

# What science can do

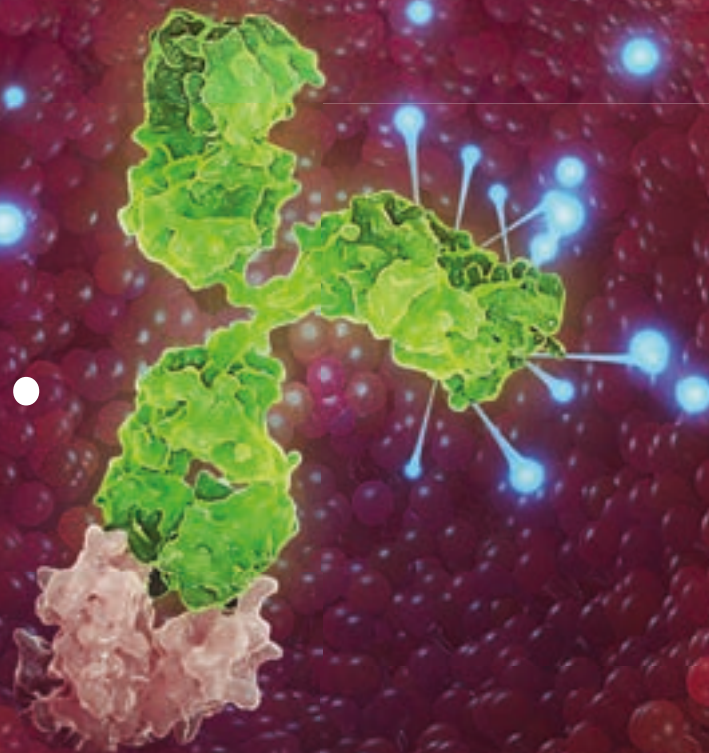
AstraZeneca Annual Report and Form 20-F Information 2019



## Welcome

We are a global, science-led, patient-focused pharmaceutical company and in this Annual Report we report on the progress we made in 2019 in pushing the boundaries of science to deliver life-changing medicines.

# What science can do... Next?



Our strategic priorities are focused on delivering value to patients and society.

### Delivering growth and therapy area leadership

by supplying medicines that can transform care and ensuring that they reach patients who need them.

☐ See Delivering growth from page 31.

### Accelerating innovative science

in search of solutions that prevent, treat, and even cure, some of the world's most serious health challenges.

☐ See Innovative science from page 25.

### Being a great place to work

by living our Values and behaviours, delivering as an enterprise team and leading in sustainability.

☐ See A great place to work: Employees from page 44 and Contributing to society from page 49.

#### Use of terms

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

#### Front cover image:

Antibody-drug conjugates (ADCs)

ADCs are among the most exciting technologies for the treatment of cancer. AstraZeneca is developing novel ADC targets that include therapy-resistant tumours and cancer stem cells. We are building a library of payloads, and using our antibody engineering expertise for site-specific conjugation and next-generation ADCs.

# Contents

## Financial highlights

### Total Revenue\*

Up 10% at actual rate of exchange to \$24,384 million (up 13% at CER), comprising Product Sales of \$23,565 million (up 12%; 15% at CER) and Collaboration Revenue of \$819 million (down 21%; 20% at CER)

|      |           |
|------|-----------|
| 2019 | \$24,384m |
| 2018 | \$22,090m |
| 2017 | \$22,465m |

**\$24.4bn**

### Net cash flow from operating activities

Up 13% at actual rate of exchange to \$2,969 million

|      |          |
|------|----------|
| 2019 | \$2,969m |
| 2018 | \$2,618m |
| 2017 | \$3,578m |

**\$3.0bn**

### Reported operating profit

Down 14% at actual rate of exchange to \$2,924 million (down 16% at CER)

|      |          |
|------|----------|
| 2019 | \$2,924m |
| 2018 | \$3,387m |
| 2017 | \$3,677m |

**\$2.9bn**

### Core operating profit

Up 13% at actual rate of exchange to \$6,436 million (up 13% at CER)

|      |          |
|------|----------|
| 2019 | \$6,436m |
| 2018 | \$5,672m |
| 2017 | \$6,855m |

**\$6.4bn**

### Reported EPS

Down 40% at actual rate of exchange to \$1.03 (down 44% at CER)

|      |        |
|------|--------|
| 2019 | \$1.03 |
| 2018 | \$1.70 |
| 2017 | \$2.37 |

**\$1.03**

### Core EPS

Up 1% at actual rate of exchange to \$3.50 (0% at CER)

|      |        |
|------|--------|
| 2019 | \$3.50 |
| 2018 | \$3.46 |
| 2017 | \$4.28 |

**\$3.50**

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

□ For more information in relation to the inclusion of Reported performance, Core financial measures and constant exchange rate (CER) growth rates as used in this Annual Report, see the Financial Review from page 78.

\* As detailed from page 173, Total Revenue consists of Product Sales and Collaboration Revenue.

## Key

- For more information within this Annual Report
- For more information, see [www.astrazeneca.com](http://www.astrazeneca.com)
- BV** Denotes sustainability information independently assured by Bureau Veritas



This Annual Report is also available on our website, [www.astrazeneca.com/annualreport2019](http://www.astrazeneca.com/annualreport2019)

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We are a global, science-led, patient-focused, pharmaceutical company. We have transformed our pipeline and returned to growth. As a result of continued pipeline delivery and commercial execution, we are now entering a new stage in our journey.

This is focused on enhanced innovation and the sustainable delivery of life-changing medicines that improve patient outcomes and health experience.

**Our strategic priorities**

□ Strategy from page 17 and Key Performance Indicators from page 20.

Reflect how we are working to achieve our Purpose: to push the boundaries of science to deliver life-changing medicines

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

**A science-led innovation strategy**

□ Innovative science from page 25.

**Distinctive R&D capabilities**

Small molecules, biologics, protein engineering and innovative delivery devices, as well as new scientific modalities, new technologies and new biology

**8** new molecular entities (NMEs) in Phase III/ pivotal Phase II or under regulatory review covering 13 indications



**Broad R&D platform in three main areas**

□ Innovative science from page 25 and Therapy Area Review from page 54.

**Oncology**

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

**Cardiovascular, Renal & Metabolism**

We are committed to the seamless management of heart failure, cardiovascular, renal and metabolic diseases, improving patient outcomes and decreasing the mortality rate

**Respiratory**

We aim to transform the treatment of respiratory diseases through our inhaled combination medicines, biologics for unmet medical need and scientific advances, with the ambition of achieving remission or even cures for patients

**Other Disease Areas**

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

**Portfolio of specialty and primary care medicines (Product Sales)**

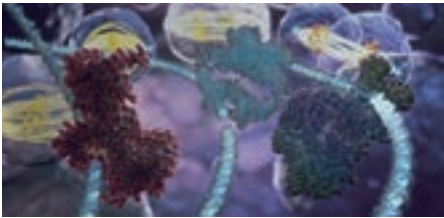
| 2019                             | 2018                             | 2017                             | 2016                             |
|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| <b>\$8,667m</b><br>37% of total  | <b>\$6,906m</b><br>29% of total  | <b>\$5,391m</b><br>23% of total  | <b>\$2,601m</b><br>11% of total  |
| 2018: \$6,028m<br>2017: \$4,024m | 2018: \$6,710m<br>2017: \$7,266m | 2018: \$4,911m<br>2017: \$4,706m | 2018: \$3,400m<br>2017: \$4,156m |

Sales growth of 44% (47% at CER), including:  
*Tagrisso* sales of \$3,189 million, representing growth of 71% (74% at CER)  
*Imfinzi* sales of \$1,469 million, representing growth of 132% (133% at CER)  
*Lynparza* sales of \$1,198 million, representing growth of 85% (89% at CER)  
 The performance of legacy medicines included a decline in *Faslodex* sales of 13% (11% at CER) to \$892 million, reflecting the launch of multiple generic medicines

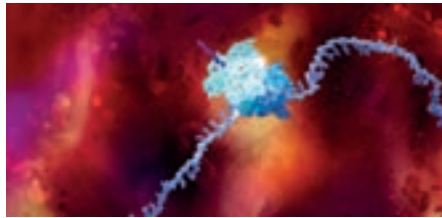
Sales growth of 3% (6% at CER), including:  
*Brilinta* sales of \$1,581 million, representing growth of 20% (23% at CER), due to continued patient uptake for ACS and post-MI  
*Farxiga* sales of \$1,543 million, with growth of 11% (14% at CER), reflecting pricing pressure in the US and a sales increase of 40% in Emerging Markets (48% at CER) to \$471 million  
*Crestor* sales of \$1,278 million, down 11% (8% at CER), reflecting generic competition and the effect of volume-based procurement in China

Sales growth of 10% in the year (13% at CER), including:  
*Symbicort* sales of \$2,495 million, down 3% (stable CER), as competitive price pressures in the US continued  
*Pulmicort* sales of \$1,466 million, representing growth of 14% (18% at CER), with Emerging Market sales up 20% (24% at CER) representing 81% of global sales  
*Fasenra* sales of \$704 million, up by 137% (139% at CER), with strong sales growth in the US, Europe and Japan

Product Sales declined by 24% (21% at CER) and represented 11% of total Product Sales, down from 16% in 2018. This included *Nexium* sales down by 13% (11% at CER) to \$1,483 million



Oncology. See page 54.



Cardiovascular, Renal & Metabolism. See page 60.



Respiratory. See page 66.

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

□ Delivering growth from page 31.

**Emerging Markets**

**\$8,165m**

35% of total  
2018: \$6,891m  
2017: \$6,149m

Product Sales increased by 18% (24% at CER). New Medicines<sup>1</sup> represented 23% of Emerging Market sales in the year, up from 15% in 2018

**US**

**\$7,747m**

33% of total  
2018: \$6,876m  
2017: \$6,169m

Product Sales increased by 13%, reflecting the success of the new Oncology medicines

**Europe**

**\$4,350m**

18% of total  
2018: \$4,459m  
2017: \$4,753m

Product Sales declined by 2% (grew 2% at CER), reflecting a strong performance by our Oncology medicines, offset by a decline in *Nexium* and legacy Respiratory medicines

**Established Rest of World**

**\$3,303m**

14% of total  
2018: \$2,823m  
2017: \$3,081m

Product Sales grew by 17% (18% at CER) reflecting the strong performance of New Medicines in Japan. We are also impacted by divestments in Canada and *Symbicort* analogues competition in Australia

**Our talented and diverse employees**

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

□ A great place to work: Employees from page 44.

