new patients with head and neck squamous cell carcinoma (HNSCC) for clinical trials of durvalumab Tremelimumab DETERMINE, <i>Lynparza</i> GOLD, selumetinib SELECT-1 trials failed to meet primary endpoint; voluntarily withdrew the marketing authorisation application submitted to the EMA for cediranib in advanced ovarian cancer The following clinical programmes were discontinued: inebilizumab for diffuse large B-cell lymphoma; MEDI3617 for solid tumours; inebilizumab (MEDI-551)+rituximab for haematological malignancies; AZD5312 for solid tumours; AZD8835 for solid tumours; <i>Tagrisso</i> +durvalumab (CAURAL) ≥2nd line advanced EGFRm T790M NSCLC; MEDI6383 for solid tumours; durvalumab+MEDI6383 for solid tumours; MEDI0639 for solid tumours

* Roche holds licence for ctDNA blood test; collaborative effort between Roche and AstraZeneca to secure approval.



Our marketed products

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

 [Full product information on page 211](#)

We are also focused on identifying and developing combination therapies. Our immuno-oncology portfolio, which we believe is one of the most comprehensive in our industry, enables us to explore and exploit scientific and biological synergies to pursue combinations that improve outcomes and maximise patient benefit.

Our 2016 focus

In total, our marketed Oncology products generated sales of \$3.4 billion worldwide in 2016. Sales from our New Oncology Growth Platform, totalled \$0.7 billion in 2016, an increase of 458% at actual rate of exchange (450% at CER) over 2015 (\$0.1 billion). We continue to explore ways to maximise the benefit of our medicines for patients.

Tagrisso is the first approved epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) indicated for patients with metastatic EGFR T790M mutation-positive non-small cell lung cancer (NSCLC). This indication was approved in November 2015 under the FDA's Accelerated Approval Programme based on tumour response rate and duration of response. Full approval for this indication is dependent on verification and description of clinical benefit in the confirmatory trial, AURA3, for which positive results were presented in December. The EMA and FDA accepted the AURA3 submission in October and November respectively, and the FDA has granted it a Priority Review.

In February 2016, *Tagrisso* was approved by the EMA for the treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC. In March 2016, it was approved in Japan and, by the end of 2016, *Tagrisso* had received regulatory approval in more than 40 countries. In September 2016, the FDA approved a blood-based companion diagnostic test for use with *Tagrisso*. This clinically-validated companion diagnostic test uses either tissue or a blood sample to confirm the presence of a T790M mutation in patients. Japan approved the same test in December 2016.

Iressa was the first EGFR-TKI to be approved in advanced NSCLC and, as of 31 December 2016, had been approved in 90 countries. Indicated for the treatment of advanced EGFR mutation NSCLC, it is the leading EGFR-TKI outside the US. *Iressa* received approval in the US in July 2015.

Lynparza is an oral poly ADP ribose polymerase (PARP) inhibitor available to patients in 31 countries for the treatment of adult patients with BRCA-mutated high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer. In October 2016, AstraZeneca announced positive high level results of SOLO-2, a Phase III randomised, double-blind, placebo-controlled, multicentre study of *Lynparza* maintenance monotherapy in platinum sensitive relapsed BRCA gene-mutated ovarian cancer patients who are in complete or partial response following platinum-based chemotherapy. Data from SOLO-2 could form the core Phase III component for an FDA NDA submission, a Japan NDA submission and an EU variation to the MAA in 2017.

Faslodex 500mg is approved in more than 80 countries, including the EU, the US and Japan. In March 2016, the FDA approved a new indication expanding the use of *Faslodex*, in combination with palbociclib (Pfizer), for the treatment of women with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer whose cancer has progressed after

endocrine therapy. In October 2016, at the European Society of Medical Oncology Congress, we presented positive results of the Phase III FALCON clinical trial comparing the efficacy and safety of *Faslodex* 500mg with *Arimidex* in the 1st line advanced breast cancer setting (hormone-naïve patients). These positive outcomes will form the basis of a continuous expansion of *Faslodex* in metastatic breast cancer.

Details of litigation relating to *Faslodex* are included in Note 28 to the Financial Statements from page 185.

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

14m

Annual cancer cases are expected to rise from 14 million in 2012 to an estimated 22 million within the next two decades.

Source: WHO Factsheet February 2014 (data from 2012).

Oncology continued

In the pipeline

Our Oncology pipeline continued to progress in 2016. It now includes 32 NMEs in development. We also expanded several of our projects to incorporate novel combinations and various types of cancer. Some of our projects from each of our platforms are outlined below.

Immuno-oncology franchise

- > Durvalumab (MEDI4736) is an anti-PD-L1 antibody in Phase III development for NSCLC as a monotherapy and in combination with tremelimumab, an anti-Cytotoxic T-Lymphocyte-Associated protein 4 antibody. The lung cancer programme includes studies in the 1st line, 2nd line and 3rd line setting. Additional registration studies are progressing in head and neck squamous cell carcinoma (1st and 2nd line), and bladder cancer (1st line). The development programme also includes additional Phase I and Phase II studies in a broad range of solid tumours and an extensive range of combination programmes. In February 2016, durvalumab was granted Breakthrough Therapy Designation by the FDA for the treatment of patients with PD-L1 positive inoperable or metastatic urothelial bladder cancer and, in December 2016, it was additionally granted Priority Review status with a Prescription Drug User Fee Act set for the second quarter of 2017.
- > MEDI0680 is an anti-programmed cell death protein 1 (PD-1) MAb that may help promote an effective anti-tumour immune response by blocking the interactions between PD-1 and its ligands. It could also improve the intrinsic functionality of T-cells by triggering internalisation of PD-1, a mechanism that may be unique to MEDI0680. MEDI0680 is in Phase I development for solid tumours as a monotherapy and in combination with durvalumab.
- > Other immuno-oncology agents in early development include: MEDI6383, a human tumour necrosis factor receptor superfamily, member 4 (OX40) agonist; MEDI9447 targeting ecto-5'-nucleotidase (CD73); and MEDI1873 targeting glucocorticoid-induced tumour necrosis factor receptor-ligand (GITRL). These agents are in Phase I development for a range of solid tumours and have the potential for combination with other molecules in the portfolio.

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 small molecules are under investigation.
- > Selumetinib is a mitogen-activated protein kinase inhibitor in Phase III development for adjuvant differentiated thyroid cancer. In May 2016, selumetinib was granted Orphan Drug Designation by the FDA for differentiated thyroid cancer. In August 2016, the selumetinib Phase III study SELECT-1 in 2nd line KRAS mutant NSCLC failed to meet its primary endpoint of progression-free survival.
- > Cediranib is an orally administered multi-Vascular Endothelial Growth Factor receptor (VEGFR) inhibitor which is currently being tested in combination with *Lynparza* in patients with platinum-sensitive relapsed (PSR) ovarian cancer and platinum-resistant/refractory (PRR) ovarian cancer. In September 2016, AstraZeneca made the decision to withdraw the MAA for cediranib in combination with platinum-based chemotherapy followed by maintenance monotherapy for the treatment of adult patients with platinum-sensitive relapsed ovarian cancer (ICON6).
- > AZD5363 is a protein kinase B (AKT) inhibitor in Phase II development for breast and prostate cancer.
- > Savolitinib (AZD6094) is a hepatocyte growth factor receptor (c-MET) inhibitor. It is in Phase II development for lung and renal cancer.
- > Vistusertib (AZD2014) 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 (SERD) in Phase I development for the treatment of breast cancer.
- > Acalabrutinib is a Bruton's tyrosine kinase (BTK) inhibitor in Phase III development in B-cell malignancies and solid tumours. In April 2016, acalabrutinib was designated as an orphan medicinal product by the

EMA for the treatment of chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL), mantle cell lymphoma (MCL) and lymphoplasmacytic lymphoma (Waldenström's macroglobulinaemia, WM).

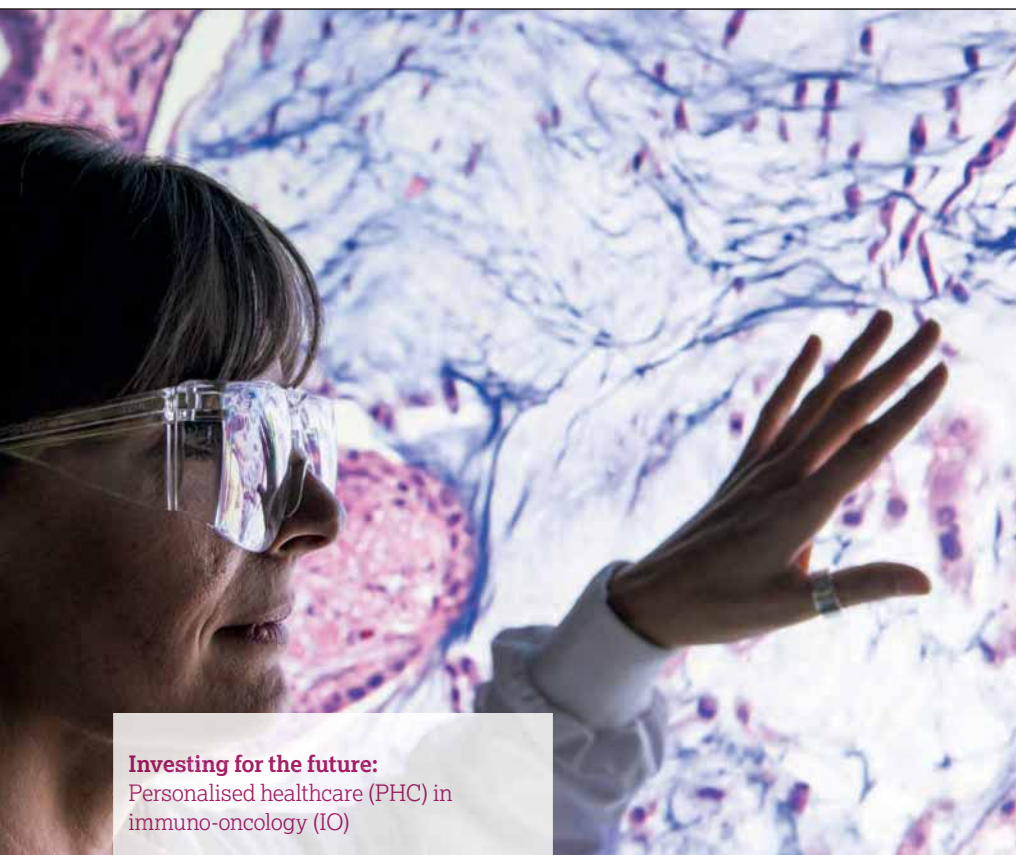
DNA damage response franchise

- > *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. *Lynparza* was granted Breakthrough Therapy Designation by the FDA for treatment of BRCA1/2 or ATM gene-mutated metastatic castration resistant prostate cancer. In May 2016, the *Lynparza* GOLD study in 2nd line gastric cancer failed to meet its primary endpoint of overall survival. In October 2016, results from the Phase III SOLO-2 trial demonstrated a clinically meaningful and statistically significant improvement of progression-free survival (PFS) among patients treated with *Lynparza* tablets (300mg twice daily) compared to placebo and provided additional evidence to support the potential use of *Lynparza* as a monotherapy for the maintenance treatment of platinum-sensitive relapsed, BRCA-mutated ovarian cancer.
- > AZD1775 is a Wee1 inhibitor in Phase II development for ovarian and other solid tumours in combination with *Lynparza*.
- > Phase I clinical studies are progressing for the ATR inhibitor AZD6738 (2nd line gastric cancer with *Lynparza* and also in combination with ionising radiation in solid tumours), the ATM inhibitor AZD0156 (for the treatment of gastric and colorectal cancers) and the aurora b kinase AZD2811 (in solid tumours).

8.2m

Cancer is a leading cause of death worldwide and accounted for 8.2 million deaths in 2012.

Source: WHO Factsheet February 2014 (data from 2012).



Investing for the future:
Personalised healthcare (PHC) in immuno-oncology (IO)

AstraZeneca has been at the forefront of PHC since its inception, with 80% of current investigative molecules using a PHC approach. This research includes investment in understanding the science of PD-L1 protein expression, which plays a role in suppressing the immune system. Testing for expression levels of PD-L1 may help to identify patients most likely to benefit from IO-based cancer therapies. However, choosing between the many PD-L1 diagnostic tests available can be challenging. We embarked on a series of studies to compare the currently available PD-L1 tests across various tumour types, and demonstrated a strong association – concordance – between most of them. This research suggests that the tests might one day be used interchangeably to enable identification of appropriate patients for IO therapies, thereby driving efficiencies in cancer care.

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.
- > MEDI4276 is a HER2 bispecific ADC, which entered clinical development for a range of solid tumours.

Key Oncology collaborations and transactions

Collaboration is key to accessing the best science and technology, achieving scientific leadership and delivering innovative, life-changing medicines. In 2016, we continued to strengthen our portfolio and accelerate clinical programmes through acquisitions and collaborations.

In January 2016, we announced a new collaboration with Incyte to evaluate the efficacy and safety of Incyte's Janus-associated kinase (JAK) 1 inhibitor, INCB39110, in combination with *Tagrisso*. This builds on an existing collaboration between the two companies to explore AstraZeneca's anti-PD-L1 immune checkpoint inhibitor, durvalumab, in

combination with Incyte's oral indoleamine dioxygenase-1 (IDO1) inhibitor, epacadostat (INCB24360).

We also extended our collaboration with Moderna to discover, co-develop and co-commercialise messenger RNA (mRNA) therapeutic candidates for the treatment of a range of cancers.

In February 2016, we completed a transaction for a majority equity stake investment in Acerta Pharma. The transaction provides AstraZeneca with a potential best-in-class irreversible oral BTK inhibitor, acalabrutinib (ACP-196), currently in Phase III development for B-cell lymphoid cancers and in Phase I/II clinical trials in multiple solid tumours.

In June 2016, we signed a definitive agreement with Foundation Medicine, Inc. to develop a novel companion diagnostic assay for *Lynparza* to support its global development programme. The companion diagnostic seeks to enable physicians to identify those patients most likely to benefit from AstraZeneca's first-in-class PARP inhibitor.

In November 2016, CancerLinQ, a non-profit subsidiary of the American Society of Clinical Oncology, announced a new non-exclusive partnership with AstraZeneca, which will use CancerLinQ Discovery, a groundbreaking offering that aims to provide insights through the analysis of real-world cancer care data. As a 'Founding Enterprise Partner', AstraZeneca will be able to gather insights on specific cancer care questions and provide critical input to maximise CancerLinQ Discovery's utility and usability.

60%

More than 60% of the world's total new annual cancer cases occur in Africa, Asia and Central and South America. These regions account for 70% of the world's cancer deaths.

Source: WHO Factsheet February 2014 (data from 2012).



Cardiovascular & Metabolic Disease

Current treatments for hyperkalaemia, a potentially life-threatening condition associated with chronic kidney disease and chronic heart failure, are poorly tolerated by patients. AstraZeneca is developing a treatment which traps potassium in the gut and removes it from the body.

We push the boundaries of science to create life-changing medicines for patients that reduce morbidity, mortality and organ damage by addressing multiple risk factors.



Following the science of cardiovascular and metabolic disease

AstraZeneca is following the science to transform how cardiovascular disease (CVD), chronic kidney disease (CKD) and diabetes are understood, interact and impact one another – ensuring the focus of treatment is across cardiovascular and metabolic disease (CVMD) to slow progression and save more lives.

Our strategic priorities

Our strategic focus is on transformative medicines that address the high unmet medical need in CVMD, including thrombosis (blood clotting), atherosclerosis (hardening of the arteries), dyslipidaemia (abnormal levels of blood lipids), chronic heart failure (CHF), diabetes and CKD.

Currently an estimated 17.5 million people die annually from CVD, representing 31% of all global deaths, and CVD is the leading cause of death in people with CKD and people with diabetes. Despite improvements in the diagnosis and treatment of CVMD, unmet medical need, as well as access and affordability challenges, remain high, while co-morbidity is common in patients living with CVMD.

We are seeking to unlock the scientific potential of our CVMD therapy area by investigating disease causes and progression, supporting our larger objective of innovating to develop novel therapeutic approaches. Our efforts aim to reduce long-term morbidity and mortality, and to ultimately reduce the burden, as well as the human, social and economic costs, of these diseases.

Our commitment is demonstrated in both our clinical development and life-cycle management programmes. More than 60,000 patients are participating in our R&D-led cardiovascular trials at more than 6,000 sites worldwide. Our focus on diabetes research includes almost 50 clinical trials worldwide with an enrolment target of 56,000 patients.

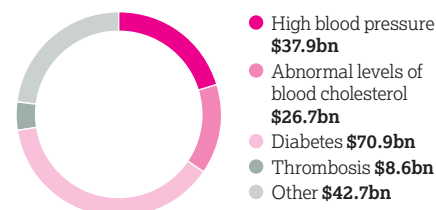
Our scientific leadership is strengthened by developing cutting edge technologies with our strategic partners:

- > Participation in the RPC2 consortium (renal precompetitive consortium) formed with the University of Michigan and Lilly to identify new therapeutic targets for the treatment of CKD.
- > Alliance with Moderna and Professor Ken Chien at the Integrated Cardio Metabolic Centre (ICMC), Karolinska Institutet in Stockholm, Sweden, to identify targets and pathways involved in repairing damaged cardiac muscle.

Therapy area world market (MAT/Q3/16)

\$186.8bn

Annual worldwide market value



- > Collaboration with the Harvard Stem Cell Institute to adapt a technique that creates human beta cells from stem cells in the search for new, transformative treatment options for diabetes.

Cardiovascular disease

Our 2016 focus

Acute coronary syndromes (ACS) is an umbrella term for sudden chest pain and other symptoms due to ischaemia (insufficient blood supply) to the heart. ACS is associated with considerable mortality and morbidity. There is a significant need to improve patient outcomes and reduce treatment costs.

Brilinta/Brilique is an oral antiplatelet treatment for ACS. It is approved in over 100 countries, including the US, Canada and Brazil under the trade name *Brilinta*, and in the EU, Iceland and Norway under the trade name *Brilique*. Since it was first launched in Europe in December 2010, it has been included in 12 major ACS treatment guidelines globally.

In February 2016, the European Commission granted marketing authorisation for *Brilique* for long-term prevention of cardiovascular death, heart attack and stroke for patients with a history of heart attack. The EU approval was based on the results from the PEGASUS TIMI-54 trial, a large-scale outcomes trial involving more than 21,000 patients.

Cardiovascular & Metabolic Disease – pipeline progressions

Regional approvals	<i>Brilinta/Brilique</i> – post myocardial infarction (EU) and acute coronary syndromes and post myocardial infarction (JP) <i>Qtern</i> (saxagliptin/dapagliflozin) – Type 2 diabetes (EU)
Expedited review	None
Regulatory submissions	ZS-9 – hyperkalaemia in response to a CRL (US) DURATION-8 (exenatide+dapagliflozin) (EU) Two further submissions await regulatory acceptance
Phase III investment decisions	<i>Forxiga</i> – heart failure; <i>Forxiga</i> – chronic kidney disease
Phase II starts/progressions	MEDI4166 – diabetes/cardiovascular disease; MEDI0382 – diabetes/obesity; AZD4076 – non-alcoholic steatohepatitis
Strategic transactions completed	Partnering with 3SBio Inc. for commercialisation of <i>Bydureon</i> and <i>Byetta</i> in China
Setbacks and terminated projects	<i>Brilinta</i> SOCRATES and EUCLID trials failed to meet primary endpoint; CRL received from FDA for ZS-9 for treatment of hyperkalaemia; <i>Epanova/Forxiga</i> combination discontinued for non-alcoholic steatohepatitis (NASH)

Cardiovascular & Metabolic Disease continued

Our marketed products

Cardiovascular disease

- > **Atacand**¹ / **Atacand HCT** / **Atacand Plus** (candesartan cilexetil)
- > **Brilinta** / **Brilique** (ticagrelor)
- > **Crestor**² (rosuvastatin calcium)
- > **Imdur**³ (isosorbide mononitrate)
- > **Plendil**⁴ (felodipine)
- > **Seloken** / **Toprol-XL**⁵ (metoprolol succinate)
- > **Tenormin**⁶ (atenolol)
- > **Zestril**⁷ (lisinopril dihydrate)

Metabolic disease

- > **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 211

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 10 October 2016.

⁴ Divested China rights to China Medical Systems Holdings Ltd effective 29 February 2016.

