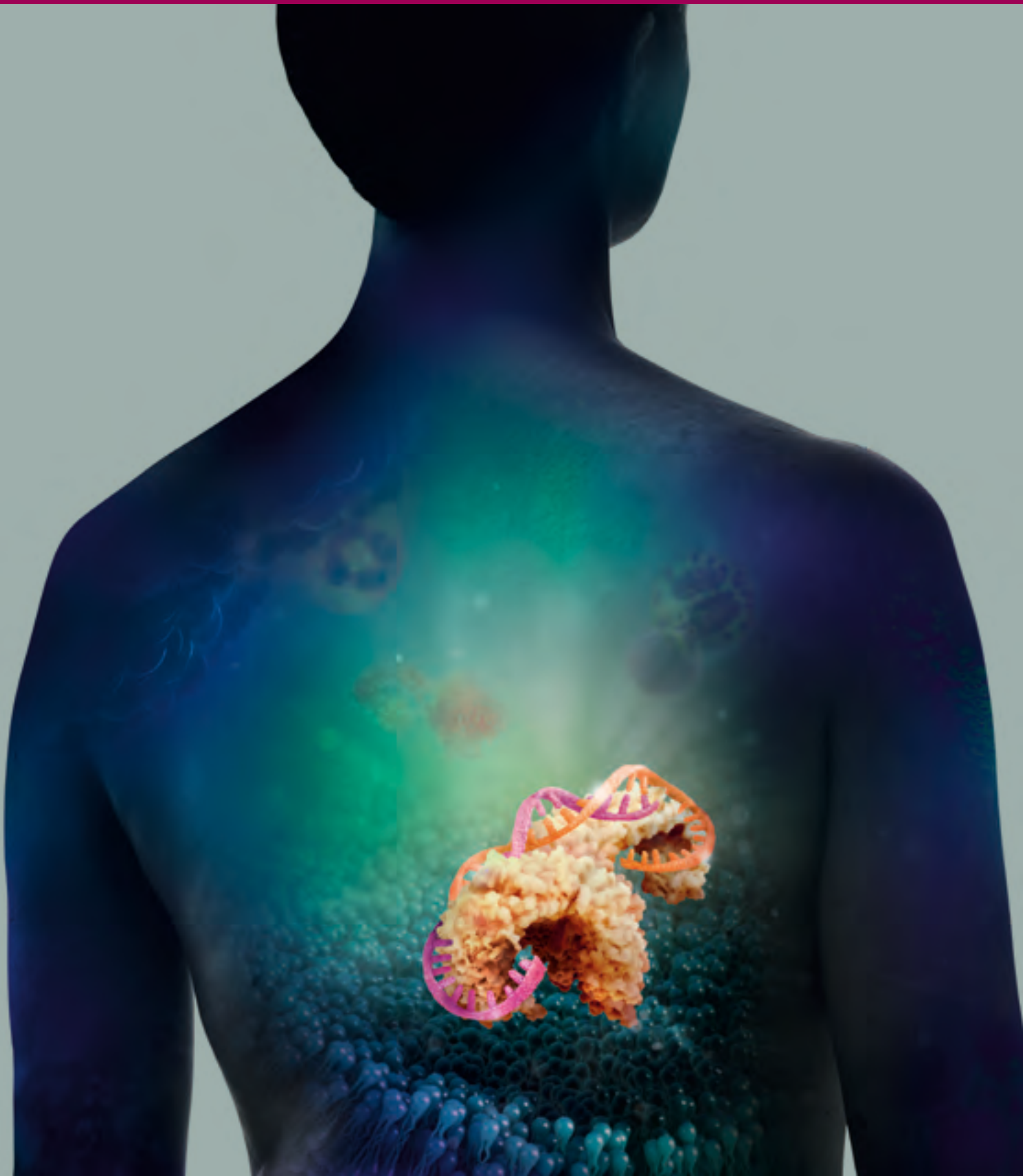


What science can do

AstraZeneca Annual Report and Form 20-F Information 2015



Welcome to the AstraZeneca
Annual Report and Form 20-F Information 2015.

We are a global, science-led biopharmaceutical business and in this Annual Report we report on the progress we made in 2015 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.

Our Chief Financial Officer, Marc Dunoyer, reviews our financial performance from page 62.

From page 82, Leif Johansson, our Chairman, reviews how our governance and approach to remuneration support delivery of the strategy.

Front cover:

New approaches in the treatment of asthma

AstraZeneca is developing a therapy aimed at producing long-term benefit in asthma by addressing imbalances in the immune system that may be an underlying cause of the disease. Rather than simply treating symptoms by relaxing airway constriction and dampening inflammation in the lung, this therapy aims to target toll-like receptor 9 in dendritic cells in the lung. This could potentially change the way immune cells communicate with each other and restore a healthy balance to the immune system.

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. Throughout this Annual Report, growth rates are expressed at CER unless otherwise stated.

Definitions

The Glossary and the Market definitions table from page 247 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 251.

Learn about our main therapy areas:



Pushing the boundaries

Respiratory, Inflammation and Autoimmunity

We have pushed the boundaries of science in respiratory disease for 40 years

 See page 26



Breaking through conventional thinking

Cardiovascular and Metabolic diseases

We take an integrated patient approach to reduce cardiovascular morbidity and mortality

 See page 30



Redefining the treatment paradigm

Oncology

We are committed to advancing the science of oncology

 See page 34

Directors' Report

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

- > Business Review: Research and Development
- > Resources Review: Employees
- > 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
- > Therapy Area Review
- > Business Review
- > Resources Review
- > Financial Review

Financial highlights

Total Revenue*

up 1% at CER to \$24,708 million (down 7% at actual rate of exchange)

2015	\$24,708m
2014	\$26,547m
2013	\$25,806m

\$24.7bn

Core operating profit

up 6% at CER to \$6,902 million (down 1% at actual rate of exchange)

2015	\$6,902m
2014	\$6,937m
2013	\$8,390m

\$6.9bn

Core EPS

for the full year up 7% at CER to \$4.26 (unchanged at actual rate of exchange)

2015	\$4.26
2014	\$4.28
2013	\$5.05

\$4.26

Net cash flow from operating activities

down 53% (at actual rate of exchange) to \$3,324 million

2015	\$3,324m
2014	\$7,058m
2013	\$7,400m

\$3.3bn

Reported operating profit

up 100% at CER to \$4,114 million (up 93% at actual rate of exchange)

2015	\$4,114m
2014	\$2,137m
2013	\$3,712m

\$4.1bn

Reported EPS

for the full year up 137% at CER to \$2.23 (up 128% at actual rate of exchange)

2015	\$2.23
2014	\$0.98
2013	\$2.04

\$2.23

 [Financial Review from page 62](#)

* As detailed on page 144, Total Revenue consists of Product Sales and Externalisation Revenue.



For more information within this Annual Report



For more information see www.astrazeneca.com



This Annual Report is also available on our website, www.astrazeneca.com/annualreport2015

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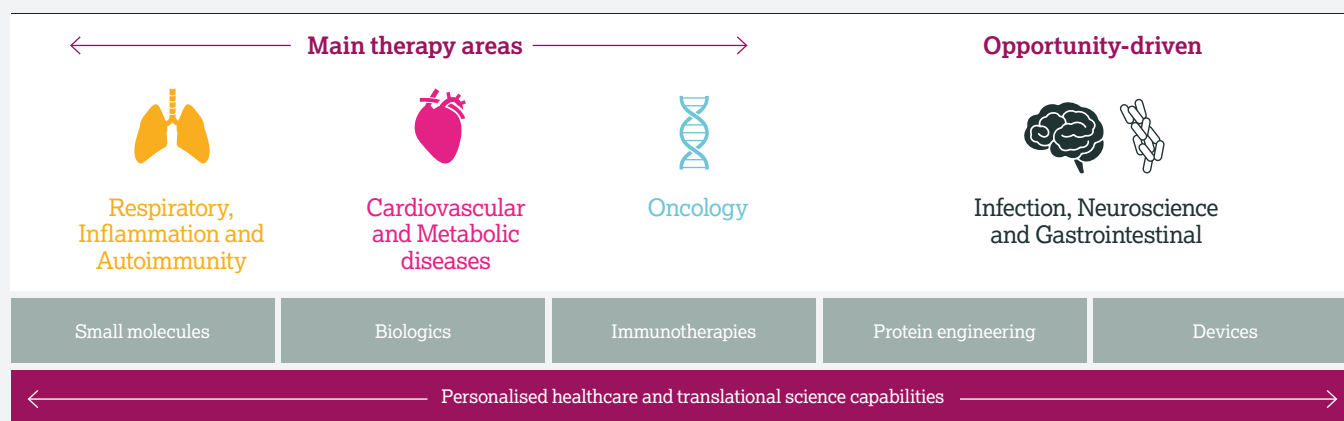
AstraZeneca at a glance

AstraZeneca is a global, science-led biopharmaceutical business...
...with an on-market portfolio in our chosen therapy areas.

Respiratory, Inflammation and Autoimmunity	Cardiovascular and Metabolic diseases	Oncology	Infection, Neuroscience and Gastrointestinal
			
\$4,987m	\$9,489m	\$2,825m	\$6,340m
Product Sales 2014: \$5,063m 2013: \$4,677m	Product Sales 2014: \$9,802m 2013: \$8,830m	Product Sales 2014: \$3,027m 2013: \$3,193m	Product Sales 2014: \$8,203m 2013: \$9,011m
Highlights			
<ul style="list-style-type: none"> > Respiratory sales up by 7%, including 25% in Emerging Markets, before completion of the acquisition of Takeda's respiratory business > Sales of <i>Symbicort</i> down by 3% 	<ul style="list-style-type: none"> > <i>Brilinta/Brilique</i> sales up by 44%, including 64% in the US > Diabetes sales up by 26%, including 76% in Emerging Markets > Sales of <i>Crestor</i> fell by 3% reflecting competition from generic statins and pricing pressure 	<ul style="list-style-type: none"> > Oncology sales up by 7% > New Oncology included for the first time (comprising <i>Lynparza</i>, <i>Iressa</i> (US) and <i>Tagrisso</i>) > <i>Lynparza</i> launched in 15 markets and sales of \$94 million 	<ul style="list-style-type: none"> > Sales of <i>Nexium</i> declined by 26%, including 52% in the US following loss of exclusivity > Sales of <i>Seroquel XR</i> fell by 12% and <i>Synagis</i> fell by 26%

 Sales and Marketing from page 48, Financial Review from page 62 and Geographical Review from page 227

We have distinctive R&D capabilities, a growing late-stage pipeline...



NMEs in Phase III, pivotal Phase II or under regulatory review

15

 Therapy Area Review from page 24 and Research and Development from page 42

2015		15
2014		13
2013		11
2012		6

...and a strong global commercial presence, with strength in Emerging Markets.

North America	Europe	International and Japan
\$10,007m Product Sales 2014: \$10,710m 2013: \$10,328m	\$5,323m Product Sales 2014: \$6,638m 2013: \$6,658m	\$8,311m Product Sales 2014: \$8,747m 2013: \$8,725m
Employees		
7,600	5,900	21,900
Highlights		
<ul style="list-style-type: none"> > Sales in the US declined by 6% reflecting entry of generic <i>Nexium</i> products and adverse <i>Synagis</i> guideline changes > Favourable performances were delivered by <i>Brilinta</i>, <i>Farxiga</i>, <i>Bydureon</i> and <i>Lynparza</i> as well as the acquired Respiratory medicines, <i>Tudorza</i> and <i>Daliresp</i> > Sales in Canada grew by 4% 	<ul style="list-style-type: none"> > Sales declined by 6% > Strong growth for Diabetes medicines was offset by generic competition facing <i>Crestor</i> and <i>Seroquel XR</i> > 14% decline in <i>Symbicort</i> sales reflected adverse pricing movements driven by competition from analogues in key markets 	<ul style="list-style-type: none"> > Emerging Markets revenue grew by 12% to \$5,822 million, including China sales growth of 15% > Sales in Japan grew by 4% to \$2,020 million > Opened facility in Russia

 Business Review from page 42

Our talented employees are committed to achieving our Purpose in a sustainable way...

61,500
employees worldwide



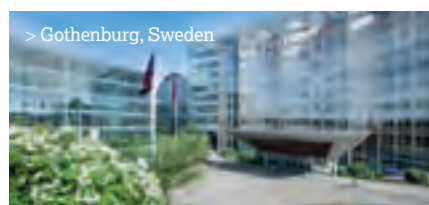
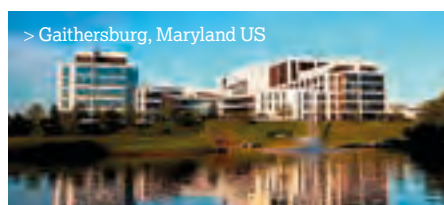
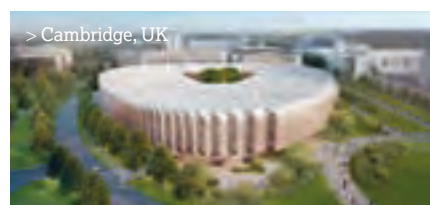
8,900
employees in R&D



12,500
employees in
Manufacturing
and Supply



Increasing our proximity to bioscience clusters and co-locating around three strategic R&D centres



 Employees from page 52

...and our disciplined capital allocation enables commitment to a progressive dividend.

\$3,443m

Net cash shareholder distributions
increased to \$3,443 million

2015		\$3,443m
2014		\$3,242m
2013		\$2,979m

\$2.80

Dividend per Ordinary Share
unchanged

2015		\$2.80
2014		\$2.80
2013		\$2.80

All growth rates at CER.
All employee numbers are approximate
as at 31 December 2015.

Chief Executive Officer's Review



2015 was an exceptional year for AstraZeneca as we made significant progress in meeting both our near- and longer-term strategic goals. Building on the solid foundations of the previous two years, our success during 2015 was based on a strong commitment to our values. It was this focus that made the year a great one for science and patients.

“It was this focus that made the year a great one for science and patients.”

The first stage of our strategic journey involved strengthening our product pipeline and building our Growth Platforms. We are now well into the second stage of that journey, as we manage a transitional period of patent expiries, and are on track to continue driving our Growth Platforms and launch our new products.

The increased momentum we built in 2015 was exemplified by a number of developments towards the end of the year in each of our main therapy areas that will help deliver our strategy.

Leadership in Oncology

The first of those events was the approval in November of *Tagrisso* in the US. This approval marks a significant milestone in AstraZeneca's journey, and in our leadership in Oncology. *Tagrisso* is the first treatment approved for patients with a very specific form of non-small cell lung cancer who present with a genetic mutation in the epidermal growth factor receptor but also have a secondary mutation, T790M. Its story is remarkable and, as shown over, it demonstrates our ability to successfully deliver our pipeline and, even more

importantly, offer patients a new treatment option in a disease where very few solutions exist.

Another significant development in Oncology came with our agreement in December to invest in a majority equity stake in Acerta Pharma, a company focused on haematology which represents a natural fit with our existing Oncology pipeline. The acquisition provides us with access to acalabrutinib (ACP-196), a potential best-in-class small molecule oral BTK inhibitor, which is expected to transform the treatment landscape for B-cell malignancies, the most common forms of blood cancers, and has potential in solid tumours and autoimmune diseases.

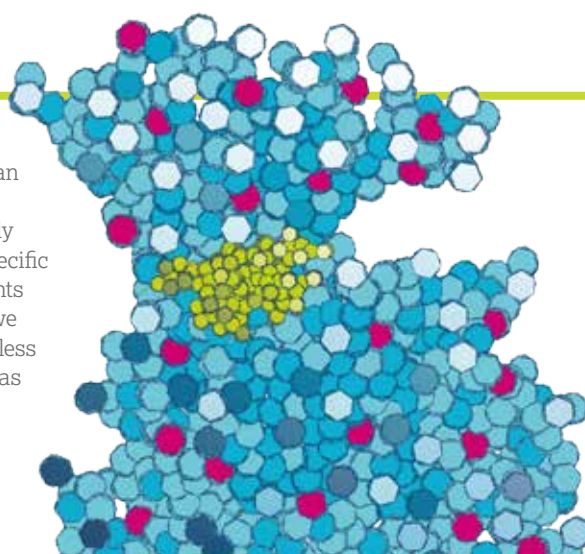
The acquisition of Acerta Pharma will also reinforce our growing position in haematology – building on our agreement with Celgene, in April, to develop durvalumab across a range of blood cancers.

Innovation in Cardiovascular and Metabolic diseases

Also in December, we completed our acquisition of ZS Pharma. This transaction provides access to the potassium-binding compound ZS-9, a potential best-in-class treatment for hyperkalaemia (high potassium levels in the bloodstream). The acquisition represents a good fit with our pipeline and portfolio in Cardiovascular and Metabolic diseases (CVM), which focuses on reducing morbidity, mortality and organ damage by addressing multiple risk factors across cardiovascular disease, diabetes and chronic kidney disease.

AstraZeneca: Values in action

Tagrisso (osimertinib) highlights how living our values can ensure we achieve our goals. It started with inspiration and effort of our scientists to design a compound precisely targeting the biological dysfunction associated with a specific form of non-small cell lung cancer. And, by putting patients first, working collaboratively and following the science, we delivered the fastest development journey in our history: less than three years from first patient dosed to approval. It was then shipped to patients in less than six hours.



Artistic impression of osimertinib binding to mutant EGFR.

Transforming Respiratory treatment

Another development in December, was our agreement to acquire Takeda's core respiratory business. When completed, this agreement will expand our ownership of rights to roflumilast (*Daliresp/Daxas*), the only approved oral PDE4 inhibitor for the treatment of COPD. The agreement builds on our acquisition from Actavis, in March, of the rights to market *Daliresp* in the US. This important agreement will also provide us with access to other marketed medicines that complement our growing portfolio. Importantly, it will support our return to growth after 2017 and our goal to transform the way respiratory disease is treated.

Achieve scientific leadership

In addition to these developments, in the week before Christmas, we received our sixth approval for the year from the FDA. Subsequently, in February 2016, we received approval from the EU for *Tagrisso* for lung cancer.

However, in what was a very busy and successful year, my Review can only give a flavour of what we achieved. The 2015 Strategic priorities overview, shown on the right, lists some of our other achievements, as well as the challenges we faced. All these are explored in more detail throughout our Strategic Report.

So far as achieving scientific leadership is concerned, one measure of the distance we have come is in the recognition we have received through 'high-impact' publications in major relevant scientific journals. AstraZeneca people had 58 such articles published in 2015 compared with seven in 2010 – a more than eightfold increase.

2015 Strategic priorities overview

Achieve scientific leadership

- > 6 approvals of NMEs or major LCM projects in major markets
 - Oncology: *Iressa* (US); *Tagrisso* (AZD9291/osimertinib) (US); *Faslodex* 500mg (China)
 - CVMD: *Bydureon* Dual Pen (Japan); *Brilinta* (US for treatment of history of heart attack)
 - RIA: *Zurampic* (US)
- > 2 Phase III NME starts:
 - anifrolumab for lupus
 - PT010 for COPD
- > 12 NME or major LCM regulatory submissions in major markets
- > Accelerated reviews included
 - *Brilinta* FDA granted Priority Review for PEGASUS
 - *Tagrisso* FDA and PMDA granted Priority Review. EMA accelerated assessment
 - FDA granted Fast Track status for anifrolumab for systemic lupus erythematosus; durvalumab for head and neck cancer; and tremelimumab for mesothelioma
- > 20 projects discontinued



Return to growth

- > 1% increase in Total Revenue to \$24,708 million at CER; comprising Product Sales of \$23,641 million (down 1%) and Externalisation Revenue of \$1,067 million (up 140%)
 - Based on actual exchange rates, Total Revenue declined by 7%, reflecting the particular weakness of key trading currencies against the US dollar
- > 11% increase in Growth Platforms revenue contributing 57% of Total Revenue
 - Respiratory: up 7%, before completion of the acquisition of Takeda's respiratory business
 - *Brilinta/Brilique*: up 44% underpinned by a recently-extended US label and positive CHMP opinion
 - Diabetes: up 26%, including 76% in Emerging Markets; global *Farxiga/Forxiga* growth of 137%
 - Emerging Markets: up 12%, including China and Latin America each growing by 15%
 - Japan revenue: up 4%
 - New Oncology: contributed \$119 million, comprising *Lynparza*, *Iressa* (US) and *Tagrisso*
- > US revenue was down 6% to \$9,474 million; Europe down 6% to \$5,323 million; and Established ROW was stable at \$3,022 million (at CER)



Great place to work

- > Our quarterly employee survey (pulse) showed belief in our strategy stood at 89% (compared with 86% in our 2014 all-employee survey)
- > Exceeded our targets for senior leaders: women (42% versus 41%) and country of origin from an Emerging Market or Japan (15.6% versus 13%)
- > Exceeded our target by screening more than one million people in Kenya for hypertension as part of our Healthy Heart Africa programme



Chief Executive Officer's Review continued

Strategic Report

In this Strategic Report, we outline our business model, the marketplace in which we operate and the strategic priorities we decided upon in response to those conditions. We define our measures of success (our key performance indicators) and the risks we have identified to achieving our strategy.

Subsequent sections explore our therapy areas as well as our business units and the resources we are able to deploy in their support.

We also highlight how commitment to our values contributes to our success.

Great people are central to our success and being a great place to work is at the heart of our efforts to release the talents of our employees.



A pipeline ahead of plan

Our pipeline is also a measure of our progress and 2015 was a year of considerable success. Of our six approvals for the year, the approval, in September, of *Brilinta* in the US for the treatment of patients with a history of heart attack beyond the first year was particularly impressive: it took just nine months to move from the presentation of top-line PEGASUS TIMI-54 data to launch.

During the year we also made 12 major regulatory submissions. After our partner Amgen decided to terminate our collaboration on brodalumab in May, our subsequent collaboration with Valeant, with their specific expertise in dermatology, enabled submissions to be made in the US and EU by the end of the year. In July, results of a Phase III study for selumetinib did not meet its primary endpoint for uveal melanoma. As for saxagliptin/dapagliflozin, its submission in the EU and elsewhere remains on track despite a Complete Response Letter being received from the FDA in October.

External recognition of the strength of our pipeline was provided by the number of accelerated reviews received by our candidate drugs during the year, including those for cancer, respiratory diseases and lupus. Internally, six Phase III investment decisions and 11 Phase II starts stand testament to the quality of the projects in development which will help deliver sustainable growth.

Even after the approvals we received during the year, and the 18 approvals of the last two years, we ended 2015 with 15 projects in late-stage development, including recently

acquired compounds. This exceeds the target set in 2013 of nine to 10 NMEs in Phase III/pivotal Phase II studies or under regulatory review by 2016.

Collaboration as a way of life

2015 was also a good year for collaborations which are an integral part of our business model and culture. They improve the productivity of our R&D and help maximise the value of our pipeline. With 10 deals we considerably exceeded our target. Some of these, such as our agreement with Celgene, are examples of strategic collaborations to broaden and accelerate the development of key pipeline assets. This is explained in more detail in the Business model on page 8.

As well as externalising some of our early development projects outside our main therapy areas, we also divest medicines that can be better deployed by a partner with a primary focus in that area. Examples in 2015 included the divestment of *Entocort*, our gastrointestinal medicine. Both routes allow us to leverage the capabilities and expertise of others, focus our own resources and deliver the greatest benefit to patients and shareholders.

Scientific collaborations also help us push the boundaries of science. For example, during the year we announced four collaborations aimed at harnessing the power of CRISPR (clustered regularly-spaced short palindromic repeats), including one with The Wellcome Trust Sanger Institute in Cambridge, UK – see over.

Values in action: We follow the science

Genetic engineering is not new. The Human Genome Project produced a complete genetic blueprint for building a human in 2003 but, until now, scientists have been unable to manipulate genes simply and effectively. A new technology called CRISPR is changing that by allowing the genome of several different species to be edited precisely. We are using CRISPR to identify new targets for medicines and develop new models to test compounds which align more closely with human disease.



Return to growth

We delivered a strong pipeline and financial performance in 2015 as we began the next phase in our strategic journey. As the 2015 Strategic priorities overview shows, Total Revenue in 2015 was up 1% at CER. The overview also shows the success we have had with our Growth Platforms where Product Sales grew by 11% and represented 57% of Total Revenue.

Our top-line and gross-margin growth underpinned continued investment in R&D. Core R&D costs were up by 21% in the year which reflected the investment in the pipeline.

Investing in China for the long term

The extent of our ambition was demonstrated by our strategic investments, announced in December, to accelerate the delivery of innovative medicines to patients in China, the world's second largest economy and our second largest market, and to support the delivery of our strategy.

These initiatives will see AstraZeneca become the first multinational pharmaceutical company operating in China to commit to local development of its innovative global portfolio from research to commercialisation. Just as importantly, these initiatives will allow us to better integrate Chinese requirements into our global portfolio decisions.

Great place to work

Great people are central to our success and being a great place to work is at the heart of our efforts to release the talents of our employees. So, for example, during 2015, we held over 70 People Development Week

events to help our staff take ownership of their personal development. A talented workforce is also diverse and I am pleased that we managed to exceed our targets for women and country of origin among our senior leaders. I take pride in the fact that our efforts are being increasingly recognised in external awards for the work environment we have instilled.

That environment is nurtured by our investment in strategic R&D centres, such as Cambridge, UK where we now have more than 1,600 employees and where the construction of our R&D centre and global headquarters is progressing rapidly. These investments help create an environment of innovation and a focus on science and patients. They also attract a lot of talent from academia and other companies.

A great place to work also has to be one where we do the right thing – for the patients who take our medicines, as well as the planet and society as a whole. If we are to deliver business success over the longer term, then sustainability has to be in our DNA. As the Chairman outlines in more detail in his Statement, the steps we are taking in this regard reflect a determination to do our fair share.

Looking ahead

The investments we made in 2015 were designed to ensure we achieved a balance between meeting our short-term goal of returning to growth and then delivering sustainable growth over the longer term as we build a sustainable, durable and more profitable business.

As we face the transitional period of patent expiry for *Crestor* in the US, we're confident that our strong execution on strategy, combined with the benefits of focused investments and new launches, keeps us on track to return to sustainable growth in line with our targets. The weakness of key trading currencies against the US dollar has continued. Based on average exchange rates in January 2016 and our published currency sensitivities, an adverse impact of around 3% from currency movements on Total Revenue and Core EPS in 2016 would be anticipated.

Appreciation

I am confident that in AstraZeneca we have the people who can overcome our short-term challenges and deliver longer-term sustainable growth. In that regard I would particularly like to welcome Pam Cheng and Sean Bohen who joined us during the year. In doing so, I would like to thank David Smith and Briggs Morrison whom Pam and Sean replaced, for the contributions they made to our strategic journey.

In closing, I would like to pay tribute to everyone in AstraZeneca for making 2015 a tremendous year. I have every confidence in their ability to continue that success in the years ahead.

Pascal Soriot
Chief Executive Officer

Business model

Our Purpose and Values drive what we do – and how we do it. This includes our business model and our determination to create sustainable value across every medicine's life-cycle.

AstraZeneca's investor proposition

Science-led biopharmaceutical company in three therapy areas

Productive R&D	Strong business	Sustainable organisation
<ul style="list-style-type: none"> > Platform of small molecules and biologics > Sustainable model and growing early-stage pipeline > Growing late-stage pipeline with immuno-oncology strength > Protein engineering 	<ul style="list-style-type: none"> > Strong portfolio of established products > Global scale with Emerging Markets strength > Six platforms driving growth towards a balanced portfolio of primary care and specialty care medicines > Durability through devices and companion diagnostics 	<ul style="list-style-type: none"> > Innovative, entrepreneurial culture > Strong talent base > Efficient and productive organisation > Balanced pipeline to drive sustainable growth
Disciplined capital allocation	Commitment to progressive dividend	

Externalisation

Our business model includes externalisation as part of our portfolio management strategy and is a result of increasing R&D productivity and a focus on three main therapy areas. Externalisation activities relate to specific risk- and reward-sharing strategic collaborations that provide greater access to strong science and broaden, accelerate and maximise the development and commercialisation potential for some of our medicines and help bring those medicines to patients faster. Milestone payments and royalties arising from externalisation activities are included in the income statement as Externalisation Revenue. Externalisation allows us to leverage the capabilities and expertise of others, focus on our main therapy areas and deliver the greatest benefit to patients and shareholders.