**70,600**

employees  
2018: 64,600  
2017: 61,100

**45.4%**

of our senior roles are filled by women

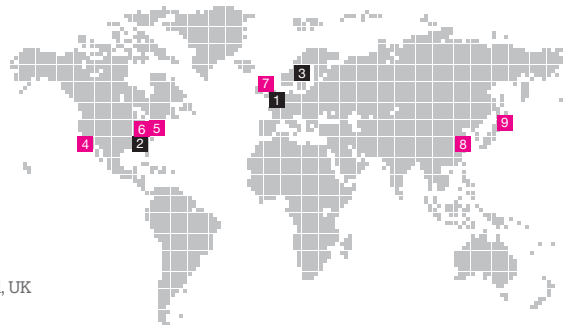
**91**

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

**>3,100**

employees with PhDs

- Strategic R&D centres**
1. Cambridge, UK (HQ)
  2. Gaithersburg, MD, US
  3. Gothenburg, Sweden
- Other R&D centres and offices**
4. South San Francisco, CA, US
  5. Boston, MA, US
  6. New York, NY, US
  7. Alderley Park and Macclesfield, UK
  8. Shanghai, China
  9. Osaka, Japan



**A sustainable business**

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

□ Sustainability from page 51.

**Priority**

**1**  
Access to healthcare



**Priority**

**2**  
Environmental protection



**Priority**

**3**  
Ethics and transparency



**100%**  
of employees trained in Code of Ethics



**Our capital allocation priorities**

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

□ Financial Review from page 78.

**Distributions to shareholders**

**Dividends**

**\$3,592m**  
2018: \$3,484m  
2017: \$3,519m

**Proceeds from issue of shares<sup>2</sup>**

**\$(3,525)m**  
2018: \$(34)m  
2017: \$(43)m

**Total**

**\$67m**  
2018: \$3,450m  
2017: \$3,476m

**R&D expenditure**

**\$6,059m**  
2018: \$5,932m  
2017: \$5,757m

**Credit rating (Standard & Poor's)**

**BBB+**  
Long-term: stable outlook

**Credit rating (Moody's)**

**A3**  
Long-term: negative outlook

<sup>1</sup> *Brilinta, Tagrisso, Imfinzi, Lynparza, Calquence, Farxiga, Lokelma, Fasenna, Bevespi and Breztri.*  
<sup>2</sup> In April 2019, the Company completed a placing of 44,386,214 new Ordinary Shares of \$0.25 each in the Company. For more information, see page 263.

In the first full year of our return to Product Sales growth, we made good progress in line with our strategy. We anticipate 2020 to be another year of progress.



“Looking ahead, ...we will maintain our focus on executing a strategy centred on science and patients.”

# \$2.80

Full-year dividend of \$2.80 per share

### Broad-based progress

AstraZeneca's financial performance in 2019 reflected a year of innovation for patients. Results from our New Medicines<sup>1</sup> and Emerging Markets accompanied positive news for patients and growing sales in all three of our therapy areas. This balance across our medicines and regions is matched by a balance across primary and specialty care treatments, which, together with our healthy pipeline of candidate medicines, forms a firm foundation for what we believe will be growth in the coming years.

### Responding to a changing world

Our return to Product Sales growth also reflects our success in responding to a changing world. It is a world of economic growth and increasing wealth, of a growing and ageing global population and challenged by an increasing burden of chronic and non-communicable diseases.

It is also a world of pricing pressures and of strong competition in which unparalleled scientific and technological advances are transforming both the pharmaceutical sector and people's ability to manage their own health.

Success will come to those companies able to grasp the opportunities offered and overcome the challenges faced. The Board and I are encouraged by AstraZeneca's re-emergence as a science leader, and how it is embracing those opportunities and driving change in the industry.

Nowhere is change more evident than in the US, where we are working with policymakers to ensure patients continue to have access to the medicines they need. We are actively supporting solutions that provide access and affordability while continuing to support scientific innovation. These include efforts to reform the system of rebates, ensuring patients are benefiting from the discounts we provide and the broader implementation of value-based reimbursement models.

### Working with stakeholders

We are only able to achieve this because of the strong team Pascal has assembled at AstraZeneca. But driving change only happens as a result of engaging successfully with a wide range of stakeholders beyond our shareholders – employees and patients, healthcare providers and governments, suppliers and the communities in which we operate. We report on how we do that in the Corporate Governance Report from page 104 and I have seen this with my own eyes when representing AstraZeneca across the world.

### Leading in sustainability

Leading in science means we have a responsibility to take a lead in applying the science to the world in which we live. It is why I am proud of our Ambition Zero Carbon strategy announced at the World Economic Forum in January 2020 to eliminate emissions by 2025 and be carbon negative across the entire value chain by 2030.

### 2019 performance and what's next

With Product Sales in 2019 up by 12% (15% at CER), we delivered a year of strong revenue growth. Good progress was also made with a pipeline that produced an extensive number of regulatory approvals and data readouts. Of course, seeking to lead and push the boundaries of science means that sometimes we do not succeed and our results in 2019 reflect an intangible asset impairment following the closure of the Phase III STRENGTH trial for *Epanova* due to its low likelihood of demonstrating a benefit to patients.

So far as 2020 is concerned, we anticipate another year of progress for AstraZeneca with continued focus on improving operating leverage and cash generation. In light of this, the Board reaffirmed its commitment to the progressive dividend policy; with a second interim dividend of \$1.90 per share taking the unchanged full-year dividend per share to \$2.80.

Our outlook for 2020 reflects our assessment of the Covid-19 virus outbreak and assumes an unfavourable impact lasting up to a few months.

Looking ahead, and as we reinforce our commitment to achieving our long-term climate change and decarbonisation targets, we will maintain our focus on executing a strategy centred on science and patients.

Leif Johansson  
Chairman

## Chief Executive Officer's Review

AstraZeneca's first full year of returning to Product Sales growth was made possible by our ability to deliver our science to patients. We are now maximising and exploring the full potential of our leading medicines, rapidly advancing the next wave of science and positioning your Company for continued success.



“Underpinning our return to growth has been our science-led innovation.”

### Science-led growth

In 2019, Product Sales grew by 12% (15% at CER) to \$23,565 million, driven by progress in all three of our therapy areas.

Underpinning our return to growth has been our science-led innovation. The panel to the right lists the medicines we have launched from our main therapy areas since 2013. The two we launched in 2019, together with the launch of roxadustat in 2020, brings the total to 12. It is these 12 new medicines that are largely responsible for the 59% growth (62% at CER) in Product Sales of our New Medicines<sup>1</sup> in 2019 to almost \$10 billion. New Medicines also represented 42% of total Product Sales, up from 30% in 2018.

2019 was also another exceptional year for our science, with our pipeline producing overwhelmingly positive news for patients. This included a record number of 63 regulatory events, either submissions or approvals for our medicines in major markets. That performance is backed by a healthy pipeline of high potential medicines, with the number of Phase II and Phase III pipeline progressions indicating our ability to deliver longer-term sustainable growth. In 2019, we had 22 pipeline progressions, and an average of 24 progressions in each of the last four years.

### Delivering our science for patients

Thanks to the strength of our science, we are reaching patients quickly.

### Oncology

As shown in the panel, our Oncology therapy area has delivered six new cancer medicines to patients since 2013 – meeting our 2020 target early.

Of these medicines, *Lynparza*, which we are developing in collaboration with MSD, is now approved in 73 countries and is the industry-leading PARP inhibitor: approved in three tumour types, ovarian, breast and pancreatic, in 2019 *Lynparza* became the only PARP inhibitor to show clinical benefit in a fourth type – prostate. A particular benefit of *Lynparza* is its administration in the 1st-line setting which brings the goal of long-term remission and cure closer. With annual sales of more than \$1 billion, *Lynparza* benefited some 15,000 new patients in 2019.

It was also another strong year for *Tagrisso*, which is approved in more than 87 countries and is our largest selling medicine, with more than 68,000 new patients in 2019. And, *Imfinzi*, which is now approved in 15 countries for bladder cancer and in 61 countries for lung cancer, benefited some 25,000 new patients in 2019 and achieved sales of more than \$1 billion.

We have a range of clinical trials under way investigating the full potential of our marketed medicines and there are plenty more projects in our pipeline. Of course, in pushing the boundaries of science, we sometimes experience setbacks which, in 2019, included disappointing results from the Phase III trial of *Imfinzi* plus tremelimumab in Stage IV non-small cell lung cancer. Overall, however, we continue to make good progress advancing new and exciting candidate medicines designed to change the practice of medicine and ultimately eliminate cancer as a cause of death.

### New medicines launched since 2013 (date of first launch)

#### Oncology

- > *Lynparza* (2014) for ovarian, breast and pancreatic cancer
- > *Tagrisso* (2015) for lung cancer
- > *Imfinzi* (2017) for lung and bladder cancer
- > *Calquence* (2017) for mantle cell lymphoma and chronic lymphocytic leukaemia
- > *Lumoxiti* (2018) for hairy cell leukaemia
- > *Enhertu* (2019) for breast cancer

#### CVRM

- > *Qtern* (2017) for diabetes
- > *Lokelma* (2018) for hyperkalaemia
- > *Roxadustat* (2020) for anaemia

#### Respiratory

- > *Fasenra* (2017) for severe asthma
- > *Bevespi Aerosphere* (2017) for chronic obstructive pulmonary disease (COPD)
- > *Breztri Aerosphere* (2019) for COPD

<sup>1</sup> *Brilinta* plus *Tagrisso*, *Imfinzi*, *Lynparza*, *Calquence*, *Farxiga*, *Lokelma*, *Fasenra*, *Bevespi* and *Breztri*. Of our remaining recently launched medicines, *Enhertu* and roxadustat will be added to this list in due course, while commercialisation rights of *Lumoxiti* were licensed to Innate Pharma for the US and EU in 2018.

# Chief Executive Officer's Review *continued*

## 59%

59% growth (62% at CER) in Product Sales of our New Medicines in 2019 to almost \$10 billion

## 63

63 regulatory submissions or approvals for our medicines in major markets

## 45%

Women now make up just over 45% of senior leaders today, compared with 40% in 2012

“By harnessing the unprecedented possibilities of science and technology, by transforming the way we work and by engaging with patients in everything we do, I am confident that we will realise our pipeline's potential to the full and deliver continued success.”

Perhaps the most exciting is *Enhertu* which was approved in the US in December for the treatment of HER2-positive breast cancer. This is a difficult to treat cancer and, together with partner Daiichi Sankyo, we are exploring *Enhertu's* full potential with five ongoing pivotal trials and over 40 clinical trials planned across HER2-expressing cancers.