⁵ Divested US rights to Aralez Pharmaceuticals Trading DAC effective 4 October 2016.

⁶ Divested US rights to *Tenormin* to Alvogen Pharma US Inc. effective 9 January 2015.

⁷ Licensed from Merck. Divested US rights to *Zestril* to Alvogen Pharma US Inc. effective 9 January 2015.

In March 2016, the SOCRATES trial top-line results were announced. The trial assessed the efficacy of *Brilinta* 90mg tablets twice daily when compared to aspirin 100mg once daily in patients with acute ischaemic stroke or transient ischaemic attack. Fewer events were observed on *Brilinta* versus the comparator in the overall trial population; the trend, however, did not reach statistical significance and the primary efficacy endpoint of time to first occurrence of any event from the composite of stroke (ischaemic or haemorrhagic), myocardial infarction (MI) and death was not met.

In March 2016, the American College of Cardiology (ACC) and American Heart Association (AHA) updated their treatment guidelines for ACS and the duration of dual antiplatelet therapy. *Brilinta* is now preferred over clopidogrel for the management of patients with ACS who have received a coronary stent and in non-ST Elevation ACS patients treated with medical therapy alone. This update was the first time that the ACC and AHA have recommended *Brilinta* over clopidogrel for patients who have experienced an ST-elevation myocardial infarction (STEMI).

The update was also the first US guideline to provide the medical community with insights drawn from the PEGASUS TIMI-54 trial. The guideline supported continuation of P2Y12 platelet inhibitor therapy beyond 12 months in prior MI patients who are not at high bleeding risk.

There were three new treatment guidelines updated in China in the first half of 2016. The ACS Emergency Room Rapid Guideline, Chinese PCI Guideline and the Coronary Artery Bypass Graft Consensus (2016) Guideline. These recommended *Brilinta* as 'first-choice treatment' over any other platelet inhibitor.

The Japanese Ministry of Health, Labour and Welfare approved *Brilinta* 90mg for patients with ACS for whom the use of other antiplatelet medicines in combination with aspirin is difficult. *Brilinta* 60mg was also approved for patients who have suffered a heart attack at least one year prior and are at high risk of developing a further atherothrombotic event.

In October 2016, the EUCLID Phase III trial in peripheral artery disease (PAD) results were announced. *Brilinta* did not demonstrate benefit over clopidogrel in a symptomatic PAD patient population and did not meet the primary endpoint of the trial. However, the safety profile observed in both this trial and the SOCRATES trial was consistent with the known safety profile of *Brilinta*. Based on the current expectations, it is unlikely that we will seek regulatory submission of an indication in PAD.

Crestor is approved in 109 countries for the treatment of dyslipidaemia and hypercholesterolaemia (elevated cholesterol). The medicine has been shown to effectively lower low-density lipoprotein cholesterol (LDL-C) and achieve LDL-C goals and to increase high-density lipoprotein cholesterol (HDL-C) and reduce atherosclerotic plaque. *Crestor* faces competition from atorvastatin (*Lipitor*) and other generic products. The substance patent protecting *Crestor* in the US expired on 8 January 2016 and the paediatric exclusivity period expired on 8 July 2016. Watson Laboratories, Inc. and Actavis, Inc. began selling generic rosuvastatin in the US in May 2016 as the result of a litigation settlement with AstraZeneca. Details of these matters are included in Note 28 to the Financial Statements, from page 185. Additional manufacturers have made generic rosuvastatin available in the US in 2016, in line with AstraZeneca's business assumptions.

Epanova (omega-3-carboxylic acids) is the first FDA approved prescription omega-3 fatty acid in free fatty acid form. It has the potential to help patients with severe hypertriglyceridaemia by reducing high triglycerides (TG) levels. *Epanova* is approved in the US as an adjunct to diet to reduce TG levels in adult patients with severe hypertriglyceridaemia (TG levels $\geq 500\text{mg/dL}$). We remain committed to the launch of *Epanova* in the US and other key markets.



Investing for the future:
Patients with chronic kidney disease (CKD) and heart failure (HF)

Farxiga/Forxiga is an SGLT2 inhibitor indicated for the treatment of Type 2 diabetes. It is also being investigated in two Phase IIIb outcome trials for the management of CKD and HF in people with and without Type 2 diabetes. This marks the first time a major outcome trial will be conducted to evaluate the effect of an SGLT2 inhibitor in CKD, for which there are currently few treatment options and a significant unmet medical need.

Clinical studies

PARTHENON is AstraZeneca's largest ever cardiovascular (CV) outcomes programme involving nearly 80,000 patients. It includes five key studies covering broad patient populations across varying timescales and aims to support four new indications for *Brilinta/Brilique* over the next four years. Following the SOCRATES and EUCLID trials, which failed to meet primary endpoint, THEMIS is the next major trial, studying the benefit of ticagrelor for the prevention of CV events among Type 2 diabetic patients. The whole programme continues to progress.

To better understand the interplay between CKD, CVD and diabetes, AstraZeneca recently announced two Phase IIIb outcomes trials designed to evaluate the potential role of an SGLT2 inhibitor, which is currently indicated for the treatment of Type 2 diabetes, in the management of both CHD and CKD in people with and without Type 2 diabetes. This marks the first time a major outcome trial will evaluate the effect of an SGLT2 inhibitor on CKD.

We are also committed to further evaluating the clinical profile of *Epanova* and identifying other patient groups it may benefit. AstraZeneca continues to advance its large-scale CV outcomes trial (STRENGTH), STatin Residual risk reduction with EpaNova in high cardiovascular risk patients with Hypertriglyceridaemia, 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.

Metabolic and renal diseases

Type 2 diabetes is a chronic progressive disease that accounts for more than 90% of diabetes cases worldwide. Disease prevalence continues to grow, particularly among those at a younger age, and many patients require multiple medications. Various oral generic and branded treatments exist and newer classes of treatments continue to enter the market.

There are more than 200 million people worldwide living with CKD and AstraZeneca is working to create an innovative standard of care to prevent, treat and manage CKD with a long-term ambition of modifying the disease itself. Complications of CKD, such as hyperkalaemia and anaemia, are associated with significant CV risk plus morbidity and mortality.

Our 2016 focus

We are focused on redefining the Type 2 diabetes treatment approach and harnessing complementary mechanisms of action, as well as evaluating potential CV outcomes benefit. Our current portfolio is intended to enable combination treatment, and data from our Phase III programmes are expected to further support the outcomes benefit of this new class approach.

In 2016, we saw ongoing approvals and launches for *Farxiga/Forxiga* for the treatment of Type 2 diabetes. Starting with the EU in 2012, it is now approved in over 85 countries. It is under regulatory review in 12 additional countries.

Xigduo is approved in 55 countries, including the US with *Xigduo XR* with ongoing approvals in 2017 expected. In 2016, we continued to receive approvals and launch the *Bydureon Pen* in new markets, which is now either approved or launched in 30 countries, including the US, Japan and key European countries. The *Bydureon Pen* is a pre-filled, single-use pen injector. In the US, we are engaged in patent litigation against multiple generic companies challenging patents listed in the FDA Orange Book with reference to *Onglyza*, and are awaiting the outcome of a trial that took place in September 2016.

17.5m

An estimated 17.5 million people die annually from CV disease, representing 31% of all global deaths. More than three-quarters of these deaths occur in low- to middle-income countries.

Source: WHO Factsheet 2016 (data from 2012).

Cardiovascular & Metabolic Disease continued

422m

The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. Diabetes prevalence has been rising more rapidly in middle- and low-income countries.

Source: WHO Factsheet November 2016.

200m

CKD affects an estimated 200 million people worldwide.

Source: Ojo A. 'Addressing the Global Burden of Chronic Kidney Disease Through Clinical and Translational Research.' *Transactions of the American Clinical and Climatological Association* 2015; 125: 229-246.

In July 2016, we also saw the approval of *Qtern* (a fixed-dose combination of saxagliptin and dapagliflozin) by the European Commission for the treatment of Type 2 diabetes in European markets – the first DPP-4i/SGLT2i combination product to be approved in Europe. The resubmission for *Qtern* in the US was completed and accepted by the FDA, and we anticipate a Prescription Drug User Fee Act date in early 2017.

In September, we saw positive results from the Phase III DURATION-8 trial, demonstrating that *Bydureon* (exenatide extended-release formulation) 2mg once-weekly in combination with *Forxiga* (dapagliflozin) 10mg once-daily, significantly reduced blood sugar as measured by HbA1c, versus the individual medicines alone in patients with Type 2 diabetes inadequately controlled on metformin.

In the pipeline

The Phase III programme for a once-weekly suspension of *Bydureon* continues to progress and the *Bydureon* auto-injector is due for submission to the FDA in 2017.

Through our strategic collaboration with FibroGen and Astellas, we continue to develop roxadustat, a potential first-in-class oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) in Phase III development for the treatment of anaemia in patients with CKD, including those who are dialysis dependent and non-dialysis dependent. Roxadustat is in Phase III in the US, Europe, Japan and China. The Phase III programme consists of 15 studies enrolling more than 7,000 patients worldwide. To date, roxadustat has been studied in over 1,100 subjects in completed Phase I and II studies.

We continue to progress ZS-9 (sodium zirconium cyclosilicate), a treatment for hyperkalaemia being developed by ZS Pharma, a wholly-owned subsidiary of AstraZeneca which was acquired in December 2015.

In May 2016, the FDA issued a complete response letter (CRL) regarding the NDA for ZS-9. The CRL referred to observations arising from a pre-approval inspection at the manufacturing facility and the FDA acknowledged the receipt of recently-

submitted data which it had yet to review. In October 2016, the FDA confirmed acceptance of the NDA resubmission. The resubmission did not require the generation of new data and a regulatory decision is expected in the first half of 2017. Interactions are ongoing with other health authorities in the EU and Australia, where ZS-9 is currently under separate regulatory review. Additional regulatory submissions in other markets are planned for 2017.

Verinurad (RDEA3170) is a potent selective uric acid reabsorption inhibitor that has been in Phase II development as a urate-lowering therapy. We will now progress development of verinurad for CKD in a Phase II trial, which is planned to start during 2017.


 For more information please see [Financial Review](#) from page 62

Clinical studies

The Dapagliflozin Effect on CardiovascuLAR Events (DECLARE) study, a large CV outcomes trial to assess the impact of *Farxiga/Forxiga* on CV risk/benefit, when added to a patient's current diabetes therapy, continued in 2016. The trial was fully enrolled in 2015 with approximately 17,000 adult patients with Type 2 diabetes and is expected to be completed in 2019.

The Exenatide Study of Cardiovascular Event Lowering (EXSCEL) study also continued during 2016. This study, which began in 2010 and is expected to end in 2018, is evaluating the impact of *Bydureon*, in addition to standard of care, on CV outcomes in patients with Type 2 diabetes.

AstraZeneca and FibroGen continue to investigate roxadustat for the treatment of anaemia in patients with CKD. The OLYMPUS and ROCKIES pivotal studies evaluate roxadustat for the treatment of anaemia in patients with CKD not on dialysis and on dialysis, respectively. The initial data read-out for our sponsored trials is expected to align with the availability of pooled safety data in coordination with our partners, expected in early 2018, and we anticipate a 2018 regulatory filing in the US.



One of our key focus areas in Respiratory is lung immunity, where we are aiming to reset immunological dysfunctions that may be underlying causes of disease.



Respiratory

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

Respiratory continued

Following the science of respiratory disease

Our 40-year heritage in respiratory medicines is just the beginning of our story. The age of targeted biologics to address the unmet needs of specific patient populations has now arrived in asthma, and AstraZeneca has three biologics in mid- or late-stage development with each one targeting different biologic pathways that play important roles in this heterogeneous disease.

Our strategic priorities

Respiratory is one of AstraZeneca's main therapy areas, and our medicines reached more than 18 million patients in 2016. We have a strong pipeline with about 22,000 patients involved in clinical trials, and we expect up to four launches of new medicines between 2016 and 2020.

Our work focuses on transforming the treatment of asthma and COPD in three areas: (i) inhaled combinations at the core of care, (ii) biologic medicines for the unmet needs of specific patient populations, and (iii) scientific advancements where our ambition is to achieve disease modification and durable remission. We have considerable capabilities in inhalation technologies, which span both pressurised metered-dose inhalers (pMDIs) and dry powder inhalers (DPIs), as well as our innovative particle Co-Suspension Delivery Technology. In our early development pipeline, we focus our research on three key areas: lung immunity, lung epithelium and lung regeneration.

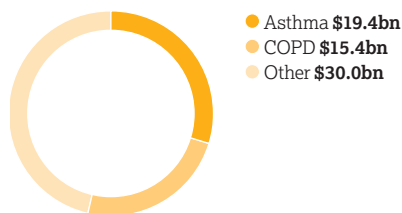
Asthma is one of the most common and chronic lung diseases worldwide and a serious global health problem, affecting the lungs' airways. Inflammation and narrowing of the airways may cause wheezing, breathlessness, chest tightness and coughing. Fixed-dose combinations (FDCs) of an inhaled corticosteroid (ICS) with a long-acting beta₂-agonist (LABA) such as *Symbicort* are the cornerstone of treatment, helping to treat moderate-to-severe asthma. For patients with mild asthma, we are investigating the use of *Symbicort* dosed 'as needed', recognising the variability and inflammatory nature of disease in these patients. For the approximately 10% of asthma patients who have severe, uncontrolled asthma despite standard-of-care medications, we are working to develop targeted biologics that address the underlying causes of disease. The FDA and EMA have accepted regulatory submissions for benralizumab, our first respiratory biologic, which is being developed for severe asthma.

COPD is a progressive and chronic disease. There are unmet needs in the treatment of COPD, such as exacerbation and symptom control, improving health status and slowing the decline of lung function and disease progression. We foresee physicians increasingly treating earlier and more actively with different strategies for inflammatory and non-inflammatory patients, and both our portfolio and development pipeline address these different needs in mild and severe disease.

Therapy area world market (MAT/Q3/16)

\$64.8bn

Annual worldwide market value



Our 2016 focus

We continue to invest in *Symbicort*, which was the number one ICS/LABA combination globally in volume terms in 2016. In the US, 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 is based on the CHASE (ChildHood Asthma Safety and Efficacy) clinical trial programme, which included the CHASE 3 Phase III trial. In addition, on 25 January 2017, the FDA granted six months of paediatric exclusivity for *Symbicort* Inhalation Aerosol. Budesonide/formoterol 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.

In the EU, two new indications were approved during 2016 – *Symbicort* pMDI for the treatment of COPD and *Symbicort* SMART for adolescents with asthma. Also, *Pulmicort* continues to be a leading ICS therapy, with significant sales growth in 2016 driven by China and other Emerging Markets.

In April 2016, the FDA approved *Bevespi* *Aerosphere* inhalation for the long-term maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema. *Bevespi* *Aerosphere* is the first combination long-acting muscarinic antagonist (LAMA) and LABA medicine to be delivered in a pMDI and the first medicine using

Respiratory – pipeline progressions

Regional approvals	<i>Bevespi</i> <i>Aerosphere</i> (PT003) – COPD (US)
Expedited review	None
Regulatory submissions	Benralizumab – severe asthma (US, EU) One further submission awaits regulatory acceptance
Phase III investment decisions	None
Phase II starts/progressions	Abediterol (AZD0548) – for asthma/COPD; AZD1419 (inhaled TLR9) – asthma
Strategic transactions completed	Acquisition of Takeda's core respiratory business
Setbacks and terminated projects	AZD8999 for COPD; MEDI7836 for asthma; AZD7624 for COPD



Our marketed products

- > **Accolate** (zafirlukast)
- > **Bevespi Aerosphere** (glycopyrrolate and formoterol fumarate)
- > **Bricanyl Respules** (terbutaline)¹
- > **Bricanyl Turbuhaler** (terbutaline)²
- > **Daliresp/Daxas** (roflumilast)
- > **Duaklir Genuair** (aclidinium/formoterol)²
- > **Eklira Genuair/Tudorza Pressair** (aclidinium)²
- > **Oxis Turbuhaler** (formoterol)²
- > **Pulmicort Turbuhaler/Pulmicort Flexhaler** (budesonide)
- > **Pulmicort Respules** (budesonide)¹
- > **Symbicort** pMDI (budesonide/formoterol)
- > **Symbicort Turbuhaler** (budesonide/formoterol)²

 Full product information on page 211

- ¹ Inhalation suspension.
² In a dry powder inhaler.

AstraZeneca's unique Co-Suspension Delivery Technology. The technology is designed to enable medicine crystals to be evenly distributed in the aerosol allowing for more consistent delivery of one or more different medicines from a single pMDI. The technology is also being applied to a range of AstraZeneca respiratory inhaled combination therapies currently in clinical development, such as the fixed-dose triple combination of LAMA/LABA/ICS (PT010).

We have launched the LAMA/LABA combination *Duaklir* for the maintenance treatment of COPD symptoms in 25 countries across Europe, Asia and Latin America. Phase III development in the US and China is underway with anticipated regulatory filings in 2018 and 2019 respectively.

In May 2016, we completed our acquisition of Takeda's core respiratory business. The deal included the acquisition of non-US rights to *Daliresp*, which is known as *Daxas* in certain countries. In December 2016, we completed the divestment of the non-US rights to *Rhinocort Aqua*, a nasal spray indicated for rhinitis nasal polyps, to Cilag GmbH International, an affiliate of Johnson & Johnson.



315m

It is estimated that approximately 315 million people worldwide suffer from asthma.



Source: To T, Stanojevic S, Moores G et al. Global asthma prevalence in adults: findings from cross-sectional world health survey. *BioMed Central Public Health*. 2012; 12(204)

In the pipeline

In COPD, PT010 is a twice-daily triple inhaled medicine combination LAMA/LABA/ICS composed of glycopyrrolate, formoterol and budesonide (key components of *Symbicort* and *Bevespi Aerosphere*) in late-stage development. PT010 is delivered in a pMDI using the Aerosphere Technology. Topline data from the KRONOS study will be available in 2017.

Benralizumab is an anti-eosinophil MAb that directly induces cellular apoptosis, which results in rapid and near-complete depletion of eosinophils. Eosinophils are the biological effector cells that drive inflammation and airway hyper-responsiveness in approximately 50% of asthma patients. The FDA and EMA have accepted regulatory submissions for benralizumab, based on our Phase III clinical trial programme. The SIROCCO and CALIMA studies demonstrated that adding benralizumab to standard-of-care medicine significantly reduced exacerbations and improved lung function and asthma symptoms in severe asthma patients with an eosinophilic phenotype compared to patients taking a placebo. These outcomes were demonstrated for the eight week dosing regimen, which may support less-frequent dosing than available medicines. An additional Phase III study showed benralizumab also reduced dependence on

oral corticosteroid use in this same patient population. Benralizumab is also in development for COPD. Phase III results and regulatory filings for COPD studies are expected in 2018.

Tralokinumab is an investigational MAb that binds to IL-13. Blocking IL-13 is a potentially important target in the treatment of certain types of severe asthma, estimated to affect around half the total severe asthma population. Analysis of the tralokinumab Phase II data suggests that IL-13 neutralisation may improve lung function and reduce asthma exacerbation rate in a subpopulation of moderate-to-severe asthma patients who are uncontrolled with standard-of-care therapy. In August 2014, we initiated a Phase III programme to evaluate the safety and efficacy of tralokinumab in reducing asthma exacerbations in adults and adolescents with severe, inadequately controlled asthma. The Phase III asthma programme is on track to deliver results in the second half of 2017.

329m

The global prevalence of COPD is estimated to be 329 million people¹ and WHO predicts that COPD will become the third leading cause of death worldwide by 2030².

¹ Source: Bereza BG, Nielsen AT, Valgardsson S et al. Patient preferences in severe COPD and asthma: a comprehensive literature review. *International Journal of COPD*. 2015; 10: 739-744.

² Source: WHO. Burden of COPD. <http://www.who.int/respiratory/copd/burden/en/>. Accessed December 2016.

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 and Neuroscience, as well as Gastroenterology, where we aim to develop best-in-class therapies and follow an opportunity-driven approach.

Our approach in our 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 (NMO) 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. NMO causes severe muscle weakness and paralysis, loss of vision, respiratory failure, problems with bowel and bladder function and neuropathic pain.

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.

Gout is a serious, chronic, progressive and debilitating form of inflammatory arthritis that affects more than 15.8 million people in major markets. The underlying cause of gout is hyperuricemia (elevated serum uric acid), which leads to the deposition of crystals primarily in the joints and in other tissues. This can result in recurrent attacks of inflammatory arthritis and, if left uncontrolled, can lead to chronic, progressive arthritis and tophus (visible soft tissue deposits of urate crystals) formation.