Externalisation activities in 2015 included our collaboration with Celgene, leveraging the expertise of AstraZeneca in immuno-oncology along with the experience of Celgene in the study and treatment of blood cancers, for the development and commercialisation of durvalumab across a range of haematological malignancies. Similarly, our collaboration with Lilly, entered into in 2014, combines the scientific expertise from our two organisations and, by sharing the risks and cost of late-stage development, aims to accelerate the advancement of AZD3293 and progress a new approach to support the treatment of Alzheimer's disease patients around the world. AstraZeneca retains significant interest, and continued participation, in the key decision making undertaken within these strategic collaborations.

 [Financial Review on page 62](#)

How it works

Strategic priorities

Our strategic priorities reflect how we aim to achieve our Purpose. They are to

 [Strategic priorities from page 16](#)

Inputs

Demographic trends are favourable to our industry's long-term growth; while innovative scientific research continues to deliver new ways of fulfilling unmet medical need. As the Marketplace section from page 12 demonstrates, however, the economic, social and political environment presents not only significant opportunities but challenges as well.


To achieve our Purpose, we seek to maximise the value of our resources, including our employees, IP and partners.

 [Resources Review from page 52](#)

We have strong commercial franchises that focus on Respiratory, Inflammation and Autoimmunity; Cardiovascular and Metabolic diseases; and Oncology. We have combined a broad portfolio of primary care and specialty care medicines with a global reach. We believe our capabilities, pipeline and portfolio will enable us to build on our leading positions in Established Markets and achieve further growth in Emerging Markets.

 [Therapy Area Review from page 24](#)

Sustainability

 [In the wider world from page 55](#)

Purpose and Values

1

Achieve scientific leadership

2

Return to growth

3


Be a great place to work

These priorities reflect the choices we have made to focus our R&D and commercial investments, prioritise and accelerate promising assets and business development, and transform our innovation model and the way we work.

Business model

We strive to operate in accordance with a disciplined, value-creation framework that supports investment to generate cash flows that we return to investors and reinvest in the business. We also invest in targeted business development to strengthen our portfolio, pipeline and capabilities.

Our success depends on the creation and protection of our IP rights. Developing a new medicine is risky, costly and time consuming; requiring significant investment over many years, with no guarantee of success. For investments to be viable, we must protect new medicines from being copied for a reasonable period of time. The loss of key product patents has affected sales significantly in recent years and will continue to do so. As such, one of our main goals is to sustain the cycle of innovation and continually refresh our portfolio of patented products.

 **Life-cycle of a medicine overleaf**

How we create and sustain value over the life-cycle of a medicine across our chosen therapy areas

Investment in the R&D, Manufacturing and Supply, and Sales and Marketing of innovative medicines. This includes targeted business development through collaboration, in-licensing and acquisitions.



Reinvestment of returns from sales, externalisation (see page 8) and divestments to develop and sustain the next generation of innovative medicines.

Outputs

Returns to shareholders

Revenue from the sale of our medicines generates cash flow, which helps us fund business investment. It also enables us to meet our debt service obligations and follow our progressive dividend policy. This involves balancing the interests of our business, financial creditors and shareholders.

 **Financial Review from page 62**

Improved health

Continuous scientific innovation is vital to achieving sustainable healthcare as it 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.

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

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. It also sets the context for our employees' activities and the roles of our teams, partners and other collaborators.

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

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

Life-cycle of a medicine

As a global science-led biopharmaceutical company, our activities span the entire life-cycle of a medicine from Research and Development to Manufacturing and Supply to the global Sales and Marketing of primary care and specialty care medicines that transform lives.

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

9

Post-exclusivity

- > Patent expiry and generic entry
- > Reinvestment of returns

Primary care and specialty care

Primary care is general healthcare provided by doctors who ordinarily have first contact with patients and who may have continuing care for them. Specialty care is specific healthcare provided by medical specialists who do not generally have first contact with patients. Specialty care medicines generally treat more severe diseases and an increasing number of specialty care medicines require a diagnostic test for patient eligibility or to achieve the best outcomes.

Small molecule drugs

- > Typically composed of 20 to 100 atoms with a well-defined chemical structure
- > Potential for off target activity
- > Manufactured through chemical synthesis. Identical copies can be made
- > Wide variety of administration routes, such as oral, inhaled, injected or topical delivery

Large molecule drugs (biologics)

- > Small biologics (eg peptides) typically 200 to 3,000 atoms. Large biologics (eg antibodies), typically 5,000 to 50,000 atoms
- > High selectivity and specificity; potentially immunogenic
- > Manufactured in a living system such as a microorganism, or plant or animal cells
- > Administration route often intravenous, intramuscular or other parenteral route



- Research and Development from page 42
- Manufacturing and Supply from page 46
- Sales and Marketing from page 48

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.

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 9.5% in 2015
- > The sector remains highly competitive
- > Patient populations are expanding and ageing
- > Non-communicable diseases kill 38 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

84.0%

Generics constituted 84.0% of prescriptions dispensed in the US.



\$140bn

Global investment in pharmaceutical R&D expected to reach an estimated \$140 billion in 2015, a 30% increase from \$108 billion in 2006.

The global context

According to the International Monetary Fund (IMF), a return to robust and synchronised global expansion remains elusive six years after the world economy emerged from its broadest and deepest post-war recession. Moreover, downside risks to the world economy appear more pronounced, particularly for emerging market and developing economies, and including renewed concerns about China's growth potential.

The demand for healthcare, however, 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.

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 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 pages 14 and 15 shows, we expect developing markets to continue to boost pharmaceutical growth.

Unmet medical need

The prevalence of non-communicable diseases (NCDs), such as cancer and cardiovascular, metabolic and respiratory diseases, is increasing worldwide. NCDs are

often associated with ageing populations and lifestyle choices, including smoking, diet and lack of exercise. Many NCDs require long-term management. WHO estimates that NCDs kill 38 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 right, global pharmaceutical sales grew by 9.5% in 2015. Established Markets saw average revenue growth of 9.3% and Emerging Markets revenue growth at 10.3%. The US, China, Japan, Germany and France are the world's top five pharmaceutical markets. In 2015, the US had 45.7% of global sales (2014: 44.6%; 2013: 43.2%).

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 are expected to account for 46% of the total sales revenue of the world's top 100 pharmaceutical products, having risen from 21% 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 with more than half the Center for Drug Evaluation and Research NME approvals in 2015 receiving a Priority Review and, almost a quarter having a Breakthrough Therapy designation. Between the inception of the Breakthrough Therapy designation programme in October 2012 and the end of 2015, the FDA has granted more than 100

such requests, 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 \$140 billion in 2015. While the growth rate of R&D spend has slowed in recent years, pharmaceutical companies continue to deliver new medicines. In 2015 the FDA approved 45 NMEs compared with 41 in 2014 and 27 in 2013. The number of approvals in 2015 is the largest since 1996 when 59 NMEs were approved.

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, passed by the House of Representatives in July 2015, and the related Senate Innovation for Healthier Americans Legislative Initiative, are focused on accelerating the discovery, development and delivery of promising new treatments for patients. Similarly, the PDUFA reauthorisation legislation considered by the US Congress in 2017 is anticipated to contain proposals aimed at accelerating innovation and modernising the 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

Global pharmaceutical sales

World \$bn

2015	904
2014	826
2013	759

\$904bn (9.5%)

US \$bn

2015	413
2014	369
2013	328

\$413bn (12.0%)

Europe \$bn

2015	194
2014	182
2013	177

\$194bn (6.3%)

Established ROW \$bn

2015	100
2014	96
2013	94

\$100bn (4.3%)

Emerging Markets \$bn

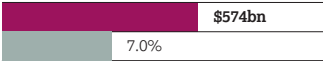
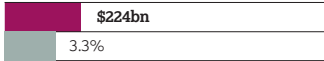
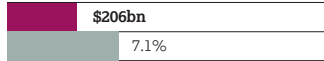
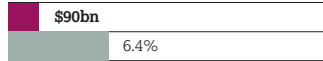
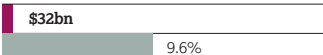
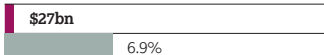
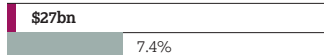
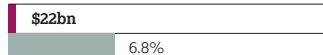
2015	198
2014	179
2013	160

\$198bn (10.3%)

Data based on world market sales using AstraZeneca market definitions as set out in the Market definitions on page 247. Source: IMS Health, IMS Midas Quantum Q3 2015 (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.

Marketplace continued

Estimated pharmaceutical sales and market growth – 2019

North America 	EU 	South East and East Asia 	Latin America 
Africa 	CIS 	Middle East 	Other Europe (Non-EU countries) 

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 piloting of a programme to implement 'adaptive pathways', or 'staggered approval', to improve timely patient access to new medicines. In Japan, the SAKIGAKE strategy is fostering a more favourable environment for drug development and accelerating the availability of currently 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, proposed revisions to China's Drug Administration Law, which are under review, may help address this issue.

Greater transparency and public access to regulatory submissions that support approval of new medicines continues to be an area of interest. A recent example involves the EMA policy 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. These clinical reports include the overviews, summaries and clinical study reports submitted by the applicant, together with documentation of statistical methods.

The study of paediatric populations 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 EMA's initiative offering free-of-charge meetings early in drug development. Increased interest in the availability of the paediatric rare disease voucher programme in the US is another noteworthy development.

Regulatory requirements for the registration of biosimilar products continue to be developed and become better defined. This includes the publication of a new pathway for China and the first biosimilar product approval in the US. However, significant areas of regulatory policy are still evolving. Among these are transparency of data 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 below.

Pricing of medicines

Pricing and reimbursement remain challenging in many markets. Most pharmaceutical sales are generated in highly regulated markets where governments, insurers and other private payers exert various controls on pricing and reimbursement. These include limitations on pharmaceutical spending and the cost of readmitting patients to hospital. Implementation of certain reforms and shifting market dynamics are further

constraining healthcare providers, while difficult economic conditions burden patients who pay out-of-pocket for medicines. Pharmaceutical companies are now expending significant resources to demonstrate the economic as well as therapeutic value of their medicines.

In the US, the Affordable Care Act (ACA) has had a direct impact on healthcare activities. It continues to reshape the market through various provisions designed to reduce cost and improve healthcare and patient outcomes. We, along with other pharmaceutical companies, are working with policymakers and regulators to help contain costs, improve outcomes and promote an environment that fosters medical and scientific innovation.

In Europe, governments continue to implement 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, Romania and Italy. In France, price negotiations are particularly challenging due to budget 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 a single reimbursement level (or reference) for each drug group.

In China, pricing practices remain a priority for regulators. Though free pricing has been introduced, 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

Japan

\$82bn
1.3%

Indian subcontinent

\$35bn
12.3%

Oceania

\$13bn
1.8%

- Estimated pharmaceutical sales – 2019. Ex-manufacturer prices at CER. Source: IMS Health.
- Estimated pharmaceutical market growth – 2014 to 2019. Compound annual growth rate. Source: IMS Health.

pricing legislation. In Japan, mandated biennial cuts are likely to continue. In Latin America, pricing is increasingly controlled by governments as, for example, in Colombia.

For more information about price controls, reductions and US healthcare reform, and price regulation in our major markets, please see Geographical Review from page 227 and Risk from page 212

Patent expiries and genericisation

Patent protection for pharmaceutical products is finite. Patents are expiring on some of the biggest-selling drugs ever produced and payers, physicians and patients have 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 2015, generics constituted 84.0% of the market by volume (2014: 83.4%).

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

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

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.

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 27 to the Financial Statements from page 186.

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. 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 continued in 2015. It is estimated that the value of mergers announced in the healthcare sector during the year amounted to more than \$650 billion, accounting for 14% of all merger and acquisition activity.

Strategic priorities

We are focused on returning to growth in our chosen therapy areas through a science-led innovation strategy. This strategy is 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. It also involves engaging in targeted business development and leveraging our strong global commercial presence, particularly in Emerging Markets.

	What do we need to do?	
Achieve scientific leadership 	Focus on innovative science in three therapy areas	
	Prioritise and accelerate our pipeline	
	Transform our innovation and culture model	
	Accelerate through business development	
Return to growth 	Focus on Growth Platforms	
	Transform through specialty care, devices and biologics	
Be a great place to work 	Evolve our culture	
	Simplify our business	
	Attract and retain the best talent	
	Deliver business success over the long term	
Achieve our Group financial targets 	Drive on-market value	
	Maintain a progressive dividend	
	Maintain a strong balance sheet	

How are we implementing this?	For more information
Our focus is on Respiratory, Inflammation and Autoimmunity; Cardiovascular and Metabolic diseases; and Oncology. We are also taking an opportunity-driven approach to Infection, Neuroscience and Gastrointestinal disorders. We are working across small molecules, biologics, immunotherapies, protein engineering and devices.	Therapy Area Review from page 24
We are accelerating and investing in key R&D programmes. 15 new molecular entities (NMEs) are in Phase III/pivotal Phase II or under regulatory review compared with our March 2013 target of nine to 10 by the end of 2016. Between 2013 and the end of 2016, we have the potential for 12 to 16 Phase II starts; 14 to 16 NME and major line extension regulatory submissions; and eight to 10 NME and major line extension regulatory approvals. We are strengthening our early-stage pipeline through novel science and technology.	Pipeline and Therapy Area Introduction from page 24 Development Pipeline from page 205
Our two autonomous biotech units, MedImmune and IMED, drive science and innovation, and GMD drives our late-stage development unit. We are focusing on novel science, such as immune-mediated therapy combinations and personalised healthcare (PHC). To increase our proximity to bioscience clusters, we are co-locating around three strategic centres in Cambridge, UK; Gaithersburg, Maryland US; and Gothenburg, Sweden. These moves will leverage our capabilities and foster collaboration with leading scientists and research organisations.	Research and Development from page 42
We are working to reinforce our therapy areas and are strengthening our portfolio and pipeline through targeted business development, including collaborations, in-licensing and acquisitions. We are collaborating strategically to broaden and accelerate the development of key pipeline assets (externalisation) and divesting non-core assets to realise value.	In the wider world from page 55
<i>Brilinta/Brilique</i> – We are working to deliver <i>Brilinta/Brilique</i> 's potential to reduce cardiovascular deaths through ongoing clinical studies and plans for market leadership.	Cardiovascular and Metabolic diseases from page 30
Diabetes – We are working to maximise the potential of our broad and innovative non-insulin, anti-diabetic portfolio to transform patient care.	Cardiovascular and Metabolic diseases from page 30
Emerging Markets – We are focused on delivering innovative medicines by accelerating our investment in Emerging Markets capabilities, with a focus on China and other leading markets, such as Russia and Brazil. We are also expanding our commercial reach through multi-channel marketing and sales force excellence and building strong local medical and scientific affairs teams. Transformation of our capabilities is supporting new products and improving access and affordability.	Sales and Marketing from page 48
Respiratory – We are working to maximise pipeline value, devices and medicines to fulfil unmet medical need and improve patient outcomes in asthma, chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF).	Respiratory, Inflammation and Autoimmunity from page 26
Japan – We are strengthening our Oncology franchise and working to maximise the success of our Diabetes medicines and established brands: <i>Symbicort</i> , <i>Nexium</i> and <i>Crestor</i> .	Sales and Marketing from page 48
New Oncology – Became our sixth Growth Platform in January 2015 and includes <i>Lynparza</i> , <i>Iressa</i> (US) and <i>Tagrisso</i> . We are aiming to deliver six new cancer medicines to patients by 2020.	Oncology from page 34
We are transforming our business to become more sustainable, durable and profitable. This involves focusing on specialty care medicines, devices and biologics. Biologics now account for half of the NMEs in development, potentially enhancing asset longevity. A greater focus on innovative and differentiated delivery devices affords patient choice while ensuring product durability. Our new specialty care portfolio is expected to balance our strength in primary care medicines.	Therapy Area Review from page 24
We are working to improve our employees' identification with our Purpose and Values and to promote greater understanding of and belief in our strategy. We are investing in and implementing tailored leadership development programmes.	Employees from page 52
We are developing simpler, more efficient processes and flattening our organisational structure to encourage accountability and improve decision making and communication.	
We are accelerating efforts to attract diverse, top talent with new capabilities.	
We are supporting the sustainable delivery of our business strategy while delivering wider benefits to society and the environment.	In the wider world from page 55
We 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.	Financial Review from page 62
Our policy is to maintain or grow dividend per share.	
Target a strong, investment-grade credit rating, operational cash balance and periodic share repurchases.	

Key performance indicators

How we performed against the indicators by which we measure our success.

Achieve Group financial targets



Total Revenue¹

\$24,708m

2015		\$24,708m
2014		\$26,547m
2013		\$25,806m

CER growth

2015 **+1%**
2014 +5%
2013 -7%

Actual growth

2015 **-7%**
2014 +3%
2013 -9%

Total Revenue comprised Product Sales of \$23,641 million (down by 1%) and Externalisation Revenue of \$1,067 million (up by 140%). 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 144, Total Revenue consists of Product Sales and Externalisation Revenue.

Net cash flow from operating activities

\$3,324m

2015		\$3,324m
2014		\$7,058m
2013		\$7,400m

Actual growth

2015 **-53%**
2014 -5%
2013 +7%

Cash generated from operating activities reflects a modest increase in investment in working capital of \$49 million compared to a decline of \$2,508 million in 2014. Working capital improvements made in 2014 have been sustained minimising the impact of increased acquired diabetes and launch product inventory balances.

Dividend per share²

\$2.80

2015		\$2.80
2014		\$2.80
2013		\$2.80

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

² First and second interim dividend for the year.

Core EPS

\$4.26

2015		\$4.26
2014		\$4.28
2013		\$5.05

CER growth

2015 **+7%**
2014 -8%
2013 -23%

Actual growth

2015 **0%**
2014 -15%
2013 -26%

Increase in Core EPS demonstrated resilience in face of patent expiries as we position ourselves for a return to growth.

Financial Review from page 62

Achieve scientific leadership

Phase III investment decisions

6

2015		6
2014		9
2013		3

Anifrolumab; AZD9291 + durvalumab; PT010; durvalumab + tremelimumab (NSCLC); durvalumab + tremelimumab (bladder and head and neck); AZD9291 adjuvant.

NME or LCM project regulatory submissions in major markets

12

2015		12
2014		6
2013		3

Brilinta PEGASUS (US, EU, Japan); CAZ AVI (EU); *Tagrisso* (AZD9291) (US, EU, Japan); cediranib (EU); saxagliptin/dapagliflozin (EU); PT003 (US); brodalumab (US, EU).

NME Phase II starts/progressions

11

2015		11
2014		13
2013		13

MEDI8897; MEDI-551; MEDI7510; AZD3241; AZD9412; AZD7594; AZD5069; AZD9150; AZD3759; MEDI6012; MEDI8852.

NME and major LCM regional approvals

6

2015		6
2014		12
2013		3

Bydureon Dual Pen (Japan); *Iressa* (US); *Brilinta* (US for treatment of history of heart attack); *Tagrisso* (AZD9291) (US); *Zurampic* (US); *Faslodex* 500mg (China).

Therapy Area Review from page 24



Clinical-stage strategic transactions

10

2015		10
2014		3
2013		7*

Licensing and/or acquisition opportunities helped us achieve our 2016 target three years ahead of schedule and contribute to meeting our target of sustainable delivery of two NMEs annually by 2020.

* Four for early-stage (Phase I/II) opportunities, and three for late-stage (Phase II+) opportunities.



Return to growth

Brilinta/Brilique

\$619m

sales

2015		\$619m
2014		\$476m
2013		\$283m

CER growth	Actual growth
2015 +44%	2015 +30%
2014 +70%	2014 +68%
2013 +216%	2013 +218%

Growth was underpinned by recently-extended US label and positive CHMP opinion. Sales in the US and EU increased by 64% and 18% respectively and Emerging Market growth also continued, most notably in China.

Diabetes

\$2,224m

sales

2015		\$2,224m
2014		\$1,870m
2013		\$787m

CER growth	Actual growth
2015 +26%	2015 +19%
2014 +139%	2014 +138%
2013 +75%	2013 +75%

Growth of 26% delivered, including 76% in Emerging Markets. *Farxiga/Forxiga* grew by 137% to \$492 million, with both US and EU growing strongly.

Japan

\$2,020m

sales

2015		\$2,020m
2014		\$2,227m
2013		\$2,485m

CER growth	Actual growth
2015 +4%	2015 -9%
2014 -3%	2014 -10%
2013 +4%	2013 -14%

Growth in sales of 4% driven by strong performance of *Nexium*, *Crestor*, *Symbicort* and the Diabetes franchise, offsetting the headwinds from generic competition.

Emerging Markets

\$5,822m

sales

2015		\$5,822m
2014		\$5,827m
2013		\$5,389m

CER growth	Actual growth
2015 +12%	2015 0%
2014 +12%	2014 +8%
2013 +8%	2013 +6%

Contributions to growth of 12% were generated from across the region. Around 60% of Emerging Markets sales were derived outside China.

Respiratory

\$4,987m

sales

2015		\$4,987m
2014		\$5,063m
2013		\$4,677m

CER growth	Actual growth
2015 +7%	2015 -2%
2014 +10%	2014 +8%
2013 +7%	2013 +6%

Growth of 7% was driven primarily by the performance of *Pulmicort Respules* in Emerging Markets, where *Pulmicort* sales grew by 35%.

New Oncology

\$119m

sales

2015		\$119m
2014		N/A
2013		N/A

New Oncology is included for the first time (comprising *Lynparza*, *Iressa* (US) and *Tagrisso*).

Sales and Marketing from page 48 and Geographical Review from page 227

Key performance indicators continued

Be a great place to work



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

71%

2015	<div></div>	71%
2014	<div></div>	75%
2013	<div></div>	70%

This is a key indicator of our progress in driving accountability and improving decision making and communication.

Employee belief in our strategy

89%

2015	<div></div>	89% ¹
2014	<div></div>	86% ²
2013	<div></div>	84% ³

This is a key indicator of employee engagement.

¹ Source: January 2016 pulse survey across a sample of the organisation.

² Source: Global FOCUS all-employee survey.

³ Source: January 2014 pulse survey across a sample of the organisation.

Employees who would recommend AstraZeneca as a great place to work

83%

2015	<div></div>	83% ¹
2014	<div></div>	82% ²
2013	<div></div>	N/A

This is a key indicator of whether employees believe AstraZeneca is a great place to work.

¹ Source: January 2016 pulse survey across a sample of the organisation.

² Source: Global FOCUS all-employee survey.

Employees from page 52

Do business sustainably

Dow Jones Sustainability Index ranking

Top 5% of companies

2015	<div></div>	84%
2014	<div></div>	79%
2013	<div></div>	85%

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 84%.

Confirmed breaches of external sales and marketing codes or regulations globally

11 confirmed breaches

2015	<div></div>	11
2014	<div></div>	6
2013	<div></div>	11

Continue to report and learn from confirmed breaches of external codes arising from external scrutiny and voluntary disclosure by AstraZeneca.

Operational carbon footprint¹

704 kt CO₂e

2015	<div></div>	704 kt CO ₂ e
2014	<div></div>	735 kt CO ₂ e
2013	<div></div>	704 kt CO ₂ e

Our 2015 operational carbon footprint met our target emission of 714 kt CO₂e and represents a 21.2% reduction from our 2010 baseline. Our overall target of a 20% reduction from a 2010 baseline of 893 kt CO₂e by the end of 2015 has been achieved.

¹ Operational carbon footprint is emissions from all sources, excluding those from patient use of our inhalers.

Screening, diagnosis and treatment of hypertension as part of Healthy Heart Africa programme

1 million patients

2015	<div></div>	1m
2014	<div></div>	N/A
2013	<div></div>	N/A

In our first full year of Healthy Heart Africa, we exceeded our 2015 target by screening one million patients in Kenya for hypertension during demonstration projects.

Sustainability from page 55

Risk overview

What may challenge the delivery of our strategic priorities.

Oversight and monitoring

Board: defines the Group's risk appetite, which enables the Group, in both quantitative and qualitative terms, to judge the level of risk it is prepared to take in achieving its overall objectives.

SET: responsible for overseeing and monitoring the effectiveness of the risk management processes implemented by management.

Management: 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.

Managing risk

As a global, science-led biopharmaceutical business, we face a diverse range of risks and uncertainties. These could adversely affect our business. Our approach to risk management is therefore 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.

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 robust processes and clear accountabilities, as described below, provide it with adequate information on the Principal Risks and uncertainties we face.

Risk management embedded in business processes

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

The Board has defined the Group's risk appetite, expressing 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. Annually, the Group develops a long-term business plan to support the delivery of its strategy. The Board reviews this to ensure that the plan conforms to its risk appetite. 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.

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 that is shared with the Board, Audit Committee and SET. Quarterly, each SET function identifies any changes to these risks, its mitigation plans and new and emerging risks. The quarterly updates 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.

We also develop 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 2018 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-term strategic plan but, given the inherent uncertainty involved, believes that the three-year statement presents readers of the Annual Report with a reasonable degree of assurance while still providing a longer-term perspective.

The three-year detailed business plan captures risks to the sales and cost forecasts at a market and SET function level and 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 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.

Risk overview continued





Principal Risks


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.

Trend key

-  Increasing risk
-  Decreasing risk
-  Unchanged

Strategy key

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

 Further information on our key risk management and assurance processes can be found in Risk from pages 212 to 226 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

Risk category and Principal Risks	Context/potential impact
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, 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 and scientific exchanges	Any failure to comply with applicable laws, rules and regulations 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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Management actions	Trend versus prior year	Link to strategy
<ul style="list-style-type: none"> > Prioritise and accelerate our pipeline > Strengthen pipeline through acquisitions, licensing and collaborations > Focus on innovative science in three 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 		
<ul style="list-style-type: none"> > Active management of IP rights 		
<ul style="list-style-type: none"> > Focus on Growth Platforms > Demonstrating value of medicines/health economics > Global footprint > Diversified portfolio 	 Global economic conditions placing downwards pressure on healthcare spending and therefore revenue	
<ul style="list-style-type: none"> > Focus on Growth Platforms > Accelerate 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 > 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 and footprint projects including Cambridge relocation in the UK	
<ul style="list-style-type: none"> > Evolve our culture > Focus on simplification > Development of our employees 	 Ongoing restructuring and footprint projects including Cambridge relocation in the UK	
<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 		
<ul style="list-style-type: none"> > Combined internal and external counsel management 		
<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 	 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 > Focus on innovative science in three therapy areas > Strengthen pipeline through acquisitions, licensing and collaborations > Appropriate capital structure and balance sheet > Portfolio-driven decision making process governed by committees 	 Increasing requirement to balance long- and short-term investments as we navigate a period of loss of exclusivity on key brands	

Pipeline and Therapy Area Introduction

Our business model describes how we create and sustain value over the life-cycle of a medicine across our therapy areas. In this section, we review our therapy areas, including our portfolio of marketed products, pipeline projects, strategic priorities, capabilities, resources and business development activities.

Overview

As outlined in Strategic priorities from page 16, a key element of our drive to achieve scientific leadership is our focus on innovative science in three therapy areas: Respiratory, Inflammation and Autoimmunity (RIA); Cardiovascular and Metabolic diseases (CVMD); and Oncology. We apply our distinctive capabilities to small molecules, biologics, immunotherapies,

protein engineering technologies and delivery devices across these therapy areas. Our goal is to deliver life-changing medicines to patients while creating value for shareholders. Our approach to Infection, Neuroscience and Gastrointestinal (ING) is opportunity-driven.

Our Global Product and Portfolio Strategy group (GPPS) leads our therapy area

activities. GPPS also serves as the bridge between our R&D and Sales and Marketing functions and works to provide strategic direction from early-stage research to commercialisation. It also helps us to integrate our corporate, portfolio, therapy area and product strategies. This, in turn, drives scientific innovation, prioritises investment, supports the growth of our therapy areas, and accelerates business development. GPPS also works closely with healthcare providers, regulatory authorities and payers to ensure our medicines help to fulfil unmet medical need and provide economic as well as therapeutic benefits.