### **CVRM**

In our CVRM portfolio, *Farxiga*, our treatment for diabetes, is now approved in more than 100 countries. While we received a Complete Response Letter (CRL) from the FDA during the year in respect of type-1 diabetes, the real excitement with this medicine is in following the science to explore its potential to go beyond diabetes and treat patients with heart failure. Here, our trials are demonstrating that *Farxiga* can reduce the risk of heart failure in patients with, and without, diabetes.

We are also following the science in our pipeline by, for example, exploring diseases such as non-alcoholic fatty liver disease, or other innovative approaches, including regenerating the heart by growing heart muscle back.

### **Respiratory**

Finally, in our Respiratory portfolio, *Fasenra* is now approved in more than 50 countries for the treatment of severe asthma with an eosinophilic phenotype. First approved in 2017, it was our first respiratory biologic medicine and has already helped 50,000 patients. We continue to explore *Fasenra's* potential in treating severe asthma as well as other diseases where eosinophils are believed to play a major role.

Approvals for *Breztri Aerosphere* (PT010) in China and Japan in 2019 on the strength of the Phase III KRONOS trial, were followed by positive results from its Phase III ETHOS trial which showed a significant reduction in the rate of moderate to very severe COPD exacerbations. This evidence will be used in response to the CRL we received from the FDA in response to our regulatory submission. We are also researching tezepelumab which has the potential to treat a broad population of asthma patients currently ineligible for biologic therapies.

Our Respiratory therapy area is expanding to include immunology, where candidate medicines include anifrolumab, a potential treatment for lupus, we hope to bring soon to patients who have only seen one new treatment in some 60 years.

### **A global, balanced business**

The contribution that each of our three therapy areas is making in delivering for patients is symptomatic of diversity and greater balance in our Company: for the first time in 2019 around half our Product Sales were in a specialty care and half in a primary care setting.

Balance is also evident in our global commercial presence, where we operate across all geographies. We have particular strength in Emerging Markets, where Product Sales increased by 18% (24% at CER) in 2019, with growth in China of 29% (35% at CER). In the US, Product Sales increased by 13%, while in Europe they declined by 2% in the year (up by 2% at CER). In Japan, Product Sales increased by 27% (26% at CER).

None of this commercial success would have been possible without the operational excellence that underpinned 106 successful market launches during the year and 31 independent inspections of our manufacturing sites with no critical observations.

### **Being a great place to work**

To be successful, we must remain a great place to work. This is because our innovation requires breakthrough ideas that can only come from people encouraged to be themselves at work, enabled to contribute to their full potential, and empowered to challenge conventional thinking. For us that means being an inclusive and diverse workplace, attracting and retaining the best people. For example, women now make up just over 45% of senior leaders today, compared with 40% in 2012, and we are aiming to reach 50% by 2022.

To ensure our organisation is best able to deliver our ambition, in January 2019, we announced changes that created therapy area-focused R&D units responsible for discovery through to late-stage development – one for Oncology and one for BioPharmaceuticals (CVRM and Respiratory). While we continue to make decisions on a Group-wide basis based on overall therapeutic considerations, these changes have enabled us to follow the science by accelerating promising early-stage assets and life-cycle management programmes, as well as making us more agile and collaborative in the way we work.



## Global Product Sales by therapy area

|                                    | 2019              |                 |              | 2018              |                 |              | 2017              |                 |              |
|------------------------------------|-------------------|-----------------|--------------|-------------------|-----------------|--------------|-------------------|-----------------|--------------|
|                                    | Product Sales \$m | Actual growth % | CER growth % | Product Sales \$m | Actual growth % | CER growth % | Product Sales \$m | Actual growth % | CER growth % |
| Oncology                           | 8,667             | 44              | 47           | 6,028             | 50              | 49           | 4,024             | 19              | 19           |
| Cardiovascular, Renal & Metabolism | 6,906             | 3               | 6            | 6,710             | (8)             | (8)          | 7,266             | (10)            | (10)         |
| Respiratory                        | 5,391             | 10              | 13           | 4,911             | 4               | 3            | 4,706             | (1)             | (1)          |
| Other Disease Areas                | 2,601             | (24)            | (21)         | 3,400             | (18)            | (19)         | 4,156             | (18)            | (17)         |
| <b>Total</b>                       | <b>23,565</b>     | <b>12</b>       | <b>15</b>    | <b>21,049</b>     | <b>4</b>        | <b>4</b>     | <b>20,152</b>     | <b>(5)</b>      | <b>(5)</b>   |

### Working with patients to deliver more

As we accelerate growth, our strategy is focused on exploring the full potential of our leading medicines and advancing our science. For us that means continued innovation – both in our science and the way we work. Throughout this Annual Report and listed to the right are examples of how we are doing that, including ideas which we crowdsourced from employees.

Putting patients at the heart of what we do is central to those efforts and an example of how we live our Values. That means recognising patients as people first and working with them to help us innovate and deliver advances across everything that a patient experiences – from prevention and awareness, diagnosis, treatment and post-treatment to wellness.

As the case studies also indicate, we are using digital technology more generally to transform the way we work and reimagine healthcare across all areas, from R&D to Commercial, and from Operations to our enabling units.

### Sustaining the planet

We are a Company that has long recognised the interconnection between business growth, the needs of society and the limitations of our planet. Climate change is an urgent threat to public health, the environment and the sustainability of the global economy. Since 2015, we have reduced our carbon emissions from operations by almost one third and our water consumption by almost one fifth. But now is the time to act even faster and, in January 2020, we announced an ambitious \$1 billion programme for zero carbon emissions from our global operations by 2025 and to ensure our entire value chain is carbon negative by 2030. This would bring forward our decarbonisation plans by more than a decade.

This announcement builds on our longstanding commitment to leading in sustainability and contributing to society. For example, 2019 was the fifth anniversary of our Healthy Heart Africa programme. It was also the tenth year of our award-winning Young Health Programme where, with our recently announced partnership with UNICEF, we will have a truly global disease prevention programme working in some of the hardest to reach areas of the world.

### Our long-term future

Our decarbonisation plans for the planet are for the long term. Our Company is also for the long term. As well as delivering our science for patients today, we have ambitious future plans built on our healthy pipeline. By harnessing the unprecedented possibilities of science and technology, by transforming the way we work and by engaging with patients in everything we do, I am confident that we will realise our pipeline's potential to the full and deliver continued success.

That confidence stems from the talented team we can draw on in AstraZeneca, as well as our many partners, and the continued support of Leif and the Board of Directors. I am grateful to them all.



**Pascal Soriot**  
Chief Executive Officer

### Delivering our strategy

Understanding disease better: Transforming the discovery and development of innovative new medicines. See page 27.

Redefining clinical trials: Making clinical trials better and easier for patients. See page 30.

Improving patient access: Exploring new value-based payment models. See page 36.

Improving outcomes for patients: Establishing Health Innovation Hubs to deliver patient-focused disease management solutions. See page 43.

Being a great place to work: Attracting and retaining the best people. See page 48.

Ambition Zero Carbon: Our strategy to eliminate emissions by 2025 and be carbon negative by 2030. See page 53.

Business model and life-cycle of a medicine

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

# Why AstraZeneca?

We are a global pharmaceutical business which has:

- > A science-led innovation strategy
- > An R&D platform across small molecules and biologics, as well as new scientific modalities
- > Three main therapy areas: Oncology; Cardiovascular, Renal & Metabolism; and Respiratory
- > A portfolio of specialty care and primary care medicines
- > A global footprint
- > A talented and diverse workforce who are committed to our Purpose and who live our Values

Lipid nanoparticle breaking the endosomal membrane to release modified mRNA into the cytoplasm.

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## Who we are

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### Our Purpose

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

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

### A focus on patients.

We aim to improve the entire patient experience and deliver the health outcomes that people care about most so that they can enjoy fulfilling lives. We can do that better if we walk in patients' shoes, listen to their experiences and embed their insights to innovate and strengthen how we work.

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### Our Values

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

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

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### Our Culture

Our Values foster a strong AstraZeneca culture in which our people are empowered and inspired to make a difference to patients, society and our Company. By performing as an enterprise team, committing to life-long learning and development and being champions of inclusion and diversity, we ensure that AstraZeneca is a great place to work. All of this is underpinned by the high ethical standards embodied in our Code of Ethics which we employ when carrying out all aspects of our business globally.

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### Our Sustainability

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

Our sustainability priorities in access to healthcare, environmental protection, and ethics and transparency support the delivery of our business strategy.

□ Business Review from page 24.

## What we do

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

### How we create financial value

#### Investment

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

#### Revenue generation

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

#### Reinvestment

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



## Life-cycle of a medicine

### Research and development phases – duration: 5–15 years

- 1. Find potential medicine**
  - > Identify unmet medical need 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 trials**
  - > Begin clinical trials with small groups of healthy human volunteers (small molecules) or patients (biologics) to understand how the potential medicine is absorbed into the body, distributed around it and excreted.
  - > Determine approximate dosage and identify side effects.
- 4. Phase II trials**
  - > Conduct trials on small- to medium-sized groups of patients to test effectiveness and tolerability of the medicine and determine optimal dose.
  - > Design Phase III trials to generate data needed for regulatory approvals and pricing/reimbursement globally.
- 5. Phase III trials**
  - > Engage in trials 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 whether to grant regulatory approvals.

### Launch phase – duration: 5–15 years

- 7. Launch new medicine**
  - > Raise awareness of patient benefit and appropriate use, market and sell the medicine.
  - > Clinicians begin to prescribe the medicine 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 the medicine's full potential.
  - > Consider additional diseases or aspects of disease to be treated by, or better ways of administering, the medicine.
  - > Submit data packages with requests for life-cycle management to regulatory authorities for review and approval.

### Post-exclusivity – duration 20+ years

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

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

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

## What does our business model require to be successful?

### A talented and diverse workforce

We need to acquire, retain and develop a talented and diverse workforce united in pursuit of our Purpose and Values and fostering a strong AstraZeneca culture.

□ See A great place to work: Employees from page 44.

### A leadership position in science

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

□ See Innovative science from page 25.

### Understand our stakeholders

We need to understand the factors and issues that are most important to the various stakeholders that interact with, and are impacted by, our business.

□ See Connecting with our stakeholders from page 104.

### Effective collaborations

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

□ See Business development on page 40.

### Commercialisation skills

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

□ See Delivering growth from page 31.

### Intellectual property (IP)

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

□ See Intellectual Property from page 41.

### A robust supply chain

We need a supply of high-quality medicines, whether from one of the 26 Operations sites in 16 countries in which we manufacture or the \$14 billion we spend on the purchase of goods, services and active pharmaceutical ingredients (APIs).