Rheumatoid arthritis is an autoimmune disease that affects about 1% of the population and causes inflammation in the joints, with joint pain and swelling symptoms. There is a need for novel treatments, since only about a third of patients treated with biologics achieve their treatment goals.

In the pipeline

We are strengthening 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 interferon (IFN) receptors, 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. Phase II trial results presented in November 2015 demonstrated that anifrolumab significantly reduced disease activity in moderate-to-severe SLE patients as measured by several SLE composite

Other Disease Areas – pipeline progressions

Regional approvals	<i>Zurampic</i> – gout (EU) <i>Zovacefta</i> (previously CAZ AVI) – serious infections (EU) Pandemic Live Attenuated Influenza Vaccine – pandemic influenza (EU)
Expedited review	Orphan Drug Designation: inebilizumab (MEDI-551) – neuromyelitis optica (US) Fast Track Designation: MEDI8852 – hospitalised influenza (US); AZD3293 – Alzheimer's disease (US)
Regulatory submissions	Lesinurad+allopurinol FDC – gout (US)
Phase III investment decisions	AZD3293 – Alzheimer's disease; ATM-AVI* for serious bacterial infections; tralokinumab* for atopic dermatitis
Phase II starts/progressions	MEDI2070 for Crohn's disease; MEDI3902 for the prevention of nosocomial pseudomonas pneumonia; MEDI8897 for RSV
Strategic transactions completed	Licensing agreements with Ironwood for the US rights to <i>Zurampic</i> and with Grünenthal GmbH for rights in the EU and Latin America; two licensing agreements with LEO Pharma on our dermatology portfolio (brodalumab for EU, and tralokinumab for atopic dermatitis); sale of small molecule antibiotics portfolio to Pfizer; licensing MEDI2070 to Allergan; agreement with ProStrakan Group (now Kyowa Kirin International plc) for the rights to <i>Movantik</i> (naloxegol) in the EU, Iceland, Norway, Switzerland and Liechtenstein
Setbacks and terminated projects	Abrilumab for Crohn's disease/ulcerative colitis; MEDI7510 for prevention of RSV disease in older patients

* Achieved as a result of partnering; will not be progressed by AstraZeneca.



Investing for the future: Breaking the lupus code

Recognition of the importance of the role played by the interferon pathway in lupus led to the development of anifrolumab, an investigational, potentially first-in-class, MAb that inhibits the activity of all type 1 interferons (IFN). Anifrolumab is being developed with an IFN gene signature diagnostic test designed to identify patients who may be more likely to benefit from treatment. The role of the interferon pathway may go beyond lupus; elevated type 1 IFN signature has been found in several other autoimmune diseases.



endpoints. It also improved symptoms of lupus such as rash and arthritis. Anifrolumab is currently in Phase III development for SLE and Phase II for lupus nephritis. A Phase I subcutaneous administration study was completed in 2016 with plans for further studies ongoing.

In March 2016, the FDA granted Orphan Drug Designation for inebilizumab (MEDI-551) for the treatment of patients with NMO as well as neuromyelitis optica spectrum disorders (NMOSD). Inebilizumab is an anti-CD19 MAb currently in Phase IIb clinical development. The FDA's Orphan Drug Designation programme provides orphan status to potential medicines intended for the safe and effective treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the US.

Brodalumab is a human MAb that targets the interleukin-17 (IL-17) receptor. Brodalumab is currently under regulatory review in the US and Europe for adult patients with moderate-to-severe plaque psoriasis, with decisions anticipated in early 2017.

Through a collaboration agreement, Valeant, an expert in dermatology, has an exclusive licence to develop and commercialise brodalumab globally, except in Japan and certain other Asian countries where rights are held by Kyowa Hakko Kirin, and in Europe, where LEO Pharma holds exclusive rights to develop and commercialise brodalumab based on an

agreement entered into in July 2016. Valeant and LEO Pharma assume decision making on future development and all development costs associated with brodalumab.

Zurampic inhibits the urate transporter, URAT1, which is responsible for the majority of the renal reabsorption of uric acid. By inhibiting URAT1, *Zurampic* increases uric acid excretion and thereby lowers serum uric acid levels. In combination with the current standard-of-care, xanthine oxidase inhibitors (XOIs) allopurinol or febuxostat, *Zurampic* provides a dual mechanism of action to increase excretion and decrease production of uric acid, enabling more patients with inadequately controlled gout to achieve target treatment goals.

In April 2016, AstraZeneca entered into a licensing agreement with Ironwood for the exclusive US rights to *Zurampic*. *Zurampic* was approved by the FDA in December 2015, in combination with an XO, for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with an XO alone. Ironwood launched *Zurampic* in the US in October 2016. In addition, Ironwood has exclusive US rights to the fixed-dose combination of lesinurad and allopurinol.

In February 2016, the European Commission granted marketing authorisation for *Zurampic* 200mg in combination with an XO for the adjunctive treatment of hyperuricemia in gout patients (with or without tophi) who have not achieved target serum uric acid levels with an adequate dose of an XO alone.

In June 2016, we licensed out the exclusive rights to *Zurampic* in the EU, Switzerland, Iceland, Norway and Liechtenstein, and in all Latin American countries to Grünenthal GmbH. The agreement includes rights to the fixed-dose combination of lesinurad and allopurinol in gout.

Verinurad (RDEA3170) is a potent selective uric acid reabsorption inhibitor, also intended for use as a combination urate-lowering therapy with XOIs. Verinurad is in Phase II development. We have recently initiated plans to study verinurad for CKD in a Phase II study.

Other Disease Areas continued

Our marketed products

Infection

- > **Fluenz Tetra/FluMist Quadrivalent**^{1,2} (influenza vaccine live)
- > **Synagis**³ (palivizumab)

 Full product information on page 211

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.

Neuroscience

- > **Movantik/Moventig** (naloxegol)
- > **Seroquel IR** (quetiapine fumarate)
- > **Seroquel XR** (quetiapine fumarate)
- > **Vimovo**¹ (naproxen and esomeprazole magnesium)
- > **Zomig** (zolmitriptan)

 Full product information on page 211

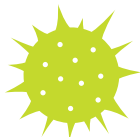
¹ Licensed from Pozen. Divested US rights to Horizon Pharma USA, Inc. effective 22 November 2013.

Gastrointestinal

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

 Full product information on page 211

3-5m



Annual influenza epidemics are estimated to result in about three to five million cases of severe illness, and about 250,000 to 500,000 deaths.

Source: WHO Factsheet November 2016.

Mavrilimumab, an investigational MAb that inhibits a key pathway in the development of rheumatoid arthritis, achieved its primary and secondary endpoints in recently completed Phase IIb trials. Results showed that mavrilimumab improved signs and symptoms of rheumatoid arthritis, measures of disability and patient-reported outcomes.

Infection

Seasonal influenza is a serious public health problem that causes severe illness and death in high-risk populations. In 2016, the US Centers for Disease Control and Prevention (CDC) issued an interim recommendation that *FluMist Quadrivalent/Fluenz Tetra* should not be used in the US for the 2016 to 2017 influenza season based on concerns regarding low effectiveness of the vaccine in the US during the last three influenza seasons (2013 to 2016). The vaccine remains licensed in the US and AstraZeneca/MedImmune remain committed to *FluMist Quadrivalent* and supporting it in the US and in the rest of the world. The FDA continues to find that the benefits of *FluMist Quadrivalent* outweigh any potential risks. We are conducting non-clinical and clinical studies in order to provide data to help support a renewed recommendation for use in the US in future seasons. The vaccine 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 recently reached an agreement with the WHO to donate and supply at reduced prices a portion of vaccine production in the event of an influenza pandemic.

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.

Since its approval in 1998, *Synagis* has helped protect at risk babies globally against respiratory syncytial virus (RSV). RSV is a common seasonal virus and the most prevalent cause of lower respiratory tract infections among infants and young children, affecting approximately two-thirds of all infants in their first year of life (68% by 12 months of age and 97% by 24 months of age). 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. *Synagis* is approved in more than 80 countries and is the global standard of care for RSV prevention. 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 requires dosing only once per RSV season – a potential breakthrough in RSV prophylaxis. In November 2016, the first patient was dosed in a Phase IIb trial. The FDA granted Fast Track status to MEDI8897 in April 2015.

Through a broad collaboration and significant funding, AstraZeneca joined in a public-private partnership with Vaccines Europe, the European Commission, the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Innovative Medicines Initiative (IMI) to further define the substantial unmet needs of RSV in paediatrics and older adults. Funding for the partnership, called RESCEU, will support the existing MEDI8897 programme and further strengthens our relationship with IMI.

In June 2016, the European Commission granted marketing authorisation for *Zavicefta* (ceftazidime-avibactam, previously known as CAZ AVI), a new combination antibiotic for the treatment of patients with serious Gram-negative bacterial infections requiring hospitalisation.

Zavicefta has been developed in response to the urgent need for new antibiotics to treat serious infections that are becoming increasingly resistant, such as multi-drug resistant *P. aeruginosa*, carbapenem-resistant Gram-negative pathogens, and ESBL-producing *Enterobacteriaceae*.

In December 2016, we confirmed the completion of an agreement to sell the development and commercialisation rights of our late-stage, small molecule antibiotics business to Pfizer. The portfolio comprised *Zinforo*, *Zavicefta*, *Merrem*, ATM-AVI and CXL in all markets where we held the rights.



Investing for the future:
Searching for a treatment for
Alzheimer's disease

Alzheimer's disease remains one of the largest areas of unmet medical need and continues to generate significant social and scientific interest. AZD3293, our BACE inhibitor in collaboration with Lilly received Fast Track Designation by the FDA in August 2016.

Neuroscience

Current commercialised AstraZeneca neuroscience molecules include *Zomig* (triptan) and *Seroquel* (atypical antipsychotics), which have lost exclusivity in all major markets. In November 2016, two licensed generics of *Seroquel XR* were launched in the US. In June 2016, AstraZeneca announced an agreement with Aspen Global Incorporated, part of Aspen Group, for the rights to the global anaesthetics portfolio 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*).

AZD3293 is our BACE inhibitor which we are progressing in collaboration with Lilly for the potential treatment of Alzheimer's disease. It experienced several critical milestones throughout 2016, including continuation of the Phase II/III trial AMARANTH into Phase III and the initiation of DAYBREAK-ALZ, a new Phase III trial to evaluate the safety and efficacy of AZD3293 in people with mild Alzheimer's dementia. The investigational treatment also received Fast Track Designation by the FDA in August 2016.

Further underpinning AstraZeneca's commitment to Alzheimer's disease, in December 2016, we announced that MEDI1814, an investigational MAb selective for toxic proteins associated with Alzheimer's disease, will be developed beyond Phase I, also in collaboration with Lilly.

We are committed to ensuring that pain patients who need to manage the side effect of opioid induced constipation continue to get access to *Movantik/Moventig*. In March 2016, AstraZeneca announced an agreement with ProStrakan Group, now Kyowa Kirin International plc, for the rights to *Movantik* (naloxegol) in the EU, Iceland, Norway, Switzerland and Liechtenstein. In December 2016, we completed a sub-licence to Knight Therapeutics Inc. to commercialise *Movantik/Moventig* in Canada and Israel. This follows the 2015 co-commercialisation agreement with Daiichi Sankyo for *Movantik* in the US. These agreements are in line with delivering on our externalisation strategy to create value by partnering on pipeline assets that are outside our three main therapy areas.

Gastrointestinal

In 2016, use of *Nexium* continued to grow in markets including 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.

Business Review



The first phase in AstraZeneca's strategy focused on strengthening and accelerating our product pipeline. Now into the second phase, our focus is on driving our Growth Platforms and launching new products. This effort is driven by a business that is organised to deliver our strategic priorities in a sustainable way.

Overview

- > Focused investment in accelerating late-stage programmes to ensure new treatments get to patients safely and as quickly as possible
- > Plans for achieving scientific leadership include researching new modalities, seeking out different kinds of collaboration and promoting personalised healthcare
- > Six Growth Platforms represented 63% of revenues in 2016, up 4% at actual exchange rates (5% at CER) over 2015
- > In April, announced further focus on our main therapy areas to drive greater productivity across the organisation, sharpen the prioritisation of investments, increase partnering and streamline our operations
- > Began to refresh our sustainability programme and embed it into our business practices, with focus on three areas: ethics and transparency; broadening access to healthcare; and environmental protection
- > Committed to delivering value in pricing our medicines with policy based on four principles
- > Continued to promote a safe and healthy work environment, coupled with our commitment to working only with those who share our ethical standards

Organisation

Our science is led by our two biotech units which conduct innovative discovery research and early-stage development from initial target selection to Phase II trial completion. The Innovative Medicines and Early Development (IMED) Biotech Unit focuses on scientific advances in small molecules, nucleotides and other emerging technologies and drug discovery platforms, while MedImmune is responsible for global biologics R&D. Both units are responsible for delivering projects to our Global Medicines Development (GMD) unit for late-stage development.

We have three strategic R&D centres: Gaithersburg, Maryland US; Gothenburg, Sweden; and Cambridge, UK. For more information on our move to Cambridge, announced in 2013, see page 7.

Our Global Product and Portfolio Strategy group (GPPS) leads our therapy area activities. 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 also works closely with healthcare providers, regulatory authorities and those who pay for our medicines, seeking to ensure those medicines help to fulfil unmet medical need and provide economic as well as therapeutic benefits.

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



Throughout this Annual Report this symbol identifies sustainability content

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

Restructuring

Since 2007, we have made significant efforts to restructure and reshape our business to improve long-term competitiveness. Full details are provided in the Financial Review from page 62. We have created a leaner and simpler organisation, focused on driving distinctive science in our main therapy areas. To advance our strategy, in April 2016, we announced plans to:

- > sharpen prioritisation of investments and focus in our main therapy areas, particularly Oncology
- > increase partnering in relation to projects in our inflammation, infection and neuroscience disease areas, and to products in markets where there is a clear rationale

- > align costs to our changing business shape and to streamline our operations at a global, regional and country level; reshaping manufacturing as we build our biologics capacity; to drive simplification; and to implement small footprint changes.

Restructuring charges of \$1,107 million were incurred in the year and we remain on track to realise the benefits and incur the costs we announced.

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. Our commitment to growing our business in a sustainable way also helps us protect our licence to operate, attract and retain talent, manage risk and, most importantly, deliver life-changing medicines to patients. The SET and Board regularly review our sustainability work as part of their risk management and business review activities.

Refreshed sustainability strategy

In 2016, we embarked on a process to refresh and focus our sustainability programme and further embed it into our business practices and strategic priorities. We worked with an independent think-tank to complete a sustainability materiality assessment to help identify priorities.

Sustainability framework

A sustainability framework is embedded in the way we operate:



Sustainability Advisory Board

Established in 2015 and meets twice annually to provide external insight, feedback and advice to help sharpen our understanding of, and responses to, established and emerging sustainability issues. The Advisory Board also helps identify opportunities for further innovation and collaboration.

Board

Non-Executive Director, Geneviève Berger, oversees implementation of the sustainability framework and reporting to the Board.

SET

SET is responsible for the framework.

Senior managers throughout the Group are accountable for operating in line with the sustainability commitments within their areas, taking into account national, functional, and site issues and priorities.

Line managers are accountable for ensuring that their teams understand the requirements and improvement targets, and that people are clear about what is expected of them as they work to achieve our business goals.

Sustainability Council

The Council is chaired by a SET member, currently Katarina Ageborg. Members comprise senior leaders from each relevant SET function. Its agenda focuses on driving long-term value creation by, among other things:

- > agreeing sustainability priorities for the Group in line with strategic business objectives
- > managing and monitoring the annual process of setting sustainability objectives and targets, as well as reviewing performance against KPIs
- > agreeing appropriate policy positions to support our objectives and reputation management.

Sustainability Working Group

A network of SET function representatives and subject matter experts supports the Council. The network reviews issues with the potential to impact AstraZeneca's sustainability agenda and helps deliver the substantive elements of our programme.



Stakeholders

Regular engagement with external stakeholders, which takes place with a range of socially responsible investors and other interest groups, provides the opportunity for sustainable issues or concerns to be raised and discussed.

Business Review continued

The assessment process identified 27 sustainability issues relevant to us. These became the basis for benchmarking analysis, engagement with external and internal stakeholders, and an internal review that examined our areas of strength, weakness and opportunity, and our alignment with the UN Sustainable Development Goals.

Through this process, we have identified three priority areas that, given their alignment with our Purpose and business strategy, will allow us to have the most impact in benefiting our patients, our Company, broader society and the planet. We remain committed to managing and building our performance in the other areas within the scope of AstraZeneca's sustainability programmes, such as human rights, diversity, and workplace health and safety. We will continue to work across our business to integrate these commitments into the way we work, engage with stakeholders and evaluate our performance. The three priority areas are as follows.

1. Broadening access to healthcare. Through collaboration and innovation we strive to expand access to our medicines by:

- > Exploring innovative ways of increasing access to healthcare for more people, tailored to meet differing patient needs and circumstances (see page 51 and Healthy Heart Africa on page 49).
- > Making a positive contribution to our local communities around the world, through community support programmes consistent with improving health and promoting science (see page 53).

2. Ethics and transparency. We will maintain integrity in everything we do by:

- > Working to consistent global standards of ethical sales and marketing practices in all our markets (see page 52).
- > Working only with suppliers who have standards consistent with our own as we increase our outsourcing to drive business efficiency (see page 52).
- > Working on continued transparency with our data in clinical trials, enhancing the understanding of how our medicines work and benefit patients (see page 47).

> Applying sound bioethics to all our work and maintaining a strong focus on patient safety (see pages 47 and 48).

3. Environmental protection. We follow the science to protect the planet by:

- > Managing our impact on the environment, across all our activities, with a particular focus on carbon emissions, waste and water use.
- > Minimising the environmental impact of our products (see pages 60 and 61).

Our focus on these three areas does not diminish our commitment to other areas of our sustainability agenda. For example:

- > Ensuring that diversity in its broadest sense is reflected in our leadership and people strategies (see page 55).
- > Continuing to develop and embed a consistent approach to human rights across our worldwide activities (see page 56).
- > Promoting the safety, health and wellbeing of all our people worldwide (see page 53).

Benchmarking and assurance

Our work in sustainability has been recognised by a number of organisations in 2016:



DJSI

- > Second in Pharmaceuticals, Biotechnology and Life Sciences industry group.
- > Sector best scores attained for: Occupational Health and Safety, Code of Conduct, Marketing Practices, Climate Strategy and Health Outcomes Contribution.



CDP

- > Climate A List – Among the top 9% of companies participating in CDP's climate change programme in recognition of our actions to reduce emissions and mitigate climate change.
- > Water A List – Among the leading 25 companies for our commitment to transparency around environmental risks and demonstration of pursuing best practice.
- > Supplier Climate A List – Among the 3% of companies awarded an A grade for our efforts and actions to combat climate change by implementing programmes to reduce emissions in both direct operations and supply chain.



Access to Medicine Index

- > Biggest riser in the Index since the last survey, moving to 7th place in 2016 from 15th in 2014.
- > Recognition for industry best practice in a number of areas, including transparent approach to intellectual property in relation to Index Countries: disclosing where we will not enforce patents, where we would consider granting a licence, and disclosing the status of our patents for products used to treat Index Diseases.



Bureau Veritas has provided independent external assurance to a limited level on the sustainability information contained within this Annual Report.

For more information on Bureau Veritas' work and benchmarking, please see Sustainability: supplementary information on page 231 and the Sustainability pages on our website, www.astrazeneca.com.

Safety, Health and Environment strategy

Throughout 2016, we worked to embed our 2016 to 2025 Safety, Health and Environment (SHE) strategy and deliver the targets we have set ourselves as regards:

- > eliminating workplace accidents and illnesses (see page 53)
- > protecting natural resources (see pages 60 and 61)
- > ensuring the environmental safety of our products (see page 61).

We have made good progress to date, attaining independent verification that our climate change targets are science-based, setting out our RE100 strategy to source 100% renewable power globally, and disclosing our climate information in public reports. We have also made a commitment to responsible water stewardship as part of The Business Alliance for Water and Climate partnership. We are working closely with our operating sites to agree on specific contributions to our 2025 strategy targets. More information on our performance in 2016 can be found in Safety, health and wellbeing on page 53 and Environment from page 60.