Key pipeline progressions	Product	Achievement
Phase III NME starts	anifrolumab	Phase III programme commenced for systemic lupus erythematosus
	PT010	Phase III programme commenced for COPD
Expedited review	<i>Brilinta</i>	FDA granted Priority Review for PEGASUS
	<i>Tagrisso</i> (AZD9291)	FDA and PMDA granted Priority Review. EMA accelerated assessment
	anifrolumab	FDA granted Fast Track status for systemic lupus erythematosus
	durvalumab	FDA granted Fast Track status for head and neck cancer
	tremelimumab	FDA granted Fast Track status for mesothelioma
Regulatory filings	<i>Brilinta</i>	Regulatory submissions accepted in US, EU and Japan for <i>Brilinta</i> to reduce the rate of cardiovascular death, myocardial infarction (MI) and stroke in patients with acute coronary syndrome or a history of MI
	cediranib	MAA accepted by EMA for treatment of recurrent platinum-sensitive ovarian cancer
	PT003	NDA accepted by FDA for treatment of COPD
	<i>Tagrisso</i> (AZD9291)	Regulatory submission accepted by the FDA, EMA and PMDA for treatment of 2nd line or greater EGFRm T790M NSCLC
	CAZ AVI	MAA accepted by EMA for treatment of serious bacterial infection, including complicated intra-abdominal infection and complicated urinary tract infection
	saxagliptin/dapagliflozin FDC	MAA accepted by EMA for treatment of Type 2 diabetes
	brodalumab	Regulatory submission accepted by EMA and FDA for psoriasis
	<i>Bydureon</i> Pen	Japanese regulatory approval for treatment of Type 2 diabetes
Regional approvals	<i>Iressa</i>	US regulatory approval for treatment of EGFRm NSCLC
	<i>Brilinta</i>	Regulatory approval in US for <i>Brilinta</i> to reduce the rate of cardiovascular death, MI and stroke in patients with acute coronary syndrome or a history of MI
	<i>Tagrisso</i> (AZD9291)	Regulatory approval in US for treatment of 2nd line or greater EGFRm T790M NSCLC; CHMP issues Positive Opinion to EMA and EU approval received in February 2016
	<i>Zurampic</i> (lesinurad)	Regulatory approval in US; CHMP issues Positive Opinion to EMA
	<i>Faslodex</i> 500mg	Regulatory approval in China for breast cancer
		20 projects discontinued
Discontinued projects		

Putting patients first

In keeping with our value of putting patients first, we formed a Patient Centricity team in 2015 to better connect patients with our science and to help ensure we deliver medicines they value. In 2015, we connected with more than 30,000 patients through our new alliance with PatientsLikeMe, a virtual patient community, and are exploring similar partnerships with other organisations to ensure we understand our patients' requirements better.

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, 30, 34 to 35, and 39 and the Development Pipeline table from page 205. For information on patent expiries of our key marketed products, please see Patent Expiries from page 210.

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.

Development pipeline overview

Our pipeline includes 146 projects of which 125 are in the clinical phase of development.

Phase I	Phase II	Late-stage development	LCM projects
44	33	35	34
<ul style="list-style-type: none"> > 44 projects in Phase I including: <ul style="list-style-type: none"> – 34 NMEs – 3 significant additional indications for projects that have reached Phase III – 7 oncology combination projects 	<ul style="list-style-type: none"> > 33 projects in Phase II, including: <ul style="list-style-type: none"> – 26 NMEs – 5 significant additional indications for projects that have reached Phase III – 2 oncology combination projects 	<ul style="list-style-type: none"> > 35 projects in late-stage development, either in Phase III/pivotal Phase II studies or under regulatory review: <ul style="list-style-type: none"> – 15 NMEs – 13 projects exploring additional indications for these NMEs – 6 projects already approved or launched in the EU, China, Japan and/or the US – MEDI-550 pandemic influenza vaccine pending acceptance of regulatory submission 	<ul style="list-style-type: none"> > 34 LCM projects*
* Only includes material projects.			

For those of our products subject to litigation, information about material legal proceedings can be found in Note 27 to the Financial Statements from page 186.

 Details of relevant risks are set out in Risk from page 212

Development pipeline

The Development pipeline overview above summarises our development pipeline as at 31 December 2015.


We continue to maintain a clinical portfolio of more than 100 projects, and are making significant progress in advancing our late-stage programmes through regulatory approval. The portfolio has reached a steady state, with new project starts and progressions netted out against project

termination and rationalisation decisions. Twenty projects were discontinued in 2015, 11 for poorer than anticipated safety and efficacy results, eight as a result of strategic shift in the environment or portfolio prioritisation, and one because of a change in regulatory requirements.

During 2015, 18 NMEs progressed to their next phase of development. We also started a number of oncology trials during the course of the year, of which 12 were oncology combination trials. Importantly, many of our late-stage programmes achieved key milestones, with 12 NME or major LCM regulatory submissions within the year, and six major approvals. Expedited regulatory reviews indicate the degree of medical need that many of these programmes aim to address.

Progress against targets

We remain on track to meet the pipeline aspirations that we have previously communicated for the period from 2013 to the end of 2016: 12 to 16 Phase II starts; 14 to 16 NME and line extension regulatory submissions; and eight to 10 NME and line extension regulatory approvals. Moreover, we had 15 NME projects in pivotal studies or under regulatory review at the end of 2015, versus 13 at the end of 2014. This demonstrates the sustainability of our pipeline and our ability to deliver new medicines to patients.

 For more information on the risks associated with biologics and our products, please see Risk from page 212

Global Product Sales by therapy area

	2015			2014			2013		
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %
Cardiovascular and Metabolic diseases	9,489	(3)	4	9,802	11	12	8,830	(7)	(6)
Oncology	2,825	(7)	7	3,027	(5)	(2)	3,193	(9)	(2)
Respiratory, Inflammation and Autoimmunity	4,987	(2)	7	5,063	8	10	4,677	6	7
Infection, Neuroscience and Gastrointestinal	6,340	(23)	(16)	8,203	(9)	(7)	9,011	(14)	(13)
Total	23,641	(9)	(1)	26,095	1	3	25,711	(8)	(6)



Respiratory, Inflammation and Autoimmunity

2015 was a year of robust performance and significant pipeline evolution with inhaled therapies and biologics for asthma and COPD. We also have promising assets in the inflammatory and autoimmune disease areas.

Our strategic priorities

We have an industry-leading pipeline in Respiratory, which is an important platform for our return to growth. Our goal is to establish a leading position in asthma and COPD treatment, by delivering a range of differentiated inhaled therapies, novel combinations and devices, and biologics.

In Inflammation and Autoimmunity, we aim to develop innovative, first- and best-in-class therapies.

Asthma and COPD

Asthma is a common and chronic condition that affects the lungs' airways. Inflammation and narrowing of the airways may cause wheezing, breathlessness, chest tightness and coughing. Asthma is a major cause of chronic morbidity. Asthma that is not well controlled by existing treatments remains a significant unmet medical need.

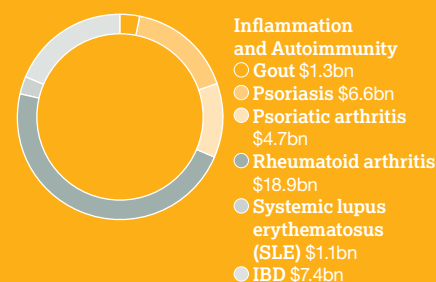
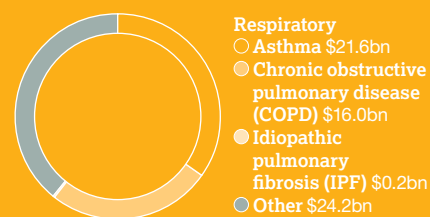
Currently, fixed-dose combinations (FDCs) of an inhaled corticosteroid (ICS) with a long-acting beta₂-agonist (LABA) such as *Symbicort* help treat moderate-to-severe asthma. We are exploring the use of *Symbicort* dosed 'as needed' in mild asthma patients. For specific patient groups, including more severe, refractory patients who experience severe or frequent exacerbations and a reduced quality of life, our effort is focused on developing targeted biologic therapies. We are also placing emphasis on better understanding patient phenotypes to enable targeted therapies and to go beyond symptom control.

COPD is a progressive and chronic disease. It includes various lung conditions, such as chronic bronchitis and emphysema. Currently, medication has only a limited impact on the course of COPD and the prognosis for patients remains poor.

Therapy area world market
(MAT/Q3/15)

\$102.0bn

Annual worldwide market value



Respiratory, Inflammation and Autoimmunity

Phase I		Phase II		Phase III		LCM Projects	
Small molecule	Large molecule	Small molecule	Large molecule	Small molecule	Large molecule	Small molecule	Large molecule
lesinurad + allopurinol	MEDI4920	abediterol	AZD9412 [#]	PT003 GFF (COPD)	brodalumab [#] (psoriasis)	Duaklir Genuair	
AZD1419 [#]	MEDI5872 [#]	AZD7594	mavrilimumab [#]	PT010 (COPD)	benralizumab [#] (severe asthma)	Symbicort SYGMA	
AZD7986	MEDI7836	AZD7624	abrilumab [#]	Zurampic (US) (gout)	benralizumab [#] (COPD)	Symbicort Breath Actuated Inhaler	
AZD8871	anifrolumab [#] (subcutaneous)	RDEA3170	MEDI9929 [#]		tralokinumab (severe asthma)		
AZD8999		PT010 (asthma)	tralokinumab (atopic dermatitis)		anifrolumab [#] (SLE)		
AZD9567			MEDI2070 [#]				
			MEDI-551 [#] (neuromyelitis optica)				
			anifrolumab [#] (lupus nephritis)				
							Key
							+ Addition
							— No change
							→ Progression
							□ Approved/launched
							# Partnered product
							F New filing



Pushing the boundaries

For 40 years, AstraZeneca has pushed the boundaries of science and helped millions of patients with respiratory disease. Now in RIA, we are advancing a pipeline of inhaled and biologic treatments, drug combinations and devices, and other therapies that aim to transform disease management.

AstraZeneca is developing a TLR-9 receptor agonist (shown here) aimed at producing long-term benefit in asthma by addressing imbalances in the immune system that may be an underlying cause of the disease.

Respiratory, Inflammation and Autoimmunity continued

Our marketed products

- > **Accolate** (zafirlukast)
- > **Bricanyl Respules** (terbutaline)
- > **Bricanyl Turbuhaler** (terbutaline)¹
- > **Daliresp/Daxas** (roflumilast)
- > **Duaklir Genuair** (aclidinium/formoterol)
- > **Eklira Genuair/Tudorza/Bretaris** (aclidinium)¹
- > **Oxis Turbuhaler** (formoterol)¹
- > **Pulmicort Turbuhaler/ Pulmicort Flexhaler** (budesonide)
- > **Pulmicort Respules** (budesonide)²
- > **Rhinocort** (budesonide)
- > **Symbicort pMDI** (budesonide/formoterol)
- > **Symbicort Turbuhaler** (budesonide/formoterol)¹

¹ In a dry powder inhaler.

² budesonide inhalation suspension.

 Full product information on page 203

The aim of COPD treatments is to reduce symptoms and prevent exacerbations. A class of FDCs of a long-acting muscarinic antagonist (LAMA) and LABA, known as LAMA/LABAs, is likely to become a 1st line therapy for symptomatic moderate-to-severe COPD patients. For patients who have either experienced or have a high risk of experiencing exacerbations, an ICS/LABA FDC such as *Symbicort* is recommended.

Our 2015 focus

Our *Symbicort* products improve the health of COPD and asthma patients by providing rapid relief of symptoms and long-term anti-inflammatory control. We continue to invest in this brand and are exploring a new indication in mild asthma through the SYGMA trial programme, enhancing our inhaled devices and patient support programmes, and by expanding indications such as the recently approved change to the *Symbicort Turbuhaler* label in Europe to include more moderate COPD patients. *Pulmicort* is a leading ICS therapy for asthma. Despite generic competition in many Established Markets, sales continue to grow, driven by Emerging Markets. More information about litigation relating to *Pulmicort Respules* can be found in Note 27 to the Financial Statements from page 186.

In 2015, we launched *Duaklir Genuair* (a LAMA/LABA) for maintenance symptom control in COPD patients. Our portfolio also includes *Eklira Genuair* (aclidinium, a LAMA) for patients with symptomatic mild-to-moderate COPD. In February 2015, we announced an agreement with Actavis to acquire the rights to its branded respiratory business in the US and Canada. This included the rights to develop and commercialise on-market products *Tudorza Pressair* (aclidinium, a LAMA) and *Daliresp* (a PDE4 inhibitor) for COPD. In December 2015, we announced that we had entered into a definitive agreement to acquire the core respiratory business of Takeda. The deal includes the acquisition of non-US rights to *Daliresp*, which is known as *Daxas* in certain countries. The transaction is anticipated to close in early 2016.

In the pipeline

We received positive results from the Phase III PINNACLE programme investigating the potential of PT003 to improve lung function in patients with COPD. PT003 is a twice-daily, fixed-dose

combination of glycopyrronium (a LAMA) and formoterol fumarate (a LABA). PT003 is the first LAMA/LABA combination to be delivered in a pressurised metered-dose inhaler (pMDI), using the proprietary porous particle co-suspension technology developed by Pearl Therapeutics. We are also developing PT010 as a twice-daily triple combination LAMA/LABA/ICS (composed of glycopyrronium, formoterol and budesonide, a key component of *Symbicort*) in a pMDI device for severe COPD. It has progressed to Phase III in COPD and may be one of the first products to deliver the three therapeutic agents via one inhaler.

Benralizumab is a biologic (MAb) in Phase III development for the treatment of severe uncontrolled asthma and COPD. It targets the IL-5 receptor and depletes eosinophils, which play a key role in inflammatory respiratory disease. The global Phase III results for benralizumab in severe asthma are expected in 2016. We anticipate making US and European regulatory submissions later in 2016. Phase III results and regulatory filing in COPD are expected in 2018.

Talokinumab is a MAb that binds to IL-13. Phase II data from talokinumab suggest that IL-13 neutralisation can 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 talokinumab 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 early 2017.

Inflammation and Autoimmunity

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 deposits of urate crystals) formation.

329m

The global prevalence of COPD is estimated to be 329 million people and WHO predicts that COPD will become the third leading cause of death worldwide by 2030.

Source: Vos et al 2012 WHO.



Values in action: Follow the science

Patients with SLE or lupus have only seen one new treatment for their disease in almost 60 years and clinical development remains challenging. With anifrolumab, we followed the science behind the potential therapeutic benefits of blocking the interferon pathway as a new treatment strategy. Our Phase II data confirmed this approach and the FDA has granted the anifrolumab SLE programme Fast Track designation.



Systemic lupus erythematosus (SLE), or lupus, is an autoimmune disease. It occurs when the immune system produces antibodies that, instead of targeting viruses or other foreign invaders, attack healthy tissue in the body 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. Current treatment of SLE focuses on suppressing symptoms and controlling disease flares and, in the case of lupus nephritis, preventing renal failure.

Although a biologic medicine was launched for SLE in 2011, most therapies used are off-label and significant unmet medical need remains. Most emerging biologics are likely to be used in combination with standard therapies, such as corticosteroids and immunosuppressants.

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 125 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.

Rheumatoid arthritis is currently treated with generic disease-modifying anti-rheumatic agents and, where appropriate, biologics. There is a need for novel treatments, since only about a third of patients treated with biologics achieve their treatment goals. Although tumour necrosis factor (TNF) alpha-blockers are currently the primary treatment for rheumatoid arthritis, use of other biologic approaches is expected to increase. Novel oral drugs targeting intra-cellular signalling pathways may provide anti-TNF-like levels of efficacy and potentially more convenient dosing, especially in patients who do not use injectable biologics.

In the pipeline

We are strengthening our pipeline and improving treatment options and clinical outcomes for patients with inflammation and autoimmunity diseases. Completion of four Phase II trials (anifrolumab and

mavrilimumab, and two RDEA3170 trials in Japan and the US), two Phase III trial programmes (brodalumab and *Zurampic*) along with the initiation of various Phase II trials, demonstrates the success of our R&D efforts to deliver new medicines quickly.

In December 2015, the FDA approved *Zurampic* 200mg tablets in combination with a xanthine oxidase inhibitor (XOI) for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with an XOI alone. Also in December 2015, the Committee for Medicinal Products for Human Use (CHMP) of the EMA adopted a Positive Opinion recommending the marketing authorisation of *Zurampic* 200mg tablets for the adjunctive treatment of hyperuricemia in adult gout patients (with or without tophi) who have not achieved target sUA levels with an adequate dose of an XOI alone.

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 sUA.

RDEA3170 is a potent selective uric acid reabsorption inhibitor, also intended for use as a combination urate-lowering therapy with XOIs. RDEA3170 is our lead investigational urate-lowering therapy (ULT) in Asia and is entering Phase IIb in both Japan and the US.

Anifrolumab is a developmental MAb that targets the type I interferon (IFN) receptor inhibiting the activity of all type I IFNs, which play a central role in lupus. Phase II trial results presented in November demonstrated that anifrolumab significantly reduced disease activity in moderate-to-severe SLE patients as measured by several

SLE composite endpoints. It also improved symptoms of lupus such as rash and arthritis. Anifrolumab is currently in Phase III development for SLE. A Phase II trial in lupus nephritis and Phase I subcutaneous administration study were initiated in late 2015. The FDA assigned anifrolumab Fast Track designation for SLE, which facilitates the development and expedites the review process of medicine candidates that treat serious conditions and fill an unmet medical need. Sifalimumab is a developmental MAb that specifically blocks the action of interferon alpha. Driven by data from the Phase II trials in SLE for both sifalimumab and anifrolumab, we have progressed anifrolumab into Phase III and therefore we do not intend to further develop sifalimumab in SLE.

Brodalumab is a human MAb that targets the interleukin-17 (IL-17) receptor to treat moderate-to-severe psoriasis. The Phase III programme in psoriasis included three studies evaluating treatment with brodalumab, two of which compared brodalumab with ustekinumab and/or placebo. Results from all three clinical trials showed that all primary and secondary endpoints were met. Brodalumab showed superiority to ustekinumab in both comparative studies. In May 2015, Amgen terminated its participation in the co-development and commercialisation of brodalumab. In September 2015, we announced a collaboration agreement with Valeant. This granted an exclusive licence for Valeant, as an expert in dermatology, to develop and commercialise brodalumab globally except in Japan and certain Asian countries. AstraZeneca submitted global regulatory filings on behalf of Valeant for brodalumab in psoriasis in late 2015. Valeant assumes decision making on future development and all development costs associated with the regulatory approval for brodalumab.

Mavrilimumab, an investigational MAb that inhibits a key pathway in the development of rheumatoid arthritis, achieved its primary endpoints in a Phase IIb study. Results, which were announced in May 2014, showed that mavrilimumab improved signs and symptoms of rheumatoid arthritis, measures of disability and patient-reported outcomes.

300m

It is estimated that approximately 300 million people worldwide suffer from asthma.

Source: Massoli et al, 2004.



Cardiovascular and Metabolic diseases

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.

Our strategic priorities

Our strategy and focus is on bringing life-changing medicines to patients to reduce morbidity, mortality and organ damage by addressing multiple risk factors across cardiovascular (CV) disease, including thrombosis (blood clotting), atherosclerosis (hardening of the arteries), dyslipidaemia (abnormal levels of blood lipids), and hypertension, diabetes and chronic kidney disease (CKD).

Despite improvements in the diagnosis and treatment of CVMD, unmet medical need remains high. The prevalence of these diseases and associated complications continues to increase worldwide.

We invest heavily in clinical development and life-cycle management. Nearly 60,000 patients participate in our R&D-led CV trials

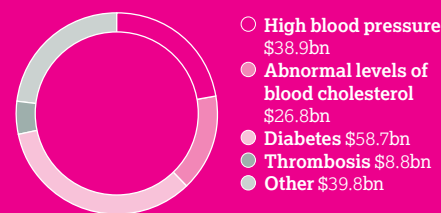
at more than 5,700 sites worldwide. We are also concentrating on diabetes research, which includes more than 50 clinical studies worldwide with an enrolment target of nearly 40,000 patients.

We are expanding our core capabilities and research programmes into new modalities and regenerative medicine. Our aim is to provide new treatment paradigms for heart failure, diabetes and CKD. To help achieve scientific leadership, we are engaging in collaborations that focus on scientific innovation in CVMD. For example, in 2015, we entered into collaborations with the French National Institute of Health and Medical Research (Inserm) to investigate new therapeutic approaches to Type 2 diabetes and CKD, with the University of Michigan to advance the treatment of CKD through the improved understanding of the

Therapy area world market (MAT/Q3/15)

\$173.0bn

Annual worldwide market value



disease and with Professor Doug Melton, Harvard Stem Cell Institute, applying revolutionary techniques transforming human stem cells into beta cells that secrete insulin.

For information on our CV collaborations, please see the Research and Development section from pages 42 to 45

Cardiovascular disease

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.

Cardiovascular and Metabolic diseases (CVMD)

Phase I		Phase II		Phase III		Applications under review		LCM projects	
Small molecule		Large molecule		Large molecule		Small molecule		Small molecule	
AZD4076 +		MEDI8111 −		MEDI6012 →		Brilinta/Brilique −		ZS-9 +	
								Brilinta/Brilique EUCLID −	
		MEDI0382 +				Epanova [#] (approved but not launched)		Brilinta/Brilique PEGASUS-TIMI 54 F□ −	
						Farxiga/Forxiga [*] −		Brilinta/Brilique SOCRATES −	
		MEDI4166 +				roxadustat [#] −		Brilinta/Brilique THEMIS −	
								Brilinta/Brilique HESTIA +	
								Bydureon EXSCEL −	
								Bydureon Dual Chamber Pen □	
								Bydureon weekly suspension −	
								Epanova STRENGTH −	
								saxagliptin/ dapagliflozin FDC F	
								Xigduo XR/ Xigduo −	

Key

+ Addition
 — No change
 → Progression
 □ Approved/launched
 F New filing
 # Partnered product
 * Farxiga in the US; Forxiga in the rest of the world
 ** Kombiglyze XR in the US; Kombiglyze in the EU



Breaking through conventional thinking

Because we know that cardiovascular disease (CVD) is a well-known consequence of diabetes and chronic kidney disease (CKD), AstraZeneca takes an integrated patient approach and seeks to further reduce cardiovascular (CV) morbidity and mortality, and organ damage by addressing multiple CV risk factors.

Pancreatic beta cells at different stages of regeneration: AstraZeneca is investing in research that could stimulate the regeneration of beta cells in the pancreas with the aim of stopping the progression of, or reversing, the course of diabetes.

Cardiovascular and Metabolic diseases continued

Our marketed products

Cardiovascular disease

- > **Atacand**¹ / **Atacand HCT** / **Atacand Plus** (candesartan cilexetil)
- > **Brilinta/Brilique** (ticagrelor)
- > **Crestor**² (rosuvastatin calcium)
- > **Plendil** (felodipine)
- > **Seloken/Toprol-XL** (metoprolol succinate)
- > **Tenormin**³ (atenolol)
- > **Zestril**⁴ (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)
- > **Symlin** (pramlintide acetate)
- > **Xigduo** (dapagliflozin and metformin HCl)
- > **Xigduo XR** (dapagliflozin and metformin HCl)

Full product information on page 203

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

⁴ Licensed from Merck. Divested US rights to *Zestril* to Alvogen Pharma US Inc. effective 9 January 2015.



Values in action: We play to win

Acquiring ZS Pharma gave us access to the potassium-binding compound ZS-9, a potential best-in-class treatment for hyperkalaemia (high potassium levels) which affects more than three million people in the US alone who suffer from chronic kidney disease and chronic heart disease. With submissions under way, we expect ZS-9 to accelerate our return to growth.

Our 2015 focus

Brilinta/Brilique, one of our Growth Platforms, 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*. It is currently under regulatory review in three additional countries. Since launch, more than one million patients have been treated with *Brilinta/Brilique*, and it has been included in 12 major ACS treatment guidelines globally. In August 2015, the European Society of Cardiology updated NSTE-ACS guidelines and continued to recommend ticagrelor over clopidogrel in ACS for all patients at moderate-to-high risk of ischaemic events, regardless of initial treatment strategy and including those pre-treated with clopidogrel.

The PEGASUS-TIMI 54 study investigated the efficacy and safety of ticagrelor at both 60mg and 90mg twice daily, plus low-dose aspirin, compared to placebo plus low-dose aspirin, for the long-term prevention of atherothrombotic events in patients who had suffered a heart attack one to three years prior to study enrolment. Both 90mg and 60mg study doses of ticagrelor with aspirin significantly reduced the primary composite endpoint of CV death, myocardial infarction (MI, also known as heart attack) or stroke compared to placebo and aspirin. The full results of the study were published in the New England Journal of Medicine in March 2015.

In September 2015, the FDA approved a new 60mg dosage strength for *Brilinta* to be used in patients with a history of heart attack beyond the initial one-year treatment with *Brilinta* 90mg to reduce the rate of cardiovascular death, MI and stroke in patients with ACS. In December, CHMP of the EMA adopted a Positive Opinion recommending approval of *Brilique* 60mg for the treatment of patients with a history of heart attack and at high risk of having a further coronary event. The opinion states that treatment may be started as continuation therapy after an initial one-year treatment with dual anti-platelet therapy. In the US, we are in early stages of patent litigation against multiple generic companies after they sent so-called 'Paragraph IV notices' challenging patents listed in the FDA Orange Book with reference to *Brilinta*.

The SOCRATES trial evaluating the efficacy of *Brilinta/Brilique* compared to aspirin in reducing thrombotic events in patients with acute ischaemic stroke and high-risk transient ischaemic attack, saw its last patient randomised in November 2015. This trial is scheduled to report data in the first half of 2016. SOCRATES involves 13,200 patients in 33 countries and is part of the broader PARTHENON life-cycle programme for *Brilinta/Brilique* (discussed further overleaf).

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 existing paediatric exclusivity period expires on 8 July 2016. Subsequently, generic competition from various companies is expected in the US market. Actavis is permitted to begin selling generic rosuvastatin in the US in May 2016 as the result of a litigation settlement with AstraZeneca. Patents protecting *Crestor* have been challenged in various jurisdictions. Details of these matters are included in Note 27 to the Financial Statements, from page 186.

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

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.*

415 million people worldwide have diabetes; WHO projects that diabetes will be the seventh leading cause of death in 2030.**

* Source: WHO Factsheet 2015 (data from 2012).

** Source: IDF Atlas 2015 and WHO Factsheet 2015.



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 $\geq 500\text{mg/dL}$).

Clinical studies

In addition to the PEGASUS and SOCRATES trial described above, *Brilinta/Brilique* is being studied in two other clinical trials under the PARTHENON programme. PARTHENON is AstraZeneca's largest ever 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.

AstraZeneca continues to explore the unmet medical need in cholesterol management, building on the well-established clinical trial programme for *Crestor*. *Crestor* has been studied in more than 120 ongoing or completed clinical trials and involving more than 67,000 patients worldwide over the past 13 years.

We are also committed to further evaluating the clinical profile of *Epanova* and identifying other patient groups it may benefit.

AstraZeneca recently commenced a 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 cardiovascular 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.

Our 2015 focus

AstraZeneca is focused on redefining the Type 2 diabetes treatment approach and harnessing complementary mechanisms of action, as well as evaluating potential cardiovascular outcomes benefit. Our current portfolio is well-positioned to enable combination treatment, and data from our Phase III programmes is expected to further

support the outcomes benefits of the new class.

We have a broad anti-diabetes portfolio with products in the three fastest growing classes of diabetes treatments (SGLT2, GLP-1 and DPP-4).

In 2015, 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 50 countries. It is under regulatory review in 20 additional countries.

Xigduo is approved in 33 countries, including the US with *Xigduo XR* (ongoing approvals in 2016 expected). In 2015, we continued to see the approval and launch of the *Bydureon Pen*, which is now launched in 17 countries globally, 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 after they sent so-called 'Paragraph IV notices' challenging patents listed in the FDA Orange Book with reference to *Onglyza*. A trial is scheduled to take place during 2016.