□ See Operations from page 37.

### Financial strength

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

□ See Financial Review from page 78.

**70,600**  
employees

**\$6.1bn**  
invested in our science

**>120m**  
Our medicines impacted more than 120 million patient lives in 2019

**>730**  
collaborations worldwide

**>100**  
countries in which we are active

**>100**  
countries where we obtain patent protection

**\$14bn**  
spent with suppliers

**\$3.0bn**  
net cash flow from operating activities

### How we add value

#### Improved health

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

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

□ See A great place to work: Contributing to society from page 49.

#### Financial value

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

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

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

□ See Financial Review from page 78.

## Healthcare in a changing world

Economic growth and increasing wealth, an expanding and ageing global population, together with technological change, are contributing to growth in the pharmaceutical industry. However, social, economic and political challenges remain in addressing unmet medical need.

### Increasing demand for healthcare

- > Economic growth and increasing wealth have raised many people out of extreme poverty
- > The world's population is growing and life expectancy is increasing
- > While communicable diseases continue to pose a threat, especially in emerging markets, chronic and non-communicable diseases (NCDs) are increasing
- > Digital and other technologies are transforming the pharmaceutical industry and enabling people to become more active participants in managing their healthcare
- > Society's expectations of business are changing and new challenges are being faced

### A growing pharmaceutical sector

- > The US is the largest pharmaceutical market, with 48% of global sales, while China now represents 8%
- > Pharmaceutical sales grew by 6.0% in 2019, led by emerging markets
- > Global healthcare spending is projected to increase at an annual rate of 4.7% from 2018-2023

### Opportunities and challenges for the sector

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

### Increasing demand for healthcare

#### Growing and shifting global economy

The October 2019 World Economic Outlook of the International Monetary Fund commented that global economic activity remained weak after slowing sharply in the last three quarters of 2018. It observed that rising trade and geopolitical tensions had increased uncertainty about the future of the global trading system and international cooperation more generally, taking a toll on business confidence, investment decisions and global trade.

Over the longer term, in the two decades to 2018, global GDP rose by some 80% to \$82.5 trillion (World Bank). Figures from the International Development Association of the World Bank indicate these decades saw significant progress in many of the world's poorest countries. The extreme poverty rate fell from more than 50% to about 30%. Child mortality declined from nearly 14% to 7%. Access to electricity increased by 57% and the share of people using at least basic drinking water and sanitation services increased by 22% and 41%, respectively.

At the same time, with markets such as China and India developing and urbanising rapidly, economic growth is shifting east and away from advanced economies such as North America, Western Europe and Japan. By some estimates, Africa could represent the fourth largest economy in the world by 2040 and, by 2050, India could overtake the US as the world's second largest economy.

## 80%

Global GDP grew by nearly 80% between 1998 and 2018. (World Bank)

## 30%

Between 1998 and 2018, the rate of extreme poverty fell from more than 50% to about 30%. (International Development Association)

# Healthcare in a changing world *continued*

## Increasing demand for healthcare *continued*

### Growing and ageing populations

As shown on the right, the world's population is rising and, with more people living longer, ageing. Indeed, in some markets, such as Japan and Western Europe, where the number of people over 65 in 2023 is forecast to be 29% and 22%, respectively, ageing populations mean the size of the labour force will stagnate or decline. This will result in a potential shortage of labour compared with the abundance of labour that has fuelled growth since the 1970s.

Estimated world population (UN, bn)

|      |      |
|------|------|
| 2100 | 11.2 |
| 2050 | 9.7  |
| 2030 | 8.5  |
| 2019 | 7.7  |

Life expectancy (Economist Intelligence Unit, years)

|      |      |
|------|------|
| 2018 | 73.7 |
| 2022 | 74.7 |

// Denotes a scale break.

### Increasing burden of chronic disease

An ageing population and changes in society are contributing to steady increases in NCDs with developing countries particularly affected as their populations grow. For example, nearly 425 million people were living with diabetes in 2017; by 2045, that number is projected to increase to 629 million.

In particular, while urbanisation presents opportunities, such as greater wealth and access to better healthcare, it also presents new hazards and healthcare challenges, including an increase in the prevalence of NCDs. These diseases include cancer and cardiovascular, metabolic and respiratory diseases which are often associated with urban lifestyle choices, including smoking, diet and lack of exercise. NCDs are also associated with ageing and, with the majority of the world's workforce ageing, healthcare costs are rising as people are living longer.

## 41m

NCDs killed 41 million people in 2016, compared with 31 million in 2000, up by one third. (WHO)

## \$47tn

The World Economic Forum has estimated that NCDs could cost the global economy a cumulative \$47 trillion in the 20 years to 2030.

## 85%

More than 85% of 'premature' deaths arising from NCDs occur in low- to middle-income countries. (WHO)

### Digital and technical breakthroughs

Advances in digitisation, analytics, artificial intelligence (AI), machine learning and automation are redefining how business and industries work. They will transform the workplace and business processes as people interact with increasingly smarter machines. New entrants from the technology sector are bringing different competencies to healthcare, applying their knowledge to accelerate scientific discovery, improve health through technology and better understanding of the patient.

At the same time, the digitisation of healthcare is improving prevention, facilitating more accurate diagnoses and treatment regimens, and putting more information in people's hands, empowering them to play a larger role in managing their own health.

## 38bn

It is estimated that by 2025, more than 38 billion internet-connected devices will be installed globally. (Strategy Analytics)

### Changing society and business

As the burden of NCDs grows, so do public expectations, while governments' ability to meet them is constrained as finances are under stress. Low- and middle-income countries are also disproportionately affected by issues such as air pollution and climate change, thereby exacerbating social, economic and demographic inequalities. Society's view of business is also changing. Organisations are no longer valued or trusted solely on the quality of products and services, and financial performance, but also their engagement with employees, customers, communities and society as a whole as well as the way in which they consider sustainability issues, such as environmental or human rights issues.

Workforce dynamics are also changing for many, as working for a single employer is replaced by working independently in a number of different roles.

**“Organisations are no longer valued or trusted solely on the quality of products and services, and financial performance, but also their engagement with employees, customers, communities and society as a whole.”**

## A growing pharmaceutical sector

### Global pharmaceutical sales

As shown in the chart on the right, global pharmaceutical sales grew by 6.0% in 2019. Established Markets saw an average revenue increase of 4.9% and Emerging Markets revenue grew at 10.1%. The US, Japan, China, Germany and France are the world's top five pharmaceutical markets by 2019 sales. In 2019, the US had 47.5% of global sales (2018: 47.9%; 2017: 47.7%).

#### World (\$bn)

|      |       |
|------|-------|
| 2019 | 1,033 |
| 2018 | 975   |
| 2017 | 930   |

**\$1,033bn** (6.0%)

#### US (\$bn)

|      |     |
|------|-----|
| 2019 | 491 |
| 2018 | 467 |
| 2017 | 440 |

**\$491bn** (5.1%)

#### Europe (\$bn)

|      |     |
|------|-----|
| 2019 | 195 |
| 2018 | 185 |
| 2017 | 177 |

**\$195bn** (5.5%)

#### Established ROW (\$bn)

|      |     |
|------|-----|
| 2019 | 115 |
| 2018 | 112 |
| 2017 | 112 |

**\$115bn** (2.5%)

#### Emerging Markets (\$bn)

|      |     |
|------|-----|
| 2019 | 232 |
| 2018 | 211 |
| 2017 | 198 |

**\$232bn** (10.1%)

// Denotes a scale break.

Data based on world market sales using AstraZeneca market definitions as set out in the Market definitions on page 268. Changes in data subscriptions, exchange rates and subscription coverage, as well as restated IQVIA data, have led to the restatement of total market values for prior years. Source: IQVIA, IQVIA Midas Quantum Q3 2019 (including US data). Reported values and growth are based on CER. Value figures are rounded to the nearest billion and growth percentages are rounded to the nearest tenth.

### Estimated pharmaceutical sales and market growth to 2023

The table of estimated pharmaceutical sales and market growth to 2023 on the right also illustrates that we expect developing markets, including Africa, the Commonwealth of Independent States (CIS), the Indian subcontinent and Latin America, to fuel pharmaceutical growth. Market growth in China is expected to remain below historical levels at a compound annual growth rate of 5.7%. This is due to the continued slowdown of the major hospital sector.

#### North America

|  |         |
|--|---------|
| Estimated pharmaceutical sales in 2023 | \$628bn |
| Estimated pharmaceutical market growth | 4.2%    |

#### EU (Including UK)

|  |         |
|--|---------|
| Estimated pharmaceutical sales in 2023 | \$302bn |
| Estimated pharmaceutical market growth | 3.6%    |

#### Other Europe (Non-EU countries)

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$26bn |
| Estimated pharmaceutical market growth | 9.7%   |

#### Japan

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$94bn |
| Estimated pharmaceutical market growth | -0.6%  |

#### Oceania

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$16bn |
| Estimated pharmaceutical market growth | 2.7%   |

#### South East Asia and East Asia

|  |         |
|--|---------|
| Estimated pharmaceutical sales in 2023 | \$234bn |
| Estimated pharmaceutical market growth | 5.8%    |

#### Latin America

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$93bn |
| Estimated pharmaceutical market growth | 10.5%  |

#### Africa

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$29bn |
| Estimated pharmaceutical market growth | 7.5%   |

#### CIS

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$31bn |
| Estimated pharmaceutical market growth | 9.3%   |

#### Middle East

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$25bn |
| Estimated pharmaceutical market growth | 4.4%   |

#### Indian subcontinent

|  |        |
|--|--------|
| Estimated pharmaceutical sales in 2023 | \$41bn |
| Estimated pharmaceutical market growth | 9.9%   |

■ Estimated pharmaceutical sales in 2023. Data are based on ex-manufacturer prices at CER. Source: IQVIA.

■ Estimated pharmaceutical market growth. Data are based on the compound annual growth rate from 2018 to 2023. Source: IQVIA.

# Healthcare in a changing world *continued*

## Opportunities and challenges for the sector

In addition to the global trends set out on the previous pages, the pharmaceutical sector faces a number of opportunities and challenges, as set out below. The Strategy section of this Annual Report includes an overview of how we are responding to this environment. More detail can be found in the relevant sections of this Annual Report as indicated below.

For more information, see Strategy from page 17.

## Innovation

Scientific innovation is critical to addressing unmet medical need but R&D productivity across the industry has fallen in recent years. For example, in its report, *Ten years on*, Deloitte charted the pressures that had led to a decline in return on investment, with the average cost of bringing a medicine to market increasing by two thirds, to almost \$2 billion, in the decade to 2019.