We are proud of the external recognition we are receiving for our work. As shown to the left, the Dow Jones Sustainability Index (DJSI) has scored our climate change strategy and occupational health and safety performance as best in our industry. Our submissions to investor benchmarking organisation, CDP achieved an A-list ranking for both climate change and water stewardship. During 2016, we committed approximately \$25 million to natural resource projects at our sites. These projects are expected to accelerate our resource efficiency performance and include: solvent recovery to reduce hazardous waste; a novel heat pump system to reduce reliance on natural gas; and a number of resource efficiency minor works programmes. Site water stress assessments and natural resource audits continue to identify further opportunities for management and investment. We continue to hold third party suppliers accountable for protecting the environment across our supply chains and we are active members of the Pharmaceutical Supply Chain Initiative to promote a collaborative approach across our industry.

1. Achieve scientific leadership



We are using our distinctive scientific capabilities in small molecules and biologics, including immunotherapies and protein engineering, as well as investing in key programmes and focused business development, to deliver life-changing medicines.

Overview

- > Launched six diagnostic tests linked to our products in line with our personalised healthcare (PHC) strategy
- > Delivered clinical trial data and submissions that resulted in 11 approvals for brand new medicines in the US, EU, China or Japan
- > Simplified programmes, processes and systems, and prioritised resources towards late-stage drug development
- > Published 75 manuscripts in 'high-impact' publications compared to seven in 2010
- > Continued to strengthen early-stage portfolio with new drug modalities, allowing us to expand into novel scientific areas while maintaining a clear focus on disease mechanisms
- > Strive to access the best science, both internal and external, in our biotech units, and we are open to exploring new and different kinds of collaborations
- > Committed to working responsibly and in accordance with our global bioethics policy

Early science

We continued to strengthen our early-stage portfolio with new drug modalities such as modified RNA, anti-micro RNA, antisense oligonucleotides, bi-specific monoclonal antibodies (MAbs) and antibody-drug conjugates (ADC). This is allowing us to expand into novel scientific areas while maintaining a clear focus on disease mechanisms. In 2016, in partnership with Regulus Therapeutics Inc., we saw AZD4076, an anti-micro RNA targeting the miR103/107 gene, being dosed into patients. These patients had non-alcoholic steatohepatitis or 'silent-liver disease', for which there are no approved medicines. Also in 2016, in partnership with Moderna, we filed the clinical trials application for AZD8601, a modified RNA for VEGF-A for

cardiac regeneration. We also extended our partnership with Moderna to include immuno-oncology programmes, combining MedImmune's protein engineering and cancer biology expertise with Moderna's technology.

 See Oncology from page 25 for more information

Working collaboratively and fostering open innovation

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. Our partnership models include in-licensing of new chemical modalities and platforms, disease understanding, technology advances, uncovering novel target opportunities, and clinical partnerships. For example, two key pieces of scientific research were published in high-impact journals by scientists at our joint centre for cardiometabolic diseases at the Karolinska Institutet. We also identify collaborations that allow us to out-license our technology platforms. For instance, we have expanded the utilisation of our ADC technology platform through an agreement with Regeneron Pharmaceuticals Inc., giving them access to MedImmune's ADC technology.

In 2016, IMED continued to pioneer new approaches to open innovation, enabling our scientists more freely to share their ideas 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 2016, our teams had reviewed more than 500 proposals for new drug projects. Of these, 26 have progressed as far as clinical trials, while more than 150 are at pre-clinical trial stage.

During 2016, MedImmune continued to forge collaborations, including a research collaboration with the University of California, San Francisco US, with an emphasis on basic research and translational sciences. We also announced an innovative programme with Johns Hopkins University, providing a first-of-its-kind industry-academic PhD programme in the US. Furthermore, in late 2016, MedImmune and a consortium of UK universities – Cambridge, Leeds, Manchester and Sheffield – announced that they will be afforded a Collaborative

Business Review continued



Investing for the future:
Listening to patients

Since 2015, we have introduced over 60,000 patients from the PatientsLikeMe network to our research teams to inform our R&D programmes. After simulating a clinical study visit with lupus patients, their feedback resulted in 16 changes to the way the study was conducted.

That study is now delivering ahead of time, demonstrating the value of working with patients to deliver more efficient research. We believe that this will improve our ability to bring more life-changing medicines, more quickly to more patients.

Training Partnership (CTP), structured as 12 PhD studentships, from the Biotechnology and Biological Sciences Research Council (BBSRC). These CTP studentships are designed to invest in the training of the next generation of scientists, providing access to facilities and expertise unavailable in an academic setting alone.

Our personalised healthcare strategy
Personalised healthcare (PHC) allows us to tailor both new and existing treatments to the needs of individual patients by means of diagnostic tests. It is an integral part of our plans to achieve scientific leadership and we are committed to bringing PHC to patients in all main disease areas. Three of our products (*Iressa*, *Lynparza* and *Tagrisso*) are coupled with companion diagnostic tests that select patients based on their molecular profiles. In addition, 80% of our clinical pipeline is following our PHC approach and over 50 planned drug launches by 2023 require a diagnostic test.

In 2016, we worked with our partners to launch six diagnostic tests linked to our products increasing our total number of diagnostics launched since 2014 to 15. Our commitment to bring PHC to patients in all main disease areas has resulted in our first diagnostic test outside oncology: the Nova Biomedical Pro Uric Acid Test. It is a hand-held serum uric acid point of care test, aligned to *Zurampic*, which can be used to measure a patient's response to gout treatment. We are also developing diagnostic tests with Abbott for treating asthma and with Qiagen for treating lupus.

Also in 2016, we announced our integrated genomics initiative which focuses on the discovery of new targets and biomarkers

linked to molecular mechanisms of disease across our main therapy areas. The initiative includes new collaborations with Human Longevity, Inc., US, the Wellcome Trust Sanger Institute, UK, and The Institute for Molecular Medicine, Finland. We are also establishing an in-house Centre for Genomics Research led by Professor David Goldstein, a leader in genomics. This Centre aims to apply genomic insight across our entire R&D pipeline by developing a bespoke database comprising genome sequences from samples donated by patients in clinical trials together with associated clinical and drug response data.

Late-stage development

GMD designs and delivers clinical trials and makes regulatory submissions to seek approval for new drugs and line extensions. During 2016, we delivered clinical trial data and submissions that resulted in 11 approvals for brand new medicines in the US, EU, China or Japan. We also had some setbacks during the year, with some disappointing Phase III data results – for example, *Brilinta* for peripheral arterial disease, selumetinib for non-small cell lung cancer, and tremelimumab for mesothelioma – see Cardiovascular & Metabolic Disease and Oncology from pages 30 and 25 respectively for more information. However, this is to be expected when we are investigating treatments for diseases that are hard to treat.

In order to maintain a focus on our main therapy areas and enable us to maximise time and resources in accelerating certain programmes, we identified opportunities to collaborate on developing assets within our late-stage pipeline. For example, we made an agreement for the development of tralokinumab for patients with atopic dermatitis (allowing us to focus on its development for asthma) and an agreement for an accelerated global development programme for savolitinib for patients with papillary renal cell carcinoma.

Accelerating the pipeline

In 2016, we presented scientific rationale that resulted in 10 regulatory designations for Priority or Fast Track review for new medicines which offer the potential to address unmet medical need in certain diseases, and we also worked to secure Orphan Drug status for the development of medicines to treat very rare diseases. For example, in the US, we were granted Breakthrough Therapy Designation for our

6



In 2016, launched six diagnostic tests linked to our products.

immunotherapy treatment – durvalumab for bladder cancer. We also received Fast Track Designation for *Lynparza* for 2nd line ovarian cancer and for MEDI8852 for patients hospitalised with Type A strain influenza. Orphan Drug Designations were granted for acalabrutinib for three haematological indications, for selumetinib for differentiated thyroid cancer, and for MEDI-551 for treating neuromyelitis optica. We are also working alongside regulatory authorities to drive change within the regulatory environment by ensuring that the clinical benefits of our medicines for patients are clearly understood. For example, using Patient Reported Outcomes data can help define how oncology medicines are used to treat patients with cancer.

With 132 drug projects in the pipeline, GMD is prioritising by focusing investment to accelerate specific programmes, so that new treatments get to patients more quickly but still safely. As a result, several immuno-oncology clinical trials, including some for lung cancer, head and neck cancer and bladder cancer, completed recruitment in 2016, with read-outs expected in 2017. Teams have also been quick to turn positive clinical trial data into regulatory submissions. In 2016, we made submissions in the US and EU for our first respiratory biologic treatment, benralizumab, for severe asthma and for our lung cancer treatment, *Tagrisso*, in China. We secured a priority review for *Tagrisso* following its accelerated development programme and previous approvals in the US, EU, Japan and 13 other countries.

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. These include new partnerships with the Department of Medical Statistics at the London School of Hygiene & Tropical Medicine and with the University of Manchester's Health eResearch Centre. These partnerships aim to deploy statistical techniques in examining clinical and healthcare data to make medicines more personalised and effective for patients, and to drive smarter clinical trials.

Our scientific reputation

Demonstrating the quality of the research conducted in our laboratories, through publication in high-quality and 'high-impact' journals, is an essential element in building our scientific reputation and achieving

scientific leadership. It is also critical for recruiting and retaining the best scientists from around the world. Scientists from IMED, MedImmune and GMD have published 75 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 1,050 in total. This represents an eleven-fold improvement since our drive to publish in 'high-impact' journals began in 2010.

Responsible research

Our commitment to working in a transparent and ethical manner is essential to achieving scientific leadership and delivering life-changing medicines. Our global standards of bioethics apply to all our research activity, whether conducted by us or third parties on our behalf. The following sections summarise our activities in this area – for more information, see our website, www.astrazeneca.com/sustainability.html

Patient safety

Patient safety is very important and we strive to minimise the risks and maximise the benefits of our medicines. Through a pharmacovigilance programme, we monitor our medicines once they are in the marketplace to learn of any side effects not identified during the development process and provide information concerning the safety profile of our medicines to regulators, healthcare professionals and, where appropriate, patients.

We have a dedicated patient safety team to help us fulfil our commitment to patient safety. Each developing and marketed medicine is allocated a Global Safety Physician and a patient safety scientist. In addition, each market is supported by a dedicated patient safety manager. Our Chief Medical Officer is accountable for the benefit/risk profiles of our products in development and on the market. He provides medical oversight and enforces risk assessment processes to help us make efficient and informed decisions about patient safety.

Clinical trials and transparency

In 2016, we conducted a range of clinical trials at many sites as shown in the chart 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 but some are conducted by CROs on our behalf. In 2016, approximately 48% of patients in our small molecule studies and 44% of patients in our biologics studies were monitored by CROs. We require these organisations to comply with our global standards and we conduct risk-based audits to monitor compliance.

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

In 2016, we implemented new global standards which give patients and researchers more information about our research. Specifically:

- > Every patient who participates in a study sponsored by us receives a note recognising their contribution as well as a copy of the study's Trial Results Summary.
- > In 2016, we launched a portal (<https://astrazenecagroup-dt.pharmacm.com>) for external researchers to allow them to request our clinical data and reports to support additional research. We have responded to over 50 requests so far.

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

Clinical trials by region

Region	Small molecule	Biologics
Europe	15%	23%
US/Canada	27%	26%
Asia Pacific	15%	11%
Central/Eastern Europe	28%	24%
Japan	2%	5%
Latin America	10%	10%
Middle East and Africa	3%	1%

Business Review continued

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 and meet regulatory concerns. 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.

To date, seven research proposals that include use of cells derived from hFT have been received for consideration, but none of these has progressed so far, either for scientific or other reasons. We continue to review our processes for the supply of hFT but, at the end of 2016, had yet to approve a single source. Currently, four projects using three different hESC lines have been approved.

Animal research

We are committed to helping the public understand our use of animals in research and our methods for reducing, refining, or replacing this use (3R approach).

We share our transparency goals externally through presentations at conferences and workshops throughout the US and EU, and

we also highlighted our latest refinement techniques and approach to implementing the 3Rs in a recent blog for the UK National Council for the 3Rs. Internally we are working to refine our study designs by improving access to a refreshed training programme on the principles of good statistical practice. The objective of this training is to ensure that scientists are better able to appropriately power their studies, account for variability and control bias wherever possible.

Animal research use varies depending on numerous factors, including our amount of pre-clinical research, the complexity of the diseases under investigation and regulatory requirements. We believe that without our active commitment to reducing, refining, or replacing animals in research, our animal use would be much greater. In 2016, we used 193,451 animals in-house (2015: 182,055). In addition, 25,651 animals were used by CROs on our behalf (2015: 33,220).

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

- > Ongoing scrutiny of pharmaceutical pricing in US and Europe
- > Despite biennial price cuts, Japan remained an attractive market
- > Third fastest growing top 10 multinational pharmaceutical company in Emerging Markets
- > Growth rate in China expected to moderate due to increased price pressure and hospital cost containment
- > Pricing policy based on principles of value, sustainability, access and flexibility
- > Sought to make our medicines more affordable for self-pay patients based on ability to pay
- > Expanded Healthy Heart Africa programme from Kenya to Ethiopia and partnered with The US President's Emergency Plan for AIDS Relief

Our plans for growth

Our Commercial teams, which comprised around 34,100 employees at the end of 2016, 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, such as *Crestor*, *Nexium* and *Seroquel*, we have witnessed increasing revenues from our growth brands and launches. This return to growth is underpinned by our internal Growth Platforms which are our growth levers. As our strategy has progressed, so our Growth Platforms have evolved, as shown in Strategy and key performance indicators from page 16. 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 4% at actual exchange rates (5% at CER) in 2016 and now represent 63% of all revenues.

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 2016 can be found in the Geographical Review from page 226](#)

US

As the eleventh largest prescription-based pharmaceutical company in the US, we have a 3.9% market share of US pharmaceuticals by sales value.

In 2016, sales in the US decreased by 22% to \$7,365 million (2015: \$9,474 million). Declines in revenue from *Nexium*, *Crestor* and *Synagis* were partially offset by the strong performance of our Growth Platforms, including *Farxiga*, *Bydureon* and *Brilinta*, the launches of *Lynparza* and



Investing for the future: Healthy Heart Africa



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.

HHA aims to reach 10 million hypertensive patients across Sub-Saharan Africa by 2025 and, after two years, it has already:

- > conducted over two million hypertension screenings in the community and in health facilities
- > trained over 3,000 healthcare workers, including doctors, nurses, community health volunteers and pharmacists to provide education and awareness, screening and treatment services for hypertension across 31 counties
- > activated 403 health facilities to provide hypertension services, including the establishment of secure supply chains for low-cost, high-quality antihypertensive medicines.

Following the success of HHA in Kenya, we developed a partnership with the Federal Ministry of Health in Ethiopia to integrate HHA programming into the Ethiopian healthcare system in support of the Government National Strategic Action Plan for NCDs.

In September, we announced a \$10 million, five-year global public-private partnership with The US President's Emergency Plan for AIDS Relief (PEPFAR) that will expand access to HIV/AIDS and hypertension services by offering them in an integrated manner at existing PEPFAR-supported HIV/AIDS sites, beginning in Kenya. For example, working-age men are a difficult population to engage for HIV care, and HHA's innovative way of working presents an opportunity for the partnership with PEPFAR to improve HIV care in this hard-to-reach population.

Tagrisso, and the impact of completing the acquisition of Actavis' rights to *Tudorza* and *Daliresp* in the US.

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 2016, the overall measurable reduction in our profit before tax for the year due to discounts on branded pharmaceuticals and an industry-wide excise fee was \$471 million (2015: \$786 million; 2014: \$714 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 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 2016, 84.7% of prescriptions dispensed in the US were generic, compared with 84.0% in 2015. 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

3,000

Trained over 3,000 healthcare workers as part of Healthy Heart Africa.

Business Review continued

out-of-pocket thresholds. We understand that our medicines will not benefit patients if they are unable to afford them, and that is why we offer a number of resources and programmes that can help patients afford their medications by reducing 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.

Ongoing scrutiny of the US pharmaceutical industry, focused largely on pricing, is placing increased emphasis on the value of medicines. This scrutiny is likely to continue from many stakeholders, including policymakers and legislators. Proposed policy and legislative changes which are being considered, include different approaches to price controls on medicines (including price transparency), potential changes to government regulated programmes (such as Medicare Part B, Medicare Part D, Medicaid or other provisions under the ACA), and changes affecting the commercial importation of medicines into the US.

While widespread adoption of a broad national price-control scheme in the near future is unlikely, we expect the increased focus on pharmaceutical prices and their impact on healthcare costs to continue for the foreseeable future.

 For more information on pricing pressure and the ACA, please see Marketplace from page 11

Europe

The total European pharmaceutical market was worth \$201 billion in 2016. We are the twelfth largest prescription-based pharmaceutical company in Europe (see Market definitions on page 239) with a 2.4% market share of pharmaceutical sales by value.

In 2016, our sales in Europe decreased by 5% at actual rate of exchange (3% at CER) to \$5,064 million (2015: \$5,323 million). Key drivers of the decline, leaving aside the impact of divestments, such as the anaesthetics portfolio, were continued competition from *Symbicort* analogues, ongoing volume erosion of *Pulmicort*, *Seroquel XR* and *Nexium* following loss of exclusivity, and pricing and volume pressure for *Crestor*. The continued macroeconomic

environment, increased government interventions (for example, on price and volume) and parallel trade across markets also affected sales. Despite these conditions, we continue to launch innovative medicines across Europe and saw significant progress within our Growth Platforms, in particular with *Forxiga*, *Xigduo*, *Brilinta*, *Lynparza* and *Tagrisso*.

Established Rest of World (ROW)*

In 2016, sales in Japan increased by 8% at actual rate of exchange (decreased 3% at CER) to \$2,184 million (2015: \$2,020 million), as a result of the biennial National Health Insurance (NHI) price cuts effective from 1 April 2016. We experienced price cuts of approximately 5% on our 2016 revenue. Despite the NHI price cuts, across our Growth Platforms we saw strong volume growth. Particularly strong performance from *Nexium* and *Crestor*, and the Diabetes franchise helped to drive this volume growth, offsetting generic competition. In addition, in May 2016, we launched *Tagrisso* in Japan which generated \$82 million of sales and we expect will continue to be a major driver of growth. We now hold ninth position in the ranking of pharmaceutical companies by sales of medicines in Japan. Despite the 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.

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 65% funded by private payers and 35% with public plans.

Our sales in Australia and New Zealand declined by 12% at actual rate of exchange (10% at CER) in 2016. This was primarily due to the continued erosion of *Crestor*, *Atacand* and *Nexium* by generic medicines. Sales declined less in 2016 than in 2015 as the pace of generic erosion has been

moderated while the sales growth from new products such as *Brilinta* and the Diabetes portfolio has started to pick up. *Brilinta* and the Diabetes portfolio grew by 18% (actual and CER) and 57% (actual and CER) respectively.

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

Emerging Markets: expansion and collaboration

Emerging Markets, as defined in Market definitions on page 239, comprise various countries with dynamic, growing economies. As outlined in Marketplace from page 11, these countries represent a major growth opportunity for the pharmaceutical industry due to strong demand 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.

With revenues of \$5,794 million, AstraZeneca was the fifth largest multinational pharmaceutical company, as measured by prescription sales, and the third fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2016.

In China, AstraZeneca is the second largest pharmaceutical company in the hospital sector, as measured by sales. Sales in China in 2016 increased by 4% at actual rate of exchange (10% at CER) to \$2,636 million (2015: \$2,530 million). We delivered sales growth above the growth rate of the hospital market sector through strategic brands investment, systematic organisational capability improvements and long-term market expansion programmes in core therapy areas. The industry growth rate is expected to be moderated to high single digits, impacted by increased price pressure and hospital cost containment. Nevertheless, the healthcare environment in China remains dynamic. Opportunities are arising from incremental healthcare investment, strong underlying demand and the emergence of innovative medicines.

Growth drivers for Emerging Markets include our new medicines, notably *Brilinta* and *Forxiga*, and our Diabetes, Respiratory, Oncology and CV portfolios. To educate



Investing for the future:
Making medicines more affordable
in Brazil

Brazil has large socio-economic disparities and, despite a universal healthcare system, the main source of funding for medicines remains the private sector, including individuals paying out-of-pocket. To improve access to our medicines, we have been exploring how we can use economic data to link an individual's ability to pay with the price of our medicines, supporting our work with lifestyle and disease awareness advice. This latest approach builds on our Faz Bem programme, which has helped some 2.5 million patients since it was launched in 2008.