In April 2015, an FDA Endocrinologic and Metabolic Drugs Advisory Committee voted 13 to one that the results of the Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus (SAVOR) study demonstrated that the use of saxagliptin in patients with Type 2 diabetes has an acceptable cardiovascular risk profile. AstraZeneca will conduct further investigation to better understand the signal of hospitalisation for heart failure found in the SAVOR results.

In the pipeline

We are developing an FDC of saxagliptin and dapagliflozin, which combines two complementary mechanisms designed to help more patients with Type 2 diabetes reach their treatment goals. In October 2015, AstraZeneca received a Complete Response Letter (CRL) from the FDA regarding the NDA for the investigational FDC of saxagliptin and dapagliflozin for the treatment of adult patients with Type 2 diabetes. The CRL states that more clinical data are required to support the application. We are working closely with the FDA to determine the appropriate next steps for the NDA and remain committed to the development of saxagliptin and dapagliflozin. We will file additional clinical data from a study which is now completed and continue our conversations with the FDA.

This announcement does not affect interactions with other health authorities as part of these application procedures for the FDC, including an ongoing review by the EU for the FDC.

The Phase III programme for a once-weekly suspension of *Bydureon* continues to progress.

Through our strategic collaboration with FibroGen and Astellas, we continue to develop roxadustat, a potential first-in-class oral compound 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 and China, and is just completing Phase II in Japan. The Phase III programme consists of seven 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.

In December 2015, we acquired ZS Pharma to strengthen our CVMD portfolio. This provided us access to ZS-9, a potential best-in-class treatment for hyperkalaemia which complements our increasing focus on CKD. ZS-9 has been submitted for approval in the US, EU and Australia. In November 2015, data presented at the American Society of Nephrology meeting showed positive interim results from ZS005, a long-term safety study of ZS-9.

 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 anti-diabetes therapy, continued in 2015.

The trial will enrol approximately 17,000 adult patients with Type 2 diabetes. DECLARE was fully enrolled in 2015 and is expected to be completed in 2019.

The Exenatide Study of Cardiovascular Event Lowering (EXSCEL) study also continued during 2015. This study, which began in 2010 and is expected to end in 2017 is evaluating the impact of *Bydureon*, in addition to usual care on CV outcomes in patients with Type 2 diabetes.



Oncology

Our combination-focused pipeline exploits the power of four scientific platforms, and we are driven by an ambition to help eliminate cancer as a cause of death through scientific discovery and collaborations.

Our strategic priorities

For more than 40 years we have developed cancer drugs. Many of these have increased survival rates for patients around the world. Significant unmet medical need remains for therapies that increase survival, cure rates and time to recurrence. Our vision is to help meet this need by redefining the cancer treatment paradigm. We are doing this through scientific innovation, accelerated clinical programmes and collaboration. Several submissions are under way and we aim to deliver at least four new cancer therapies 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 approaches: immunotherapy, tumour drivers and resistance mechanisms, DNA damage repair, and antibody-drug conjugates.

Therapy area world market
(MAT/Q3/15)

\$72.2bn

Annual worldwide market value



- Chemotherapy \$19.2bn
- Hormonal therapies \$10.0bn
- Monoclonal antibodies (MAbs) \$22.4bn
- Small molecule tyrosine kinase inhibitors (TKIs) \$18.6bn
- Immunotherapies \$2.0bn

Oncology

Phase I				Phase II				Phase III								
Small molecule		Large molecule		Combination molecules		Small molecule		Large molecule		Combination molecules		Small molecule		Large molecule		
AZD0156	+	MEDI0562 [#]	+	Tagrisso (AZD9291) combination TATTON	—	AZD1775 [#]	—	MEDI-551 [#]	—	AZD5069 + durvalumab [#] AZD9150 [#] + durvalumab [#]	+	cediranib ICON6	F	durvalumab [#] HAWK	+	
AZD2811	+	MEDI0639 [#]	—	durvalumab [#] + dabrafenib + trametinib	—	AZD2014	—	MEDI-573 [#]	—	durvalumab [#] + tremelimumab (gastric cancer)	+	selumetinib [#] ASTRA	—	durvalumab [#] PACIFIC	—	
AZD5312 [#]	—	MEDI0680	—	durvalumab [#] + Iressa	—	Tagrisso (AZD9291) BLOOM AZD3759 BLOOM	→	durvalumab [#]	—			selumetinib [#] SELECT-1	—	moxetumomab [#]	—	
AZD6738	—	MEDI1873	+	durvalumab [#] + MEDI0680	—	AZD4547	—					Tagrisso (AZD9291) AURA, AURA 2	F □	tremelimumab DETERMINE	—	
AZD8186	—	MEDI3617 [#]	—	durvalumab [#] + MEDI6383 [#]	+	AZD5363 [#]	—					acalabrutinib	+			
AZD8835	—	MEDI4276	+	durvalumab [#] + tremelimumab (solid tumours)	—	savolitinib [#]	—					Tagrisso (AZD9291) AURA 3	—			
AZD9150 [#]	—	MEDI-565 [#]	—	MEDI-551 [#] + rituximab	—	selumetinib [#]	—									
AZD9496	—	MEDI6383 [#]	—													
MEDI9197	+	MEDI9447	+													
		durvalumab [#]	—													

Key

+ Addition

— No change

→ Progression

□ Approved/launched

F New filing

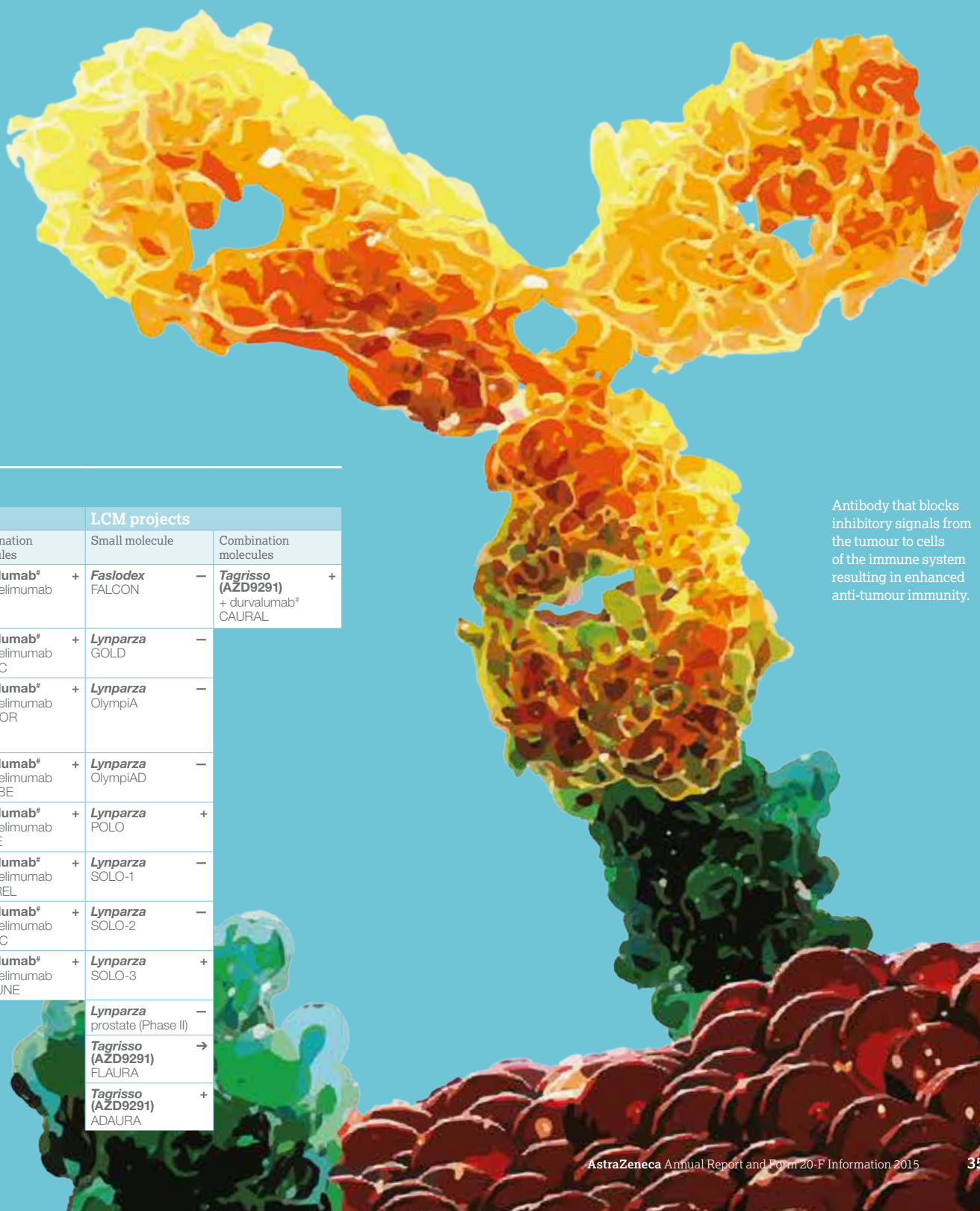
Partnered product

Key

- + Addition
- No change
- Progression
- Approved/launched
- F New filing
- # Partnered product

Redefining the treatment paradigm

Even as research and development continues to break boundaries in how we understand and fight cancer, there are still more than eight million lives lost every year to the disease. At AstraZeneca, we are committed to advancing the science of oncology to deliver life-changing medicines to people most in need.



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

		LCM projects	
Combination molecules		Small molecule	Combination molecules
durvalumab[†] + tremelimumab ALPS	+	Faslodex FALCON	— Tagrisso (AZD9291) + durvalumab [†] CAURAL
durvalumab[†] + tremelimumab ARCTIC	+	Lynparza GOLD	—
durvalumab[†] + tremelimumab CONDOR	+	Lynparza OlympiA	—
durvalumab[†] + tremelimumab DANUBE	+	Lynparza OlympiAD	—
durvalumab[†] + tremelimumab EAGLE	+	Lynparza POLO	+
durvalumab[†] + tremelimumab KESTREL	+	Lynparza SOLO-1	—
durvalumab[†] + tremelimumab MYSTIC	+	Lynparza SOLO-2	—
durvalumab[†] + tremelimumab NEPTUNE	+	Lynparza SOLO-3	+
		Lynparza prostate (Phase II)	—
		Tagrisso (AZD9291) FLAURA	→
		Tagrisso (AZD9291) ADAURA	+

Oncology continued

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 204



Values in action: We follow the science

The DNA inside our cells, our genetic blueprint, is continually being damaged by environmental factors, ultraviolet light and even natural growth and division. Cells contain multiple repair mechanisms to fix damage to DNA strands because, if this isn't repaired, the cells die. Cancer cells very commonly have one repair mechanism missing or not functioning, which creates an 'Achilles Heel' – making them sensitive to being killed if another repair mechanism is targeted by a medicine. Our scientists are exploiting this 'Achilles Heel' of sensitivity to develop new medicines which specifically block DNA repair and cause cancer cells to die, while sparing the normal cells which have multiple repair mechanisms intact. One such treatment is *Lynparza* which blocks PARP – a protein involved in DNA repair in cancer cells that already have loss of the BRCA protein which is a critical part of the 'homologous repair' pathway.

> **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 repair:** 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 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.

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 2015 focus

Our marketed oncology products generated sales of more than \$2.8 billion worldwide in 2015. We continue to explore ways to maximise the benefit of our medicines for patients.

Iressa was the first EGFR-TKI to be approved in advanced NSCLC. Now approved in 90 countries, it is the leading EGFR-TKI for patients with advanced EGFRm NSCLC in Europe and Asia.

It received US approval in July 2015.

Iressa is also the first EGFR-TKI to include blood-based diagnostic testing where a suitable tumour sample is not available in its European label.

Faslodex 500mg is approved in more than 80 countries, including the EU, the US and Japan. We are currently exploring the efficacy and safety of *Faslodex* 500mg compared with *Arimidex* in the 1st line advanced breast cancer setting (hormone-naïve patients) in the Phase III FALCON trial. We are engaged in patent litigation, including in the US and Europe, in relation to generic challenges to *Faslodex*. Details of litigation relating to *Faslodex* are included in Note 27 to the Financial Statements from page 186.

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

Lynparza is an oral PARP inhibitor approved in 36 countries for the treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer.

Tagrisso is the first approved EGFR-TKI indicated for patients with metastatic EGFR T790M mutation-positive NSCLC. This indication was approved in November 2015 under the FDA's Accelerated Approval Programme based on tumour response rate and duration of response. Conversion to full approval for this indication is contingent upon verification and description of clinical benefit in confirmatory trials.

In December 2015, *Tagrisso* received a Positive Opinion by CHMP for the treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC. In Japan, *Tagrisso* was granted Priority Review by the PMDA. Interactions with regulatory authorities in the rest of the world are ongoing.



In the pipeline

Our Oncology pipeline continued to progress in 2015. It now includes five NMEs in late-stage development and another 26 NMEs in Phases I and II. 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 include:

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 and *Tagrisso*. The lung cancer programme includes studies in the 1st line, 2nd line and 3rd line setting. Additional registration studies are progressing in squamous cell carcinoma of the head and neck (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.

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).

> Tremelimumab, an anti-Cytotoxic T-Lymphocyte-Associated protein 4 antibody, is being investigated as a monotherapy in a pivotal study for the treatment of malignant mesothelioma.

> MEDI0680 is an antiprogrammed 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.
- > Some of our 2015 strategic collaborations include:
 - A collaboration with Immunocore, a UK-based biotechnology company, to combine durvalumab (PD-L1) with IMCgp100, Immunocore's lead T-cell receptor-based investigational therapeutic, for the treatment of patients with metastatic myeloma.
 - A collaboration between MedImmune and Innate Pharma, a biopharmaceutical company focused on cancer and inflammation. The aim is to accelerate and broaden the development of Innate's proprietary anti-NKG2A antibody (IPH2201), including in combination with durvalumab (PD-L1) across a broad range of solid tumours.
 - A collaboration between MedImmune and Mirati Therapeutics, an oncology company focused on genetic and epigenetic drivers of cancer. We are evaluating the safety and efficacy of durvalumab (PD-L1) in combination with mocetinostat, Mirati Therapeutics' investigational spectrum-selective histone deacetylase inhibitor.
 - An agreement with Heptares under which AstraZeneca will acquire exclusive global rights to develop, manufacture and commercialise the adenosine A2A receptor antagonist, HTL-1071.

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).

Tumour drivers and resistance mechanisms franchise

- > *Tagrisso* (AZD9291) 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 and immunotherapies are under investigation.
- > Selumetinib is a mitogen-activated protein kinase inhibitor in Phase III development for 2nd line Kirsten rat sarcoma viral oncogene homolog (KRAS) mutant NSCLC. The selumetinib programme also includes a Phase III study for adjuvant differentiated thyroid cancer and a Phase II study for 2nd line KRAS mutation not detected NSCLC.
- > 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.
- > 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.



Oncology continued



DNA damage repair franchise

- > *Lynparza* (olaparib) is being evaluated in a broad range of Phase III trials, including advanced gastric cancer, BRCAm adjuvant and metastatic breast cancer, gBRCAm pancreatic cancer, and gBRCAm ovarian cancer. *Lynparza* is also in Phase II development for prostate cancer.
- > AZD1775 is a Wee1 inhibitor in Phase II development for ovarian and other solid tumours.
- > Phase I clinical studies are progressing for the ATR inhibitor AZD6738 (2nd line gastric cancer with *Lynparza* and also in combination with ionizing radiation in solid tumours) and the ATM inhibitor AZD0156 (for the treatment of gastric and colorectal cancers).

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.
- > A strategic collaboration with Tanabe Research Laboratories (TRL), a subsidiary of Mitsubishi Tanabe Pharma Corporation, is looking at ways to combine MedImmune's pyrrolobenzodiazepine based cytotoxic molecules and linker technology with TRL's antibodies. The aim is to generate monospecific and bispecific conjugates (ADCs) for a broad range of cancer types.

Our Oncology collaborations

Collaboration is key to accessing the best science and technology, achieving scientific leadership and delivering innovative, life-changing medicines. In 2015, we continued to strengthen our portfolio and accelerate clinical programmes through acquisitions and collaborations.

In December 2015, we announced entry into an agreement to invest in a majority equity stake in Acerta Pharma. The transaction provides AstraZeneca with a potential best-in-class irreversible oral

Bruton's tyrosine kinase (BTK) inhibitor, acalabrutinib (ACP-196), currently in Phase III development for B-cell blood cancers and in Phase I/II clinical trials in multiple solid tumours.

For more information please see Note 30 to the Financial Statements on page 193

Earlier in 2015, we established several collaborations that reflect the attractiveness of our immuno-oncology portfolio, as demonstrated by:

- > Our externalisation agreement with Celgene, a global leader in haematological cancers, for the development and commercialisation of durvalumab, anti-programmed death-ligand 1 antibody (PD-L1) across a range of blood cancers, including non-Hodgkin lymphoma (NHL), myelodysplastic syndromes and multiple myeloma.
- > The expansion of our existing immuno-oncology collaboration with Lilly to further explore novel combinations across the companies' complementary portfolios. This collaboration will include evaluations of the safety and efficacy of durvalumab (PD-L1), with select Lilly agents targeting the immune system or tumour drivers and resistance mechanisms.
- > Our collaboration with Juno Therapeutics, a biopharmaceutical company. This focuses on re-engaging the body's immune system to treat cancer and to evaluate safety, assess tolerability, and preliminary efficacy of durvalumab combinations with CD19-directed chimeric antigen receptor (CAR) T-cell candidates for patients with NHL.

In addition to the collaborations mentioned above, during 2015 we have also entered into a range of collaborations in early science with several scientific and research institutions and biotechnology and diagnostic companies. These additional collaborations include:

- > Two Co-operative Research and Development Agreements between MedImmune and the National Cancer Institute (NCI), a part of the National

Institutes of Health (NIH), to advance early-stage research and development in immunotherapy and tumour-targeted therapies for cancer.

- > A five-year collaboration between MedImmune and the University of Cambridge's Department of Chemical Engineering and Biotechnology (CEB) designed to generate breakthrough research in biopharmaceutical development, including activities in cell engineering and formulation and analytical science.
- > A five-year agreement with the University of Manchester to harness clinical bioinformatics to deliver personalised healthcare for cancer patients. The research will be carried out in partnership with the state-of-the-art clinical trials unit of The Christie National Health Service (NHS) Foundation Trust, which is at the forefront of experimental cancer medicine in the UK.
- > A licence agreement and collaboration between MedImmune and Inovio Pharmaceuticals, a biotechnology company developing DNA-based immunotherapies for cancer and infectious diseases, to acquire exclusive rights to Inovio's INO-3112 immunotherapy. This agent targets cancers caused by the human papillomavirus (HPV) types 16 and 18 and is in Phase I/II development for cervical, and head and neck cancers. MedImmune intends to study INO-3112 in combination with selected immunotherapy molecules within its pipeline in HPV-driven cancers.

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).



Infection, Neuroscience and Gastrointestinal

Our opportunity-driven strategy seeks to maximise the value of our pipeline and portfolio through focused R&D, licensing and collaboration. In 2015, we made progress in developing several assets and launched *Movantik/ Moventig* in the US, Canada and in key markets across the EU. In partnership with Lilly, we also made advances in clinical trials for our BACE inhibitor, AZD3293, a potential treatment for Alzheimer's disease.

attenuated influenza vaccine MAA for a global influenza pandemic virus in March 2015. In September 2015, AstraZeneca entered into an agreement with Daiichi Sankyo for the development and commercialisation of *FluMist* Quadrivalent in Japan. We continue to engage in discussions with other governments to help protect children against influenza, the most common vaccine-preventable disease in the developed world.

Respiratory syncytial virus

Since its approval in 1998, *Synagis* has helped protect more than 2.8 million babies globally against respiratory syncytial virus (RSV). RSV affects approximately half of all infants in their first year of life. It is the leading cause of hospitalisations and admissions to paediatric intensive care units. *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. In July 2014, the American Academy of Pediatrics Committee on Infectious Diseases (COID) issued guidance to further restrict premature infants from eligibility for preventive therapy with *Synagis*. A majority of the payers in the US implemented these guidelines this year. As a result, demand in the US was adversely impacted with the majority of the impact seen in the 2014 to 2015 season, when volume declined approximately 40% versus the prior season. The 2015 to 2016 season started in November in most parts of the US and season-to-date volume has been in line with expectations. We have not seen a direct replication of these guidelines in other countries at a national level.

Infection

We have a long history in the fields of Infection, Neuroscience, and Gastrointestinal (ING) diseases, which represent a significant area of unmet medical need for patients around the world. We group these fields into one therapy area. This helps to support existing medicines, develop and commercialise new therapies, prioritise resources, enable effective and efficient investment and maximise value for patients and shareholders. In February 2015, we created a new company, Entasis Therapeutics, to develop programmes in our small molecule early-stage anti-infective portfolio. In July 2015, we also announced the creation of a new antibiotics organisation in order to develop and commercialise effective antibiotics to combat the growth of resistant infections.

Our strategic priorities

Our focus in Infection is on respiratory viruses and serious bacterial infections. Our differentiated and leading on-market portfolio and pipeline were active in 2015.

Influenza virus

Seasonal influenza is a serious public health problem that causes severe illness and death in high-risk populations. Clinical data from *Fluenz* Tetra/*FluMist* Quadrivalent has demonstrated superiority to traditional inactivated influenza vaccines in children. In addition to being used in the UK's largest vaccination programme to date, *Fluenz* Tetra was included in Finland's National Immunization Program for the 2015/2016 influenza season. The regulatory filing in Australia in July 2015 followed on from the submission of an EU pandemic live

Infection, Neuroscience and Gastrointestinal

Phase I		Phase II		LCM projects		Applications under review					
Small molecule	Large molecule	Small molecule	Large molecule	Small molecule							
ATM AVI [#]	—	MEDI3902	—	CXL [#]	—	MEDI4893	—	linacotide [#]	F	CAZ AVI [#] (serious infection)	F
AZD8108	—	MEDI1814	—	AZD3241	→	MEDI7510	→	Nexium (paediatrics)	—	CAZ AVI [#] (HAP/VAP)	F
				AZD3293 [#]	—	MEDI8897	→	Nexium (stress ulcer prophylaxis)	—	MEDI-550*	F
Key											
— No change						MEDI8852	→	Diprivan	—	Zinforo	—

Key

— No change
→ Progression
F New filing
Partnered product
* Regulatory acceptance is anticipated in H1 2016

Infection, Neuroscience and Gastrointestinal continued

Our marketed products

Infection

- > **Fluenz/FluMist¹** (influenza vaccine live)
- > **Fluenz Tetra/FluMist Quadrivalent^{1,2}** (influenza vaccine live)
- > **Merrem/Meronem³** (meropenem)
- > **Synagis⁴** (palivizumab)
- > **Zinforo⁵** (ceftaroline fosamil)

 Full product information on page 204

¹ Intra-nasal.

² Daiichi Sankyo holds rights to *Fluenz Tetra/FluMist Quadrivalent* in Japan.

³ Licensed from Dainippon Sumitomo Pharmaceuticals Co., Limited.

⁴ US rights only. AbbVie holds rights to *Synagis* outside the US.

⁵ Licensed from Forest (now a wholly-owned subsidiary of Allergan). AstraZeneca holds global rights, excluding the US, Canada and Japan.

Neuroscience

- > **Diprivan** (propofol)
- > **EMLA** (lidocaine and prilocaine)
- > **Movantik/Moventig** (naloxegol)
- > **Naropin** (ropivacaine)
- > **Seroquel IR** (quetiapine fumarate)
- > **Seroquel XR** (quetiapine fumarate)
- > **Vimovo¹** (naproxen and esomeprazole magnesium)
- > **Xyllocaine** (lidocaine)
- > **Zomig** (zolmitriptan)

 Full product information on page 204

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 204

In 2015, we strengthened our leadership position in RSV, securing FDA Fast Track designation for MEDI8897, a MAb that may require dosing only once per RSV season. We also launched Phase IIa clinical trials. Additionally, we launched Phase II clinical trials to assess the efficacy of MEDI7510, MedImmune's RSV sF antigen plus the synthetic molecule GLA, for the prevention of acute RSV-associated respiratory illness in older adults.

Serious bacterial infections

Governments increasingly recognise antibiotic or anti-microbial resistance as a major public health threat. We have a broad and innovative portfolio of medicines for serious Gram-positive and Gram-negative bacterial infections. We are now developing additional medicines to fight these infections. As bacteria develop resistance to current antibiotics, deadly infections could, again, become uncontrollable. In May 2015, AstraZeneca submitted a filing to the EMA for CAZ AVI, an innovative combination of ceftazidime and avibactam. We are seeking full approvals for complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), and nosocomial pneumonia (NP) (including hospital-acquired pneumonia and ventilator-associated pneumonia). In April 2015, we announced full Phase III results from CAZ AVI pivotal studies RECLAIM-1, -2, and -3 and REPRISE, with positive Phase III cUTI results for RECAPTURE-1 and -2 announced in September. During the year, we launched antibiotic *Zinforo* in Mexico; the product is now available in 34 markets.

In addition to CAZ AVI in our late-stage pipeline, we are developing aztreonam avibactam (ATM AVI), a Phase I compound being developed jointly with Forest (now a wholly-owned subsidiary of Allergan). It targets Gram-negative bacteria with a metallo-beta-lactamase resistance mechanism. This bacteria is endemic in India and spreading throughout the world. In September 2015, AstraZeneca entered into a public-private partnership agreement with the US Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response (ASPR) to develop a portfolio of medicines, of which ATM AVI is the first candidate medicine in the portfolio, to combat bioterrorism threats and other life-

threatening bacterial infections. ASPR's Biomedical Advanced Research and Development Authority (BARDA) and AstraZeneca will manage and fund the portfolio over the next five years. In the arrangement, BARDA initially will provide \$50 million towards ATM AVI development and could provide up to a total of \$170 million for development of additional products in the portfolio during the five-year period.

Neuroscience

Our strategic priorities

We have a long history in anaesthesia and analgesia, and a sizeable business in psychiatry rooted in *Seroquel IR* and *Seroquel XR*. The patent protecting the active ingredient in *Seroquel IR* and *Seroquel XR*, quetiapine, expired worldwide in 2012. However, in most European countries, the formulation patent covering *Seroquel XR* does not expire until 2017. As such, *Seroquel XR* remains a key product. We are vigorously defending the patent protecting *Seroquel XR*. The patent, however, has been subject to various challenges and revocations. Details of litigation relating to *Seroquel XR* are included in Note 27 to the Financial Statements from page 186.



Values in action: We are entrepreneurial

The antibiotics organisation has been created with a clear vision – to be a global leader in the development and commercialisation of life-saving antibiotics by 2020. With the formation of this separate and dedicated unit, we will focus on the fast growing global health threat of multidrug resistant bacterial infections and continue to bring scientific innovation from our antibiotics portfolio to doctors and patients around the world.



Neurology

Alzheimer's disease remains one of the largest areas of unmet medical need and continues to generate significant social and scientific interest. To address this, in addition to our BACE inhibitor, AZD3293, which is currently advancing in our externalisation collaboration with Lilly in Phase II/III clinical trials as a potential treatment for Alzheimer's disease, we continued to develop MEDI1814 in Phase I clinical trials. We also entered into multiple collaborations with academic and scientific institutions to advance disease understanding and identify potential new medicines. For example, we started a collaboration with the University of Cambridge (focusing on advancing research in neurodegenerative diseases), and continued to work with the Karolinska Institutet (Sweden), the Banner Alzheimer's Institute (US), the National Institute of Radiological Sciences (Japan) and Vanderbilt University (US), focusing on psychosis and other neuropsychiatric symptoms associated with major brain diseases, such as Alzheimer's disease and schizophrenia. We also renewed or continued our collaborations with the Lieber Institute for Brain Development (US) and Tufts University (US), focusing on understanding brain diseases and disorders, including Alzheimer's disease and autism spectrum disorders. In another collaboration, we joined the Medical Research Council Dementias Platform UK, a large public-private partnership, to accelerate and share dementia research. In addition, we are developing AZD3241, a myeloperoxidase inhibitor, to potentially delay progression of disability in patients with multiple system atrophy. The National Institute on Drug Abuse in the US is conducting and funding a Phase II trial of AZD8529 in smoking cessation. AZD7325 is in a clinical trial sponsored by the National Institute of Mental Health in the US to be tested as a potential treatment for autism spectrum disorders.