R&D models are therefore changing in an effort to be more productive. For example, scientific and technological breakthroughs in the next generation of therapeutics have the potential to help accelerate innovation and are leading to new treatment options. Such advances have already resulted in significant numbers of FDA Priority Reviews and Breakthrough Therapy Designations.

Innovation can also be accelerated through the use of large volumes of data from disease biology and genomics, which is driving precision medicine, while advances in data management and integration can improve the speed and quality of clinical trials. Additionally, a better understanding of disease biology can assist the delivery of new medicines and new approaches to health, including improved methods of prevention.

Against this background, and as shown to the right, the FDA approved 48 novel drugs in 2019. The role of regulation in the pharmaceutical sector is explored further below.

# 48

### FDA novel medicine approvals

|      |    |
|------|----|
| 2019 | 48 |
| 2018 | 59 |
| 2017 | 46 |
| 2016 | 22 |
| 2015 | 45 |

### Link to strategy

 Accelerate Innovative Science

For more information, see Risk from page 246.

## Regulatory environment

Public expectation of safe, effective and high-quality medicines is reflected in a highly regulated biopharmaceutical industry. At the same time, we are seeing instances of government policy and regulation being introduced to stimulate innovation in drug development, and of regulatory health authorities implementing programmes intended to speed up patient access to transformative medicines. Examples include the 21st Century Cures Act of 2016 and the FDA Reauthorization Act of 2017 in the US; the EMA Regulatory Science to 2025 in Europe; a new conditional early approval system in Japan; worksharing processes between authorities in Australia, Singapore, Canada and Switzerland; and proposed changes to regulations in China. Facilitated review pathways relying on assessments conducted in a reference agency have been introduced in many developing authorities to speed up patient access to medicines. In addition, international harmonisation of regulatory requirements is being advanced in many areas and will contribute to faster access to new medicines for patients and promote public health.

There are also uncertainties. In Europe, they include how the UK will work with the EU regulatory system after the end of the transition period, which runs to 31 December 2020 following its exit from the EU on 31 January 2020 and the approach the UK will take to establishing its own regulatory system outside the EU. Additionally, the relocation of the EMA from London to Amsterdam, Netherlands has created some disruption and delay to regulatory processes.

The implementation of the EU Clinical Trials Regulation has also been delayed. Nevertheless, paediatrics, use of digital tools, and of data sources other than randomised controlled clinical trials in clinical development, as well as patients' access to innovative medicines and stakeholders' interactions to improve drug development, are high on the EU and US agenda as well as being key objectives of the China regulatory reforms. In the EU, there is now stronger evidence that the Commission and the Member States are reviewing the full pharmaceutical legislation framework and may put forward relevant actions to the new Commission which was established in 2019.

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

Increased transparency of data used for regulatory decision making continues to be an area of interest to regulatory authorities in the EU, the US and now Canada. New policies continue to be evaluated by other regulatory authorities around the world.

“Public expectation of safe, effective and high-quality medicines is reflected in a highly regulated biopharmaceutical industry.”

### Link to strategy

 Accelerate Innovative Science

For more information, see Risk from page 246. For more information about biosimilars, see Loss of exclusivity and genericisation opposite.



## Pricing of medicines

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

The need and desire for payers to manage drug expenditure has been heightened by the shift over the last decade from a primary care to a specialty care focus. Specialty drugs are used for the treatment of complex, chronic or rare conditions, such as cancers, and pricing for these products reflects the higher value they bring to patients and payers, as well as the smaller patient numbers as a result of targeted treatment options.

Pricing controls and transparency measures remain a priority in key markets such as China, where the National Reimbursement Drug List was updated in 2017. In 2019, China expanded value-based procurement (VBP), placing downward pressure on the pricing of products that have lost exclusivity in the VBP.

In Europe, governments continue to implement and expand price control measures for medicines, and the EU has committed to introducing a harmonised health technology assessment (HTA) review. In other markets, there has been a trend towards rigorous and consistent application of pricing regulations, including reference pricing and group/alliance purchasing.

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

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

[Link to strategy](#)

 [Deliver Growth and Therapy Area Leadership](#)

 For more information, see Risk from page 246.

## Loss of exclusivity and genericisation

Patent protection for pharmaceutical products is finite and, after protection expires, payers, physicians and patients gain greater access to generic alternatives (both substitutable and analogue) in many important drug classes. These generic alternatives are primarily lower priced because generic manufacturers are largely spared the costs of R&D and market development. As a result, demand for generics is high. For prescriptions dispensed in the US in 2019, generics constituted 84.8% of the market by volume (2018: 84.8%).

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.

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

**84.8%**

For prescriptions dispensed in the US in 2019, generics constituted 84.8% of the market by volume (2018: 84.8%).

[Link to strategy](#)

 [Deliver Growth and Therapy Area Leadership](#)

 For more information, see Intellectual Property from page 41.



## Opportunities and challenges for the sector *continued*

### Trust

The pharmaceutical industry continues to face challenges in building and maintaining its reputation and the trust of its stakeholders. This reflects sales and marketing practices by some companies, for example in connection with the selling of opioid pain relievers, or pricing practices, including price gouging. It also reflects inquiries or investigations by government and regulatory authorities. For example, companies have been investigated by the US Department of Justice (DOJ) and Securities and Exchange Commission (SEC), under the Foreign Corrupt Practices Act, and by the UK Serious Fraud Office under the UK Bribery Act.

To address these challenges, companies are seeking to operate in a way that meets the expectations of all stakeholders, for example, by:

- > embedding a culture of ethics and integrity
- > adopting higher governance standards
- > promoting sustainability programmes
- > improving relationships with employees, shareholders and other stakeholders.

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

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

[Link to strategy](#)

 [Be a Great Place to Work](#)

 For more information, see Ethics and transparency on page 52.

### Reshaping of the sector

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

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

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

The speed of technological change may also transform current business models. Existing and new entrants to the sector, for example from the technology sector, are focusing on patient outcomes rather than just products and services, and prediction and prevention rather than just diagnosis and treatment. This may also entail new ways of competing. If new approaches such as outcomes-based pricing are to be successful, companies will need to develop systems that capture outcomes data linked to the use of their medicines. The sustainability and growth of a more patient-centric pharmaceutical industry is predicated on organisations being able to take full advantage of these breakthroughs in digital and other technologies.

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

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

[Link to strategy](#)

[Global, science-led, patient-focused pharmaceutical company](#)

 For more information, see Risk from page 246.

# What's Next?

In 2018, we achieved a significant milestone by returning to Product Sales growth. In 2019, we refreshed our strategy to focus on what comes next, and where we want our business to be in 2025. Our strategy is set out on the following pages. It reflects ideas which we crowdsourced from our employees and is underpinned by the following initiatives intended to accelerate delivery of our strategy.

## Understanding disease better

Transforming the discovery and development of innovative new medicines.

☐ See page 27.

## Redefining clinical trials

Making clinical trials better and easier for patients.

☐ See page 30.

## Improving patient access

Exploring new value-based payment models.

☐ See page 36.

## Improving outcomes for patients

Establishing Health Innovation Hubs to deliver patient-focused disease management solutions.

☐ See page 43.

## Being a great place to work

Attracting and retaining the best people.

☐ See page 48.

## Ambition Zero Carbon

Our strategy to eliminate emissions by 2025 and be carbon negative by 2030.

☐ See page 53.

Biocatalysis: enabling efficient and sustainable synthesis of AstraZeneca drug molecules.

The fundamentals of our strategy are clear. We focus on innovative science and leadership in our three main therapy areas: Oncology; Cardiovascular, Renal & Metabolism; and Respiratory. With a broad R&D platform and portfolio of specialty and primary care medicines, we have a global presence, with strength in Emerging Markets, particularly China.


### Our strategic priorities


While the fundamentals of our strategy are unchanged, the world around us is changing and the burden of disease is increasing. We are responding by enhancing our focus on growth through innovation – fostering a patient-centric culture and embedding it across our organisation, doing more with technology, digital and data, and advancing cutting-edge science.

All this is reflected in our strategic priorities, listed below, which were refreshed in 2019 to support delivery of the next phase of our strategy.

These priorities are accompanied by our unwavering commitment to being a trusted partner for all our stakeholders, having a positive impact on society, and being an indispensable ally in the quest to meet rising global demand for effective healthcare.

 **1. Deliver Growth and Therapy Area Leadership**

 **2. Accelerate Innovative Science**

 **3. Be a Great Place to Work**

 **Achieve Group Financial Targets**

Effective delivery of our three strategic pillars will help us achieve our financial targets. We aim to deliver great medicines to patients while maintaining cost discipline and a flexible cost base, driving operating leverage, and increased cash generation.

We wish to maintain a progressive dividend policy and a strong balance sheet.

### How we report our progress

#### Key Performance Indicators (KPIs)

The following pages present our KPIs for the year ending 31 December 2019. Our KPIs are aligned to our three strategic priorities and are the indicators against which we measure our productivity and success. We also monitor financial targets, which indicate whether we have delivered our strategy in a way that allows us to continue to operate as a successful business.

Our remuneration arrangements are also aligned to our strategic priorities as set out in our Group scorecard and reflected in our KPIs. Deliver Growth and Therapy Area Leadership, Accelerate Innovative Science and Achieve Group Financial Targets are included in the annual bonus targets.

 For more information, see the Directors' Remuneration Report from page 125.

#### Strategic Report

Our operating model comprises key business functions that are aligned to the delivery of our strategy. In addition, our therapy areas provide strategic direction for each of our disease areas all the way from early-stage development to commercialisation.

Our Strategic Report therefore includes three types of review and our Principal Risks:

#### Business Review

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

#### Therapy Area Review


Looks at each of our therapy areas, their developments and focus for 2019, as well as what is in the pipeline.

#### Financial Review

Reviews our financial performance during the year.

#### Risks

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

 For more information, see Business Review from page 24, Therapy Area Review from page 54, Risk Overview from page 74 and Financial Review from page 78.

## Strategic priority



## Deliver Growth and Therapy Area Leadership



## Accelerate Innovative Science



## Be a Great Place to Work

## What this means

Driving growth through successful innovation and commercial excellence, and creating sustainable profitability by managing costs and scaling efficiently as we build.

Impacting and improving the whole patient experience, from disease prevention and awareness, diagnosis, treatment, post-treatment to wellness.

Collaborating with the funders of healthcare to increase the use of value-based pricing solutions that focus on the outcomes our medicines deliver to patients and healthcare systems.

Advancing high-potential late-stage pipeline projects with a continued focus to ensure sustainable delivery of new products.