2.5m



Our Faz Bem programme in Brazil has helped some 2.5 million patients.

physicians about our broad portfolio, we are selectively investing in sales capabilities where opportunities from unmet medical need exist. We are also expanding our reach through multi-channel marketing and external partnerships.

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 11, 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.

Pricing and 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 user 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. Our new pricing strategy addressing out-of-pocket funding, developed in 2016, focuses on two of our therapy areas, Respiratory and CVMD, and uses socio-economic evaluation on a country-by-country basis to determine affordable price points for self-pay patients based on ability to pay.

Our efforts to price medicines affordably were seen by the Access to Medicine Foundation as an important step and, together with our approach to IP and our capacity building strategy in markets such as Brazil and China, contributed to our rise from 15th place in 2014 to 7th place in 2016 in the Foundation's biennial Access to Medicine Index. For more information on our initiatives, see Healthy Heart Africa on page 49, affordability programme in Brazil on this page, and our Young Health Programme on page 53. We will continue to work with partners and patients to develop sustainable access initiatives for as many patients as possible.

Business Review continued

3. Be a great place to work



Great people (see Employees from page 54) 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

- > We continued to train employees on the ethical standards that govern the way we operate
- > We identified six confirmed breaches of external sales and marketing regulations or codes
- > We carried out 8,977 risk assessments on third parties as part of our risk management process
- > We are developing a health and wellbeing framework based on the WHO Healthy Workplace Model
- > Over 1.6 million young people across five continents were provided with skills and information to improve their health

Sales and marketing ethics

We are committed to employing high ethical standards of sales and marketing practice worldwide, which are detailed in our Code of Conduct and supporting Global Policies on Ethical Interactions. Approximately 34,100 employees are engaged in our Commercial activities. We report publicly on the number of:

- > confirmed breaches of external sales and marketing codes
- > breaches of our Code of Conduct, Global Policies or supporting requirements by employees and third parties in our Commercial Regions, and associated corrective actions.

Alongside our Company Values, our Code of Conduct guides us on how we can make the best day-to-day choices on behalf of AstraZeneca and act in a consistent, responsible way, worldwide. There are two mandatory training courses dedicated to the

Code of Conduct; one is for new starters to introduce the Code, while the other is the annual training for all employees, which serves as an important reminder of our key commitments and principles.

During 2016, we continued to train employees on the ethical standards that govern the way we operate. We maintain a robust compliance programme in our efforts to ensure that there is compliance with all applicable laws, regulations and adopted industry codes, and that our business is operating with high ethical standards. Our compliance programme is delivered by dedicated compliance professionals who advise on and monitor adherence to our Code of Conduct, Global Policies and supporting requirements. These professionals also support our line managers locally, seeking to ensure that their staff meet our high ethical standards. A network of nominated signatories reviews our promotional materials and activities against applicable requirements. In 2016, audit professionals in Internal Audit Services also conducted compliance audits on selected marketing companies. When engaging third parties for sales and marketing activities or other services, we are committed to working with only those third parties who embrace high standards of ethical behaviour consistent with our own.

We identified six confirmed breaches of external sales and marketing regulations or codes in 2016 (2015: 11).

There were 1,729 instances, most of them minor, of non-compliance with our Code of Conduct, Global Policies or supporting requirements in our Commercial Regions, including instances by employees and third parties (2015: 1,749).

We removed a total of 222 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 429 others and provided further guidance or coaching on our policies to 1,283 more. The most serious breaches were raised with the Audit Committee.

The US Foreign Corrupt Practices Act investigation involving AstraZeneca was resolved in 2016 following a civil settlement agreed with the SEC; the DOJ closed its investigation without taking action against

the Company. More information about material legal proceedings can be found in Note 28 to the Financial Statements from page 185.

Transparency reporting

AstraZeneca is committed to the highest standards of conduct in all of our operations, including transparency in how we partner with physicians and medical institutions. In the US, our external transparency reporting meets the requirements of the Physician Payments Sunshine Act (Open Payments), as well as relevant state transparency laws. In Europe, AstraZeneca's reporting meets the requirements of the European Federation of Pharmaceutical Industries and Associations (EFPIA) Disclosure Code, as well as applicable local transparency requirements.

Working with suppliers

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.

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 8,977 assessments in 2016, taking our total number of assessments to 21,622 since May 2014. Of these, 6,622 were in the Asia Pacific region, 6,488 in Europe and 5,712 in the Americas. The remaining 2,800 assessments relate to global suppliers and those based in the Middle East and Africa.

In 2016, we conducted 66 audits on high-risk suppliers, seeking to ensure that they employ appropriate practices and controls. Thirty two percent of suppliers met our expectations, with a further 42% implementing improvement plans to address minor instances of non-compliance. Through our due diligence process, we rejected 40 suppliers because of reputational concerns.

Safety, health and wellbeing

We work to promote a safe, healthy and energising work environment for employees and partners. As outlined in our Safety, Health and Environment (SHE) strategy on page 45, we have established a set of safety, health and wellbeing targets aimed at supporting our people and keeping AstraZeneca among the sector leaders in SHE performance.

We made good progress against our new strategic targets in 2016, achieving a 16% reduction in the reportable injury rate and a 12% reduction in vehicle collision rate from 2015 baseline. Building on our previous success in establishing a culture of health and wellbeing, we are developing a health and wellbeing framework, based

on the World Health Organization's Healthy Workplace Model, which will give sites and marketing companies a blueprint for continuous improvement in this area.

In 2016, we carried out a number of activities and initiatives focused on delivery of improvements in key areas of concern, including driver safety, fall prevention, behavioural SHE, risk management, industrial hygiene and stress management. We also continued to focus on learning from incidents, using a dedicated website where all employees can access the learning to help ensure incidents are not repeated.

Vehicle collisions

Year	Collisions per million km	Target
2016	3.62	4.00
2015	4.13	5.60

Reportable injuries

Year	Reportable injury rate per million hours worked	Target
2016	1.45	1.64
2015	1.73	N/A

Community investment

Our global community investment strategy focuses on healthcare in the community and science. For example, 2016 was the sixth year of our partnership with the UK educational charity Career Ready to support increased participation by 16- to 19-year-olds in science, technology, engineering and maths subjects.

In 2016, we spent a total of approximately \$501 million (2015: approximately \$680 million) on community investment sponsorships, partnerships and charitable donations worldwide, including our product donation and patient assistance programmes which make our medicines available free of charge or at reduced prices.

In 2016, we provided more than \$466 million (2015: over \$617 million) in savings to almost 200,000 patients in the US and Puerto Rico through our AZ&Me Prescription Savings

Program. Additionally, we donated over \$20 million in products across multiple therapeutic areas to our NGO partners AmeriCares and Direct Relief International in support of public health needs and disaster relief.

Young Health Programme

We continued to develop the three strands of our Young Health Programme (YHP): on-the-ground programmes; advocacy; and research and evidence generation. Our on-the-ground programmes focus on the primary prevention of NCDs and associated adolescent risk behaviours. From 2010 to 2016, the programme has provided over 1.6 million young people in communities across five continents with the skills and information they need to improve their health. Over 47,000 of these young people have been trained to share this health information with their peers and the community. The programmes have also trained more than 12,600 frontline health workers in adolescent health. 2016 saw the launch of a programme in Kenya, the extension of the India programme to 2020 and a new programme in Canada. Further programmes are in development for 2017.

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

Disaster relief

The British Red Cross continues to act as our global disaster relief partner, channelling the bulk of our disaster relief donations. In addition to the charitable donations referenced in Community investment above, in July 2016 we donated \$200,000 via the British Red Cross to the Kuala Lumpur Emergency Response Unit, and \$25,000 to replenish stocks of hygiene kits at the British Red Cross/Crescent Panama Warehouse following Hurricane Matthew.

21,000



Carried out more than 21,000 supplier assessments since May 2014.

Resources Review



If we are to achieve our strategic priorities, we need to ensure that we deploy our assets efficiently and manage our resources to best effect. Our employees are our greatest asset but we also rely on our intellectual property and our R&D investment, our manufacturing resources and our information services support. We also seek to manage our environmental resources efficiently.

Overview

- > 59,700 employees in more than 100 countries
- > People strategy built around four key pillars: build and develop organisations and capabilities; develop a strong and diverse pipeline of leaders; drive a vibrant, high-performing culture; and generate a passion for people development
- > Commit significant resources to establishing and defending our patent and related IP protections for inventions
- > 31 sites in 18 countries where we are working on the development, manufacture and supply of our products
- > Launched our Operations 2020 strategy to enhance supply capabilities in order to respond better to patient and market needs
- > Three strategic R&D centres: in the US (Gaithersburg, MD); UK (Cambridge); and Sweden (Gothenburg). A total of nine R&D sites in five countries
- > Our vision for IT focuses on areas that will enable competitive advantage for us
- > Embedding our 2025 Safety, Health and Environment strategy into our business

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 Values.

Overview

- > Hired 9,200 permanent employees to help us achieve our strategic priorities
- > Piloted an online Leading People development experience
- > Established a global target for all employees to have a development conversation with their manager and associated development plan
- > Increased the gender diversity of our leadership
- > Piloted a global Women as Leaders programme

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

During 2016, we hired 9,200 permanent employees. An additional 200 employees joined us through acquisitions, most notably Takeda and Acerta Pharma. We are committed to hiring and promoting talent ethically and in compliance with applicable laws. Our policies and procedures 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. 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 procurement, quality, engineering, IT and supply chain 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 30% of our global workforce (up from 20% in 2012). This provides a greater balance in terms of refreshing talent and retaining organisational experience. The composition of our international workforce has also changed with our business focus. This can be seen in the Sales and Marketing figures to the right, which shows a greater concentration in Emerging Markets.

Voluntary employee turnover increased marginally to 9.6% in 2016 from 8.6% in 2015 (restated 2015 number). The voluntary employee turnover rate among our high performers also increased in 2016 to 6.1%. We seek to reduce regretted turnover through more effective hiring and induction, high-level reviews of resignations, risk assessments and retention plans.

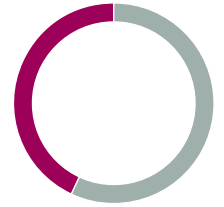
Develop a strong and diverse pipeline of leaders

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.

During 2016, we implemented new talent management and succession planning processes. This focused on the deliberate identification, sourcing and accelerated development of our highest potential talent, seeking to ensure that we have credible successors with the capabilities and experiences necessary for our business critical roles.

Sales and Marketing workforce composition (%)

- Emerging Markets 57%
- Established Markets 43%



We continue to focus on diversity and inclusion with a goal to increase the presence of women on our leadership teams. In 2016, we piloted a European Women as Leaders experience to support the accelerated development of high potential women in AstraZeneca. In 2017, this programme will be offered globally. As shown in the gender diversity figure on the next page, women comprise 49.9% of our global workforce. There are currently three women on our Board (30%). 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 43.2% in 2016, which exceeded our Scorecard target of 42.5% for this measure and compares favourably to external benchmarks.

A global business

59,700 employees by geographical area

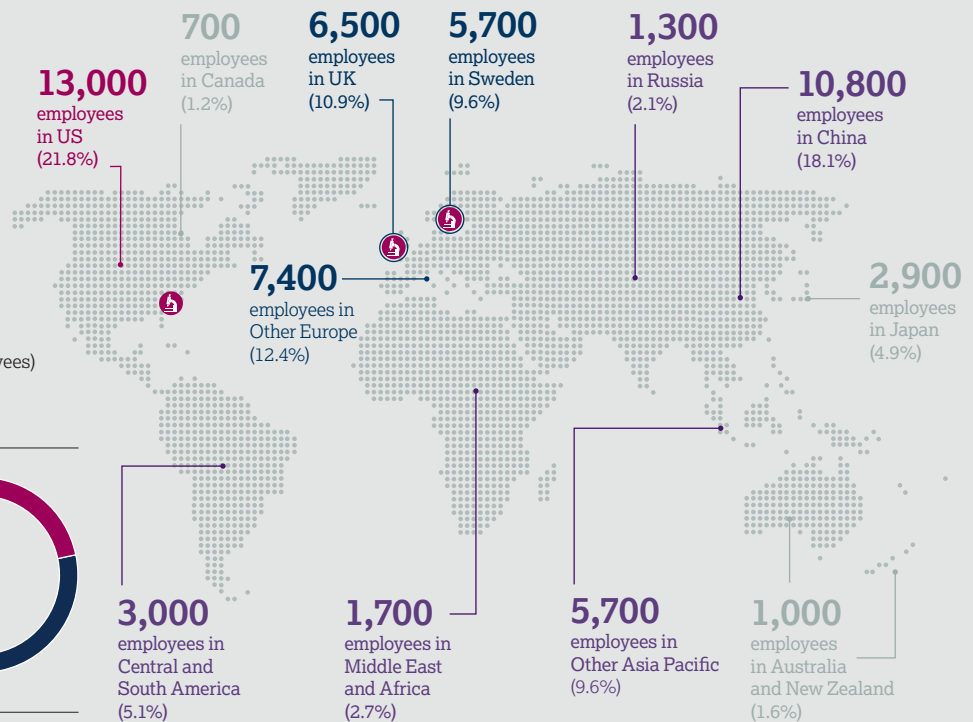
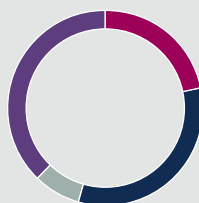


Co-locating around three strategic R&D centres

- > Cambridge, UK (2,000 employees)
- > Gaithersburg, Maryland US (2,900 employees)
- > Gothenburg, Sweden (2,200 employees)

Employees by reporting region (%)

- US 21.8%
- Europe 32.9%
- Established Rest of World 7.7%
- Emerging Markets 37.6%



All numbers as at 31 December 2016

Resources Review continued

We continue to develop high-quality leaders. In 2016, 15% of the approximately 130 leadership roles that report to our senior leadership team were either promoted into the leadership population, or moved roles within the leadership population. 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 2016, 14.5% 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).

Drive a vibrant, high-performing culture

Continuing our emphasis on high performance, in 2016, we extended our single global performance management framework and approach to cover 94% of the workforce. We also implemented a global annual salary and incentive review process which covers 60% of the workforce. 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.

Equally important are our performance-related bonus and incentive plans. We encourage participation in various employee share plans, some of which are described in the Directors' Remuneration Report from page 103, and also in Note 27 to the Financial Statements, from page 182.

Employee opinion surveys help us measure employee satisfaction and engagement and how we are doing in our aim of being a great place to work. Our most recent survey, carried out in December 2016, showed a decline compared to the survey at the start of the year in scores for all 10 items common to both surveys. Although this might not be unexpected given the action we are taking to reshape our business to improve long-term competitiveness, we are continuing to focus on improving areas identified in our surveys as being important drivers of employee engagement. For example, we are driving our agenda around people development, encouraging improved dialogue between colleagues and their line managers on development. We have also continued our efforts to simplify the work environment for colleagues, whether this be through simplifying business processes or improving the IT tools we use in the workplace.

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, in 2016 we implemented a global platform to increase the visibility and accessibility of job opportunities.

We strive to attract talent by offering rewarding careers that connect the potential of our people with the capabilities required by our business. We are focusing on ensuring development opportunities are available to all employees, alongside our investment in our highest potential talent. In 2016, we piloted a new best-practice technology-enabled leadership experience, rooted in social learning, with 180 supply and manufacturing leaders based in West Chester and Mount Vernon in the US, and Vorsino in Russia. This experience can be accessed on any device at any time, with the goal of implementing global technology enabled development programmes in 2017.

Human rights

We are committed 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 policies, 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 will be published on our website, www.astrazeneca.com, later in 2017.

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.

In 2016, we began conducting our third biennial Human Rights labour review in all countries where we have a presence. The review focuses on ILO core themes, including freedom of association and collective bargaining, child labour,

Gender diversity

Board of Directors of the Company 10

- Male 70%
- Female 30%



Directors of the Company's subsidiaries* 435

- Male 71.7%
- Female 28.3%



SET* 12

- Male 67%
- Female 33%



AstraZeneca employees 59,700

- Male 50.1%
- Female 49.9%



* 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.

discrimination, working hours and wages, including questions on the Living Wage. Where a gap to ILO minimum standards is identified, we will put in place local plans to close those gaps. In 2016, AstraZeneca became accredited with the Living Wage Foundation in the UK and will treat this as an experience to be evaluated alongside all other associated evidence in respect of seeking a global solution, for example, monitoring impact on our cost base.

Managing change

In 2013, we announced plans to invest in three strategic R&D centres as outlined in Organisation on page 42. This affected employees in the US and the UK. We encouraged and supported employees to relocate and have made good progress. For example, as at 31 December 2016, 2,000 employees were working in Cambridge and, of these employees, 500 have relocated from other sites in the UK. In addition to the 750 employees hired in 2015 and 2016, we expect to hire a further approximately 350 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 Cambridge, see page 7; on our restructuring programme, please see Restructuring from page 69 and Financial Review from page 62

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.

Intellectual Property

Discovering and developing medicines requires a significant investment of resources by research-based pharmaceutical companies. The process can take a decade or more. For this to be a viable investment, new medicines must be safeguarded from being copied with a reasonable amount of certainty for a reasonable period of time.

Our industry's principal economic safeguard is a well-functioning patent system 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 185. For more information on the risks relating to patent litigation and early loss and expiry of patents, please see Risk from page 214.

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 tables on pages 211 to 213 set out certain patent expiry dates and sales for our key marketed products.

Other exclusivities

In addition to patent protection, regulatory data protection (RDP or 'data exclusivity') is an important IP right, which 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. 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. RDP generally expires prior to patent expiry in all major markets.

Resources Review continued

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 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' exclusivity under the Federal Food, Drug and Cosmetic Act. This period of exclusivity runs parallel to any pending or granted patent protection and starts at the approval of the new application. As with RDP, there are circumstances where this protection could be the sole IP right protecting a product from being copied. Further, under the Biologics License Application process, the FDA will grant 12 years' data exclusivity for a new biologic to an innovator manufacturer.

Under Orphan Drug laws in the EU and US, exclusivity is granted to an innovator who gains approval for a pharmaceutical product developed to treat a rare disease. What qualifies as a rare condition 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 Patente) 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.

Manufacturing

Our 2020 strategy provides a focus for our investments to help ensure we are able to respond to patient and market needs for our medicines.

Overview

- > Operations 2020 strategy started with a number of global initiatives in 2016
- > Biologics manufacturing footprint increased in preparation for new product launches
- > The Pharmaceutical Technology & Development teams have been integrated into Operations to enhance the way we design, develop, manufacture and launch new products

Strategy

Operations 2020 strategy was launched in 2015 to enhance supply capabilities in order to respond better to patient and market needs. Our strategy 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 objective is to be recognised as a leader in biopharmaceutical supply chain by the end of 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 2016, we hosted 33 independent inspections from 18 regulatory authorities. We reviewed observations from these

inspections together with the outcomes of internal audits and, where necessary, implemented improvement actions.

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

Pharmaceutical Technology & Development (PT&D)

In January 2016, the integration of PT&D into Global Operations commenced to support further and accelerate successive new product launches, new device platforms and manage an increase in the overall product portfolio complexity. The integration is also expected to enhance collaboration and alignment and our focus on late-stage development, adding substantial scientific expertise and leadership to Operations.

We are actively working on over 150 drug projects across our R&D and Commercial portfolios, supporting more than 300 AstraZeneca clinical studies worldwide and an additional 400 External Sponsored Research studies. We also support over 100 in-line brands and small molecule products.

Our continued science and technology innovation allows us to enable and differentiate products including *Lynparza*, *Tagrisso*, *acalabrutinib*, *Brilinta* and new respiratory products such as PT010 as they are introduced into the marketplace and ultimately into the hands of patients globally.

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.



Investing for the future: Manufacturing biologics

We are investing in our supply network, with a focus on increasing production capacity to support the growing demand for biologics. The addition of three new high-tech biologics manufacturing facilities (Gärtuna in Sweden (above), and Boulder and Longmont, both in Colorado in the US) to our supply network will leave us well-positioned for the future.

For biologics, our principal commercial manufacturing facilities are in the US (Frederick, Maryland; Greater Philadelphia, Pennsylvania; Boulder and Longmont, Colorado), 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.