Pain control

Our anaesthesia portfolio consists of various compounds, including an intravenous general anaesthetic/sedative and local anaesthetics available in different formulations. The portfolio includes injectables, creams, gels, sprays and suppositories.

Biologics are an emerging treatment for pain control. We are exploring treatments in focused pain areas, with patients selected on the basis of their characteristic symptoms.

Movantik/Moventig is the first orally administered, once-daily, peripherally-acting mu-opioid receptor antagonist to be approved for the treatment of opioid-induced constipation (OIC) in adult patients. The indication varies by jurisdiction. OIC is the most common side effect of chronic use of opioid pain medicines. These are taken by over 69 million people worldwide, and the incidence of OIC in patients with chronic pain varies and has been suggested to be as high as 81%. Of these patients, only about half achieve desired treatment outcomes with current options, such as OTC and prescription laxatives, which treat general constipation symptoms. *Movantik/Moventig* was developed using Nektar Therapeutics' oral small molecule polymer conjugate technology as part of a 2009 licence agreement with Nektar Therapeutics.

In March 2015, AstraZeneca announced a co-commercialisation agreement with Daiichi Sankyo, for *Movantik* in the US, in line with delivering on our externalisation strategy to create value from the science that exists in the product pipeline. The brand launched in the US, UK, Canada, Sweden, Denmark, Norway, Finland and Germany in 2015. Additional launches will occur through the first half of 2016.

Gastrointestinal Our strategic priorities

Nexium remains one of the most used therapies in the world. In 2015, its use continued to grow in markets including China and Japan. Demand for *Nexium* in China is expected to grow significantly and will complement its position in Japan as the top-selling medicine in its class.

Nexium is generally subject to generic competition in Europe. In the US, we expected the first generic entry in 2014 but that did not occur. In January 2015, Teva received approval from the FDA to market a generic version of *Nexium*. Since then, Mylan, Hetero/Camber, Dr Reddy Labs and Torrent received approval for generic versions of *Nexium*. *Nexium* is also subject



Values in action: We play to win

In 2015, we made *Movantik/Moventig*, the first peripherally-acting mu-opioid receptor antagonist (PAMORA), available to patients suffering from opioid-induced constipation in the US, Canada, UK, Germany, Ireland and the Nordic countries.

to generic competition in Australia, where the first generic entry occurred in August 2014. Patents protecting *Nexium* have been subject to a number of challenges in different jurisdictions. Details of these matters are included in Note 27 to the Financial Statements from page 186.

Pfizer acquired the exclusive global rights to market *Nexium* for OTC indications worldwide in 2012, and launched OTC *Nexium* 20mg in the US and Europe in 2014.

In July 2015, we announced the completion of an agreement with Tillotts Pharma, part of the Zeria Group. This covered the divestment of global rights, outside the US, to *Entocort* (budesonide), a gastroenterology medicine for patients with mild-to-moderate Crohn's disease and ulcerative colitis. In December 2015, we entered into an agreement with Perrigo for the divestment of US rights to *Entocort*, granting Perrigo the rights to sell *Entocort* capsules and the authorised generic *Entocort* capsules marketed by Par Pharmaceuticals.

Research and Development



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

Overview

- > Focused on science-led innovation across small molecules, biologics, immunotherapies, protein engineering and devices
- > Strengthened our pipeline, portfolio and capabilities in 2015 through focused investment and business development
- > Simplified programmes, processes and systems while prioritising resources towards late-stage development
- > Launched seven diagnostic tests linked to our products in line with our personalised healthcare (PHC) strategy
- > Promoted open innovation and collaboration by co-locating to strategic R&D centres and collaborating with leading research organisations
- > Published 58 articles in 'high-impact' publications compared to seven in 2010
- > Committed to working responsibly and in accordance with our global bioethics standards

Achieve scientific leadership

As outlined in Strategic priorities from page 16, achieving scientific leadership is critical to our success.

During 2015, we

- > continued to redeploy R&D spend towards late-stage development
- > further expanded our immuno-oncology research and development activities
- > entered into numerous strategic collaborations to access novel science and technology.

Our biotech-style operating model enables us to access the best science, both internal and external, which is a prerequisite for achieving scientific leadership. Further, our productivity and pipeline continue to benefit from investments in key capabilities, such as payer partnering, PHC, predictive science and clinical trial design.

In recent years, we have created a leaner, simpler and smaller organisation, focused on driving distinctive science across our key therapy areas. We have also made progress in co-locating our teams to our strategic R&D centres. The move to Gaithersburg, Maryland US is complete and the move to Cambridge, UK is progressing rapidly with 1,600 roles now located in Cambridge where the new R&D centre and corporate headquarters is under construction.

58

Record number of 'high-impact' publications



7

Launched seven diagnostic tests linked to our products



Research and early clinical development

Our two biotech units conduct innovative discovery research and early-stage development from initial target selection to Phase II trial completion. Our IMED biotech unit focuses on scientific advances in small

molecules, oligonucleotides and other emerging technologies and drug discovery platforms. The MedImmune biotech unit is responsible for global biologics research and early-stage development. Both units are responsible for delivering projects to our Global Medicines Development (GMD) unit for late-stage development.

Working collaboratively and fostering open innovation

In order to enhance our innovation capabilities and ensure that we have access to the best science, we are open to exploring new and different kinds of collaborations. Current small molecule partnership models include in-licensing of new chemical modalities and platforms; partnerships to leverage our compound collection to uncover novel target opportunities; and strategic collaborations designed to build our understanding of the mechanisms of disease. In biologics, we are actively engaged in strategic university research collaborations, clinical partnerships designed to explore the full potential of our immuno-oncology assets, and numerous in-licensing and joint development arrangements. In both biotech units our scientists work side-by-side with partner scientists, advancing science together as a single team.

In 2015, our IMED biotech unit announced several scientific collaborations. A number of collaborations enhanced the use of clustered regularly-interspaced short palindromic repeats (CRISPR) technologies across our discovery platforms, including those with the Innovative Genomics Initiative, the Whitehead Institute at the Massachusetts Centre for Technology, The Sanger Institute and Thermo Fisher Scientific. We also expanded our collaboration with Ionis Pharmaceuticals Inc. to discover and develop antisense therapies for cardiovascular, metabolic and renal diseases. MedImmune also forged several key collaborations in 2015, including a research collaboration with Joslin Diabetes Center to develop new medicines to treat diabetes, obesity, and related metabolic disorders. In addition, we launched a biotherapeutics research centre in collaboration with Cambridge Research UK. MedImmune was also very active in finalising collaborations to maximise the value of the immuno-oncology portfolio, such as through the externalisation

collaboration with Celgene to extend our extensive anti PD-L1 inhibitor programme, durvalumab, into trials for serious blood cancers. The recent exchange of chemical compounds with Sanofi is an example of our open innovation collaborations.

 **For more information on our collaborations please refer to the Oncology section from pages 34 to 38**

To better understand the biology of disease, our biotech units announced the first wave of projects from our joint venture with the MRC Laboratory of Molecular Biology and have agreed to support more than 80 PhD scholarships and eight clinical lectureships with the University of Cambridge.

Additionally, and through our IMED open innovation portal, our teams reviewed more than 350 proposals for new drug projects in 2015.

 **For an analysis of our R&D spend, please see Infrastructure on page 61**

Our personalised healthcare strategy

2015 saw us using the science of PHC to match many more patients to AstraZeneca medicines from which they are most likely to benefit. We launched seven diagnostic tests linked to our products – a total of 11 in two years. Three of our products (*Iressa*, *Lynparza* and *Tagrisso*) are now coupled with companion diagnostic tests that select patients for therapy based on their molecular profiles. PHC expanded in our clinical pipeline to over 80% – with over 60 planned drug launches by 2024 requiring a diagnostic test.

Our increasing investment in diagnostic partnerships achieved two world firsts: the EGFR mutation test for *Tagrisso* is the first diagnostic test for both circulating tumour DNA and tumour tissue (EU, with Roche Molecular Systems), while our PD-L1 Class I diagnostic (with Ventana) was the first immuno-oncology test launched in the US. In addition, we launched tests for tumour BRCA analysis for *Lynparza* (EU, with Myriad); for EGFR T790M for *Tagrisso* (US, with Roche Molecular Systems); for circulating tumour DNA EGFR for *Iressa* (EU, with Qiagen); and for PD-L1 (EU, with Ventana).

Scientific innovation is the life-blood of PHC. We are now expanding the benefits of PHC to patients in all core disease areas, such as asthma, where we are developing diagnostics for periostin and DPP-4 for potential use with tralokinumab (with Abbott) and lupus, where we are evaluating a type-I-IFN-inducible gene signature for use with anifrolumab (with Qiagen).

 **Oncology from page 34**

 **Respiratory, Inflammation and Autoimmunity from page 26**

Looking ahead, we announced a collaboration with the Montreal Heart Institute to search the genomes of up to 80,000 patients for genes associated with cardiovascular diseases and diabetes. Finally, our membership of the GENE Consortium, a public-private consortium with Genomics England in the UK, is aimed at accelerating the development of new diagnostics and treatments arising from the 100,000 Genomes Project.

 **Cardiovascular and Metabolic diseases from page 30**

Late-stage development

GMD is our R&D function focused on large Phase III clinical trial programmes across our therapy areas that support the approval, launch and reimbursement of new medicines, as well as life-cycle management. GMD also delivers studies that demonstrate evidence of how our medicines work in the 'real world' to help healthcare professionals and payers understand the therapeutic as well as economic value of our medicines. During 2015, we have continued to sharpen focus on our three therapy areas by identifying opportunities to collaborate on developing assets within our late-stage pipeline – for example, an externalisation agreement for the development of brodalumab for patients with psoriasis and the divestment of one of our established products *Caprelsa*, as a treatment for rare diseases.

Accelerating the pipeline and increasing efficiency

GMD is pushing boundaries to help ensure new treatments get to patients more quickly and still safely. Improvements include the development and use of smart clinical trials, data-modelling techniques and proactive

Research and Development continued



Values in action: We put patients first

Personalised healthcare aims to match medicines to patients who will benefit from them most. Advances in science mean we can now design diagnostic tests to tell us how individual patients are likely to respond to a medicine before prescribing it. We are also using new technology, such as blood-based tests in lung cancer, so that this science reaches more patients. Developing medicines in this way helps deliver the right medicine to the right patient and means better, more effective treatment.

regulatory approaches, as well as accelerating drug formulation and supply chain solutions. Examples in 2015 included presenting regulators with scientific rationale based on robust early clinical data in respect of *Tagrisso*, while fast delivery times to secure data from PEGASUS-TIMI 54, our 21,000-patient study for *Brilinta*, supported wider approvals in the US and additional regulatory submissions in the EU and US. GMD has created dedicated oncology delivery teams and recruited more medical expertise to bring potential new cancer treatments to patients more quickly, where there is significant unmet medical need.

 [See Therapy Area Review from page 24](#)

GMD also pursues opportunities to simplify processes to increase efficiency and productivity. A new information management system for all regulatory submissions, registrations and product changes provides improved access to documentation. We have also completed the outsourcing of routine regulatory maintenance and publishing tasks to a data-handling provider, so our internal resources can focus solely on activities to support our regulatory submission priorities. In clinical operations, we are adopting new technology and approaches to improve monitoring of clinical trials and ensure patients are protected.

Investment in disease area and scientific capabilities

With the consolidation of R&D activities to strategic centres, we continue to hire new employees to strengthen our disease area expertise and technical capabilities. This helps to meet the needs of our expanded late-stage portfolio and support the increasing number of clinical trials.

Payer and real-world evidence capabilities are helping us to show how our medicines may improve outcomes compared to other treatments, and to demonstrate how they may reduce the need for hospital or specialist care, and make a difference to patients' lives.

We continue to engage with medical experts to provide important insight into our drug programmes. Such engagements will

help ensure our medicines address the needs of patients as well as healthcare professionals. In support of this as detailed in the Pipeline and Therapy Area Introduction on page 24, we have signed an agreement with PatientsLikeMe.

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 a record number of 'high-impact' publications with 58 manuscripts in peer-reviewed journals with impact factor exceeding 15 (Thomson Reuters 5yr IF score). This represents an eight-fold improvement since our drive to publish in 'high-impact' journals in 2010, and demonstrates recognition of the quality of our science by industry and academic peers.

Responsible research†

We are committed to achieving scientific leadership and delivering life-changing medicines in a trustworthy and ethical manner. Our global standards of bioethics apply to all our research activity, whether conducted by us or third parties on our behalf.

Patient safety

Patient safety is very important to us and we strive to minimise the risks and maximise the benefits of our medicines. Through a pharmacovigilance programme, we monitor our medicines 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 also work with regulatory authorities worldwide to raise pharmacovigilance awareness.

Our patient safety team helps 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 has accountability for the benefit/risk profiles of our products in development and on the market. He provides medical oversight and enforces risk assessment processes to facilitate efficient and informed safety decision making.

Clinical trials and transparency

In 2015, we conducted clinical trials at multiple sites in various countries and regions as shown in the chart over. 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 for determining where we locate clinical trials 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 2015, approximately 36% of patients in our small molecule studies and 56% 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 also engage and collaborate with external scientific experts to support the design and interpretation of these clinical studies. Committees oversee study execution and progress, and we frequently collaborate with academic research organisations, particularly for larger multicentre outcome trials.

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.

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

During 2015, we implemented a number of changes in response to the new EU Clinical Trial Regulation, EMA's Policy 70 and the EFPIA/PhRMA Responsible Data Sharing principles.

Clinical trials by region

	Small molecule	Biologics
Europe	16%	14%
US/Canada	26%	34%
Asia Pacific	15%	6%
Central/Eastern Europe	27%	25%
Japan	3%	12%
Latin America	10%	7%
Middle East and Africa	3%	2%

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, thereby helping to develop effective, new and personalised medicines.

In carrying out this important area of research, we maintain policies and processes to ensure that we both 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 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, AstraZeneca may use human fetal tissue or embryonic stem cells. 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. AstraZeneca also insists its 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.

Animal research

We are committed to helping the public understand our use of animals in research and our methods for reducing, refining, or replacing them. Our commitment is reflected in our Global Bioethics Policy, and along with other signatories, progress has been published in the 2015 Annual Report on the 'Concordat on Openness in Animal Research in the UK'.

In response to a routine internal audit of our animal welfare assurance, we have improved our governance structure by providing a single point of accountability with oversight across AstraZeneca effective 1 January 2016. Our approach will provide consistent implementation of policies and procedures, and will ensure that all new organisations that join AstraZeneca have support in fulfilling their obligations under the Code of Conduct.

□ Further information on our governance structure can be found on our website, www.astrazeneca.com

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 2015, we used 182,055 animals in-house (2014: 194,162). In addition, 33,220 animals were used by CROs on our behalf (2014: 15,634).

† For further information on AstraZeneca's approach to doing business sustainably please refer to In the wider world from page 55 and on our website, www.astrazeneca.com.

Manufacturing and Supply



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

Overview

- > Developed a new transformational operations 2020 strategy focused on helping AstraZeneca to achieve its strategic purpose
- > Opened our new facility in Russia to supply local markets better
- > Announced plans to invest more than \$285 million in our Sweden biologics centre, and acquired a facility in the US to meet growing demand for manufacturing biologics
- > Continued to combine internal capabilities with cost-efficient external resources using established process for third party risk management including suppliers, their partners and local business development partners

\$285m

Plan to invest more than \$285 million in our Sweden biologics centre



11,236

Undertook 11,236 risk assessments in 2015



New operations strategy

In 2015, we developed a new transformational strategic framework for Global Operations to help ensure we are fit for the future. Our strategy, which is focused around a set of strategic imperatives and strong foundations, will drive our thinking and actions in the years ahead as we strive to become more agile, flexible and able to respond to patient and market needs.

New manufacturing facilities

Following the successful introduction of our Taizhou facility in China at the end of 2014, regulatory validation work continues at our Vorsino facility in Russia, which opened in 2015. This marks the largest foreign investment in the construction of a new pharmaceutical plant in Russia. First commercial production is scheduled to commence in early 2016, improving our ability to supply local markets. Also during 2015, we announced major investment plans to develop our capability in biologics, including the acquisition of Amgen's facility in Boulder, Colorado in the US, as well as a \$285 million investment in a new manufacturing facility in Södertälje, Sweden. These projects, in addition to a previously announced expansion plan at Frederick, Maryland US, will increase production capacity to support the growing demand for biologics, which represents half of our development pipeline.

Innovation

Partnerships and innovation are playing an increasingly important role for Operations in delivering medicines to patients. New science, and ways of working are continually assessed, with pilots progressed to challenge established practices. During 2015, we have seen innovative practices

Values in action: We put patients first

We have established a secure and low-cost supply chain in support of our Healthy Heart Africa programme (see page 51). Understanding the patient's circumstances was key as we worked to enable access to, and affordability of, high-quality anti-hypertensives to middle- and lower-income patients. We are working with our distributors and NGO partners to gather and share reliable data so that we can respond to changing patient needs.



employed around readiness for launch of *Tagrisso*, while our Healthy Heart Africa programme has been further developed as we aim to reach 10 million patients across Africa. Further pilots are already under development for 2016, as we look to improve the end-to-end supply chain performance.

Product quality and supply chain

We are committed to high product quality, which underpins the safety and efficacy of our medicines. To help assure compliance and quality, we maintain a comprehensive quality management system.

Our continuous improvement programme allows us to upgrade our systems and minimise environmental impact. By applying Lean methodology to our manufacturing plants and supply chain, we have been successful in reducing waste and inventory costs. We have also improved efficiency, quality, lead times, equipment effectiveness and overall customer responsiveness. We are continuing to establish more efficient processes, with global supply chain experts providing support throughout the organisation.

Regulation and compliance

Manufacturing facilities and processes are subject to rigorous regulatory standards. These continuously evolve and are not harmonised globally. They are also 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 2015, we hosted 38 independent inspections from 16 regulatory authorities. We reviewed observations from these inspections, together with the outcomes of internal audits, and, where necessary, implemented improvement actions.

Our strategy reflects our commitment 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 EFPIA and PhRMA.

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, which consists of four steps and applies to all our suppliers, downstream supply chain partners and local business development partners, 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 ensure the partner understands and can meet our standards. We conducted a total of 11,236 assessments in 2015, taking our total number of assessments to 13,845. Of these 4,613 were in the Asia Pacific region, followed by 4,115 in Europe and 3,538 in the Americas. The remaining 1,579 assessments relate to global suppliers and those based in the Middle East and Africa.

In addition, we conducted 49 audits on direct materials suppliers to ensure they employ appropriate quality, health and safety practices. 35% of suppliers met our expectations and 65% implemented improvements to address minor instances of non-compliance. During our due diligence process, we identified and rejected 326 suppliers, including 65 for reputational related concerns.

† For further information on AstraZeneca's approach to doing business sustainably please refer to In the wider world from page 55 and on our website, www.astrazeneca.com.

Sales and Marketing



Our return to growth strategy is built on maximising the potential of our strong portfolio of primary care and specialty care medicines by leveraging our global commercial presence, particularly in Emerging Markets. We are also investing in our Growth Platforms.

Overview

- > Our Sales and Marketing teams operate in more than 100 countries
- > Sales increased by 15% in China, which is now our second largest market
- > In the US, declines in revenue from *Nexium*, *Crestor* and *Synagis* were offset by strong performance of our Growth Platforms
- > Despite an austere macroeconomic climate, we continued to launch innovative medicines in Europe
- > Japan continues as one of our Growth Platforms with revenue growth of 4% in 2015
- > We worked closely with payers and providers to help deliver cost-effective medicines
- > We increased access to healthcare through programmes in Emerging Markets, serving some 3.5 million people
- > We reaffirmed our commitment to ethical sales and marketing activity through employee training, monitoring, corrective actions and reporting

Organisation and approach

To improve health and bring benefits to patients around the world, we need to ensure the right medicines are available and that patients have access to them. To that end, our Sales and Marketing teams, which comprised around 34,800 employees at the end of 2015, are active in more than 100 countries. In most countries, we sell our medicines through wholly-owned local marketing companies. We also sell through distributors and local representative offices.

We market our products largely to primary care and specialty care physicians. We aim to meet their needs by having highly accountable local leaders who understand their customers and focus on business growth.

We group our Sales and Marketing function into Japan, one of our Growth Platforms, and three Commercial Regions: North America (US and Canada); Europe; and International (Emerging Markets, Australia and New Zealand). Underpinning all our efforts is a commitment to operate responsibly and conduct sales and marketing activity in accordance with applicable laws and our Values.

For more information on Product Sales in our markets, please see Geographical Review from page 227

US

As the sixth largest prescription-based pharmaceutical company in the US, we have a 4.5% market share of US pharmaceuticals by sales value.

In 2015, sales in the US decreased by 6% to \$9,474 million (2014: \$10,120 million). Declines in revenue from *Nexium*, *Crestor*

100

Active in more than 100 countries



3.5m

Patient access programmes in Emerging Markets reached 3.5 million people by the end of 2015



and *Synagis* were partially offset by strong performance of our Growth Platforms, including *Farxiga*, *Bydureon* and *Brilinta*, the launches of *Lynparza* and *Tagrisso* as well as the impact of completing the acquisition of Actavis' rights to *Tudorza* and *Daliresp* in the US.

The Affordable Care Act (ACA) has had, and is expected to continue to have, a significant impact on our US sales and the US healthcare industry. In 2015, the overall reduction in our profit before tax for the year, due to discounts on branded pharmaceutical sales to Medicare Part D beneficiaries and an industry-wide excise fee, was \$786 million (2014: \$714 million).

 For more information on pricing pressure and the ACA, please see Marketplace from page 12 and Geographical Review from page 227

While there is no direct governmental price control for commercial prescription drug sales in the US, some publicly funded programmes, such as Medicaid and TRICARE (Department of Veterans Affairs), have statutorily mandated rebates and discounts. These effectively serve as price controls for such programmes. Other challenges include continuing pressure on pricing, and the availability and use of prescription drugs for commercial and public payers continues to increase. This is due to, among other things, an increased focus on generic alternatives. Increased generics use is also due to rising patient co-insurance or co-payments for branded pharmaceuticals and budgetary policies of healthcare systems and providers, including policies about the use of 'generics only' formularies. In 2015, 84.0% of prescriptions dispensed in the US were generic compared with 83.4% in 2014. While the adoption of a broad national price-control scheme in the near future is unlikely, increased focus on pharmaceutical prices and their impact on healthcare costs is likely to continue.

Europe

The total European pharmaceutical market was worth \$194 billion in 2015. We are the twelfth largest prescription-based pharmaceutical company in Europe with a 2.5% market share of prescription sales by value. Europe comprises countries as defined in Market definitions on page 247.

In 2015, our sales in Europe decreased by 6% to \$5,323 million (2014: \$6,638 million). Key drivers of the decline were continued competition from *Symbicort* analogues, ongoing volume erosion of *Atacand* and *Seroquel XR* following loss of exclusivity, pricing and volume pressure for *Crestor* and *Nexium*, and lower net pricing on *Synagis*. 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.

Established Rest of World (ROW)*: opportunities and challenges

In 2015, sales in Japan increased by 4% to \$2,020 million (2014: \$2,227 million). Strong performance of *Nexium* and *Crestor*, and the Diabetes franchise helped to drive this, offsetting the headwinds from generic competition. In Japan, we hold ninth position in the ranking of pharmaceutical companies by sales of medicines. Despite biannual 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. The higher EGFR prevalence in Asian markets makes Japan a key market for the launch of *Tagrisso* expected in 2016.

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 (CADTH), 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 66% funded by private payers and 34% with public plans.

Our sales in Australia and New Zealand declined by 19% in 2015. This was primarily due to the continued erosion of *Crestor* and *Atacand* by generic medicines. *Nexium* lost exclusivity in Australia in 2014 and generic medicines were launched.

Emerging Markets: expansion and collaboration

Emerging Markets, as defined in Market definitions on page 247, comprises various countries with dynamic, growing economies. As outlined in Marketplace from page 12, 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 \$5,822 million, AstraZeneca was the eighth largest, as measured by prescription sales, and the fourth fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2015.

In China, AstraZeneca is the second largest pharmaceutical company, as measured by sales. We are driving sustainable growth through strategic brands investment, expanded hospitals coverage and systematic organisational capability improvements. Sales in China in 2015 increased by 15% to \$2,530 million (2014: \$2,242 million). We delivered sales growth at above the growth rate of the market, and initiated several long-term market expansion programmes in therapy areas. The industry growth rate is expected to be moderated to high single digits, impacted by increased price pressure, hospital cost containment and delays in new product registration. 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 our Diabetes, Respiratory, Oncology, CV and Gastrointestinal portfolios. To educate physicians about our broad portfolio, we are selectively investing in sales capabilities where opportunities from unmet medical need exist. We are also expanding our reach through multi-channel marketing and external partnerships.

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


Sales and Marketing continued

Innovative collaborations are giving us access to novel science, technology and medicines. These complement and strengthen our portfolio. One example is our collaboration with FibroGen in China to develop and commercialise roxadustat, a potential first-in-class oral compound for treating anaemia in patients with CKD.

Increasing access to healthcare[†]

We have made significant progress in broadening the access to our products by making medicines more affordable and we are working towards greatly increasing access, particularly in low income countries, through our patient access programmes. Our efforts to improve affordability are particularly focused on ability to pay based on disposable household income. We continue to grow our capabilities and build on the experience of wellbeing initiatives and patient access programmes which provide discounts on our medicines and other patient services, for example FazBern in Brazil, Disfruto Mi Salud in Central America and the Caribbean, MAZ Salud in Mexico and Karta Zdorovia in Russia. We have significantly expanded these initiatives across Latin America, the Middle East and Africa, and Asia Pacific, and the number of patient access programmes in Emerging Markets has more than doubled since 2013, reaching 3.5 million patients in total by the end of 2015.

Improved access is bringing down healthcare barriers, particularly in developing countries. In 2015, we expanded our efforts in Africa to enable greater access to hypertension medication and other essential services for patients who are otherwise unable to access medication or other forms of treatment.

 For more information, please see the [Healthy Heart Africa case study](#) over

Pricing and delivering value

Our global pricing policy helps to ensure appropriate patient access while optimising the sustained profitability of our products. When setting the price of a medicine, we consider its full value to patients, payers and society generally. We also pursue a flexible pricing approach. For example, we support the concept of differential pricing, provided that appropriate safeguards are in place to

help ensure lower-priced products reach the patients who need them and are not diverted for sale and use in more affluent markets.

Our medicines help treat unmet medical need, improve health and create economic and therapeutic benefits. Effective treatments can lower healthcare costs by reducing the need for more expensive care, preventing more serious and costly diseases and increasing productivity by reducing or preventing days lost to illness. Nevertheless, pricing pressure remains, as outlined in Marketplace on page 12. We are acutely aware of the economic challenges faced by payers and remain committed to delivering value to payers and patients alike. We work closely with payers and providers to understand their priorities and requirements. We also conduct real-world evidence studies to demonstrate how our products improve health outcomes, offer value and support cost-effective healthcare.

Sales and marketing ethics[†]

We are committed to employing high ethical standards of sales and marketing practice worldwide. This is consistent with our Global Policy on Ethical Interactions. We report publicly on the number of

- > confirmed breaches of external sales and marketing codes
- > breaches of our Code of Conduct or supporting policies by employees and contractors in our Commercial Regions, and associated corrective actions.

During 2015, we continued to train employees on the global standards that govern the way we operate. We have comprehensive processes as well as dedicated compliance professionals who monitor adherence to our Code of Conduct and Global Policies. These professionals also support our line managers locally in supervising their staff. A network of nominated signatories review our promotional materials against applicable requirements. In 2015, audit professionals also conducted compliance audits on selected marketing companies.

We identified 11 confirmed breaches of external sales and marketing regulations or codes in 2015 (2014: six).

There were 1,749 instances, most of them minor, of non-compliance with our Code of Conduct, Global Policies or related control standards in our Commercial Regions, including instances by contract staff and other third parties (2014: 1,847).