Pursuing the next wave of disruptive biology with new scientific modalities, such as ProTACs, in vivo biologics and cell therapy; new technologies, such as OMICs; and new biology, such as the microbiome.

Accelerating efforts in artificial intelligence (AI) data science and digital technology, enabling new insights, accelerated processes and an improved patient experience and adherence.

Making a difference to medicine and patients, delivering the next wave of science, shaping the patient ecosystem and focusing on outcomes.

Leading in sustainability which means improving access to healthcare, environmental protection and maintaining ethics and transparency.

Performing as an enterprise team, building a culture of lifelong learning and development and also being champions of inclusion and diversity.

Living our Values and behaviours.

## How our current strategy responds to market trends

Our strategy, on which we report in this Annual Report, including the initiatives listed on page 17, reflects the way we have chosen to respond to the opportunities and challenges posed by the marketplace in which we operate, as outlined in Healthcare in a changing world from page 11.

Aiming to shift from a focus on treatment to improve the whole patient experience and develop new payer models that improve access to our medicines:

- > Fostering a patient-immersed culture, building fully-integrated therapy area ecosystem models, and establishing 'health innovation hubs'.
- > Engaging with policymakers to support improvements in access, coverage, care delivery, quality of care and patient care outcomes.
- > Leveraging technology across prevention and awareness, diagnosis, treatment and post-treatment to wellness to deliver better patient outcomes more efficiently.
- > Enabling our Emerging Markets to deliver better and broader patient access through faster submissions, innovative and targeted equitable pricing strategies and practices.
- > Partnering with industry, governments and academia to find ways to bring new medicines to market more quickly and efficiently.
- > Basing pricing policy on four principles: value, sustainability, access and flexibility; and develop novel and flexible ways to assess and pay for medicines.
- > Pursuing a strong patent strategy – building robust patent estates that protect our pipeline and products to defending and enforcing patent rights.

□ See Delivering growth from page 31.

Aiming to lead in new science platforms, leveraging technology to transform R&D productivity and the patient's experience:

- > Focus on innovative science in three main therapy areas, a range of drug modalities, emerging drug platforms and new technologies, such as cell therapy, ProTACs and OMICs.
- > Strengthening our ability to match targeted medicines to patients who need them most.
- > Driving R&D productivity by focusing on quality rather than quantity at all stages of drug discovery and development, and leveraging technology including the provision of enhanced data and clinical insights, as well as digital and AI approaches.
- > Partnering with academia, governments, industry, and scientific and patient organisations to access the best science, drive innovation and streamline and standardise regulatory processes to increase access to our medicines worldwide.
- > Maintaining effective working relationships with health authorities worldwide.
- > Making information about our clinical research publicly available to enhance scientific understanding while ensuring respect for the privacy of patients.

□ See Innovative science from page 25 and Therapy Area Review from page 54.

Aiming to be a great and sustainable organisation, trusted by all our stakeholders:

- > Empowering employees through our Code of Ethics to make decisions in the best interests of the Group and society.
- > Refusing to tolerate bribery or any other form of corruption.
- > Recruiting the best talent which underpins our innovation and growth.
- > Living our Values and engendering a high-performing culture and lifelong learning.
- > Harnessing different perspectives, talents and ideas to create an inclusive culture, as well as ensuring that employees reflect the diversity of the communities in which we operate.
- > Contributing to society in support of the United Nations Sustainable Development Goals.
- > Broadening access to healthcare solutions for life-changing treatment and prevention.
- > Addressing the environment's impact on human health.

□ See A great place to work: Employees from page 44 and Contributing to society from page 49.

# Key Performance Indicators

## Our KPIs and remuneration

A number of KPIs on the following pages are used to measure the remuneration of Executive Directors.

In 2019, we made changes to our KPIs to reflect shareholder feedback. As a result of requests to simplify the metrics used for determining remuneration,

as well as improve transparency by disclosing targets, we have introduced three additional 'total' KPIs in 2019.

These additional KPIs have been used for remuneration purposes and allow us to disclose aggregated targets without

## Key Performance Indicators

### Deliver Growth and Therapy Area Leadership

Focus on revenue performance of our sales platforms:

#### Emerging Markets

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

Total<sup>1</sup>

**\$21,894m**

Product Sales from sales platforms



| Actual growth | CER growth |
|---------------|------------|
| 2019 +19%     | 2019 +22%  |
| 2018 +13%     | 2018 +12%  |

#### Respiratory

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

#### New CVRM

Since 2017, the New CVRM sales platform has included *Brilinta*, *Onglyza* franchise (*Onglyza* and *Kombiglyze*), *Farxiga* franchise (*Farxiga* and *Xigduo*), *Exenatide Total* (*Byetta* and *Bydureon*), *Symlin*, *Qtern*, *roxadustat* and *Lokelma*. *Epanova* was previously included but we have now terminated the Phase III STRENGTH trial.

#### Japan

Strengthen the performance of our New Medicines, particularly our Oncology brands.

#### Oncology

Includes entire Oncology portfolio. We have met our target of delivering six new cancer medicines to patients by 2020: *Lynparza*, *Tagrisso*, *Imfinzi*, *Calquence*, *Lumoxiti* and *Enhertu* that make a meaningful difference to patients.

#### Emerging Markets

**\$8,165m**

Product Sales



| Actual growth | CER growth |
|---------------|------------|
| 2019 +18%     | 2019 +24%  |
| 2018 +12%     | 2018 +13%  |
| 2017 +6%      | 2017 +8%   |

#### Respiratory

**\$5,391m**

Product Sales



| Actual growth | CER growth |
|---------------|------------|
| 2019 +10%     | 2019 +13%  |
| 2018 +4%      | 2018 +3%   |
| 2017 -1%      | 2017 -1%   |

#### New CVRM

**\$4,376m**

Product Sales



| Actual growth | CER growth |
|---------------|------------|
| 2019 +9%      | 2019 +12%  |
| 2018 +12%     | 2018 +12%  |
| 2017 +9%      | 2017 +9%   |

#### Japan

**\$2,548m**

Product Sales



| Actual growth | CER growth |
|---------------|------------|
| 2019 +27%     | 2019 +26%  |
| 2018 -9%      | 2018 -11%  |
| 2017 +1%      | 2017 +4%   |

#### Oncology

**\$8,667m**

Product Sales



| Actual growth | CER growth |
|---------------|------------|
| 2019 +44%     | 2019 +47%  |
| 2018 +50%     | 2018 +49%  |
| 2017 +19%     | 2017 +19%  |

<sup>1</sup> Reconciliation of Total Product Sales from sales platforms to total Product Sales is shown in the Financial Review from page 78. This reconciliation is shown for 2018 and 2019 only.

## Changes to KPIs in 2019

The total of Product Sales from sales platforms is a new KPI as outlined in Our KPIs and remuneration above and combines the five sales platforms' metrics. It removes the double-counting of certain Product Sales which are included in more than one platform. Reconciliation to the number used for calculating annual bonus is shown from page 135.

 Delivering growth from page 31; Therapy Area Review from page 54.

**90%**

Revenue from sales platforms of \$21,894 million in 2019 represented 90% of Total Revenue

disclosing sensitive commercial information at the individual KPI level. These changes are explained in more detail

throughout this section and more information can be found in the Directors' Remuneration Report from page 125.

Any variances between the KPI and values used in determining remuneration are explained in the Directors' Remuneration Report from page 125.

**KPI key**  
 ● New in 2019  
 ● Used for remuneration of Executive Directors  
 // Denotes a scale break.

**Key Performance Indicators**

**Accelerate Innovative Science**

The Accelerate Innovative Science KPIs measure the performance of the pipeline. Pipeline progression events (Phase II NME starts/progressions and Phase III investment decisions) measure innovation and sustainability. Regulatory events demonstrate the advancement of this innovation to patients and the value to the Group.

By measuring both Phase II and Phase III pipeline progressions, we are focused on both near-term and longer-term delivery. Phase II NME starts ensure the ongoing robustness and future stability of the pipeline (and reflect the outcome of nearer-term strategic investment decisions). Phase III investments measure assets that will deliver nearer-term value (and reflect the outcome of longer-term strategic investment decisions).

Submissions and approvals metrics demonstrate the advancement of this innovation through filing and approval in our four major markets (US, EU, Japan and China).

**Pipeline progression events**

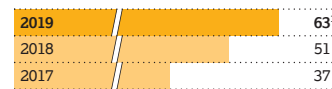
**22**



<sup>1</sup> 17 against our Group scorecard for determining annual bonus.

**Regulatory events**

**63**



<sup>1</sup> 37 against our Group scorecard for determining annual bonus.

**NME Phase II starts/progressions**

**8**



<sup>1</sup> 6 against our Group scorecard for determining annual bonus.

**NME or LCM project regulatory submissions in major markets**

**35**



<sup>1</sup> 14 against our Group scorecard for determining annual bonus.  
<sup>2</sup> 24 for determining annual bonus.  
<sup>3</sup> 13 for determining annual bonus.

**Phase III investment decisions**

**14**



<sup>1</sup> 11 against our Group scorecard for determining annual bonus.

**NME and major LCM regional approvals**

**28**



<sup>1</sup> 23 against our Group scorecard for determining annual bonus.

**Changes to KPIs in 2019**

The totals of Pipeline progression and Regulatory events are new KPIs as outlined in Our KPIs and remuneration above. The former is a total of NME Phase II starts/progressions and Phase III investment decisions. The latter represents the total of NME or LCM regulatory submissions and approvals.

□ Innovative science from page 25; Therapy Area Review from page 54; Development Pipeline from page 238.

**“In 2019, we had 22 pipeline progressions, and an average of 24 progressions in each of the last four years.”**

# Key Performance Indicators *continued*

## Key Performance Indicators

### Be a Great Place to Work

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

A great place to work from page 44.

#### Employee belief that AstraZeneca is a great place to work<sup>1</sup>

# 86%



<sup>1</sup> Source: December Pulse survey for each year. 2019 was a full census survey, 2018 and 2017 surveyed a 50% sample of the organisation.

#### Contribution to the enterprise

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

A great place to work: Employees from page 44.

<sup>2</sup> December Pulse survey: 2019 was a full census survey, 2018 and 2017 surveyed a 50% sample of the organisation.

#### Performing as an enterprise team<sup>1,2</sup>

# 77%



<sup>1</sup> Source: December Pulse survey for each year, based on the question 'effective collaboration between teams'.

#### Building a culture of lifelong learning and development<sup>1,2</sup>

# 83%



<sup>1</sup> Source: December Pulse survey for each year, based on the question 'opportunity for personal development and growth'.