We are developing our manufacturing capability in biologics and expect our bulk manufacturing facility in Boulder, Colorado US to be licensed for commercial production by the end of 2017. In Sweden, we expect our new \$285 million biologics manufacturing facility to be available for clinical trial programmes by the end of 2018 and fully operational by 2019. These projects, in addition to an expansion plan at Frederick, Maryland US, will increase production capacity to support the growing demand for biologics, which represents about half of our development pipeline. We acquired our facility in Longmont, Colorado US, in 2016 which will both support our operations in Boulder and provide space for additional biologics expansion as required.

For small molecules we are constructing a new small scale development and launch facility alongside our existing manufacturing facility in Wuxi, China. In addition, regulatory validation work continues at Vorsino, Russia, which opened in 2015. First commercial production commenced in early 2016, improving our ability to supply local markets.

At the end of 2016, approximately 12,200 people were employed at 31 Operations sites in 18 countries.

R&D resources

We have approximately 8,400 employees in our R&D organisation, working in various sites around the world.

Our small molecule sites are located in the UK (Alderley Park, Cambridge and Macclesfield), Sweden (Gothenburg), the US (Gaithersburg, Maryland, Waltham, Massachusetts and California), Japan (Osaka) and China (Shanghai). Our biologics sites are located in the UK (Cambridge) and in the US (Gaithersburg, Maryland and California). Our Gaithersburg, Maryland US; Cambridge, UK; and Warsaw, Poland sites focus on late-stage development for small molecules and biologics across our entire portfolio.

In 2016, R&D expenditure was \$5,890 million in our R&D organisation (2015: \$5,997 million; 2014: \$5,579 million), including core R&D costs of \$5,631 million (2015: \$5,603 million; 2014: \$4,941 million). In addition, we spent \$821 million on acquiring product rights (such as in-licensing) (2015: \$1,341 million; 2014: \$907 million). We also invested \$178 million on the implementation of our R&D restructuring strategy (2015: \$258 million; 2014: \$497 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

	2016	2015	2014
Discovery and early-stage development	36%	39%	47%
Late-stage development	64%	61%	53%

8,400

Around 8,400 employees in our R&D organisation.



Resources Review continued

Information technology and information services resources

Our continuing vision for IT is to focus on areas that may provide a competitive advantage for AstraZeneca.

At the end of 2016, we successfully completed our three-year IT Transformation Programme. The wide-ranging programme has delivered improved productivity, efficiency, responsiveness and innovation allowing us to better support our business priorities while at the same time significantly reducing cost.

First, to implement our vision for IT, we seek to identify, prioritise and drive adoption of new technologies to support the business and enable our science. Second, we aim to make significant investments in data and analytics to allow the business to manage information more effectively in order to drive faster, more effective decision making. Finally, we seek to drive operational excellence and improvements in the performance, stability, security and cost of the underlying application landscape and infrastructure of our IT.

Protecting our IT systems, IP and confidential information against cyberattacks 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 cybersecurity risk landscape. To help guard against cybercrime, we have adopted a comprehensive cybersecurity 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 cybersecurity risk.

At the end of 2016, our IT organisation comprised approximately 3,500 people across our sites in the UK, Sweden, the US, and our new technology centres in India (Chennai) and Mexico (Guadalajara).

Environment

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

Overview

- > Independent verification of science-based climate change targets and commitment to responsible water stewardship
- > 2016 greenhouse gas footprint reduced by 5%
- > 2016 waste management generation increased by 1%
- > 2016 water consumption performance reduced by 5%

Natural resource efficiency

As outlined in Safety, Health and Environment strategy on page 45, we have begun work on delivering our 2016 to 2025 Safety, Health and Environment (SHE) targets. Our 2016 natural resource targets included reducing:

- > operational greenhouse gas footprint by 2% to 1,708,335 tonnes CO₂e
- > waste generation by 2% to 36,760 tonnes
- > water use by 2% to 4.13 million m³.

The table to the right provides data on our global greenhouse gas emissions, waste production and water consumption for 2016. The data coverage includes 100% of our owned and controlled sites globally. 2015 data was recalculated to include acquired sites that form part of the 2016 to 2025 strategy baseline.

We continue to integrate environmental considerations across a medicine's entire life-cycle, from discovery, R&D to manufacturing, commercialisation and disposal. This considers the natural resources used to manufacture our products and the environmental impact of our active pharmaceutical ingredients (APIs).

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 2016, site energy use improved to reduce consumption by 0.2% and procurement of electricity from certified renewable sources increased to represent 58% of total electricity imports. Our travel and freight transport emissions decreased due to reduced business air travel, increased fuel efficiency of our commercial sales fleet and continued achievement in switching freighting of goods from air to sea.

Operational greenhouse gas footprint emissions (tonnes CO₂e)

2016	1,656,917
2015	1,743,199
2014	N/A

Waste production (tonnes)

2016	37,923
2015	37,510
2014	35,797

Water use (million m³)

2016	3.99
2015	4.21
2014	3.79



Investing for the future:
Following the science to protect
the environment



We were one of only four FTSE 350 companies to have had our climate change targets approved by the Science Based Targets initiative which is a partnership with CDP, the UN Global Compact, World Resources Institute, and World Wide Fund for Nature. The initiative seeks to create a systematic change in how targets are set, so that companies contribute their fair share of the challenging emissions reduction needed to limit global temperature increase to under two degrees centigrade.

Our pMDI inhaler therapy relies on hydrofluoroalkane (HFA) propellants which affects our 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 2016, we continued to explore practical opportunities to reduce the climate impact of these devices while continuing to fulfill patient needs. Including emissions from patient use of our inhaler therapies, our aim by 2016 was to reduce our operational greenhouse gas footprint by 2% from our 2015 level. We achieved this, with our operational greenhouse gas footprint totalling 1,656,917 metric tonnes in 2016, a reduction of 5% from our 2015 baseline.


 **For more information on carbon reporting, please see Sustainability: supplementary information from page 231**

Waste management is another key aspect of our commitment to minimise environmental impact. In 2016, we targeted a 2% reduction in waste generation from our 2015 baseline. In 2016, our total waste was 37,923 metric tonnes, a 1% increase on 2015. Although we initiated waste reduction projects, such as major investment to enable solvent reuse at a Swedish manufacturing site, these were insufficient to offset the increase in activity across our network. While waste prevention is an essential goal, we seek to maximise treatment by material recycling and avoiding landfill disposal when prevention is impractical.

We recognise the need to use water responsibly and, where possible, to minimise water use in our facilities. In 2016, we targeted a 2% reduction from our 2015 water use. In 2016, our water footprint was 3.99 million m³, a 5% reduction. This was achieved in part by investing in water efficiency projects such as the reclamation and reuse of water at a number of our manufacturing sites in Australia and the US. During 2016, our major sites completed Water Conservation Plans and we standardised the assessment of water stress across our network, enabling prioritisation of water efficiency in areas where water scarcity is of greatest concern.

We are also working on measuring and reporting the environmental impact of our external manufacturing activity and work to set appropriate environmental targets with our suppliers. We capture data for more than 90% (based on spend) of the globally managed outsourced manufacture of key intermediates and APIs, formulation and packaging for our established brands. Understanding and management of our external supplier footprint will be a continued focus of our SHE commitment going forward.

With regard to pharmaceuticals in the environment (PIE), we manage the manufacturing emissions 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. Our proactive SHE research also addresses some of the key risks posed by PIE. In 2016, we signed an industry declaration presented to the United Nations General Assembly ensuring the responsible use, patient access and production of antibiotics to help combat the threat of antimicrobial resistance.

 **Further information, including environmental risk assessment data for our medicines, is available on our website, www.astrazeneca.com/sustainability/environmental-sustainability.html**

Financial Review



In 2016, our financial performance reflected the ongoing impact from patent expiries; the biggest of which was *Crestor* in the US. Overall, Total Revenue declined by 7% (CER: declined by 5%) to \$23.0 billion.

In 2016, continued growth in Emerging Markets and Diabetes, coupled with strong sales of our New Oncology medicines and further progress for *Brilinta*, resulted in a 4% increase (CER: 5% increase) in our Growth Platform Sales.

However, the continued effect of patent expiries, in particular the US entry of *Crestor* generic medicines, resulted in a decline in Total Revenue of 7% (CER: decline of 5%) in the year. Our continued focus on cost discipline delivered a decrease of 2% (CER: increase restricted to 2%) in Reported R&D costs and stable (CER: increase restricted to 5%) Core R&D costs, despite the absorption of Acerta Pharma and ZS Pharma costs. The decline of 15% (CER: decline of 12%) in Reported SG&A costs, which also benefited from fair value adjustments to long-term liabilities, and the decline of 12% (CER: decline of 9%) in Core SG&A costs, reflected the evolving shape of the business and efficiency savings. This, combined with a non-recurring benefit resulting from agreements on transfer pricing between various tax authorities, delivered Reported EPS of \$2.77 and Core EPS of \$4.31.

Product Sales in Emerging Markets were stable compared to 2015 (CER: grew by 6%) in the year at \$5.8 billion, against a background of challenging macro-economic conditions in Latin America. We have reduced our activities in Venezuela and there were also cuts in healthcare spending

in Saudi Arabia. However, China maintained growth of 4% (CER: growth of 10%), ahead of the overall market, and Russia grew at 1% (CER: growth of 13%).

Our Diabetes franchise grew by 9% (CER: grew by 11%) to \$2.4 billion and *Farxiga* became our largest-selling diabetes medicine, consolidating its position as global leader in the SGLT2 class. *Brilinta* sales increased by 36% (CER: increased by 39%) to \$839 million, reflecting updated preferred guidelines from the American College of Cardiology and the American Heart Association. In addition, sales of our New Oncology medicines reached \$664 million in the year, with *Tagrisso* and *Lynparza* growing strongly. Respiratory declined by 5% (CER: declined by 3%) in the year, impacted by US pricing pressure on *Symbicort*. Japan Product Sales increased by 8% (CER: declined by 3%).

Patent expiries continued to impact negatively in our Established Markets and more than offset the performance of the Growth Platforms. US sales fell by 22% to \$7.4 billion and reflected the competition from generic *Crestor* medicines that entered the US market from July and the continued decline of *Nexium* sales following the loss of US exclusivity in 2015. Sales in Europe were down by 5% (CER: down 3%) and sales in other Established Markets grew by 2% (CER: fell by 4%).

Product Sales were supplemented by \$1.7 billion of Externalisation Revenue arising from partnerships including the global agreement with Aspen for the commercial rights to the anaesthetics portfolio and local agreements in China for *Plendil* and in the US for *Toprol-XL*. The level of sustainable and ongoing income from such partnerships and collaborations has continued to increase during 2016.

Excluding the impact of Externalisation Revenue, the Reported Gross Profit margin was broadly stable in the year, with lower restructuring and amortisation charges offset by the adverse impact from the mix of sales and a write-down of *FluMist* inventory in the US. Excluding the lower restructuring and amortisation charges, Core Gross Profit margin declined by one percentage point to 82%.

Reported Other Operating Income was \$1.7 billion in the year and included receipts from the divestments of the small molecule antibiotics business to Pfizer and *Rhinocort Aqua* to Cilag.

Reported Operating Profit increased by 19% (CER: increased by 9%) to \$4.9 billion and Core Operating Profit declined by 3% (CER: declined by 7%) to \$6.7 billion. Reported earnings per share increased by 24% (CER: increased by 9%) to \$2.77 and Core earnings per share increased by 1% (CER: declined by 5%) to \$4.31. Both Reported and Core EPS included a non-recurring benefit of \$0.36, following agreements between the Canadian tax authority and the UK and Swedish tax authorities in respect of transfer pricing arrangements for the period from 2004 to 2016.

We generated a net cash inflow from operating activities of \$4.1 billion in the year with a continued improvement in working capital investment. We maintain a strong, investment-grade credit rating and, in May, issued a total of \$2.5 billion of loans for general corporate purposes. We ended the year with net debt of \$10.7 billion.

Marc Dunoyer
Chief Financial Officer

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The purpose of this Financial Review is to provide a balanced and comprehensive analysis of the financial performance of the business during 2016, the cash flow and liquidity position of the business, the financial position as at the end of the year, and the main business factors and trends which could affect the future financial performance of the business.

Business background and results overview

The business background is covered in the Marketplace section from page 11, the Therapy Area Review from page 23 and the Geographical Review from page 226, 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 generic competitor in the same class as one of our products, with the 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 211.

- > The adverse impact on pharmaceutical prices as a result of the macroeconomic and regulatory environment. For instance, although there is no direct governmental control on prices in the US, action from federal and individual state programmes and health insurance bodies is leading to downward pressures on realised prices. In other parts of the world, there is a variety of price and volume control mechanisms and retrospective rebates based on sales levels that are imposed by governments.
- > The timings of new product launches, which can be influenced by national regulators, 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, pounds sterling, Chinese renminbi and Swedish krona.
- > Macro factors such as greater demand from an ageing population and increasing requirements of Emerging Markets.

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 2016 are:

- > Total Revenue down 7% to \$23,002 million (CER: down 5%). Product Sales were down 10% (CER: down 8%) reflecting the entry in the US of multiple *Crestor* generic medicines, as well as the reducing impact of *Nexium* generic medicines in the US and the impact of pricing pressure in the US on *Symbicort*. Product Sales of *Crestor*, *Nexium* and *Symbicort* in the US declined by 57%, 39% and 18% respectively.
- > Revenues of our Growth Platforms increased 4% (CER: increased 5%) and constituted 63% of our Total Revenue, with

- Emerging Markets flat at actual exchange rates (CER: 6% growth) supported by China, up by 4% (CER: up by 10%)
- Diabetes up 9% (CER: up 11%), which included growth of 70% (CER: growth of 72%) on *Farxiga* which became our largest-selling diabetes medicine
- Japan up 8% (CER: down 3%) to \$2,184 million
- *Brillinta* Product Sales up 36% (CER: up 39%) to \$839 million
- Respiratory down 5% (CER: down 3%) reflecting an 18% fall in US Product Sales of *Symbicort*
- New Oncology Product Sales of \$664 million.
- > Reported operating profit was up 19% (CER: up 9%) to \$4,902 million (2015: \$4,114 million). The increase reflected the reduction in SG&A costs, largely due to fair value gains on contingent consideration and lower legal charges. This reduction in SG&A costs more than offset the decline in Product Sales, while we continued to invest in our pipeline and Growth Platforms.
- > Revaluations of contingent consideration resulted in a reduction of \$1,158 million in SG&A costs in the year, and included a decrease of \$999 million relating to the acquisition of BMS's share of the Global Diabetes Alliance, based on revised milestone probabilities, and revenue and royalty forecasts. Total restructuring costs associated with the global programme to reshape the cost base of our business were \$1,107 million in 2016.
- > Core operating profit was down 3% (CER: down 7%) to \$6,721 million (2015: \$6,902 million).
- > Reported operating margin of 21.3% of Total Revenue was up 4.6 percentage points (CER: 2.6 percentage points). Core operating margin was 29.2% of Total Revenue (2015: 27.9%).
- > Reported EPS was up 24% (CER: up 9%) to \$2.77. Core EPS for the full year was \$4.31, up 1% (CER: down 5%).
- > Dividends paid amounted to \$3,561 million (2015: \$3,486 million).

Financial Review continued

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).
- > Core financial measures. These are non-GAAP measures because, unlike Reported performance, they cannot be derived directly from the information in the Group Financial Statements. These measures are adjusted to exclude certain significant items, such as
 - amortisation and impairment of intangibles, including impairment reversals but excluding any charges relating to IT assets
 - charges and provisions related to our global restructuring programmes (this includes such charges that relate to the impact of our global restructuring programmes on our capitalised IT assets)
 - other specified items, principally comprising legal settlements and acquisition-related costs which include fair value adjustments and the imputed finance charge relating to contingent consideration.

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 2016 Reconciliation of Reported results to Core results table on the opposite page for a reconciliation of Reported to Core performance.

- > 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 previous year's 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 2016 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.
- > Net funds/debt. This represents our cash and cash equivalents, current investments and derivative financial instruments less interest-bearing loans and borrowings.

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 revenues growth can be further analysed into the impact of revenues 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 Core financial and growth measures, in addition to our Reported financial information, enhances investors' ability to evaluate and analyse the underlying financial performance of our ongoing business and the related key business drivers. As detailed in our 2012 Annual Report, we revised our definition of Core financial measures in 2013, with consistent application thereafter. The adjustments are made to our Reported financial information in order to show Core

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 2016 Reconciliation of Reported results to Core results table on the page opposite, 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.

Core financial measures are non-GAAP measures. All items for which Core financial measures are adjusted are included in our Reported financial information as they represent actual costs of our business in the periods presented. 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 2016 Reported operating profit table below and our reconciliation of Core financial measures to Reported financial information in the Reconciliation of Reported results to Core results table below 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 2016

2016 Reported operating profit

	2016			2015 Reported \$m	Percentage of Total Revenue		2016 compared with 2015	
	Reported \$m	CER growth \$m	Growth due to exchange effects \$m		Reported 2016 %	Reported 2015 %	Actual growth %	CER growth ¹ %
Product Sales	21,319	(1,990)	(332)	23,641			(10)	(8)
Externalisation Revenue	1,683	634	(18)	1,067			58	59
Total Revenue	23,002	(1,356)	(350)	24,708			(7)	(5)
Cost of sales	(4,126)	332	188	(4,646)	(17.9)	(18.8)	(11)	(7)
Gross profit	18,876	(1,024)	(162)	20,062	82.1	81.2	(6)	(5)
Distribution costs	(326)	(4)	17	(339)	(1.5)	(1.4)	(4)	1
Research and development expense	(5,890)	(150)	257	(5,997)	(25.6)	(24.3)	(2)	2
Selling, general and administrative costs	(9,413)	1,373	326	(11,112)	(40.9)	(44.9)	(15)	(12)
Other operating income and expense	1,655	178	(23)	1,500	7.2	6.1	10	12
Operating profit	4,902	373	415	4,114	21.3	16.7	19	9
Net finance expense	(1,317)			(1,029)				
Share of after tax losses of joint ventures and associates	(33)			(16)				
Profit before tax	3,552			3,069				
Taxation	(146)			(243)				
Profit for the period	3,406			2,826				
Basic earnings per share (\$)	2.77			2.23				

¹ As detailed on page 64, CER growth is calculated using prior year actual results adjusted for certain exchange effects including hedging.

2016 Reconciliation of Reported results to Core results

	2016 Reported \$m	Restructuring costs \$m	Intangible amortisation and impairments \$m	BMS's share of diabetes alliance \$m	Legal provisions and other \$m	2016 Core ¹ \$m	Core ¹ 2016	
							Actual growth %	CER growth %
Gross profit	18,876	130	124	–	–	19,130	(7)	(6)
Product Sales gross margin % ²	80.8%					82.0%		
Total Revenue gross margin %	82.1%					83.2%		
Distribution costs	(326)	–	–	–	–	(326)	(4)	1
Research and development expense	(5,890)	178	81	–	–	(5,631)	–	5
Selling, general and administrative costs	(9,413)	823	1,000	(627)	48	(8,169)	(12)	(9)
Other operating income and expense	1,655	(24)	86	–	–	1,717	13	14
Operating profit	4,902	1,107	1,291	(627)	48	6,721	(3)	(7)
Operating margin as a % of Total Revenue	21.3%					29.2%		
Net finance expense	(1,317)	–	–	389	267	(661)		
Taxation	(146)	(232)	(307)	23	4	(658)		
Basic earnings per share (\$)	2.77	0.69	0.78	(0.17)	0.24	4.31		

¹ Each of the measures in the Core column in the above table are non-GAAP measures.

² Gross margin as a % of Product Sales reflects gross profit derived from Product Sales, divided by Product Sales.

Financial Review continued

Total Revenue

Total Revenue for the year was down 7% to \$23,002 million, comprising Product Sales of \$21,319 million (down 10%) and Externalisation Revenue of \$1,683 million (up 58%). At CER, Total Revenue declined by 5% in the year.

Product Sales

The decline in Product Sales primarily reflected the entry in the US of multiple *Crestor* generic medicines.

By Geography

US Product Sales were down 22% to \$7,365 million, reflecting the competition from multiple generic *Crestor* medicines that entered the US market from July 2016 as well as lower Product Sales of *Nexium* and *Symbicort*. In Europe, strong growth in Product Sales of *Forxiga* and *Brilique* were more than offset by a decline in *Symbicort*, leading to a decrease of 5% (CER: decrease of 3%) in the region in total to \$5,064 million.