We removed 339 employees or contractors from their roles as a result of these breaches (a single breach may involve more than one person). We also formally warned 490 others and provided further guidance or coaching on our policies to 1,476 more. The most serious breaches were raised with the Audit Committee.

US Corporate Integrity Agreement and The Physician Payments Sunshine Act reporting

In April 2010, AstraZeneca signed an agreement with the DOJ to settle an investigation relating to the sales and marketing of *Seroquel* IR. The requirements of the associated Corporate Integrity Agreement (CIA) between AstraZeneca and the Office of the Inspector General of the US Department of Health and Human Services (OIG) included a number of monitoring and self-reporting obligations that differ from the self-reporting required by authorities in the rest of the world. To meet these obligations, AstraZeneca provided notices to the OIG describing the outcomes of particular investigations potentially relating to violations of certain laws. We also submitted an annual report to the OIG, summarising monitoring and investigation outcomes relevant to the CIA requirements. Under the CIA, AstraZeneca also disclosed, on a publicly available website, certain payments to US physicians and institutions. The CIA was for a period of five years and successfully concluded on 30 April 2015. AstraZeneca continues to maintain a robust compliance framework to ensure compliance with all applicable laws and regulations, and that the business is operating with high ethical standards. AstraZeneca also continues to report to the US government, detailed information relating to payments to physicians and teaching hospitals in the US, as required by The Physician Payments Sunshine Act.

[†] For further information on AstraZeneca's approach to doing business sustainably please refer to In the wider world from page 55 and on our website, www.astrazeneca.com.



Healthy Heart Africa

Healthy Heart Africa (HHA) is our innovative programme to support African governments in reducing the burden of heart disease and, specifically, hypertension. This challenge is huge. According to WHO, Africa is home to the highest prevalence of adults living with hypertension and an estimated 46% have high blood pressure.

The programme was launched in October 2014 in collaboration with the Kenyan Ministry of Health and a portfolio of well-respected implementing partners. Addressing non-communicable diseases such as hypertension in middle- and low-income populations in a healthcare system that, historically, has prioritised communicable diseases and infections, remains a challenge. However, in a short space of time, the programme has achieved remarkable progress which will enable HHA to expand operations to other geographies in order to achieve our ambition of reaching 10 million hypertensive patients across sub-Saharan Africa by 2025 – in line with WHO's goal of a 25% reduction in the prevalence of raised blood pressure by that date.

By the end of 2015, we had:

- > Screened one million patients in Kenya.
- > Trained over 2,600 healthcare workers, including doctors, nurses, community health volunteers and pharmacists to provide education and awareness, screening and treatment services for hypertension.
- > Equipped at least 250 health facilities – ranging from small dispensaries staffed by a handful of people to large-scale facilities – to provide hypertension services, including the establishment of secure supply chains for low-cost, high-quality antihypertensive medicines.
- > Worked with the Ministry of Health and key scientific societies to develop a hypertension treatment protocol.

- > Created training materials for healthcare providers and community health workers on hypertension prevention, screening, diagnosis and treatment. In many cases, these community healthcare workers had never received training about hypertension before.

To reach our objectives, HHA has adopted an innovative model:

- > Raising awareness by leveraging community health worker networks.
- > Training providers and driving care to lower levels in the healthcare system.
- > Ensuring access to and availability of treatment by ensuring that healthcare workers are equipped to provide screening and have a consistent supply of appropriate medicines.

“We especially appreciate AstraZeneca's approach to partnership in order to design and implement a leading programme that is integrated into healthcare platforms.”

Dr Joseph Kibachio, Head of Division of Non-Communicable Diseases, Ministry of Health, Kenya

1m

Screened one million patients in Kenya for hypertension in 2015



Watch the video at www.astrazeneca.com



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 11,700 permanent employees to help us achieve our strategic priorities
- > Continued to offer customised leadership programmes through MIT
- > Established a global personal development campaign and defined associated targets
- > Increased the diversity of our leadership
- > Continued the STAR programme to teach emerging talent about enterprise leadership
- > Continued to simplify our organisational structure

We value the talents and skills of our 61,500 employees in more than 100 countries. Our people strategy, which supports our strategic priority of being a great place to work, is 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.

Build and develop organisations and capabilities

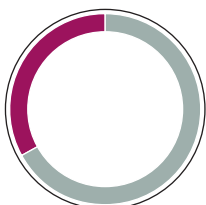
During 2015, we hired 11,700 permanent employees. Additional employees joined us through acquisitions, most notably the transition of 560 BMS employees at our Mount Vernon, Indiana US manufacturing site. We are committed to hiring and promoting talent ethically and in compliance with applicable laws. 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.

Gender diversity

Board of Directors of the Company 12

● Male
● Female

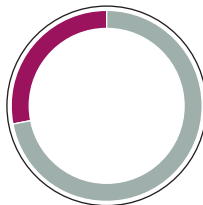
67%
33%



Directors of the Company's subsidiaries* 360

● Male
● Female

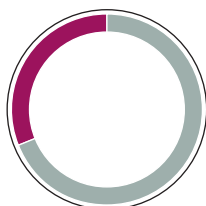
72.1%
27.9%



SET* 13

● Male
● Female

69%
31%



AstraZeneca employees 61,500

● Male
● Female

50.2%
49.8%



* For the purposes of section 414C(8)(c)(iii) 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.

A global business

61,500

employees by geographical area



Co-locating around three strategic R&D centres

- > Cambridge, UK (1,600 employees)
- > Gaithersburg, Maryland US (2,900 employees)
- > Gothenburg, Sweden (2,200 employees)



Hiring over recent years means that employees with less than two years' service now represent 36% 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 below, which shows an increasing concentration in Emerging Markets.

Voluntary employee turnover increased marginally to 9.2% in 2015 from 8.8% in 2014. However, the voluntary employee turnover rate among our high performers in 2015 reduced to 4.0% from 6.8% in 2014. 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 2015, we reviewed our talent management and succession planning processes, and implemented a revised approach which is focused on ensuring we have robust succession plans in place for our most business critical roles. Embedded in this new approach is a focus on both external sourcing and the development of our people to ensure that we have the right capabilities and leaders in place to deliver our strategy.

As shown in the gender diversity figure on the previous page, women comprise 49.8% of our global workforce. There are currently four women on our Board (33%). 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 42.0% in 2015, which exceeded our Scorecard target of 41% for this measure. We continue to hire high-quality leaders: 13% of the approximately 130 leadership roles that report to our senior leadership team joined AstraZeneca in 2015. 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 2015, 15.6% 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), which exceeded our Scorecard target of 13% for this measure.

To maximise our employees' potential, we use leadership programmes, both online and instructor-led, to help build the right capabilities and culture. In 2015, we continued our programme for emerging leaders with the Massachusetts Institute of Technology (MIT). These programmes aim to foster openness, inclusivity and innovation and are a part of a wider effort

to offer leaders at all levels of the organisation appropriate, globally consistent leadership development opportunities.

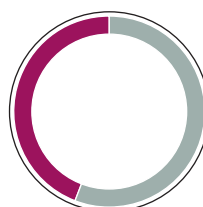
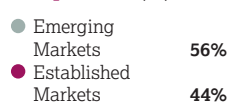
In 2015, a further 270 people participated in our various talent development programmes. We continued to offer the STAR programme which teaches our emerging talent about enterprise leadership and provides an opportunity to discuss AstraZeneca case studies and interact with senior leaders. We also continued our Insight Exchange programme to help foster diversity and inclusion, and strengthen our pool of emerging talent.

Our efforts received external recognition in 2015. AstraZeneca was ranked second among 400 businesses in Bloomberg's inaugural survey of 'The best place to work in corporate Britain', while the National Association for Female Executives ranked us as one of its 50 leading companies for the seventh year running. We also featured among Working Mother Magazine's 100 Best Companies.

Drive a vibrant, high-performing culture

Continuing our emphasis on high performance, in 2015 we implemented a single global performance management framework and approach. We require every employee to have been set 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.

Sales and Marketing workforce composition (%)



Employees continued



Values in action:

We are entrepreneurial

People development is a key global priority. In order to encourage a growth mindset and connect individual development to achievement of our strategic ambitions, we held People Development Week events in 2015. AstraZeneca employees participated in more than 70 face-to-face events held in more than 50 countries. Engagement by staff was demonstrated by 6,600 comments on people development in our sample employee surveys.

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 26 to the Financial Statements, from page 182.

We regularly conduct employee surveys and an area of improvement highlighted by our FOCUS 2014 employee survey was the need to further simplify our organisation, and we use the scores for survey questions relating to simplification as a measure of our success towards achieving our Scorecard objective.

Across the Group, individuals, teams and departments are encouraged to identify opportunities for simplification by removing obstacles to efficiency and improving the way in which they work. In 2015, these efforts were highlighted and shared in a virtual 'Simplification Week' using our new global intranet, Nucleus, and our global social platform, Chatter.

To support our drive for simplification further, we continue to widen the average span of control (7.2 employees reporting to each manager in 2015, up from 6.3 in 2012) and limit the number of reporting layers in the organisation. We believe this will increase the speed of decision making, drive accountability and improve communication.

We continue to track our progress with these initiatives through our sample employee survey which shows an eight percentage point increase in the view that AstraZeneca has been successful at eliminating obstacles to efficiency when compared to FOCUS 2014.

Generate a passion for people development

We endeavour to ensure that all our employees use their talents and abilities to the full and are provided opportunities for development. In addition to simplification, another area of improvement highlighted by our FOCUS 2014 employee survey was career development. As a result, we are strengthening our efforts in this area. In 2015, for example, we conducted over 70 Development Week events covering almost all our sites globally.

We encourage employees to take ownership of their own development and encourage leaders to spend time discussing their employees' development.

The ability of managers and leaders to develop their employees is critical, and is measured through our sample employee surveys. The scores for the survey questions pertaining to people development now contribute to our global Scorecard objective of being a great place to work.

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 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 2015, we completed a human rights labour review in all countries where we have a presence. The review focused on ILO core themes, including freedom of association and collective bargaining, child labour, discrimination, working hours and wages. In this second survey we added questions

on the living wage, data management and recruitment and the results have remained positive. Where a gap to ILO minimum standards was identified, we are putting in place local plans to close those gaps. As well as measuring living wage progress internally, we also conducted an independent external review so that we can assess developments in this area to inform our approach better. As a first step we are seeking accreditation from 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

As outlined in Strategic priorities on page 16 and 17, in 2013, we announced plans to invest in three strategic R&D centres which are shown on the map on the previous page. This affected employees in the US and the UK. We encouraged and supported employees to relocate and have made good progress. For example, 1,600 employees now work in Cambridge and, of these employees, 500 have relocated from other sites in the UK. In addition to the 410 employees hired in 2015, over the next two years we expect to hire approximately a further 600 new employees to Cambridge. We are using interim infrastructure in and around Cambridge to house these employees until our new site is ready. For employees who do not accept offers to relocate to Cambridge we provide career support, outplacement support and competitive severance packages.

 For more information on our restructuring programme, please see Financial Review from page 68

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.

† For further information on AstraZeneca's approach to doing business sustainably please refer to In the wider world from page 55 and on our website, www.astrazeneca.com.

In the wider world



Our employees are critical to achieving our strategic priorities. To realise our full potential, however, we also depend on a wider set of stakeholders and are committed to operating our business in a sustainable manner – that is, in a way that delivers real value for our company, our planet and society as a whole.

Our stakeholders include the patients and physicians for whom we provide medicines for some of the most serious diseases, and the universities and institutes that collaborate with our scientists. Governments, regulators, payers, suppliers, other commercial organisations and the communities in which we operate are among our other stakeholders. We outline our stakeholder relationships throughout our Business Review, including Research and Development from page 42 and Sales and Marketing from page 48. In Manufacturing and Supply from page 46, we examine our relationships with suppliers and our commitment to working only with those that embrace standards of ethical behaviour consistent with our own. This commitment extends to joint venture and co-promotion partners, and research and licensing partners.

Partnering

As outlined in Strategic priorities on page 16 and 17, business development, specifically partnering, is an important element of our business. It supplements and strengthens our pipeline and our efforts to achieve scientific leadership. As noted in Research and Development from page 42, we strive to access leading science from within and outside our laboratories. Our partners include academia, governments, industry, scientific organisations and patient groups.

We pursue strategically aligned value-enhancing business development opportunities and focus on

- > increasing early-stage research transactions and academic alliances
- > exploring value-creating peer collaborations

Overview

- > Over 240 major or strategically important business development transactions over the past three years
- > Created external Sustainability Advisory Board to help confirm our sustainability priorities and shape our strategy
- > Undertaking a materiality assessment to identify the most significant sustainability issues for AstraZeneca
- > Met our aggressive 2010 to 2015 carbon footprint reduction target
- > Surpassed our 2015 reduction targets for lost time injury and illness rate and vehicle collision rate
- > Finalised, with SET and Board approval, a new 2016 to 2025 Safety, Health and Environment Strategy
- > Community investment strategy focuses on healthcare in the community and science education
- > Young Health Programme has reached over 1.4 million young people

240



More than 240 major or strategically important business development transactions over the past three years

1.4m



Young Health Programme has reached over 1.4 million young people

In the wider world continued

Vehicle collisions

Year	Collisions per million km	Target
2015	4.15	5.60
2014	4.66	6.10

Lost time injury/illness

Year	Lost time injury/illness rate per million hours worked	Target
2015	1.37	1.91
2014	1.59	2.10

> pursuing partnering, in-licensing and acquisitions to strengthen our therapy area portfolios.

Our business model also encompasses externalisation as a component of our portfolio management strategy. This includes strategic collaborations to broaden and accelerate the development of key pipeline assets in our three therapy areas. We also leverage opportunities in other areas where we retain an interest in the future development of projects. Our collaborations with Lilly and Celgene are examples of this approach. For more information on these externalisation partnerships, see Business model on pages 8 and 9, and Financial Review from page 62. We also divest medicines that can be deployed better by a partner with a primary focus in the relevant area.

Over the past three years we have completed more than 240 major or strategically important business development transactions, including some 122 in 2015. Of these transactions, 24 were related to clinical stage assets or programmes, 48 to pre-clinical assets or programmes and 11 to PHC and biomarkers. Thirty-nine transactions helped expand our biologics capabilities. Approximately 30 agreements related to our expanding commitment to Open Innovation. Acquisitions completed in the year included the acquisition of Actavis' respiratory franchise in the US and the acquisition of ZS Pharma. Agreements regarding the acquisition of Takeda's respiratory portfolio and the acquisition of a controlling equity position in Acerta Pharma were signed in 2015. These were not, however, included in the 2015 data as the Takeda transaction is due to complete

Sustainability framework

A sustainability framework is embedded in the way we operate:



Sustainability Advisory Board

Established in 2015 and will meet 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 will also help 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 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 will focus 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

The Working Group of SET function representatives supports the Council. The Working Group reviews issues with the potential to impact AstraZeneca's sustainability agenda. As appropriate, it prepares proposals for the Council's consideration.



Stakeholders

Regular engagement with 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.

in the first half of 2016 and the transaction with Acerta Pharma completed in February 2016. In addition, four transactions that contribute to Externalisation Revenue were completed in 2015 with a further 10 divestments or out-licences also completed.

For more information on our partnering activity in 2015, please see Therapy Area Review from page 24, Research and Development from page 42, Financial Review from page 62 and Note 24 to the Financial Statements from page 173

Sustainability

We want to be valued and trusted by our stakeholders as a source of great medicines over the long term. That means operating in a way that recognises the interconnection between business growth, the needs of society, and the limitations of our planet. Our sustainability efforts are aligned to, and support the delivery of, our business strategy in five core areas that are most relevant to our business

- > Increasing access to healthcare (see page 50 and Healthy Heart Africa on page 51)
- > Natural resource efficiency (below)
- > Responsible research (from page 44)
- > Ethical business practices (see Working with suppliers, Sales and marketing ethics and Community investment on pages 47, 50 and 58 respectively)
- > Being a great place to work (see Develop a strong and diverse pipeline of leaders, Human rights and Safety, health and wellbeing on pages 53, 54 and 57 respectively).

Further information about our sustainability agenda is available on the Sustainability pages on our website, www.astrazeneca.com

During 2015, we commissioned an independent think-tank to review our current focus areas, examine our areas of strength and weakness, and help identify our priorities going forward. An internal focus group meeting took place to refine and calibrate the high-level findings. This involved assessing risks and opportunities, as well as the current level of integration, for each issue. This assessment is continuing and, will become the foundation for the priorities and improvement targets that define the next stage of our journey. Our goal is to ensure that sustainability is effectively aligned to our business strategy and truly embedded into the way in which we operate and define success.

For more information on our approach to sustainability, benchmarking and assurance, see Sustainability: supplementary information from page 234 and the Sustainability pages on our website, www.astrazeneca.com

Safety, health and wellbeing

We work to promote a safe, healthy and energising work environment in which our employees and partners are able to express their talents, drive innovation and improve business performance. Our five-year target period ended in 2015. The targets for 2015 included

- > no fatalities
- > lost time injury/illness rate per million hours worked of no more than 1.91 (a 25% reduction from the 2010 baseline)
- > no more than 5.6 collisions per million kilometres driven (40% reduction from 2008 baseline)
- > at least 80% of sites and marketing companies to offer six essential health activities.

Our highest priority remains driver safety, particularly among our sales force who form the largest group of employees driving on AstraZeneca business. We monitor performance centrally to assess progress and identify areas for improvement. In 2015, we delivered our five-year target for reducing collisions per million kilometres driven, achieving a 55% reduction from baseline. We regret, however, that one employee was killed in a traffic accident while driving on AstraZeneca business. We carried out a detailed investigation into this accident and developed an action plan to address the findings. Actions were monitored and what was learnt from the incident was shared widely across the business. Having already achieved our 2015 lost time injury/illness rate target two years early, we achieved a further reduction in 2015. This equates to a 46% overall reduction from the 2010 baseline.

The 2015 health and wellbeing target was missed, with 60% of sites offering six essential health activities, compared to the 80% target. Although this is disappointing, 84% of sites now offer at least five activities, compared to only 28% in 2011.

Natural resource efficiency

Our 2015 targets¹ included reducing

- > operational greenhouse gas footprint to 714,375 tonnes CO₂

Operational greenhouse gas footprint emissions (tonnes CO₂)

2015	704,073
2014	735,218
2013	704,273

Waste production (tonnes)

2015	38,452
2014	35,797
2013	32,750

Water use (m³)

2015	3,932,598
2014	3,786,963
2013	3,714,674

Note: Significant site purchases in 2014 and 2015 have been absorbed into the annual data without historical rebasing of data.

- > hazardous waste to 0.633 tonnes/\$m sales and non-hazardous waste to 0.473 tonnes per employee
- > water use to 3.4 million m³.

We are working to reduce our greenhouse gas emissions by, among other things, improving energy and fuel efficiency and pursuing lower-carbon alternatives to fossil fuels. During 2015, our air and road travel and freight transport emissions decreased due to greater achievement in switching freighting of goods from air to sea and reducing business air travel significantly. Procurement of energy from certified renewable sources increased to represent 6.1% of total consumption.

Our pMDI inhaler therapy relies on hydrofluoroalkane (HFA) propellants which affects our carbon 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 greenhouse gases. Excluding emissions from patient use of our inhaler therapy, our aim by 2015 was to reduce our operational greenhouse gas footprint by 20% from our 2010 level. We achieved this, with our operational greenhouse gas footprint totalling 704,073 metric tonnes in 2015, a reduction of 21.2% from our 2010 baseline.

For more information on carbon reporting, please see Sustainability: supplementary information from page 234

In the wider world continued



Values in action: Do the right thing

Michael Baldinger, CEO of RobecoSAM, said: "As one of the top-scoring companies in the pharmaceutical industry, AstraZeneca PLC has qualified for inclusion in the 2016 Sustainability Yearbook and has received the Silver Class distinction for its excellent sustainability performance."

Waste management is another key aspect of our commitment to minimise environmental impact. We aimed to reduce our hazardous and non-hazardous waste by 15% from our 2010 levels, indexed appropriately. While waste prevention is an essential goal, we seek to maximise treatment by material recycling and avoiding landfill disposal when prevention is impractical. In 2015, our total waste was 38,452 metric tonnes with a tonnes/\$m index of 1.56. We have reduced hazardous waste by 22% since 2010, due principally to changing production patterns and major investment at a UK manufacturing site in 2012 to enable recycling and reuse of solvent wastes. Hazardous waste generation indexed to \$m revenues increased 5%, missing our 2015 target. We reduced non-hazardous waste by 14% since 2010, but when indexed against staff numbers the metric has not improved due to staff reductions since the baseline was set.

We recognise the need to use water responsibly and, where possible, to minimise water use in our facilities. To reach our 2015 water use reduction target of 25% from 2010 levels, we initiated water conservation plans at our largest sites. In 2015, our water use was 3.9 million m³, a reduction of 14% from our 2010 baseline. This fell some distance short of achieving our very ambitious five-year target. Water use indexed to revenues was 159 m³/\$m (+16% from 2010 baseline).

We are also working on measuring and reporting the environmental impact of our external manufacturing activity and encourage setting of appropriate environmental targets with our suppliers. We believe we have captured 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 Safety, Health and Environment (SHE) improvement efforts going forward.

We continue to integrate environmental considerations across a medicine's entire life-cycle, from discovery, research and development to manufacturing, commercialisation and disposal. We follow a progressive compliance programme to ensure that our manufacturing emissions

of APIs do not exceed our internal standards for safe discharges at our manufacturing sites and we periodically conduct compliance assessments. We also follow a progressive approach to ensure ecopharmacovigilance. This involves regularly reviewing emerging science and literature for new information that might impact the environmental risk management plans for our products.

Further information, including environmental risk assessment data for our medicines, is available on our website, www.astrazeneca.com

New Safety, Health and Environment Strategy

In 2015, we finalised a new 2016 to 2025 SHE Strategy to build on our 2010 to 2015 performance and ensure that we are protecting the health and safety of our people and doing our 'fair share' to protect the planet. As an output of this strategic initiative, we have established a set of targets aimed at keeping AstraZeneca among the sector leaders in SHE performance. Our targets for 2025 are shown over.

Achieving these targets during a period of expected strong business growth will require significant business engagement and investment in resource efficiency. In light of this challenge, and in recognition that we narrowly missed our 2010 to 2015 water and waste efficiency targets, we have established a dedicated fund for capital projects that can drive substantial improvement in natural resource efficiency. We disclose our carbon and water performance and targets to external indices including the Carbon Disclosure Project (CDP). In the build up to COP 21, the 2015 Paris Climate Conference, we signed up to the CDP commitments for science-based targets and public disclosure of information associated with climate change performance.

Community investment

Our global community investment strategy focuses on healthcare in the community and science education. We are committed to operating responsibly, which means supporting our community and maximising the benefit of our investment for all stakeholders. For example, 2015 was the fifth 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 2015, we spent a total of approximately \$680 million (2014: approximately \$880 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. Through our three patient assistance programmes⁴ in the US we donated products valued at an average wholesale price of over \$617 million (2014: over \$800 million). We also donated products worth over \$17 million, valued at average wholesale price, to charitable organisation AmeriCares.

Young Health Programme

We continued to develop the three strands of our Young Health Programme (YHP): advocacy; research; and evidence generation. These on-the-ground programmes focus on the primary prevention of non-communicable diseases (NCDs) and associated adolescent risk behaviours. With over 1.4 million young people in communities across five continents directly provided with the skills and information they need to improve their health, we have well exceeded our Clinton Global Initiative Commitment to Action of reaching 250,000 young people directly by the end of 2015. Over 14,600 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 12,000 frontline health workers in adolescent health.

We continue to support research evidencing the importance of adolescence in future health, and undertake advocacy activities to ensure adolescent health and the prevention of NCDs are global and local priorities. The engagement and involvement of youth is at the core of the YHP. Activities in 2015 included commissioning research on NCD risk behaviours and participation in the development of an NCD prevention chapter for UNICEF Facts for Life book. We also funded YHP side meetings at WHO Geneva (May 2015) and United Nations General Assembly in September 2015.

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

New Safety, Health and Environment Strategy targets, 2016 to 2025



Eliminate workplace accidents and illnesses

Accidents:

75%

75% reduction in total injury rate from 2015 baseline

Health and wellbeing:

80%

80% of sites/marketing companies have all four 'Essential Health Activities'²

Driver safety:

55%

55% reduction in collisions per million kilometres driven

Protect natural resources

Carbon:

30%

Compared to a 2015 baseline, operational carbon at the same level and reduce overall carbon intensity by 30%³

Waste:

10%

10% absolute reduction from 2015 baseline

Water:

Cap usage from 2015 baseline

90%

90% of API syntheses meet resource efficiency targets at launch and establish equivalent targets for biologics

Ensure the environmental safety of our products

Ensure effective environmental management of our products from pre-launch through to product end-of-life

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 April 2015 we donated £50,000 via British Red Cross to the Nepal Earthquake Appeal, \$200,000 in July to fund the replenishment of the Kuala Lumpur Emergency Response Unit and £50,000 in September to Europe Refugee Crisis Appeal. In December, and as part of wider AstraZeneca support for those affected by the floods in Chennai, where over 1,000 AstraZeneca employees are based, we donated \$30,000 to SEWA International.

¹ Figures have been revised from those previously published to incorporate our biologics capabilities into our targets. Our targets for 2011 to 2015 were set in 2010.

² Healthy Eating & Drinking, Tobacco Cessation, Physical Activity, Workplace Pressure Management.

³ Carbon target follows the science and uses the Science-Based Target Setting tool developed by the World Resources Institute. Operational footprint = energy and process emissions, business travel, waste incineration, freight/logistics, 1st tier supply chain energy and patient use of inhalers. Carbon intensity = CO₂ tonnes/\$m sales.

⁴ For 2015 we have revised our reporting to reflect what was shipped from AstraZeneca for use in our Patient Assistance Programs as opposed to what was actually dispensed to patients, and have also moved to reporting the wholesale acquisition cost as opposed to average wholesale price. As a result, the 2015 numbers reported are lower than reported in 2014.

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 27 to the Financial Statements from page 186. For more information on the risks relating to patent litigation and early loss and expiry of patents, please see Risk from page 212.

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 210 and 211 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 pending patent protection. RDP generally expires prior to patent expiry in all major markets. If a product takes an unusually long time to secure marketing approval, or if patent protection has not been secured, has expired or has been lost, then RDP may be the sole IP right protecting a product from copying. Generic manufacturers 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.

Under the Generating Antibiotics Incentives Now Act, the FDA may grant Qualified Infectious Disease Product (QIDP) status. An antibiotic achieving QIDP status is granted five years' exclusivity while QIDPs that are also NCEs are entitled to 10 years' exclusivity, extending to 12 years' if the disease state is an orphan. The period of exclusivity granted to a product with QIDP status runs concurrently with any pending or granted patent protection.

Compulsory licensing

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

Infrastructure

The Group owns and operates R&D and production facilities and conducts sales and marketing activities around the world. Significant information technology and information services resources support these activities.

R&D resources

We have approximately 8,900 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 and Waltham, Massachusetts), Japan (Osaka) and China (Shanghai). Our biologics sites are located in the UK (Cambridge) and in the US (Gaithersburg, Maryland and Mountain View, 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. Our strategic expansion in Emerging Markets continues and includes the ongoing growth of our R&D facility in China (Shanghai).

R&D spend analysis

	2015	2014	2013
Discovery and early-stage development	39%	47%	55%
Late-stage development	61%	53%	45%
Core R&D expenditure ¹	\$5,603m	\$4,941m	\$4,269m

¹ Reported R&D expenditure was \$6.0 billion (2014: \$5.6 billion; 2013: \$4.8 billion).

In 2015, Core R&D expenditure was \$5.6 billion in our R&D organisation (2014: \$4.9 billion; 2013: \$4.3 billion). In addition, we spent \$1,341 million on acquiring product rights (such as in-licensing) (2014: \$907 million; 2013: \$635 million). We also invested \$258 million on the implementation of our R&D restructuring strategy (2014: \$497 million; 2013: \$490 million). The allocations of spend by early-stage and late-stage development are presented in the R&D spend analysis table above.