#### Inclusion and diversity<sup>1</sup>

# 45.4%



<sup>1</sup> Women representation at career level F+ (the most senior 12% of the employee population).

#### Contribution to society – Leading in sustainability

The Leading in sustainability KPIs measure the progress of our environmental, social and governance practices. They are representative indicators of each of the three priorities for our sustainability approach – to broaden access to healthcare, to protect the environment, and to foster ethics and transparency.

A great place to work: Contributing to society from page 49.

#### Access to healthcare: through our access to healthcare programmes<sup>1,2</sup>

# 19.8m

people



<sup>1</sup> Our access to healthcare programmes, including Healthy Heart Africa, Healthy Lung, Phakamisa, and Young Health Programme (YHP), have reached 19.8 million people through education, screenings, diagnosis and treatment cumulatively since the start of each programme. See from page 49 for more information.

<sup>2</sup> We expanded this measure to include the YHP for all years. Totals for each programme individually are reported in the Sustainability Data Summary at [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

#### Environmental protection: operational greenhouse gas (GHG) footprint<sup>1</sup>

# 1,975 kt CO<sub>2</sub>e



<sup>1</sup> Operational GHG footprint is emissions from all Scope 1, 2 and selected Scope 3 sources. See page 266.

#### Ethics and transparency: non-compliance with our Code of Ethics<sup>1</sup>

# 63.3

per 1,000 employees in Commercial Regions



<sup>1</sup> There were 2,597 instances, most of them minor, of non-compliance with our Code of Ethics or supporting requirements in our Commercial Regions by employees and third parties. See page 35 for more information.

#### Changes to KPIs in 2019

The Contribution to the enterprise KPIs have been revised from previous years to align to our strategy. Previous metrics are available in the Sustainability Data Summary at [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

A great place to work from page 44.

“...we announced an ambitious \$1 billion programme for zero carbon emissions from our global operations by 2025 and to ensure our entire value chain is carbon negative by 2030.”



## Key Performance Indicators

 Achieve Group Financial Targets

## Product Sales

Growth in Product Sales demonstrates our ability to deliver medicines to patients.

## Net cash flow from operating activities

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

## EPS

EPS is an important profitability metric, and a key driver of shareholder value. For more information on our Core measures, please see from page 81 in the Financial Review.

 Financial Review from page 78.

<sup>1</sup> Reconciliation to the number used for calculating annual bonus is shown from page 135.

Product Sales<sup>1</sup>

**\$23,565m**



| Actual growth | CER growth |
|---------------|------------|
| 2019 +12%     | 2019 +15%  |
| 2018 +4%      | 2018 +4%   |
| 2017 -5%      | 2017 -5%   |

// Denotes a scale break.

## Reported EPS

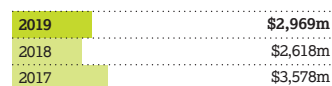
**\$1.03**



| Actual growth | CER growth |
|---------------|------------|
| 2019 -40%     | 2019 -33%  |
| 2018 -28%     | 2018 -29%  |
| 2017 -14%     | 2017 -15%  |

Net cash flow from operating activities<sup>1</sup>

**\$2,969m**



| Actual growth |
|---------------|
| 2019 +13%     |
| 2018 -27%     |
| 2017 -14%     |

Core EPS<sup>1</sup>

**\$3.50**



| Actual growth | CER growth |
|---------------|------------|
| 2019 +1%      | 2019 0%    |
| 2018 -19%     | 2018 -19%  |
| 2017 -1%      | 2017 -2%   |

## Changes to KPIs in 2019

We have removed dividend per share as a KPI as it is not a measure used by the Group to determine performance against strategy.

 Financial Review from page 78.

**“AstraZeneca’s financial performance in 2019 represented a year of innovation for patients.”**

## Business Review

Following our return to Product Sales growth in 2018, our renewed focus is on delivering growth through innovation. This focus is underpinned by embedding patient centricity across the organisation, doing more with technology, digital and data, and advancing more cutting-edge science.

Oncology tumour drivers – cell surface and lipid bilayer with receptor.

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



1. Deliver Growth and Therapy Area Leadership



2. Accelerate Innovative Science



3. Be a Great Place to Work

In January 2019, we announced organisational changes to support continued scientific innovation and commercial success as we enter the next phase in our strategic development. We wanted AstraZeneca to be more agile, collaborative and focused on bringing innovative medicines to patients.

The changes were designed to further integrate R&D and accelerate decision making and the launches of new medicines, consolidating what we believe is already one of the most exciting and productive pipelines in the industry. We also enhanced our commercial functions to increase collaboration with our R&D organisation, enabling greater commitment to our main therapy areas.

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

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

Full details are provided in the Financial Review from page 78.

### Research & Development (R&D)

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

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

### Operations

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

### Commercial

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

In January 2019, we created two commercial units – one for Oncology and one for BioPharmaceuticals. These units align product strategy and commercial delivery across the US and Europe-Canada and sharpened our focus on our main therapy areas. The International commercial organisation remains unchanged and Japan continues to be reported separately.



## Innovative science

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

### 2019 Overview

- > Created new R&D organisations
- > Published 91 manuscripts in 'high-impact' publications
- > Embarked on collaboration with BenevolentAI to help understanding of disease biology
- > Began strategic collaboration with Daiichi Sankyo for *Enhertu* as part of our efforts to create next generation of therapeutics
- > Piloted ways to better predict clinical effectiveness and make clinical trials easier for patients
- > Delivered clinical trial data and submissions that resulted in 28 approvals
- > Scientific rationale resulted in 18 regulatory designations
- > Bioethics Advisory Group ensured continued focus on bioethics
- > Construction continued at Cambridge, UK R&D centre, new centre announced in Shanghai, China and new office opened in New York, NY, US

### Research & Development

In 2019, we created therapy-area focused R&D organisations responsible for discovery through to late-stage development – BioPharmaceuticals R&D focuses on CVRM and respiratory diseases, and Oncology R&D focuses on cancer. The span across the entire life-cycle of a potential new medicine is designed to enable us to follow the science by accelerating promising early-stage assets and life-cycle management programmes, as well as providing new opportunities for combinations.

Our drug discovery and development is guided through a 5R framework – right target, right patient, right tissue, right safety and right commercial potential. In the four years after its introduction in 2012, the proportion of pipeline molecules advancing from pre-clinical investigation to completion of Phase III clinical trials has increased from 4% to 19% within the small molecules portfolio. To further improve our R&D productivity, we are exploring emerging technologies to accelerate the design and testing of potential medicines. Artificial intelligence (AI) is being used increasingly in the pharmaceutical sector, building on the emergence of novel computing technologies and the exponential increase in data and deep learning algorithms. Our teams are looking to harness new technologies to further automate processes and create efficiencies.

One of the measures of our success in accelerating innovative science and demonstrating the quality of our research is the

number of publications in high-quality and 'high-impact' journals. It is also critical for recruiting and retaining the best scientists from around the world. Our scientists from R&D have published 91 manuscripts in 'high-impact' peer-reviewed journals, each with an impact factor exceeding 15 (Thomson Reuters 5yr IF score) and a score exceeding 870 in total. This represents a thirteen-fold improvement since 2012, when the 5R framework was first introduced.

We are determined to advance our understanding of disease biology to uncover novel drivers for the diseases we aim to treat, prevent, and even cure. We aim to foster an environment where our scientists can freely share their ideas and collaborate with the best external partners. Our approach to science is exemplified by the number of joint research facilities we have established with leading scientific centres, such as the Karolinska Institutet in Sweden and the CRUK Cancer Institute in Cambridge. In 2019, we opened the Functional Genomics Research Centre at the Milner Therapeutics Institute in Cambridge to better understand gene changes and disease onset, using CRISPR-gene editing technology. We also embarked on a long-term collaboration with BenevolentAI to use AI and machine learning to build biomedical knowledge graphs for chronic kidney disease (CKD) and idiopathic pulmonary fibrosis, in order to contextualise scientific data and the relationships between them. For more information on knowledge graphs, see page 27. Such collaborations aim to uncover the underlying biology of these complex diseases and accelerate drug discovery.

### Next generation of therapeutics

We continue to design new ways to target the drivers of disease to create the next generation of therapeutics. In 2019, 12 new modalities were in clinical development, compared with six in 2012, which demonstrated the diversity of technology in our early pipeline. In conjunction with Ionis Pharmaceuticals, we are developing antisense oligonucleotides (ASOs) in two of our therapy areas: Oncology and CVRM. Danvatirsen (AZD9150) is currently in Phase II clinical trials, and is being evaluated for anti-tumour activity in combination with *Imfinzi*. We are also exploring ASOs in CKD, in non-alcoholic steatohepatitis. In 2019, we initiated a new collaboration with Seres Therapeutics to evaluate microbiome-based approaches to predict which patients may respond best to cancer immunotherapies. Additionally in 2019, our work with Pieris Pharmaceuticals allowed us to progress AZD1402 through Phase I clinical development as a novel inhaled medicine for asthma based on its proprietary Anticalin protein platform. In our long-standing relationship with Moderna, we have worked on AZD8601 and produced the largest batch ever of modified ribonucleic acid (mRNA) suitable for clinical testing. We continue to partner with Bicycle Therapeutics to develop potential new therapies

for respiratory and cardiovascular diseases, using their novel bicyclic peptide platform. We are also working with Ethris GmbH to enhance our respiratory expertise using the stabilised non-immunogenic mRNA (SNIM) technology, and APT Therapeutics to access their therapeutic protein platform. Finally, in 2019, we announced a strategic collaboration with Daiichi Sankyo to accelerate and expand development of *Enhertu*, a novel antibody-drug conjugate (ADC).

□ For more information, see Therapy Area Review from page 54.

### Predicting clinical effectiveness

We are adopting cutting-edge technologies to improve our ability to predict the clinical effectiveness of our candidate drug molecules. Our work with Definien focuses on developing analytical tools to characterise the immuno-oncology landscape of tumours, as well as the expression of biomarkers for many of the drugs in our pipeline. Advances in humanised models have generated improved data about toxicity and efficacy compared with previous methods. In 2019, our collaboration with Emulate published research which demonstrated the ability of its Liver-Chip to model liver toxicity of eight previously studied compounds. With the University of Colorado, US, we continue to show how different patient derived xenograft models can help define new combination therapies in oncology. To recreate the mechanical and electrical forces in a beating heart, we have partnered with Novoheart to leverage their 3-D human ventricular cardiac organoid chamber – 'heart-in-a-jar' – technology to reproduce key characteristics of heart failure with preserved ejection fraction. Our progress in ctDNA monitoring has the potential to identify patients with high risk of recurrence post-surgery and patients with micro-metastatic disease prior to relapse. We are capturing exquisite cellular detail using mass-spectrometry imaging to inform pre-clinical decision making, for example for how drug-drug interactions influence blood-brain barrier permeability, which was previously difficult to predict without this technology.