Established Markets were up 2% (CER: down 4%) at \$3,096 million including an increase of 8% in Japan (CER: decrease of 3%) to \$2,184 million, with *Crestor* Product Sales in Japan stable at \$521 million. Product Sales in Emerging Markets were flat (CER: up 6%) at \$5,794 million in 2016 despite growth in China of 4% (CER: growth of 10%) to \$2,636 million, as we encountered challenging macro-economic conditions in Latin America, where full-year Product Sales declined by 20% (CER: declined by 7%) to \$516 million.

By Product

Our largest selling products in 2016 were *Crestor* (\$3,401 million), *Symbicort* (\$2,989 million), *Nexium* (\$2,032 million) and *Pulmicort* (\$1,061 million). Global Product Sales of *Crestor* declined in the year by 32% (CER: declined by 32%), which primarily reflected the market entry of multiple *Crestor* generic medicines. *Symbicort* global Product Sales declined by 12% (CER: down 10%) including

a reduction of 18% in the US due to the impact of a competitive environment on net pricing. *Nexium* Product Sales were down 19% (CER: down 18%), including a 39% decrease in the US, reflecting lower demand and inventory de-stocking as a result of the loss of exclusivity in 2015. Strong underlying volume growth in Emerging Markets drove a 5% Global Product Sales increase (CER: 8% increase) in *Pulmicort*, with 66% of Product Sales of the medicine coming from that region in the year.

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 4% (CER: 5%), representing 63% of Total Revenue after removing the effect of certain Product Sales which are included in more than one Growth Platform.

Growth Platforms

	2016 Product Sales \$m	2015 Product Sales \$m	Actual growth %	CER growth %
Respiratory	4,753	4,987	(5)	(3)
<i>Brilinta</i>	839	619	36	39
Diabetes	2,427	2,224	9	11
Emerging Markets	5,794	5,822	-	6
Japan	2,184	2,020	8	(3)
New Oncology ¹	664	119	n/m	n/m
Total Growth Platform Product Sales ²	14,491	14,003	4	5

¹ New Oncology comprises *Lynparza*, *Iressa* (US) and *Tagrisso*.

² 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

	2016 \$m	2015 \$m
Milestones		
Global non-US anaesthetics portfolio (Aspen) – upfront	520	-
<i>Plendil</i> (China Medical System Holdings) – upfront	298	-
<i>Toprol-XL</i> (Aralez) – upfront	175	-
tralokinumab (LEO Pharma) – upfront	115	-
AZD3293 (Lilly) – milestone	100	50
durvalumab (Celgene) – upfront	-	450
<i>Movantik</i> (Daiichi Sankyo) – upfront	-	200
brodalumab (Valeant) – upfront	-	100
<i>Nexium</i> (Daiichi Sankyo) – milestone	-	123
Others	356	57
Total upfront/milestones	1,564	980
Royalties	119	87
Total Externalisation Revenue	1,683	1,067

Product Sales of our Respiratory medicines declined by 5% (CER: declined by 3%) reflecting pricing pressure in the US for *Symbicort*.

Sales of *Brilinta* in the year were \$839 million, an increase of 36% (CER: increase of 39%). *Brilinta* sales in the US were up 45% to \$348 million, as it remained the branded oral anti-platelet market leader in the US.

Our Diabetes Product Sales were 9% higher than in 2015 (CER: 11% higher), driven primarily by growth of 70% (CER: growth of 72%) on *Farxiga* with global sales of \$835 million as it became our largest-selling Diabetes medicine.

Product Sales in Emerging Markets were flat compared to 2015 (CER: increase of 6%). Product Sales in China increased by 4% in 2016 (CER: increased by 10%) representing 45% of Emerging Markets Product Sales in the year.

Japan Product Sales increased by 8% (CER: declined by 3%).

Product Sales of New Oncology medicines were up to \$664 million in 2016 (2015: \$119 million), \$423 million of which came from *Tagrisso* (2015: \$19 million) which became our leading medicine for the treatment of lung cancer in the year.

Externalisation Revenue

Externalisation Revenue, alongside Product Sales, is included in Total Revenue. Externalisation Revenue includes development, commercialisation and collaboration revenue, such as royalties and milestone receipts. Income is recorded as Externalisation Revenue when we have a significant ongoing interest in the product and/or it is repeatable business and there is no derecognition of an intangible asset. Disposals of assets and businesses, where we do not retain an interest, are recorded in other operating income.

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

- > In October 2016, we 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 us \$175 million upon completion of the transaction. Aralez will also pay us up to \$48 million in milestone and sales-related payments, as well as mid-teen percentage royalties on sales. We will continue to manufacture and supply *Toprol-XL* and the authorised generic medicine to Aralez. We will retain a significant ongoing interest in *Toprol-XL* in the rest of the world, and significant interest in the US through the ongoing manufacture and supply of the product.
- > In June 2016, we entered into a licence agreement with LEO Pharma for the global development and commercialisation of tralokinumab in dermatology indications. We will continue to develop tralokinumab in asthma, and will manufacture and supply tralokinumab to LEO Pharma at a mark-up of 10% on cost. LEO Pharma have 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 to us of \$115 million for the exclusive licence. LEO Pharma will also pay us up to \$1 billion in commercially-related milestones and up to mid-teen tiered percentage royalties on Product Sales.
- > In June 2016, we announced that we 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*, *Marcaïne*, *Naropin*, *Carbocaine* and *Citanest*). Under the terms of the agreement, Aspen acquired the commercialisation rights for an upfront consideration of \$520 million (\$410 million paid on completion and \$110 million to be paid in 2017). Additionally, Aspen will pay us up to \$250 million on a Product Sales-related payment, as well as double digit percentage trade mark royalties on

Product Sales. For an initial period of 10 years, we will manufacture and supply the products to Aspen at cost plus 20%. Aspen have assumed responsibility for all activities relating to the sale of the portfolio in all relevant markets.

- > In February 2016, we entered into a licensing agreement with China Medical System Holdings Ltd (CMS) for the commercialisation rights in China to our calcium channel blocker, *Plendil* (felodipine). *Plendil* achieved Product Sales in China of \$189 million in 2015. Under the terms of the agreement, CMS paid us \$155 million in 2016 for the licence to sell *Plendil* in China, and committed to pay us a further \$155 million in 2017 (recognised as Externalisation Revenue in 2016 after applying a discount factor of 8%). We will manufacture and supply the medicine to CMS and retain the global rights to *Plendil* outside China. The transaction did not include the transfer of any of our employees or facilities. Over the term of the licence, we will supply finished product to CMS for a supply value equivalent to approximately 40% of the net sales value booked by CMS for *Plendil* in each given year and will sit on the Joint Steering Committee governing the commercialisation of the product in China.
- > In September 2015, we announced that we had entered into a collaboration agreement with Valeant under which we will grant an exclusive licence for Valeant to develop and commercialise brodalumab. Under the agreement, Valeant will hold the exclusive rights to develop and commercialise brodalumab globally, except in Japan and certain other Asian countries where rights are held by Kyowa Hakkō Kirin under a prior arrangement with Amgen. Valeant will assume all development costs associated with the regulatory approval for brodalumab. Under the terms of the agreement, Valeant made an upfront payment to us of \$100 million and may also pay pre-launch milestones of up to \$170 million and further sales related milestone payments of up to \$175 million. If approved, we will share profits with Valeant.

Financial Review continued

- > In April 2015, we signed a Collaboration and License Agreement with Celgene, a global leader in haematological cancers, to develop and commercialise durvalumab across a range of blood cancers including non-Hodgkin lymphoma, myelodysplastic syndromes and multiple myeloma. Under the terms of the agreement, Celgene made an upfront payment of \$450 million to us in relation to durvalumab, which is recorded within Externalisation Revenue. Celgene will 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. We will manufacture and record all sales of durvalumab 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 durvalumab in haematological indications over a period of four years.
- > In March 2015, we announced a co-commercialisation agreement with Daiichi Sankyo, for *Movantik* in the US. The drug was launched on 31 March 2015. Under the terms of the agreement, Daiichi Sankyo paid a \$200 million upfront fee and will pay subsequent sales-related payments of up to \$625 million. \$200 million was recorded in Externalisation Revenue in 2015. We 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.
- > In September 2014, we entered into an agreement with Lilly to jointly develop and commercialise AZD3293, an oral beta secretase cleaving enzyme (BACE) inhibitor currently in development as a potential treatment for Alzheimer's disease. Under the terms of the agreement, Lilly will pay us up to \$500 million in development and regulatory milestone payments. We received the first milestone payment of \$50 million in 2015, and a further \$100 million in 2016. The companies will equally share all future costs for the development and commercialisation of AZD3293, as well as net global revenues post-launch. Lilly lead the clinical development, working with researchers from our Innovative Medicines Unit for neuroscience, while

we will be responsible for manufacturing. The companies are jointly responsible for the commercialisation of AZD3293.

As detailed in Risk from page 214, 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 margin as a percentage of Product Sales was 80.8% in the year, 0.5 percentage points higher than last year. Excluding the impact of Externalisation Revenue, the Reported gross margin was broadly flat compared to 2015 at CER, with lower restructuring and amortisation charges offset by an adverse impact from the mix of sales, the market entry of multiple *Crestor* generic medicines in the US and a write-down of *FluMist* inventory in the US.

Reported R&D expense in the year was down 2% (CER: up 2%) to \$5,890 million, as we continued our focused investment in the pipeline. Adjusting for exchange rate movements, the full-year increase at CER reflected the number of potential medicines in pivotal trials as well as the inclusion of the R&D costs of ZS Pharma and Acerta Pharma. These costs were partially offset by lower restructuring costs and impairment charges.

Reported SG&A costs declined by 15% (CER: declined by 12%) to \$9,413 million reflecting the fair value adjustment to acquisition-related liabilities based on revised milestone probabilities and revenue and royalty forecasts relating to the acquisition of BMS's share of the Global Diabetes Alliance and the acquisition of Almirall. The decline was also driven by the movement to a more even split between the sale of primary and specialty care medicines and efficiency savings in sales and marketing operations and further reductions in IT costs. These actions included a material reduction in the sales and head-office structure in the US marketing business.

Reported other operating income in the year was up 10% (CER: up 12%) at \$1,655 million which, in addition to royalty income of \$165 million for *Crestor* and \$134 million for Human Papillomavirus (HPV) vaccine, includes \$368 million on the sale of our small-molecule antibiotics business to Pfizer, \$321 million on the sale of our non-US rights to *Rhinocort Aqua* to Cilag, \$183 million on the sale of our non-US rights to *Imdur* and \$148 million (after deduction of \$83 million payable to Amgen) on the disposal of global rights to MEDI2070 to Allergan. 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 continue to be recorded as other operating income.

In 2015, Reported other operating income included \$380 million for the divestment of rights to the *Entocort* business in the US to Elan Pharma International Limited, part of the Perrigo Group, \$215 million for the divestment of the rights to sell and develop *Entocort* capsules and enema formulations outside the US to Tillotts Pharma AG, \$193 million gain on the divestment of the global rights to develop, manufacture and commercialise *Myalept* subject to an existing distributor licence with Shionogi covering Japan, South Korea, and Taiwan with Aegerion and \$165 million for the divestment of *Caprelsa* in an agreement with Genzyme Corporation, part of Sanofi S.A.

Reported operating profit increased by 19% (CER: increased by 9%) to \$4,902 million in the year. The Reported operating margin increased by 4.6 percentage points (CER: 2.6 percentage points) to 21.3% of Total Revenue. The increase reflected the reduction in SG&A costs which more than offset the decline in Product Sales and Externalisation Revenue, while we continued to invest in our pipeline and Growth Platforms.

Core operating profit declined by 3% (CER: declined by 7%) in the year to \$6,721 million. Fair value adjustments to acquisition-related liabilities reduced SG&A costs and increased Reported operating profit by \$1,158 million in the current year (2015: \$432 million). These fair value movements reflected estimates for future liabilities that can change materially over time.

Reported net finance expense was \$1,317 million (2015: \$1,029 million). The increase of \$288 million was largely due to an increase in Net Debt that was driven by the acquisition of ZS Pharma and the majority investment in Acerta Pharma. Excluding the discount unwind on acquisition-related liabilities and other adjustments, Core Net Finance Expense increased by 31% (CER: increased by 46%) in the year to \$661 million.

Profit before tax amounted to \$3,552 million in 2016 (2015: \$3,069 million). Pre-tax adjustments to arrive at Core profit before tax amounted to \$2,475 million in 2016 (2015: \$3,312 million), comprising \$1,819 million adjustments to operating profits (2015: \$2,788 million) and \$656 million to net finance expenses (2015: \$524 million). Excluded from Core results were:

- > Restructuring costs totalling \$1,107 million (2015: \$1,034 million), incurred as we continued to enhance productivity through the implementation of our restructuring initiatives. To continue the focus on cost discipline, 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. We incurred restructuring costs totalling \$555 million relating to this programme in 2016. We also disposed of our R&D facility in Bangalore, India in the period and announced plans to bring together five of our San Francisco Bay Area, US sites into one location.
- > Amortisation totalling \$1,247 million (2015: \$1,460 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 157.
- > Intangible impairment charges of \$44 million (2015: \$143 million) excluding those related to IT. Further details relating to intangible asset impairments are included in Note 9 to the Financial Statements from page 157.
- > Net credit associated with our acquisition of BMS's share of our Global Diabetes Alliance in February 2015 amounting to \$238 million (2015: net cost of \$463 million). A contingent consideration fair

value decrease of \$999 million reflecting lower expected Diabetes portfolio revenues in line with latest forecasts was partially offset by \$372 million of amortisation charges and \$389 million of interest charges relating to a discount unwind on contingent consideration arising on the acquisition.

- > Net legal provisions and other charges of \$315 million (2015: \$211 million), including \$267 million discount unwind charges, offset by \$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 164. The net charge of \$315 million also included legal charges relating to the unsuccessful defence of the validity of *Crestor*-related patents in Australia, damages claims in Europe relating to *Seroquel XR* and other matters. Further details of legal proceedings we are currently involved in are contained within Note 28 to the Financial Statements from page 185.

Reported EPS of \$2.77 in the year represented growth of 24% (CER: growth of 9%), partly reflecting the revaluation of acquisition-related liabilities described above. Core EPS in the year increased by 1% (CER: declined by 5%) to \$4.31. The CER decline of 5% mirrored the rate of decline in Total Revenue. Both Reported and Core EPS in the year included a non-recurring benefit of \$0.36, following agreements between the Canadian tax authority and the UK and Swedish tax authorities.

The Reported taxation charge for the year of \$146 million (2015: \$243 million) consisted of a current tax charge of \$370 million (2015: \$633 million) and a credit arising from movements on deferred tax of \$224 million (2015: \$390 million). The current tax charge included a prior period current tax credit of \$14 million (2015: \$404 million).

The Reported tax rate for the year was 4% (2015: 8%). The Reported tax rate of 4% benefited from a \$453 million adjustment following agreements between the Canadian tax authority and the UK and Swedish tax authorities. Excluding these effects, the Reported tax rate for the year was 17%. The Core tax rate for the year was 11%. Excluding the benefit following agreements between the Canadian tax

authority and the UK and Swedish tax authorities in respect of transfer pricing arrangements for the 13-year period from 2004-2016, the Core tax rate was 18%.

The tax paid for the year was \$412 million (12% of Reported profit and 7% of Core profit). The cash tax paid for the year was \$266 million higher than the tax charge for the year as a result of certain items with no cash impact including a \$453 million adjustment following the agreement between the Canadian tax authority and the UK and Swedish tax authorities referred to above, other net reductions in provisions for tax contingencies of \$52 million, \$244 million of deferred tax credits, net cash refunds received following agreement of prior period tax liabilities and audit settlements of \$274 million and other cash tax timing differences.

Reported post-tax profit for the year was \$3,406 million, an increase of 21% (CER: increase of 6%). Reported earnings per share was up 24% (CER: up 9%) to \$2.77.

Total comprehensive income decreased by \$860 million from the prior year, resulting in a net income of \$1,628 million for 2016. This was driven by the increase in profit for the year of \$580 million being more than offset by a reduction of \$1,440 million in other comprehensive income. The decrease in other comprehensive income arose principally from losses recorded on the remeasurement of our defined benefit pension liability of \$575 million (2015: gains of \$652 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, and foreign exchange losses arising on consolidation of the Group numbers of \$1,050 million (2015: losses of \$528 million) as a result of the strong performance of the US dollar against other major currencies in 2016.

Restructuring

Since 2007, we have undertaken significant efforts to restructure and reshape our business to improve long-term competitiveness, the first two phases of which were completed in 2011.

In 2013, we announced our Phase 4 restructuring programme, which was subsequently expanded in 2014. This consisted of centralisation of our global R&D footprint into three strategic centres,

Financial Review continued

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 2016, the Phase 4 programme had incurred costs of \$3.3 billion and realised annual benefits of \$0.9 billion, creating headroom for investment in our pipeline and launch capability. The Phase 4 programme is now expected to complete in 2018 with total programme costs estimated to be \$3.6 billion and annualised benefits \$1.2 billion. During the latter part of 2015, we implemented further targeted restructuring of our Commercial business.

This resulted in \$102 million of restructuring costs in 2015, with a further \$47 million incurred in 2016. Furthermore, as part of our ongoing commitment to improve productivity, we initiated multi-year transformation programmes within our G&A functions (principally Finance and HR) with anticipated costs by the end of 2018 of \$258 million. Once complete, we expect these transformation programmes to deliver annualised benefits of \$100 million by the end of 2018. By the end of 2016, these programmes had incurred costs of \$124 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 are expected to be \$1.5 billion by the end of 2017 and generate net annualised benefits of \$1.1 billion by 2018. We incurred restructuring costs totalling \$555 million relating to this programme in 2016.

The aggregate restructuring charge incurred in 2016 across all our restructuring programmes was \$1,107 million. Final estimates for programme costs, benefits and headcount impact in all functions are subject to completion of the requisite consultation in the various areas. Our priority as we undertake these restructuring initiatives is to work with our affected employees on the proposed changes, acting in accordance with relevant local consultation requirements and employment law.

Cash flow and liquidity – 2016

Summary cash flows

	2016 \$m	2015 \$m	2014 \$m
Net (debt)/funds brought forward at 1 January	(7,762)	(3,223)	39
Profit before tax	3,552	3,069	1,246
Sum of changes in interest, tax, depreciation, amortisation, impairment, and share of after tax losses on joint ventures and associates	3,707	3,897	4,173
Movement in working capital and short-term provisions	926	(49)	2,508
Tax paid	(412)	(1,354)	(1,201)
Interest paid	(677)	(496)	(533)
Gains on disposal of intangible assets	(1,301)	(961)	–
Fair value movements on contingent consideration arising from business combinations	(1,158)	(432)	512
Non-cash and other movements	(492)	(350)	353
Net cash available from operating activities	4,145	3,324	7,058
Disposal/(purchase) of intangibles (net)	559	(330)	(1,740)
Upfront payments on business acquisition	(2,564)	(2,446)	(3,804)
Payment of contingent consideration from business combinations	(293)	(579)	(657)
Other capital expenditure (net)	(1,405)	(1,326)	(924)
Investments	(3,703)	(4,681)	(7,125)
Dividends	(3,561)	(3,486)	(3,521)
Share proceeds	47	43	279
Distributions	(3,514)	(3,443)	(3,242)
Other movements	177	261	47
Net debt carried forward at 31 December	(10,657)	(7,762)	(3,223)

Net debt/funds reconciliation

	2016 \$m	2015 \$m	2014 \$m
Cash and cash equivalents	5,018	6,240	6,360
Other investments ¹	898	613	795
Net derivative financial instruments	235	438	465
Cash, short-term investments and derivatives	6,151	7,291	7,620
Overdraft and short-term borrowings	(451)	(849)	(1,486)
Finance leases	(93)	(95)	(108)
Current instalments of loans	(1,769)	–	(912)
Loans due after one year	(14,495)	(14,109)	(8,337)
Loans and borrowings	(16,808)	(15,053)	(10,843)
Net debt	(10,657)	(7,762)	(3,223)

¹ Other investments in 2016 includes \$14 million of non-current investments which is not separately disclosed on the Statement of Financial Position.