Manufacturing and supply resources

Our principal small molecule manufacturing facilities are in the UK (Avlon and Macclesfield), Sweden (Gärtna and Södertälje), the US (Newark, Delaware;

Westborough, Massachusetts; West Chester, Ohio; Mount Vernon, Indiana and Coppell, Texas), China (Wuxi and Taizhou), Russia (Vorsino), France (Reims and Dunkerque), Japan (Maihara), Australia (North Ryde), Indonesia (Jakarta), Egypt (Cairo), India (Bangalore), Puerto Rico (Canóvanas), Germany (Wedel), Mexico (Lomas Verdes), Brazil (Cotia) and Argentina (Buenos Aires). Our Taizhou supply site won the 2015 Facility of the Year award in the category of Project Execution by the International Society for Pharmaceutical Engineering.

We operate sites for the manufacture of APIs in the UK and Sweden, complemented by the efficient use of external sourcing. Our principal tablet and capsule formulation sites are in the UK, Sweden, Puerto Rico and the US. We also have major formulation sites for the global supply of parenteral and/or inhalation products in Sweden, France, Australia and the UK.

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

At the end of 2015, approximately 12,500 people at 29 sites in 17 countries were working on the manufacture and supply of our products.

Information technology and information services resources

At the end of 2015, our IT organisation comprised approximately 2,800 people across our sites in the UK (Alderley Park and Macclesfield), Sweden (Södertälje and Gothenburg), the US (Wilmington, Delaware and Gaithersburg, Maryland), and our new technology centre in India (Chennai). A further 250 IT people worked in our R&D and operations sites and key marketing companies.

In the beginning of 2014, we launched a wide-ranging IT Transformation Programme to better support our business priorities. Since then, we have made various changes to our operating model and organisational structure to improve efficiency, responsiveness and innovation.

Our IT vision is to deliver world-class performance in terms of speed, quality, cost and innovation. At the same time, we are relying on IT to enable simplification of our business processes. To achieve this we need to improve our current performance significantly while reducing our overall spend. We will measure our success by tracking customer satisfaction and recording the number and severity of incidents with business impacts as well as the speed with which we respond to and mitigate such incidents. We will also take into account project delivery and cost (absolute and as a percentage of revenue) as compared to industry benchmarks.

Protecting our IT systems, IP and confidential information against cyberattacks is a key concern. Our IT organisation is constantly 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 are equally vigilant in monitoring our systems and data with sophisticated technology. This includes educating our employees about cybercrime, internet use and best practices to mitigate the risk of attack.

Financial Review



In 2015, a double-digit increase in our Growth Platforms helped our top-line to remain resilient, despite headwinds that included the loss of exclusivity of *Nexium* in the US.

This, combined with a strong gross margin and disciplined cost management, allowed us to continue to make important long-term investment in our three main therapy areas, while delivering a 7% growth in Core earnings.

In 2015, our financial performance reflected continued progress from our Growth Platforms, which grew by 11% in the year and now contribute 57% of Total Revenue, which increased by 1% to \$24.7 billion in the year. Our Respiratory franchise grew by 7% during 2015, driven by a strengthening portfolio, our Emerging Markets business and the availability of new products in the US and EU. *Brilinta/Brilique* grew by 44% in the year, with particular strength in the US and Emerging Markets, led by China, and Diabetes delivered an impressive performance, with encouraging growth driven by *Farxiga/Forxiga* and the *Bydureon* Pen. Strong growth in Emerging Markets continued throughout the year with China, Brazil and Russia all delivering double-digit increases and our Japan business maintained solid growth, with *Symbicort*, *Crestor* and *Nexium* all maintaining leading market share positions in a competitive market environment. For the first time, New Oncology, which includes the launches of *Lynparza*, *Iressa* (US) and *Tagrisso*, was included as a Growth Platform, given our belief in its long-term importance for our future growth.

The performance of the Growth Platforms was supplemented by over \$1 billion of Externalisation Revenue arising from entering into collaborations including the

strategic collaboration in haematology with Celgene Corporation and the co-development and co-commercialisation arrangement with Daiichi Sankyo for *Movantik* in the US. These offset the headwinds from ongoing patent expiries, including that of *Nexium* in the US in February 2015, as well as the adverse impacts from *Synagis* guideline changes in the second half of 2014.

Excluding the impact of Externalisation Revenue, the Core Gross Profit margin increased by one percentage point, helped by the mix of Product Sales and manufacturing efficiencies, and Core SG&A costs declined by 2% to \$9.3 billion. We have progressed a number of ongoing programmes designed to address Core SG&A costs including targeting sales, marketing and medical cost effectiveness, improving efficiencies across support functions and IT, and optimising the global footprint.

This allowed us to continue to focus on our pipeline and Core R&D costs were up 21% in the year to \$5.6 billion as Oncology attracted over 40% of total Core R&D expenditure in the year, reflecting a number of active trials.

Core Other Operating Income was \$1.5 billion in the year and included \$380 million to divest US and \$215 million for Rest of World rights to *Entocort*. Core Operating Profit increased by 6% to \$6.9 billion and Core Earnings per Share increased by 7% to \$4.26. Reported Operating Profit, at \$4.1 billion, included fair value adjustments to contingent consideration, which reduced SG&A costs by \$432 million, primarily in relation to the acquisition of BMS's share of the Global Diabetes Alliance.

We generated a cash inflow from operating activities of \$3.3 billion in the year with a continued improvement in working capital investment. We maintained a strong, investment-grade credit rating and, in November, issued a total of \$6 billion of bonds to fund corporate and business development activity, repay certain outstanding commercial paper obligations and for general corporate purposes. We ended the year with net debt of \$7.8 billion.

As we look to the future, we expect a low to mid single-digit percentage decline in Total Revenue at CER in 2016. A low to mid single-digit percentage decline in Core EPS at CER is also expected. This guidance incorporates the dilutive effects arising from the Acerta Pharma and ZS Pharma transactions announced in 2015. The guidance also assumes the loss of exclusivity for *Crestor* in the US from May 2016. Externalisation Revenue is expected to be ahead of that in 2015, including an increasing element of recurring income arising from prior agreements. This is in line with our long-term business model. Core R&D costs are expected to be at a similar level to 2015 while we are committed to materially reducing Core SG&A costs in 2016. The weakness of key trading currencies against the US dollar has continued. Based on average exchange rates in January 2016 and our published currency sensitivities, an adverse impact of around 3% from currency movements on Total Revenue and Core EPS in 2016 would be anticipated.

Marc Dunoyer
Chief Financial Officer

“Our financial performance in 2015 reflected continued progress from our Growth Platforms, which grew 11% in the year and now contribute 57% of Total Revenue.”

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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 2015, 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.

All growth rates in this Financial Review are expressed at CER unless noted otherwise.

Business background and results overview

The business background is covered in the Marketplace section from page 12, the Therapy Area Review from page 24 and the Geographical Review from page 227, 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 the Patent expiries section on page 60.
- > 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 are 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 2015 are

- > Total Revenue up 1% at CER to \$24,708 million (Actual: down 7%).
- > Revenues of our Growth Platforms increased 11% at CER and constituted 57% of our Total Revenue, with

- Respiratory up 7% at CER ahead of the proposed acquisition of Takeda’s respiratory business
- *Brilinta/Brilique* up 44% at CER, underpinned by a recently-extended US label and positive CHMP opinion
- Diabetes up 26% at CER, including 76% in Emerging Markets and global *Farxiga/Forxiga* growth of 137%
- Emerging Markets up 12% at CER, including China and Latin America
- each growing by 15% at CER
- Japan up 4% at CER, including 8% in the fourth quarter
- New Oncology \$119 million, comprising *Lynparza*, *Iressa* (US) and *Tagrisso*.
- > Core operating profit was up 6% at CER (Actual: down 1%) to \$6,902 million. The increase reflected a reduction in our Core SG&A costs and an increase in Externalisation Revenue and Core other operating income. We are continuing to invest in our pipeline and Growth Platforms.
- > Reported operating profit was up 100% at CER (Actual: 93%) to \$4,114 million. Total restructuring costs associated with the global programme to reshape the cost base of our business were \$1,034 million in 2015.
- > Our Core operating margin of 27.9% of Total Revenue was up 1.3 percentage points (Actual: 1.8 percentage points). Reported operating margin was 16.7% of Total Revenue.
- > Core EPS for the full year was \$4.26, up 7% at CER (Actual: flat). Reported EPS was up 137% at CER (Actual: 128%) to \$2.23.
- > Dividends paid amounted to \$3,486 million (2014: \$3,521 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, principally 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 will include 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 2015 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 2015 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. The adjustments made to our Reported financial information in order to show Core financial measures 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 following costs that the Core measures exclude:

- Amortisation of intangible assets which generally arise from business combinations and individual licence acquisitions. 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. Our Core financial measures do not include such costs but 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 2015 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 2015 Reported operating profit table below, our reconciliation of Core financial measures to Reported financial information in the Reconciliation of Reported results to Core

results table below, and to the Results of operations – summary analysis of year ended 31 December 2014 section from page 236 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 2015

2015 Reported operating profit

	2015			2014	Percentage of Total Revenue		2015 compared with 2014	
	Reported \$m	CER growth \$m	Growth due to exchange effects \$m	Reported Restated ¹ \$m	Reported 2015 %	Reported 2014 Restated ¹ %	CER growth ² %	Actual growth %
Product Sales	23,641	(387)	(2,067)	26,095			(1)	(9)
Externalisation Revenue	1,067	631	(16)	452			140	136
Total Revenue	24,708	244	(2,083)	26,547			1	(7)
Cost of sales	(4,646)	700	496	(5,842)	(18.8)	(22.0)	(12)	(20)
Gross profit	20,062	944	(1,587)	20,705	81.2	78.0	5	(3)
Distribution costs	(339)	(56)	41	(324)	(1.4)	(1.2)	17	5
Research and development expense	(5,997)	(850)	432	(5,579)	(24.3)	(21.0)	15	7
Selling, general and administrative costs	(11,112)	1,008	880	(13,000)	(44.9)	(49.0)	(8)	(15)
Other operating income and expense	1,500	1,189	(24)	335	6.1	1.2	355	348
Operating profit	4,114	2,235	(258)	2,137	16.7	8.0	100	93
Net finance expense	(1,029)			(885)				
Share of after tax losses of joint ventures	(16)			(6)				
Profit before tax	3,069			1,246				
Taxation	(243)			(11)				
Profit for the period	2,826			1,235				
Basic earnings per share (\$)	2.23			0.98				

¹ 2014 comparatives have been restated to reflect the reclassification of Externalisation Revenue from other operating income and expense as detailed in Group Accounting Policies from page 144.

² As detailed on page 64, CER growth is calculated using prior year actual results adjusted for certain exchange effects including hedging.

2015 Reconciliation of Reported results to Core results

	2015 Reported \$m	Restructuring costs \$m	Intangible amortisation and impairments \$m	BMS's share of diabetes alliance \$m	Legal provisions and other \$m	2015 Core ¹ \$m	CER growth %	Core ¹ 2015 Actual growth %
Gross profit	20,062	158	369	–	–	20,589	2	(5)
Product Sales gross margin % ²	80.3%					82.6%		
Total Revenue gross margin %	81.2%					83.3%		
Distribution costs	(339)	–	–	–	–	(339)	17	5
Research and development expense	(5,997)	258	136	–	–	(5,603)	21	13
Selling, general and administrative costs	(11,112)	618	921	54	254	(9,265)	(2)	(9)
Other operating income and expense	1,500	–	178	–	(158)	1,520	104	100
Operating profit	4,114	1,034	1,604	54	96	6,902	6	(1)
Operating margin as a % of Total Revenue	16.7%					27.9%		
Net finance expense	(1,029)	–	–	409	115	(505)		
Taxation	(243)	(217)	(344)	(152)	(34)	(990)		
Basic earnings per share (\$)	2.23	0.65	1.00	0.24	0.14	4.26		

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

As detailed above, all growth rates in this section are expressed at CER unless noted otherwise.

Total Revenue

Total Revenue for the year was up 1% at CER to \$24,708 million, comprising Product Sales of \$23,641 million (down 1%) and Externalisation Revenue of \$1,067 million (up 140%). Based on actual exchange rates, Total Revenue declined by 7% in the year reflecting the particular weakness of key trading currencies against the US dollar.

Product Sales

The decline in Product Sales was driven by the US market entry of *Nexium* generic products from February 2015 as well as an adverse impact from *Synagis* guideline changes in 2014 and the change in accounting for the US Branded Pharmaceutical Fee, following issuance of final regulations in 2014. Further details of the effect of these regulations are contained in the Financials (Prior year) section of the Annual Report from page 236.

US Product Sales were down 6% to \$9,474 million, with Europe down 6% at \$5,323 million. Established Markets were flat at \$3,022 million and Emerging Markets were up 12% to \$5,822 million, mainly driven by

growth in China of 15% to \$2,530 million. Further details of our product performance are contained in the Geographical Review from page 227.

Our Growth Platforms, which include New Oncology, grew by 11%, representing 59% of total Product Sales.

Product Sales of Respiratory medicines were up 7% ahead of the proposed acquisition of Takeda's respiratory business (as detailed on page 28). Sales of *Brilinta/Brilique* in the year were \$619 million, an increase of 44%. The FDA approved *Brilinta* tablets at a new 60mg dose to be used by patients with a history of heart attack beyond the first year of treatment in 2015. Our Diabetes Product Sales were 26% higher than in 2014, which included growth of 137% on *Farxiga/Forxiga* with global sales of \$492 million and several successful launches in the year in a number of international markets. Product Sales in Emerging Markets increased by 12% to \$5,822 million in 2015 as we continued to focus on delivering innovative medicines to these markets in the year, with a particular focus on China and other leading markets such as Russia and Brazil. Product Sales in Japan increased by 4% to \$2,020 million, with *Crestor* continuing to grow strongly in the year, up 8% to \$468 million. Global

Product Sales of *Crestor* declined in the year by 3% to \$5,017 million, which primarily reflected ongoing competition from generic statins. *Symbicort* global Product Sales declined by 3% to \$3,394 million, with sales in Europe down 14% to \$1,076 million, with a modest volume decline and a significant price decline reflecting increased competition from recently-launched analogue medicines. Global Product Sales of *Seroquel XR* declined by 12% to \$1,025 million, as a result of generic product competition.

Externalisation Revenue

The Group updated its revenue accounting policy with effect from 1 January 2015. As detailed earlier in the Annual Report, the Group's business model now includes an increasing level of externalisation activity to broaden and accelerate the development and commercialisation of, as well as maximising patient access to, key pipeline assets in our three main therapy areas. Historically, our Reported revenue reflected only Product Sales, with Externalisation Revenue forming part of other operating income presented below gross profit. Reflecting the increased level of externalisation activity, Externalisation Revenue, alongside Product Sales, is now included in Total Revenue. Externalisation Revenue includes development, commercialisation and collaboration

Growth Platforms

	2015 Product Sales \$m	2014 Product Sales \$m	CER growth %
Respiratory	4,987	5,063	7
<i>Brilinta/Brilique</i>	619	476	44
Diabetes	2,224	1,870	26
Emerging Markets	5,822	5,827	12
Japan	2,020	2,227	4
New Oncology	119	–	n/m
Total Growth Platform Product Sales ¹	14,003	13,928	11

¹ 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

Milestones	2015 \$m	2014 \$m
Durvalumab (Celgene)	450	–
<i>Movantik</i> (Daiichi Sankyo)	200	–
Brodalumab (Valeant Pharmaceuticals)	100	–
<i>Nexium</i> (Daiichi Sankyo)	123	–
<i>Nexium</i> OTC (Pfizer)	–	250
<i>Forxiga</i> (Ono Pharmaceuticals)	–	80
Others	107	69
Total milestones	980	399
Royalties	87	53
Total Externalisation Revenue	1,067	452

revenue, such as royalties and milestone receipts. Income is recorded as Externalisation Revenue when the Group has 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 the Group does not retain an interest, continue to be recorded in other operating income. The updated financial presentation was adopted to reflect the Group's expanded entrepreneurial approach and is considered to provide a clearer picture of this important additional revenue stream. The updated revenue accounting policy results in a presentational change to the results of operations only, and has no impact on the Group's net results or net assets. Prior year comparatives have been restated to reflect this change, resulting in \$452 million of income being reclassified from other operating income to Externalisation Revenue for 2014.

Further details of the arrangements giving rise to the above revenues are included in the Investments, divestments and capital expenditure section of this Financial Review from page 72.

Gross margin, operating margin and earnings per share

Core gross margin as a percentage of Product Sales was 82.6% in the year, 0.8 percentage points higher than last year at CER due to the mix of Product Sales and manufacturing efficiencies.

Core R&D expense in the year was up 21% to \$5,603 million, as the Group continued its focused investment in the pipeline. Oncology attracted over 40% of total Core R&D expenditure in the year, reflecting a number of active trials.

Core SG&A costs declined by 2% to \$9,265 million. Core SG&A costs declined in the year by 1.1 percentage points as a proportion of Total Revenue. A number of ongoing programmes to reduce SG&A costs are progressing. These initiatives are centred on: sales, marketing and medical cost effectiveness; centralisation of selected functions and process improvements; reduced third party spend; additional efficiencies gained across support functions; and IT and continued footprint optimisation, including presence in the UK and US. Resources are being deployed more selectively to meet changing

customer needs and the evolving portfolio, while driving top-line growth more efficiently.

Core other operating income in the year was up 104% at \$1,520 million which, in addition to royalty income of \$322 million, includes \$380 million of income on the disposal of the US rights to *Entocort*, \$215 million on the disposal of Rest of World rights to *Entocort*, \$193 million on the disposal of *Myalept* and \$165 million on the disposal of *Caprelsa*. As these elements of our income arose from product divestments, where AstraZeneca no longer retains 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.

Core operating profit increased by 6% to \$6,902 million in the year. The Core operating margin increased by 1.3 percentage points to 27.9% of Total Revenue. The increase reflected the reduction in Core SG&A costs and the increase in Externalisation Revenue and Core other operating income, while we continued to invest in our pipeline and Growth Platforms.

Core EPS was \$4.26, up 7% compared with last year (Actual: flat).

Pre-tax adjustments to arrive at Core profit before tax amounted to \$3,312 million in 2015 (2014: \$5,192 million), comprising \$2,788 million adjustments to operating profits (2014: \$4,800 million) and \$524 million to net finance expenses (2014: \$392 million). Excluded from Core results were:

- > Restructuring costs totalling \$1,034 million (2014: \$1,558 million), incurred as the Group continued the fourth phase of restructuring announced in March 2013 and subsequently expanded.
- > Amortisation totalling \$1,460 million (2014: \$1,784 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). The decrease was driven by reduced amortisation charges arising from our Merck exit arrangements (which commenced in 1998) as certain associated intangible assets became fully amortised. Further information on our intangible assets is contained in Note 9 to the Financial Statements from page 158.

- > Intangible impairment charges of \$143 million (2014: \$99 million) excluding those related to IT. Further details relating to intangible asset impairments are included in Note 9 to the Financial Statements from page 158.
- > Net cost associated with our acquisition of BMS's share of our Global Diabetes Alliance in February 2014 amounting to \$463 million (2014: \$1,423 million). Included within this are \$432 million of amortisation charges and \$409 million of interest charges relating to a discount unwind on contingent consideration arising on the acquisition in 2014, offset by a contingent consideration fair value decrease of \$378 million reflecting lower expected Diabetes portfolio revenues in line with latest forecasts.
- > Net legal provisions and other charges of \$211 million (2014: \$328 million), including \$115 million discount unwind charges, offset by \$54 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 \$211 million also included legal charges relating to patent proceedings in the US for *Pulmicort Respules*, charges relating to the unsuccessful defence of the validity of *Crestor*-related patents in Australia, and damages paid to AbbVie following a contract dispute over *Synagis*. Further details of legal proceedings the Group is currently involved in are contained within Note 27 to the Financial Statements from page 186.

Reported operating profit of \$4,114 million was \$1,977 million higher than in 2014. Fair value adjustments to contingent consideration reduced SG&A costs and increased Reported operating profit by \$432 million in the current year (2014: fair value adjustments to contingent consideration reduced Reported operating profit by \$512 million). These fair value movements reflected estimates for future liabilities that can change materially over time. In addition, restructuring costs of \$1,034 million in 2015 were significantly lower than restructuring costs of \$1,558 million in 2014.

Reported net finance expense was \$1,029 million (2014: \$885 million). The increase of \$144 million was driven by increased charges related to the discount unwind

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on contingent consideration arising on business combinations driven by underlying increases in the contingent consideration value held on the balance sheet in 2014 (including a full year's discount unwind on the contingent consideration arising from our acquisition of BMS's share of our Global Diabetes Alliance).

The Reported taxation charge for the year of \$243 million (2014: \$11 million) consisted of a current tax charge of \$633 million (2014: \$872 million) and a credit arising from movements on deferred tax of \$390 million (2014: \$861 million). The current tax charge included a prior period current tax credit of \$404 million (2014: \$109 million).

The Reported tax rate for the year was 8%. This Reported tax rate was impacted by a one-off benefit of \$186 million following agreement of US federal tax liabilities of open years up to 2008, other net reductions in provisions for tax contingencies partially offset by the impact of internal transfers of intellectual property resulting in a net credit of \$181 million and non-Core revaluations of contingent consideration arising on business combinations (credit of \$432 million with related tax charge of \$39 million). Excluding these effects, the Reported tax rate for the year would have been 22%. The Core tax rate for the year was 16%. Excluding the benefit following agreement of US federal tax liabilities of open years up to 2008 and other net reductions in provisions for tax contingencies partially offset by the impact of internal transfers of intellectual property, the Core tax rate would have been 21%.

The tax paid for the year was \$1,354 million (44% of Reported profit and 21% of Core profit). The cash tax paid for the year was \$1,111 million higher than the tax charge for the year as a result of certain items with no cash impact including the benefit of \$186 million following agreement of US federal tax liabilities of open years up to 2008, other net reductions in provisions for tax contingencies of \$259 million, \$390 million of deferred tax credits, cash payments made in respect of audit settlements of \$240 million and other cash tax timing differences.

Reported post-tax profit for the year was \$2,826 million, an increase of 137%. Reported earnings per share was up 137% to \$2.23.

Total comprehensive income increased by \$2,759 million from the prior year, resulting in a net income of \$2,488 million for 2015. This was driven by the increase in profit for the year of \$1,591 million and an increase of \$1,168 million in other comprehensive income. The increase in other comprehensive income arose principally from gains recorded on the remeasurement of our defined benefit pension liability of \$652 million (2014: losses of \$766 million) due to an increase in the discount rate applied to our pension liabilities reflecting an increase in corporate bond yields and other reference interest rate instruments.

Restructuring

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

Further to the announcement in 2012 of a third phase of the programme, we announced another restructuring programme in 2013, which was combined with the third phase to create a combined Phase 4 programme. This combined programme initially entailed an estimated global headcount reduction of about 5,050 over the 2013 to 2016 period. The combined programme of changes is estimated to incur \$2.5 billion in one-time restructuring charges, of which \$1.7 billion were expected to be cash costs, and deliver \$800 million of annualised benefits by the end of 2016.

The Phase 4 programme was expanded in 2013 to include additional activities such as a transformation of our IT organisation and infrastructure, the exit of R&D activities in Bangalore, India, and the exit from branded generics in certain Emerging Markets to further reduce costs and increase flexibility. When completed, the expanded restructuring programme is expected to deliver a further \$300 million in annual benefits by the end of 2016, bringing total anticipated annualised benefits of the Phase 4 programme to \$1.1 billion, and to affect a further approximately 550 positions, bringing the total global headcount reduction under the Phase 4 programme to around 5,600 over the 2013 to 2016 period. Total incremental programme costs from these new initiatives, together with revisions to cost estimates for the original programme, are estimated to be \$700 million, of which \$600 million is cash,

bringing the total anticipated cost of our Phase 4 programme to \$3.2 billion by the end of 2016.

In addition to this programme, we announced an additional \$600 million of restructuring costs which are estimated to be incurred by the end of 2016 (of which \$494 million were incurred by the end of 2015), associated with previously-announced site exits (including Avlon in the UK) and the integration of the Diabetes and Respiratory businesses acquired from BMS and Almirall, respectively. We anticipate that, once completed, the total annualised benefits of these additional actions will be \$200 million.

During the latter part of 2015, the Company implemented further targeted restructuring of our commercial business, principally in Venezuela (in response to challenging economic conditions) and Europe. This resulted in \$102 million of restructuring costs and is expected to deliver \$30 million of annualised benefit in 2016. Furthermore, as part of the Company's ongoing commitment to improve productivity, we are initiating multi-year transformation programmes within our G&A functions (principally Finance and HR) with anticipated costs by the end of 2018 of \$270 million. Once complete, we expect these transformation programmes to deliver annualised benefits of \$100 million by the end of 2018.

The aggregate restructuring charges incurred in 2015 across all our restructuring programmes was \$1,034 million, as we continued to make progress in implementing our restructuring plans.

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.

Earnings before interest, tax, depreciation, amortisation and impairments includes adjustments for amortisation and depreciation charges of \$2,676 million (2014: \$3,160 million) and interest of \$1,029 million (2014: \$885 million) including \$570 million (2014: \$453 million) for discount unwinds.

Cash flow and liquidity – 2015

All data in this section is on a Reported basis.

Summary cash flows

	2015 \$m	2014 \$m	2013 \$m
Net (debt)/funds brought forward at 1 January	(3,223)	39	(1,369)
Earnings before interest, tax, depreciation, amortisation and impairment (EBITDA)	6,966	5,419	8,295
Movement in working capital and short-term provisions	(49)	2,508	166
Tax paid	(1,354)	(1,201)	(844)
Interest paid	(496)	(533)	(475)
Gains on disposal of intangible assets	(961)	–	–
Non-cash and other movements	(782)	865	258
Net cash available from operating activities	3,324	7,058	7,400
Purchase of intangibles (net)	(330)	(1,740)	(1,281)
Upfront payments on business acquisition	(2,446)	(3,804)	(1,158)
Payment of contingent consideration on business acquisitions	(579)	(657)	–
Other capital expenditure (net)	(1,326)	(924)	(673)
Investments	(4,681)	(7,125)	(3,112)
Dividends	(3,486)	(3,521)	(3,461)
Share proceeds	43	279	482
Distributions	(3,443)	(3,242)	(2,979)
Other movements	261	47	99
Net (debt)/funds carried forward at 31 December	(7,762)	(3,223)	39

Net debt/funds reconciliation

	2015 \$m	2014 \$m	2013 \$m
Cash and cash equivalents	6,240	6,360	9,217
Short-term investments	613	795	796
Net derivative financial instruments	438	465	402
Cash, short-term investments and derivatives	7,291	7,620	10,415
Overdraft and short-term borrowings	(849)	(1,486)	(992)
Finance leases	(95)	(108)	(102)
Current instalments of loans	–	(912)	(766)
Loans due after one year	(14,109)	(8,337)	(8,516)
Loans and borrowings	(15,053)	(10,843)	(10,376)
Net (debt)/funds	(7,762)	(3,223)	39

Net cash generated from operating activities was \$3,324 million in the year ended 31 December 2015, compared with \$7,058 million in 2014. Working capital increased by \$49 million in the year. This compared to a decline of \$2,508 million in 2014 which was driven by a significantly higher level of rebate accruals in the US, the phasing of costs increasing accruals in the fourth quarter of 2014 and the accrual of an additional year's US Branded Pharmaceutical Drug Fee following the change of regulations in 2014. In the current year, the liabilities in relation to these items normalised and, in addition, rebate accruals were further reduced following the loss of exclusivity for *Nexium*.

Gains on disposal of intangible assets of \$961 million includes \$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*. Non-cash and other movements decreased operating cash by \$782 million and included \$432 million relating to fair value adjustments on contingent consideration arising on business combinations (2014: increased operating cash by \$865 million including \$512 million increase on contingent consideration arising on business combinations).

Investment cash outflows of \$4,681 million (2014: \$7,125 million) included \$2,446 million relating to the acquisition of ZS Pharma. This compared to cash payments relating to business acquisitions in 2014 of \$4,461 million, primarily related to the BMS diabetes alliance and Almiral acquisitions. Further details of business combination acquisitions and their impact on our cash flows and balance sheet are given in the table on page 72. Investment cash outflows also include \$579 million (2014: \$657 million) of payments against contingent consideration arising on business combinations and \$1,460 million (2014: \$1,740 million) for the purchase of other intangible assets, which included \$684 million on the acquisition of the rights to Actavis' branded respiratory portfolio in the US and Canada. The comparative

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Bonds issued in 2015

	Repayment dates	Face value of bond \$m	Net book value of bond at 31 December 2015 \$m
Floating rate notes	2018	400	399
1.750% Callable bond	2018	1,000	997
2.375% Callable bond	2020	1,600	1,586
3.375% Callable bond	2025	2,000	1,971
4.375% Callable bond	2045	1,000	976
Total		6,000	5,929

period of 2014 included a \$409 million payment to Merck on the consummation of our Second Option and \$310 million on the settlement of pre-existing launch and sales-related milestones with BMS. Investment cash inflows include \$1,130 million (2014: \$nil) from the sale of intangible assets, including 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. Further details of the divestments giving rise to our investment cash inflows are included in the Investments, divestments and capital expenditure section of this Financial Review from page 72.

Net cash distributions to shareholders were \$3,443 million (2014: \$3,242 million) including dividends of \$3,486 million (2014: \$3,521 million). Proceeds from the issue of shares on the exercise of share options amounted to \$43 million (2014: \$279 million).

In November 2015, the Group 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, the Group repaid a 5.125% non-callable euro bond which had a 31 December 2014 carrying value of \$912 million.

At 31 December 2015, outstanding gross debt (interest-bearing loans and borrowings) was \$15,053 million (2014: \$10,843 million). Of the gross debt outstanding at 31 December 2015, \$916 million is due within one year (2014: \$2,446 million). Net debt at 31 December 2015 was \$7,762 million, compared to \$3,223 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 table below sets out our minimum contractual obligations at the year end.

In 2015, net assets decreased by \$1,137 million to \$18,509 million. The decrease in net assets is broadly as a result of dividends of \$3,537 million and adverse movements on exchange taken to reserves of \$861 million, partially offset by the Group profit of \$2,826 million.

Business combinations

In 2015, we completed the acquisition of ZS Pharma. In 2014, we completed the acquisition of BMS's share of our Global Diabetes Alliance, the acquisition of the rights to Almirall's respiratory franchise and the acquisition of the Definiens Group.

Payments due by period

	Less than 1 year \$m	1-3 years \$m	3-5 years \$m	Over 5 years \$m	2015 Total \$m	2014 Total \$m
Bank loans and other borrowings ¹	1,419	4,183	3,469	14,192	23,263	17,261
Finance leases	66	63	12	–	141	130
Operating leases	95	148	97	69	409	438
Contracted capital expenditure	518	–	–	–	518	438
Total	2,098	4,394	3,578	14,261	24,331	18,267

¹ Bank loans and other borrowings include interest charges payable in the period, as detailed in Note 25 to the Financial Statements on page 177.

Financial position – 31 December 2015

All data in this section is on a Reported basis.

Summary statement of financial position

	2015 \$m	Movement \$m	2014 \$m	Movement \$m	2013 \$m
Property, plant and equipment	6,413	403	6,010	192	5,818
Goodwill and intangible assets	34,514	1,983	32,531	6,503	26,028
Inventories	2,143	183	1,960	51	1,909
Trade and other receivables	7,529	(815)	8,344	(1,402)	9,746
Trade and other payables	(19,120)	757	(19,877)	(7,163)	(12,714)
Provisions	(1,242)	(135)	(1,107)	282	(1,389)
Net income tax payable	(1,096)	929	(2,025)	557	(2,582)
Net deferred tax liabilities	(1,439)	(862)	(577)	1,045	(1,622)
Retirement benefit obligations	(1,974)	977	(2,951)	(690)	(2,261)
Non-current other investments	458	(44)	502	221	281
Investment in joint ventures	85	26	59	59	–
Net (debt)/funds	(7,762)	(4,539)	(3,223)	(3,262)	39
Net assets	18,509	(1,137)	19,646	(3,607)	23,253

Further information on our business combinations can be found in the Investments, divestments and capital expenditure section of the Financial Review from page 72.

Property, plant and equipment

Property, plant and equipment increased by \$403 million to \$6,413 million. Additions of \$1,422 million (2014: \$1,607 million), including \$21 million (2014: \$515 million) arising from business combinations, were offset by depreciation of \$677 million (2014: \$776 million), impairments of \$28 million (2014: \$nil) and disposals of \$70 million (2014: \$582 million).

Goodwill and intangible assets

The Group's goodwill of \$11,868 million (2014: \$11,550 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 \$456 million arising on the acquisition of ZS Pharma was capitalised in 2015.

Intangible assets amounted to \$22,646 million at 31 December 2015 (2014: \$20,981 million). Intangible asset additions were \$4,640 million in 2015 (2014: \$8,548 million), including product rights acquired in the acquisition of ZS Pharma of \$3,162 million

(2014: \$7,501 million on 2014 business combinations). Amortisation in the year was \$1,999 million (2014: \$2,384 million). Impairment charges in the year amounted to \$148 million (2014: \$122 million), including \$64 million for AMP-110 and \$35 million for Ardelyx. Disposals of intangible assets totalled \$169 million in the year (2014: \$nil) including \$123 million on the sale of global rights to *Myalept*.

Further details of our additions to intangible assets, and impairments recorded, are included in Note 9 to the Financial Statements from page 158.

Receivables, payables and provisions

Trade and other receivables decreased by \$815 million with trade receivables reduced by \$129 million to \$4,633 million and prepayments and accrued income increasing by \$20 million. Non-current other receivables decreased by \$205 million to \$907 million driven by a reduction in the Shionogi *Crestor* royalty prepayment as detailed in Note 13 to the Financial Statements on page 162.

Trade and other payables decreased by \$757 million in 2015 to \$19,120 million, including \$223 million lower rebates and chargebacks, and \$571 million in other non-current payables. Non-current payables

includes the long-term element of contingent consideration, which as indicated above, included an adjustment of \$432 million to the total fair value in 2015, and the accrual for our minimum committed Shionogi *Crestor* royalty payments.

The increase in provisions of \$135 million in 2015 included \$706 million of additional charges recorded in the year, partially offset by \$557 million of cash payments. Included within the \$706 million of charges for the year were \$338 million for our global restructuring initiatives and \$313 million in respect of legal charges. Cash payments included \$408 million for our global restructuring programmes. Further details of the charges made against provisions are contained in Notes 19 and 27 to the Financial Statements on page 165, and 186 to 192, respectively.

Tax payable and receivable

Net income tax payable has decreased by \$929 million to \$1,096 million, principally due to a \$186 million adjustment following agreement of US federal tax liabilities of open years up to 2008, other net reductions in provisions for tax contingencies (\$259 million), cash payments made in respect of audit settlements (\$240 million) and foreign exchange (\$194 million). The tax receivable balance of \$387 million (2014: \$329 million)

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comprises tax owing to AstraZeneca from certain governments expected to be received on settlements of transfer pricing audits and disputes (\$192 million) (see Note 27 to the Financial Statements from page 186) and cash tax timing differences (\$195 million). Net deferred tax liabilities increased by \$862 million in the year mainly due to deferred tax liabilities arising from the acquisition of ZS Pharma. Additional information on the movement in deferred tax balances is contained in Note 4 to the Financial Statements from page 151.

Retirement benefit obligations

Net retirement benefit obligations decreased by \$977 million in 2015 (2014: increase of \$690 million). Employer contributions to the pension scheme of \$402 million, net remeasurement adjustments of \$652 million driven by an increase in the discount rate applied to our pension liabilities under IAS 19 and beneficial exchange movements of \$182 million were offset by service cost charges of \$167 million and net financing costs of \$77 million. Benefits paid amounted to \$580 million (2014: \$571 million).

Approximately 97% of the Group's obligations are concentrated in the UK, the US, Sweden and Germany. In recent years, the Group has undertaken several initiatives to reduce its net pension obligation exposure. For the UK defined benefit pension scheme, which is AstraZeneca's 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. In addition to the cash contributions to be paid into the UK pension scheme, AstraZeneca makes contributions to an escrow account which is held outside the pension scheme. The escrow account assets are payable to the fund in agreed circumstances, for example, in the event of AstraZeneca and the pension fund trustee agreeing a change to the current long-term investment strategy.

Further details of the Group's pension schemes are included in Note 20 to the Financial Statements from page 166.

Commitments and contingencies

The Group has 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 144. The Group also has taxation contingencies. These are described in the Taxation section in the Critical accounting policies and estimates section on page 81 and in Note 27 to the Financial Statements from page 186.

Research and development collaboration payments

Details of future potential R&D collaboration payments are also included in Note 27 to

the Financial Statements from page 186. As detailed in Note 27 to the Financial Statements, 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

The Group has completed over 240 major or strategically important business development transactions over the past three years, eight of which were accounted for as business acquisitions under IFRS 3 'Business Combinations', being 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 2014; and Pearl Therapeutics, Omthera, Amplimmune and Spirogen in 2013, and all others being in-licences, strategic alliances and collaborations.

Fair values of assets and liabilities acquired, and consideration for the acquisitions in 2015 and 2014, as at the acquisition date, are summarised below.

Business combinations

	2015	2014			
	ZS Pharma \$m	BMS's share of diabetes alliance \$m	Rights to Almirall's respiratory franchise \$m	Definiens Group \$m	2014 total \$m
Assets acquired:					
Non-current assets					
Property, plant and equipment	21	478	37	–	515
Goodwill	456	1,530	311	–	1,841
Intangible assets	3,162	5,746	1,400	355	7,501
Current assets	169	480	24	–	504
Current liabilities	(50)	(278)	(2)	–	(280)
Non-current liabilities	(1,058)	(84)	(11)	(117)	(212)
Total assets	2,700	7,872	1,759	238	9,869
Consideration:					
Upfront consideration	2,700	2,703	878	150	3,731
Contingent consideration	–	5,169	881	88	6,138
Total consideration	2,700	7,872	1,759	238	9,869

Contingent consideration arising on business combinations

	2015			2014		
	Acquisition of BMS's share of diabetes alliance \$m	Other business combinations \$m	Total 2015 \$m	Acquisition of BMS's share of diabetes alliance \$m	Other business combinations \$m	Total 2014 \$m
At 1 January	5,386	1,513	6,899	–	514	514
Acquisitions	–	–	–	5,169	969	6,138
Settlements	(325)	(254)	(579)	(657)	–	(657)
Fair value adjustments	(378)	(54)	(432)	529	(17)	512
Discount unwind	409	115	524	345	46	391
Foreign exchange	–	(1)	(1)	–	1	1
At 31 December	5,092	1,319	6,411	5,386	1,513	6,899

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 acquisition of ZS Pharma in the year 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 Almirall includes further payments of up to \$1.2 billion for future development, launch, and sales-related milestones and various other sales-related payments. 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'.

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 2015, we recorded an interest charge of \$524 million on the discount unwind on contingent consideration arising on our business combinations, and a net fair value decrease on contingent consideration of \$432 million (which resulted in a credit to our income statement for the same amount) driven, principally, by revised forecasts for revenues for our Diabetes franchise. At 31 December 2015, our contingent consideration balance held on the balance sheet amounted to \$6,411 million (2014: \$6,899 million) with the movements of the balance detailed in the table above.

Further details of our business acquisitions in the past three years are contained in Note 24 to the Financial Statements from page 173. Details of our significant business development transactions are given below:

> In September 2015, AstraZeneca announced that it had entered into a collaboration agreement with Valeant under which it 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 Hakko Kirin under a prior arrangement with Amgen Inc. 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 AstraZeneca 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, AstraZeneca and Valeant will share profits.

> In April 2015, AstraZeneca entered into two oncology agreements with Innate Pharma S.A (Innate), firstly, a licence which provides AstraZeneca 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. Currently in Phase II development, IPH2201 is a potential first-in-class humanised IgG4 antibody. Under the terms of the combination licence, AstraZeneca assumed exclusive Global rights to research, develop, and commercialise IPH2201 in combination with durvalumab. AstraZeneca and Innate jointly fund Phase II studies and AstraZeneca leads the execution of these studies. Under the terms of the agreements, AstraZeneca made an initial payment to Innate 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. AstraZeneca records all sales and will pay Innate double-digit royalties on net sales. The arrangement includes the right for Innate to co-promote in Europe for a 50% profit share in the territory.

> In April 2015, AstraZeneca signed a Collaboration and License Agreement with Celgene Corporation, a global leader

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- in haematological cancers, to develop and commercialise durvalumab across a range of blood cancers including non-Hodgkin lymphoma, myelodysplastic syndromes and multiple myeloma. Durvalumab is an investigational immune checkpoint inhibitor, directed against programmed cell death ligand 1 (PD-L1). Signals from PD-L1 help tumours avoid detection by the immune system. Durvalumab blocks these signals, countering the tumour's immune-evading tactics. Under the terms of the agreement, Celgene made an upfront payment of \$450 million to AstraZeneca in relation to durvalumab, which is recorded within Externalisation Revenue. Celgene will lead on development across all clinical trials within the collaboration and have taken on all research and development costs until the end of 2016, after which they will take on 75% of these costs. Celgene will also be responsible for global commercialisation of approved treatments. AstraZeneca will manufacture and record all sales of 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, AstraZeneca announced a co-commercialisation agreement with Daiichi Sankyo, Inc. for *Movantik* in the US. *Movantik* is a first-in-class once-daily oral peripherally-acting mu-opioid receptor antagonist (PAMORA) for opioid-induced constipation (OIC). Opioids play an important role in chronic pain relief and work by binding to mu-receptors in the central nervous system, but they also bind to mu-receptors in the gastrointestinal tract, which can result in patients suffering from OIC. The drug was launched on 31 March 2015. Under the terms of the agreement, Daiichi Sankyo Inc. 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. AstraZeneca will be responsible for manufacturing, will record all sales and will make sales-related commission payments to Daiichi Sankyo, Inc. Both companies will be jointly responsible for commercial activities.
 - > In March 2015, AstraZeneca completed the acquisition of the rights to Actavis Plc's branded respiratory business in the US

- and Canada. The deal gave AstraZeneca the ownership of the development and commercial rights in the US and Canada to *Tudorza Pressair* (aclidinium bromide inhalation powder), a twice-daily long-acting muscarinic antagonist (LAMA) for COPD, and to *Daliresp* (roflumilast), the only once-daily oral PDE4 inhibitor currently on the market for COPD, in the US. AstraZeneca also owns the development rights in the US and Canada for LAS40464, a combination of a fixed dose of aclidinium with formoterol long-acting beta-agonist (LAMA/LABA) in a dry powder inhaler, which is approved in the EU under the brand name *Duaklir Genuair*. On completion of the acquisition, AstraZeneca paid Actavis \$600 million and agreed to pay low single-digit royalties above a certain revenue threshold.
- > In September 2014, AstraZeneca and Lilly entered into an agreement 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. AZD3293 is an oral, potent and selective small molecule inhibitor of BACE that has been shown in Phase I studies to significantly and dose-dependently reduce levels of amyloid beta in the cerebro-spinal fluid of Alzheimer's patients and healthy volunteers. Under the terms of the agreement, Lilly will pay AstraZeneca up to \$500 million in development and regulatory milestone payments. AstraZeneca received the first milestone payment of \$50 million in 2015. The companies will equally share all future costs for the development and commercialisation of AZD3293, as well as net global revenues post-launch. Lilly will lead clinical development, working with researchers from AstraZeneca's Innovative Medicines Unit for neuroscience, while AstraZeneca will be responsible for manufacturing. The companies will take joint responsibility for commercialisation of AZD3293.
 - > In July 2013, AstraZeneca 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 CKD and 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. The AstraZeneca-FibroGen joint effort will be focused on the development of roxadustat to treat anaemia in CKD and ESRD, and may be extended to other anaemia indications. AstraZeneca and FibroGen plan to undertake an extensive roxadustat Phase III development programme for the US, and to initiate Phase III trials in China, with anticipated regulatory filings in China in 2016 and in the US in 2018. Under the arrangement, AstraZeneca agreed to pay FibroGen upfront and subsequent non-contingent payments totalling \$350 million, as well as potential development-related milestone payments of up to \$465 million, and potential future sales-related milestone payments, in addition to tiered royalty payments on future sales of roxadustat in the low 20% range. Additional development milestones will be payable for any subsequent indications which the companies choose to pursue. AstraZeneca 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 AstraZeneca will oversee promotional activities and commercial distribution.
- > In March 2013, AstraZeneca signed an exclusive agreement with Moderna Therapeutics 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, AstraZeneca made an upfront payment of \$240 million. AstraZeneca will have exclusive access to select any target of its 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 Therapeutics is entitled to an additional \$180 million for the achievement of three technical milestones. Through this agreement, AstraZeneca has the option to select up to 40 drug products for clinical development and Moderna

Therapeutics will be entitled to development and commercial milestone payments as well as royalties on drug sales. AstraZeneca will lead the pre-clinical, clinical development and commercialisation of therapeutics resulting from the agreement and Moderna Therapeutics will be responsible for designing and manufacturing the *messenger RNA Therapeutics* against selected targets. AstraZeneca is 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.

The Group determines 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.

In aggregate, payments capitalised under the Group's externalisation arrangements, other than those detailed above, amounted to \$1,401 million in 2015 (2014: \$201 million), including \$684 million on the acquisition of the Actavis branded respiratory portfolio in the US and Canada.

Details of our significant divestments are given below:

> In November 2015, AstraZeneca signed an agreement with Elan Pharma International Limited, part of the Perrigo Group (Perrigo), for the divestment of rights to the *Entocort* business in US. The *Entocort* business in the US consisted of

a branded product marketed by AstraZeneca (*Entocort* EC) and an authorised generic marketed by PAR Pharmaceuticals under an exclusive distribution agreement. Under the terms of the agreement, Perrigo paid AstraZeneca \$380 million upon completion of the transaction to acquire the rights to sell *Entocort* capsules and the authorised generic *Entocort* capsules marketed by Par Pharmaceuticals. The transaction involved the full divestment of US rights in *Entocort*, including relevant clinical data, regulatory documentation and contracts, and inventory of finished pack *Entocort* EC and authorised generic capsules. The transaction did not include the transfer of any AstraZeneca employees or facilities.

> In September 2015, AstraZeneca completed an agreement with Genzyme Corporation (Genzyme), part of Sanofi S.A., for the divestment of *Caprelsa*, a rare-disease medicine. *Caprelsa* was granted Orphan Drug Designation by the US FDA in 2005 and is currently available in 28 countries for the treatment of aggressive and symptomatic medullary thyroid carcinoma. Under the terms of the agreement, Genzyme paid an upfront payment of \$165 million to acquire the global rights to sell and develop *Caprelsa*, and further development and sales milestone payments of up to \$135 million. The transaction did not include the transfer of any AstraZeneca employees or facilities.

> In July 2015, AstraZeneca signed an agreement with Tillotts Pharma AG for the divestment of global rights, outside the US, to *Entocort* (budesonide). *Entocort* is a gastroenterology medicine for patients with mild to moderate Crohn's disease and ulcerative colitis. *Entocort* is currently available in over 40 countries, with total Product Sales of \$53 million outside the US in 2014. Under the terms of the agreement, Tillotts paid AstraZeneca \$215 million upon completion of the transaction to acquire the rights to sell and develop *Entocort* capsules and enema formulations outside the US. The transaction did not include the transfer of any AstraZeneca employees or facilities.

> In January 2015, AstraZeneca completed an agreement with Aegerion Pharmaceuticals, to divest *Myalept* (metreleptin for injection). *Myalept* was originally developed by Amylin and

acquired by BMS in collaboration with AstraZeneca in July 2012 and subsequently acquired in whole by AstraZeneca in February 2014. Aegerion paid AstraZeneca \$325 million, in a single upfront payment, to acquire the global rights to develop, manufacture and commercialise *Myalept*, subject to an existing distributor licence with Shionogi covering Japan, South Korea, and Taiwan. On completion, the *Myalept* intangible was \$123 million, which was derecognised along with inventory of \$9 million, resulting in a gain on disposal of \$193 million being recognised as other operating income.

Capitalisation

The total number of shares in issue at 31 December 2015 was 1,264 million (2014: 1,263 million). One million Ordinary Shares were issued in consideration of share option exercises for a total of \$43 million. Shareholders' equity decreased by \$1,137 million to \$18,490 million at the year end. Non-controlling interests were \$19 million (2014: \$19 million).

Dividend and share repurchases

The Board has recommended a second interim dividend of \$1.90 (131.0 pence, 16.26 SEK) to be paid on 21 March 2016. This brings the full year dividend to \$2.80 (188.5 pence, 23.97 SEK). Based on a measure of Core earnings per share against Core operating profit, the Group has a dividend cover ratio of 1.5 with respect to 2015 (2014: 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.

Financial Review continued

Capitalisation and shareholder return

Dividends for 2015

	\$	Pence	SEK	Payment date
First interim dividend	0.90	57.5	7.71	14 September 2015
Second interim dividend	1.90	131.0	16.26	21 March 2016
Total	2.80	188.5	23.97	

Summary of shareholder distributions

	Shares repurchased (million)	Cost \$m	Dividend per share \$	Dividend cost \$m	Shareholder distributions \$m
2000	9.4	352	0.70	1,236	1,588
2001	23.5	1,080	0.70	1,225	2,305
2002	28.3	1,190	0.70	1,206	2,396
2003	27.2	1,154	0.795	1,350	2,504
2004	50.1	2,212	0.94	1,555	3,767
2005	67.7	3,001	1.30	2,068	5,069
2006	72.2	4,147	1.72	2,649	6,796
2007	79.9	4,170	1.87	2,740	6,910
2008	13.6	610	2.05	2,971	3,581
2009	–	–	2.30	3,339	3,339
2010	53.7	2,604	2.55	3,604	6,208
2011	127.4	6,015	2.80	3,653	9,668
2012	57.8	2,635	2.80	3,496	6,131
2013	–	–	2.80	3,522	3,522
2014	–	–	2.80	3,537	3,537
2015	–	–	2.80	3,539¹	3,539
Total	610.8	29,170	29.625	41,690	70,860

¹ Total dividend cost estimated based upon number of shares in issue at 31 December 2015.

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, and to achieve \$45 billion Total Revenue by 2023 (based on constant exchange rates).

We expect 2016 Total Revenue to decline by low to mid single-digit percent at CER compared to 2015. Core R&D costs as a percentage of Total Revenue are expected to be broadly in line with 2015. We are also committed to reducing Core SG&A costs in 2016 versus 2015. Core earnings per share is expected to decrease in 2016 by low to mid single-digit percent at CER. This guidance incorporates the dilutive effects arising from recent transactions.

Financial risk management

Financial risk management policies

Insurance

Our risk management processes are described in Risk overview from page 21. 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 the Group has not purchased in the market product liability insurance since February 2006.

Taxation

Tax risk management forms an integrated part of the Group's risk management processes. Our tax strategy is to manage tax risks and tax costs in a manner consistent with shareholders' best long-term interests, taking into account both economic and reputational factors. We draw a distinction between tax planning using artificial structures and optimising tax treatment of business transactions, and we engage only in the latter.

Treasury

The principal financial risks to which the Group is exposed are those arising from liquidity, interest rate, foreign currency and credit. The Group has 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, the Group's 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 25 to the Financial Statements from page 177 and in Risk overview from page 21.

Sensitivity analysis of the Group's exposure to exchange rate and interest rate movements is also detailed in Note 25 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 144. 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
- > 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. Income from royalties and from disposals of IP, brands and product lines is included in other operating income.

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. Chargebacks are paid 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 \$13,993 million in 2015 (2014: \$13,181 million) with increases in adjustments for regulatory and chargebacks, and sales initiatives recorded within other, driving the movement.

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

	2015 \$m	2014 \$m	2013 \$m
Gross Product Sales	23,467	23,301	21,345
Chargebacks	(2,985)	(2,794)	(2,449)
Regulatory – US government and state programmes	(1,714)	(1,389)	(1,435)
Contractual – Managed-care and group purchasing organisation rebates	(7,543)	(7,730)	(6,918)
Cash and other discounts	(472)	(436)	(399)
Customer returns	(333)	(295)	(112)
Other	(946)	(537)	(341)
Net Product Sales	9,474	10,120	9,691

Movement in provisions – US pharmaceuticals

	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 – US government and state programmes	707	1,809	(95)	(1,644)	777
Contractual – Managed-care and group purchasing organisation rebates	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
Other	163	947	(1)	(923)	186
Total	4,044	14,254	(261)	(14,033)	4,004

	Brought forward at 1 January 2014 \$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 – US government and state programmes	784	1,544	(155)	(1,466)	707
Contractual – Managed-care and group purchasing organisation rebates	1,714	7,703	27	(7,078)	2,366
Cash and other discounts	32	436	–	(435)	33
Customer returns	222	295	–	(199)	318
Other	74	537	–	(448)	163
Total	3,181	13,353	(172)	(12,318)	4,044

	Brought forward at 1 January 2013 \$m	Provision for current year \$m	Adjustment in respect of prior years \$m	Returns and payments \$m	Carried forward at 31 December 2013 \$m
Chargebacks	313	2,439	10	(2,407)	355
Regulatory – US government and state programmes	825	1,447	(12)	(1,476)	784
Contractual – Managed-care and group purchasing organisation rebates	1,348	6,951	(33)	(6,552)	1,714
Cash and other discounts	33	399	–	(400)	32
Customer returns	211	99	13	(101)	222
Other	45	341	–	(312)	74
Total	2,775	11,676	(22)	(11,248)	3,181

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 2015 net US pharmaceuticals revenue by 2.8% (2014: 1.7%; 2013: 0.2%). However, taking into account the adjustments affecting both the current and the prior year, 2014 revenue would have been increased by 0.9% and 2013 revenue would have been increased by 1.5%, 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 66, the Group's 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 is underpinned by our marketed products and development portfolio. The R&D expenditure on internal activities to generate these products is generally charged to profit in the year that it is incurred. Purchases of IP and product rights to supplement our R&D portfolio are capitalised as intangible assets. Further details of this policy are included in the Group Accounting Policies section of our Financial Statements from page 144. Such intangible assets are amortised from the launch of the underlying products and are tested for impairment both before and after launch. This policy is in line with practice adopted by major pharmaceutical companies.

Impairment testing of goodwill and intangible assets

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 157. 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 AstraZeneca's 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

Financial Review continued

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 24 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 2015 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 158.

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 27 to the Financial Statements from page 186.

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 the Group has a valid contract which provides the right to reimbursement (from insurance or otherwise) of legal costs and/or all or part of any loss incurred or for which a provision has been established and we consider recovery to be virtually certain, 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. AstraZeneca believes that the provisions recorded are adequate based on currently available information and that the insurance recoveries recorded will be received. However, given the inherent uncertainties involved in assessing the outcomes of these cases and in estimating the amount of the potential losses and the associated insurance recoveries, we could in 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 166.

Taxation

Accruals for tax contingencies require management to make judgements and estimates in relation to tax audit issues and exposures. Amounts accrued are based on management's interpretation of country-specific tax law and the likelihood of settlement. Tax benefits are not recognised unless the tax positions are probable of being sustained. 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. Any recorded exposure to interest on tax liabilities is provided for in the tax charge.

AstraZeneca faces a number of transfer pricing audits in jurisdictions around the world and, in some cases, is in dispute with the tax authorities. These disputes usually result in taxable profits being increased in one territory and correspondingly decreased in another. Our balance sheet positions for these matters reflect appropriate corresponding relief in the territories affected.

Further details of the estimates and assumptions we make in determining our recorded liability for transfer pricing audits and other tax contingencies are included in the Tax section of Note 27 to the Financial Statements on page 192.

Sarbanes-Oxley Act Section 404

As a consequence of our NYSE listing, AstraZeneca is 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, such as financial consolidation and reporting,

treasury operations and taxation, 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 2015 and the assessment is set out in the Directors' Responsibilities for, and Report on, Internal Control over Financial Reporting on page 135. KPMG LLP has audited the effectiveness of our internal control over financial reporting at 31 December 2015 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 136, 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
- > 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
4 February 2016