Bonds issued in 2016 and 2015

	Repayment dates	Face value of bond \$m	Net book value of bond at 31 December 2016 \$m
Bonds issued in 2016:			
0.25% Euro bond	2021	566	522
0.75% Euro bond	2024	1,016	937
1.25% Euro bond	2028	897	827
Total 2016		2,479	2,286
Bonds issued in 2015:			
Floating rate notes	2018	400	399
1.750% Callable bond	2018	1,000	998
2.375% Callable bond	2020	1,600	1,589
3.375% Callable bond	2025	2,000	1,976
4.375% Callable bond	2045	1,000	979
Total 2015		6,000	5,941

Net cash generated from operating activities was \$4,145 million in the year ended 31 December 2016, compared with \$3,324 million in 2015. The increase of \$821 million reflected improved cash management performance and one-off tax refunds in 2016 compared to an increase of \$49 million in working capital and short-term provisions in the prior year.

Gains on disposal of intangible assets of \$1,301 million included \$368 million on the disposal of our late-stage antibiotics business, \$321 million on the sale of our rights to *Rhinocort Aqua* outside of the US, \$231 million on the out-licence agreement for MEDI-2070, and \$183 million for the divestment of the global rights to *Imdur* outside the US. 2015 included \$380 million on the disposal of US rights to *Entocort*, \$215 million on the disposal of Rest of World rights to *Entocort*, \$193 million on the disposal of global rights to *Myalept* and \$165 million on the disposal of global rights to *Caprelsa*. Fair value adjustments on acquisition-related liabilities were a credit of \$1,158 million in 2016 (2015: a credit of \$432 million) including \$999 million on our acquisition of BMS's share of our Global Diabetes Alliance in February 2015. Other non-cash movements amounted to \$492 million in 2016 (2015: \$350 million).

Investment cash outflows of \$3,703 million (2015: \$4,681 million) included \$2,383 million relating to the majority investment in Acerta Pharma. This compared to cash payments relating to business acquisitions in 2015

of \$2,446 million, primarily related to the ZS Pharma acquisition. Further details of business combination acquisitions and their impact on our cash flows and balance sheet are given in the table on page 73. Investment cash outflows also include \$293 million (2015: \$579 million) of payments against contingent consideration arising on business combinations and \$868 million (2015: \$1,460 million) for the purchase of other intangible assets, which included \$561 million on the purchase of the core respiratory assets of Takeda. The comparative period of 2015 included \$684 million on the acquisition of the rights to Actavis' branded respiratory portfolio in the US and Canada.

Investment cash inflows include \$1,427 million (2015: \$1,130 million) from the sale of intangible assets, including \$552 million for the disposal of our late-stage antibiotics business, \$330 million for the sale of our rights to *Rhinocort Aqua* outside of the US and \$250 million on the out-licence agreement for MEDI-2070. The comparative period in 2015 included the divestments of *Entocort* in the US for \$380 million, and in the Rest of World for \$215 million and of *Myalept* for \$325 million.

Net cash distributions to shareholders were \$3,514 million (2015: \$3,443 million) including dividends of \$3,561 million (2015: \$3,486 million). Proceeds from the issue of shares on the exercise of share options amounted to \$47 million (2015: \$43 million).

In May 2016, we issued €2.2 billion of bonds in the euro debt capital markets with maturities of 5, 8 and 12 years.

In November 2015, we issued bonds worth \$6 billion to fund the acquisition of ZS Pharma, to repay certain of our outstanding commercial paper obligations and for general corporate purposes. The bonds are listed in the table above.

In 2015, we repaid a 5.125% non-callable euro bond which had a 31 December 2015 carrying value of \$912 million.

At 31 December 2016, outstanding gross debt (interest-bearing loans and borrowings) was \$16,808 million (2015: \$15,053 million). Of the gross debt outstanding at 31 December 2016, \$2,307 million is due within one year (2015: \$916 million). Net debt at 31 December 2016 was \$10,657 million, compared to \$7,762 million at the beginning of the year, as a result of the net cash outflow as described above.

Off-balance sheet transactions and commitments

We have no off-balance sheet arrangements and our derivative activities are non-speculative. The following table on page 72 sets out our minimum contractual obligations at the year end.

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Payments due by period

	Less than 1 year \$m	1-3 years \$m	3-5 years \$m	Over 5 years \$m	2016 Total \$m	2015 Total \$m
Bank loans and other borrowings ¹	2,829	3,421	3,843	14,796	24,889	23,263
Finance leases	42	40	13	–	95	141
Operating leases	98	145	102	96	441	409
Contracted capital expenditure	629	–	–	–	629	518
Total	3,598	3,606	3,958	14,892	26,054	24,331

¹ Bank loans and other borrowings include interest charges payable in the period, as detailed in Note 26 to the Financial Statements on page 178.

In 2016, net assets decreased by \$1,840 million to \$16,669 million. The decrease in net assets is broadly as a result of dividends of \$3,540 million and adverse movements on exchange taken to reserves of \$1,641 million, partially offset by the Group profit of \$3,406 million.

Business combinations

In 2016, we acquired a majority equity stake in Acerta Pharma. In 2015, we completed the acquisition of ZS Pharma. During 2016 we revised our assessment of the fair values of the assets and liabilities acquired with ZS Pharma, as a result of new information obtained about facts and circumstances that existed at the date of acquisition that impact the value of deferred tax. This has resulted in a reduction to both deferred tax liabilities and goodwill of \$68 million. Further details of our business combinations are contained in Note 25 to the Financial Statements from page 173.

Fair values of assets and liabilities acquired, and consideration for the acquisitions in 2016 and 2015, as at the acquisition date, are summarised on the opposite page.

Contingent consideration

The majority of our 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.

Our agreement with BMS provides for potential further payments of up to \$0.7 billion for future regulatory, launch and sales-related milestones, and various sales-related royalty payments up until 2025. Our transaction with Ammiral includes further payments of up to \$1.0 billion for future development, launch, and sales-related milestones and various other sales-related

payments as detailed in Note 18 to the Financial Statements on page 164. All these future payments are treated as contingent consideration on our balance sheet, 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 balance sheet reporting date to reflect our latest estimate of the probabilities of these key assumptions. Given the long-term nature of our contingent consideration payments, 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'.

Financial position – 31 December 2016

All data in this section is on a Reported basis.

Summary statement of financial position

	2016 \$m	Movement \$m	2015 As restated ¹ \$m	Movement \$m	2014 \$m
Property, plant and equipment	6,848	435	6,413	403	6,010
Goodwill and intangible assets	39,244	4,798	34,446	1,915	32,531
Inventories	2,334	191	2,143	183	1,960
Trade and other receivables	5,474	(2,055)	7,529	(815)	8,344
Trade and other payables	(19,974)	(854)	(19,120)	757	(19,877)
Provisions	(1,418)	(176)	(1,242)	(135)	(1,107)
Net income tax payable	(954)	142	(1,096)	929	(2,025)
Net deferred tax liabilities	(2,854)	(1,483)	(1,371)	(794)	(577)
Retirement benefit obligations	(2,186)	(212)	(1,974)	977	(2,951)
Non-current other investments (excluding Treasury investments of \$14 million in 2016)	713	255	458	(44)	502
Investment in associates and joint ventures	99	14	85	26	59
Net debt	(10,657)	(2,895)	(7,762)	(4,539)	(3,223)
Net assets	16,669	(1,840)	18,509	(1,137)	19,646

¹ 2015 comparatives have been restated to reflect an adjustment to the acquisition accounting for ZS Pharma.

Business combinations

	2016 Acerta Pharma \$m	2015 ZS Pharma As Restated \$m
Assets acquired:		
Non-current assets		
Property, plant and equipment	–	21
Goodwill	19	388
Intangible assets	7,307	3,162
Current assets		
	253	169
Current liabilities		
	(90)	(50)
Non-current liabilities		
	(1,777)	(990)
Non-controlling interests		
	(1,903)	–
Total assets	3,809	2,700
Consideration:		
Upfront consideration	2,477	2,700
Deferred consideration	1,332	–
Total consideration	3,809	2,700

Contingent consideration arising on business combinations

	2016			2015		
	Acquisition of BMS's share of Diabetes Alliance \$m	Other business combinations \$m	Total 2016 \$m	Acquisition of BMS's share of Diabetes Alliance \$m	Other business combinations \$m	Total 2015 \$m
At 1 January	5,092	1,319	6,411	5,386	1,513	6,899
Settlements	(242)	(51)	(293)	(325)	(254)	(579)
Fair value adjustments	(999)	(159)	(1,158)	(378)	(54)	(432)
Discount unwind	389	108	497	409	115	524
Foreign exchange	–	–	–	–	(1)	(1)
At 31 December	4,240	1,217	5,457	5,092	1,319	6,411

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 2016, we recorded an interest charge of \$497 million on the discount unwind on contingent consideration arising on our business combinations, and a net fair value decrease on contingent consideration of \$1,158 million (which resulted in a credit to our income statement for the same amount) driven, principally, by revised forecasts for revenues for our Diabetes franchise reflecting the competitive marketplace. At 31 December 2016, our contingent consideration balance held on the balance sheet amounted to \$5,457 million (2015: \$6,411 million) with the movements of the balance detailed in the table above.

Further details of our business combinations in the past three years are contained in Note 25 to the Financial Statements from page 173. Further information on our business combinations can also be found in the Investments, divestments and capital expenditure section of the Financial Review from page 75.

Property, plant and equipment

Property, plant and equipment increased by \$435 million to \$6,848 million. Additions of \$1,449 million (2015: \$1,422 million) were offset by depreciation of \$609 million (2015: \$677 million), impairments of \$2 million (2015: \$28 million) and disposals of \$74 million (2015: \$70 million).

Goodwill and intangible assets

Our goodwill of \$11,658 million (2015: \$11,800 million) principally arose on the acquisition of MedImmune in 2007, the

restructuring of our US joint venture with Merck in 1998 and the acquisition of BMS's share of the Global Diabetes Alliance. Goodwill of \$19 million arising on the acquisition of Acerta Pharma was capitalised in 2016.

Intangible assets amounted to \$27,586 million at 31 December 2016 (2015: \$22,646 million). Intangible asset additions were \$8,205 million in 2016 (2015: \$4,640 million), including product rights acquired in the acquisition of Acerta Pharma of \$7,307 million (\$3,162 million on the acquisition of ZS Pharma in 2015). Amortisation in the year was \$1,701 million (2015: \$1,999 million). Impairment charges in the year amounted to \$45 million (2015: \$148 million), including \$15 million for RDEA119. Disposals of intangible assets totalled \$331 million in the year (2015: \$169 million).

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Further details of our additions to intangible assets, and impairments recorded, are included in Note 9 to the Financial Statements from page 157.

Receivables, payables and provisions

Trade and other receivables decreased by \$2,055 million with trade receivables reduced by \$2,050 million to \$2,583 million as a result of more factored invoices during the year and lower gross invoiced sales in the US. Non-current other receivables decreased by \$6 million to \$901 million, the majority of which is the Shionogi *Crestor* royalty prepayment as detailed in Note 13 to the Financial Statements on page 161.

Trade and other payables increased by \$854 million in 2016 to \$19,974 million, including a \$1,901 million put option, and \$1,332 million deferred consideration on the majority investment in Acerta Pharma, partially offset by reductions in contingent consideration of \$954 million, a decrease in trade payables of \$479 million, and a decrease of \$495 million on rebates and chargebacks driven by reduced Product Sales in the US. Further details on the put option are included in Note 25 to the Financial Statements from page 173.

The increase in provisions of \$176 million in 2016 included \$988 million of additional charges recorded in the year, partially offset by \$686 million of cash payments. Included within the \$988 million of charges for the year were \$578 million for our global restructuring initiatives and \$223 million in respect of legal charges. Cash payments included \$433 million for our global restructuring programmes. Further details of the charges made against provisions are contained in Notes 19 and 28 to the Financial Statements on page 165, and 185 to 191, respectively.

Tax payable and receivable

Net income tax payable has decreased by \$142 million to \$954 million, principally due to a \$453 million adjustment following agreements between the Canadian tax authority and the UK and Swedish tax

authorities in respect of transfer pricing arrangements for the 13-year period from 2004-2016, partially offset by net cash refunds received following agreement of prior period tax liabilities and audit settlements of \$274 million. The tax receivable balance of \$426 million (2015: \$387 million) comprises tax owing to us from certain governments expected to be received on settlements of transfer pricing audits and disputes of \$161 million (see Note 28 to the Financial Statements from page 185) and cash tax timing differences of \$265 million.

Net deferred tax liabilities increased by \$1,483 million in the year mainly due to deferred tax liabilities arising from the acquisition of Acerta Pharma. Additional information on the movement in deferred tax balances is contained in Note 4 to the Financial Statements from page 150.

Retirement benefit obligations

Net retirement benefit obligations increased by \$212 million in 2016 (2015: decrease of \$977 million) to \$2,186 million. Net remeasurement adjustments of \$575 million in the UK, Sweden and Germany arising from reductions in discount rate assumptions were partially offset by a \$312 million impact of exchange rate movements in the year as the US dollar strengthened against pound sterling, euro and Swedish krona and employer contributions to the pension scheme of \$192 million. Benefits paid amounted to \$500 million (2015: \$580 million).

Approximately 92% of our obligations are concentrated in the UK, the US and Sweden. 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. During 2016, we realised a credit of \$74 million on our Pensions Increase Exchange ('PIE') exercise which offered certain pensioner members the option of taking a higher amount of pension right away, in exchange for giving up any potential future inflation linked increases on all or part of their pension.

From 2017, for our largest pension plans, we will move to a multiple discount rate approach. This will result in separate discount rates for defined benefit obligations, service cost and interest cost. This change had no effect on the 2016 expense, and will not affect the future measurement of the defined benefit obligations, but will impact the service cost and interest cost in future years.

Further details of our pension schemes are included in Note 20 to the Financial Statements from page 165.

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 142. We also have taxation contingencies. These are described in the Taxation section in the Critical accounting policies and estimates section on page 81 and in Note 28 to the Financial Statements from page 185.

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 185.

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. As part of our overall externalisation strategy, 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 270 major or strategically important business development transactions over the past three years, five of which were accounted for as business acquisitions under IFRS 3 'Business Combinations', being the majority investment in Acerta Pharma in 2016, the acquisition of ZS Pharma in 2015, the acquisition of BMS's share of our Global Diabetes Alliance, the rights to Almirall's respiratory franchise and the acquisition of Definiens in 2015.

In addition to the business development transactions detailed under Externalisation Revenue from page 67 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 durvalumab, 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 durvalumab. 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 durvalumab, 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 (CKD) 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 externalisation 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.

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Capitalisation and shareholder return

Dividends for 2016

	\$	Pence	SEK	Payment date
First interim dividend	0.90	68.7	7.81	12 September 2016
Second interim dividend	1.90	150.2	16.57	20 March 2017
Total	2.80	218.9	24.38	

Capitalisation

The total number of shares in issue at 31 December 2016 was 1,265 million (2015: 1,264 million). 1.1 million Ordinary Shares were issued upon share option exercises for a total of \$47 million. Shareholders' equity decreased by \$3,636 million to \$14,854 million at the year end. Non-controlling interests were \$1,815 million (2015: \$19 million), with the increase in the year as a result of the acquisition of a 55% equity stake in Actera Pharma.

Dividend and share repurchases

The Board has recommended a second interim dividend of \$1.90 (150.2 pence, 16.57 SEK) to be paid on 20 March 2017. This brings the full-year dividend to \$2.80 (218.9 pence, 24.38 SEK). Against Core earnings per share the Group has a dividend cover ratio of 1.5 in 2016 (2015: 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.

We expect 2017 Total Revenue to decline by low to mid single-digit percent at CER compared to 2016. Core R&D costs as a percentage of Total Revenue are expected to be broadly in line with 2016. We are also anticipating a further reduction in Core SG&A costs in 2017 versus 2016. Core earnings per share is expected to decrease in 2017 by low to mid teens percent at CER. This guidance reflects a significantly higher expected effective Core tax rate of 16 to 20% (2016: 11%).

Financial risk management

Financial risk management policies

Insurance

Our risk management processes are described in Risk overview from page 20. 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. Insurance for product liability has not been available on commercially acceptable terms for several years and we have not purchased in the market product liability insurance since February 2006.

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 also 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.

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 177 and in Risk overview from page 20. 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 177.

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 142. 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 at the point of delivery, 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 a monthly 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 \$12,275 million in 2016 (2015: \$14,167 million) with the decrease driven by an overall reduction in our US Product Sales.

Cash discounts are offered to customers to encourage prompt payment. Accruals are calculated based on historical experience and are adjusted to reflect actual experience.

Financial Review continued

Gross to net Product Sales – US pharmaceuticals

	2016 \$m	2015 \$m	2014 \$m
Gross Product Sales	19,640	23,641	23,414
Chargebacks	(3,449)	(2,985)	(2,794)
Regulatory – Medicaid and state programmes	(1,903)	(1,714)	(1,389)
Contractual – Managed-care and Medicare	(5,219)	(7,543)	(7,730)
Cash and other discounts	(358)	(472)	(436)
Customer returns	(130)	(333)	(295)
US Branded Pharmaceutical Fee	(145)	(174)	(113)
Other	(1,071)	(946)	(537)
Net Product Sales	7,365	9,474	10,120

Movement in provisions – US pharmaceuticals

	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

	Brought forward at 1 January 2014 \$m	Recognition of US Branded Pharmaceutical Fee as a revenue deduction \$m	Provision for current year \$m	Adjustment in respect of prior years \$m	Returns and payments \$m	Carried forward at 31 December 2014 \$m
Chargebacks	355	–	2,838	(44)	(2,692)	457
Regulatory – Medicaid and state programmes	784	–	1,544	(155)	(1,466)	707
Contractual – Managed-care and Medicare	1,714	–	7,703	27	(7,078)	2,366
Cash and other discounts	32	–	436	–	(435)	33
Customer returns	222	–	295	–	(199)	318
US Branded Pharmaceutical Fee	–	132	113	–	–	245
Other	74	–	537	–	(448)	163
Total	3,181	132	13,466	(172)	(12,318)	4,289

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 preceding 12 months for established products together with market-related information, such as estimated stock levels at wholesalers and competitor activity, which we receive via third party information services. For newly launched products, we use rates based on our experience with similar products or a 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 2016 net US pharmaceuticals revenue by 6.0% (2015: 3.1%; 2014: 1.7%). However, taking into account the adjustments affecting both the current and the prior year, 2015 revenue would have been increased by 1.6% and 2014 revenue would have been increased by 1.2%, 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 balance sheet. We also own acquired intangible assets which are included on the balance sheet. As detailed on page 67, our externalisation 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 164.

Financial Review continued

Where not all of the equity of a subsidiary is acquired, the non-controlling interest is recognised either at fair value or at the non-controlling interest's proportionate share of the net assets of the subsidiary, on a case-by-case basis. Put options over non-controlling interests are recognised as a financial liability 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 156. The Group, including acquisitions, is considered a single cash-generating unit 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. Sales forecasts and specific allocated costs (which have both been subject to appropriate senior management sign-off) are discounted using appropriate rates based on our risk-adjusted, pre-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. In building to the range of rates used in our internal investment appraisal of future projects and capital investment decisions, we adjust our weighted average cost of capital for other factors which reflect, without limitation, local matters such as risk on a case-by-case basis.

A significant portion of our investments in intangible assets and goodwill arose from the restructuring of the joint venture with Merck in 1998, the acquisition of MedImmune in 2007, and the payments arising from the restructuring of the joint venture with Merck in the US. 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 2016 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 157.

Further details of the estimates and assumptions we make in impairment testing of intangible assets are included in Note 9 to the Financial Statements.

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 185.

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, Sweden and Germany 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. All 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 trustees follow a strategy of awarding mandates to specialist, active investment managers, which results in a broad diversification of investment styles and asset classes. The investment approach is intended to produce less volatility in the plan asset returns.

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 20 to the Financial Statements from page 165.

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. Any liability to interest on tax liabilities is provided for in the tax charge.

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 185.

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 2016 and the assessment is set out in the Directors' Responsibilities for, and Report on, Internal Control over Financial Reporting on page 133. KPMG LLP has audited the effectiveness of our internal control over financial reporting at 31 December 2016 and, as noted in the Auditor's Reports on the Financial Statements and on Internal Control over Financial Reporting (Sarbanes-Oxley Act Section 404) on page 134, their report is unqualified.

Strategic Report

The Strategic Report, which has been prepared in accordance with the requirements of the Companies Act 2006, comprises the following sections:

- > AstraZeneca at a glance
- > Chief Executive Officer's Review
- > Strategy, including Risk overview
- > Therapy Area Review
- > Business Review
- > Resources Review
- > Financial Review

and has been approved and signed on behalf of the Board.

A C N Kemp

Company Secretary
2 February 2017