### Pioneering new approaches to engagement in the clinic

In 2019, we conducted more than 270 global clinical trials and we piloted several trials using digital solutions to help patients to find clinical trials easier. For more information, please see Redefining clinical trials on page 30. Through the use of digital tools, we are also starting to design and drive the performance of our clinical trials, adopt electronic health records to improve clinical trial implementation and accurately forecast clinical trial drug supplies to investigator sites to avoid waste or delays.

We are also working towards digital solutions to improve disease understanding and patient outcomes. In several early clinical trials, we are exploring new digital markers, for example in the

# Business Review

## Innovative science

### continued

Phase IIa INCONTRO programme to assess the relevance of FeNO (fractional exhaled nitric oxide) as a biomarker in the assessment of lung inflammation and exacerbation risk. We are developing novel digital therapeutics to improve clinical outcomes, optimise medication use and adherence, and to reduce, manage or prevent adverse events. For example, with Voluntis and the National Cancer Institute in the US, we are developing a digital therapeutic for women undergoing treatment for recurrent platinum-sensitive high-grade ovarian cancer in clinical trials of cediranib plus *Lynparza*. This digital solution supports patients through tolerability and management of adverse effects, and recently won the Prix Galien award for best patient engagement technology.

### Development pipeline

During 2019, we delivered clinical trial data and submissions that resulted in 28 approvals for new medicines in the US, EU, China and Japan. As shown in the table below, our pipeline includes 167 projects, of which 144 are in the clinical phase of development. We are making significant progress in advancing our late-stage programmes through regulatory approval with 35 NME or major LCM regulatory submissions in the US, EU, China and Japan during 2019.

At the end of the year, we had eight NME projects in pivotal trials or under regulatory review (covering 13 indications), compared with eight at the end of 2018.

Also in 2019, 20 NMEs progressed to their next phase of development and 18 projects were discontinued: 12 for poorer than anticipated safety and efficacy results; five as a result of a strategic shift in the environment or portfolio prioritisation; and one for economic reasons.

### Accelerating our pipeline

We are prioritising our investment in specific programmes, focusing on scientific innovation. As a result, we had numerous positive trial read-outs in 2019 including: *Lynparza* in germline BRCA-mutated metastatic pancreatic cancer (POLO); *Calquence* in previously treated patients with chronic lymphocytic leukaemia (CLL) and in patients with previously untreated CLL; *Imfinzi* in patients with previously untreated extensive-stage small cell lung cancer (CASPIAN); *Enhertu* in patients with HER2-positive metastatic breast cancer (DESTINY-Breast01); *Lynparza* in men with metastatic castration-resistant prostate cancer (PROfound); *Lynparza* in women with advanced ovarian cancer (PAOLA-1); *Imfinzi* + tremelimumab in previously untreated Stage IV (metastatic) non-small cell lung cancer (NSCLC) (POSEIDON); roxadustat for the treatment of patients with anaemia in CKD that are either non-dialysis dependent or dialysis dependent; *Brilinta* in patients with established coronary artery disease and type-2 diabetes (THEMIS); *Farxiga* for the treatment of patients with heart failure (DAPA-HF); *Breztri Aerosphere* in patients with moderate to very severe chronic obstructive pulmonary disease (ETHOS); and anifrolumab for the treatment of systemic lupus erythematosus (TULIP 2).

In January 2020, we announced positive high-level results from the registrational Phase II trial for *Enhertu* for gastric cancer (DESTINY-Gastric01) and from the Phase III *Brilinta* trial for stroke (THALES).

As is to be expected when we are investigating treatments for diseases that are hard to address, we also had some setbacks during the year. These included disappointing Phase III data results. For example, the results from the Phase III NEPTUNE trial with *Imfinzi* in combination with tremelimumab in patients with Stage IV NSCLC. The trial did not meet its primary endpoint of improving overall survival (OS) compared to standard of care (SoC) chemotherapy. We also discontinued development of savolitinib as a monotherapy treatment for papillary renal cell carcinoma and closed the Phase III STRENGTH trial for *Epanova* due to its low likelihood of demonstrating a benefit to patients with mixed dyslipidaemia who are at increased risk of cardiovascular (CV) disease.

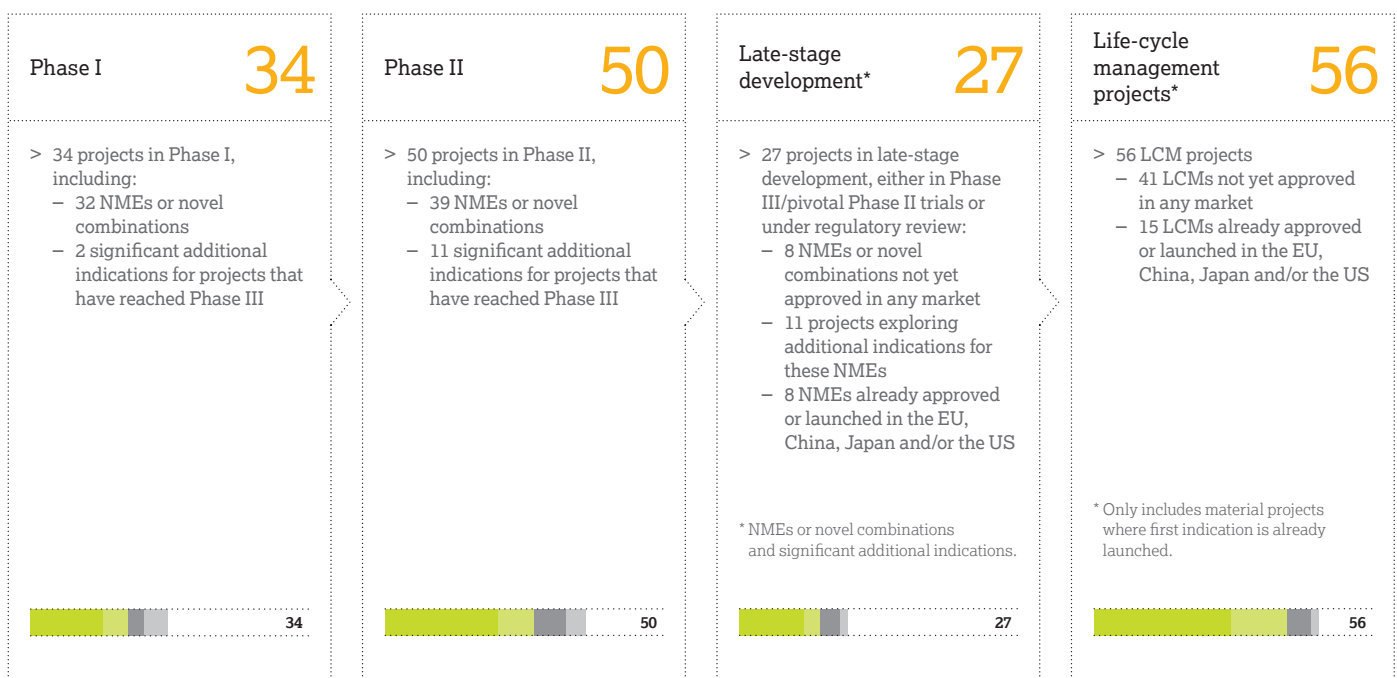
In 2019, we presented scientific rationale that resulted in 14 Regulatory Designations for Breakthrough Therapy, Priority Review or Fast Track for new medicines which offer the potential to address unmet medical need in certain diseases. We also secured Orphan Drug Designation for the development of four medicines to treat very rare diseases.

For more information, see Development Pipeline from page 238.

### Development pipeline overview (as at 31 December 2019)

#### 167 projects

Our development pipeline includes projects in early- and late-stage development as outlined below. Projects are counted here until they have launched in all applicable major regions.



■ Oncology ■ CVRM ■ Respiratory ■ Other

# Next leaps are ~~impossible~~



Link to strategy: Accelerate Innovative Science

## Understanding disease better

Using artificial intelligence and machine learning to transform the discovery and development of innovative new medicines.

By better understanding what causes or drives diseases, we hope to find new ways to treat, prevent or even cure them.

We are using knowledge graphs – networks of contextualised scientific data facts such as genes, proteins, diseases and compounds, and the relationship between them – to give scientists new insights.

Our collaboration with BenevolentAI aims to build knowledge from the masses of data to better understand disease biology. We are combining AstraZeneca's disease area expertise and large, diverse datasets with BenevolentAI's leading AI and machine learning capabilities to build knowledge graphs for idiopathic pulmonary fibrosis and chronic kidney disease.

We are working together to interpret these knowledge graphs to understand better the underlying mechanisms of these complex diseases and identify more quickly new potential drug targets.

□ For more information see Research & Development on page 25.



"We are generating and have access to more data than ever before. By harnessing artificial intelligence and machine learning to unlock this wealth of data, we have the potential to transform the way we discover and develop innovative new medicines."

**Mene Pangalos**  
EVP, BioPharmaceuticals R&D

# Business Review

## Innovative science

### *continued*

#### Bioethics BV

'Bioethics' refers to the range of ethical issues that arise from the study and practice of biological and medical science. We are committed to working in a transparent and ethical manner across all our bioethics subject matter areas. Our Global Standard on Bioethics sets out our principles which apply to all our research activity, whether conducted by us or by third parties acting on our behalf. The following sections summarise our activities in the main areas, and our Global Standard on Bioethics is available on our website, [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

Our Bioethics Advisory Group (BAG) is sponsored by the Chief Medical Officer and oversees the operation of the Global Standard on Bioethics. It acts as a source of bioethical advice to the business, bringing together the subject matter leads for each of the key bioethical areas, supported by other experts and specialists. BAG receives reports on governance and practice from subject matter leads, responds to requests for advice and support from the business, and carries out horizon-scanning activities to identify emerging scientific, technological and regulatory issues. BAG met six times in 2019. Ethical discussions in 2019 included the use of precision genome editing in research and development, potential impacts of AI on healthcare, and potential delays to supply of influenza vaccines resulting from any change to the scope of the Nagoya Protocol to include non-human genetic sequence data.

#### Clinical 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.

In 2019, we conducted a range of clinical trials across regions as shown in the charts on the right. This broad span helps ensure that study participants reflect the diversity of patients for whom our medicines are intended and identifies the patients for whom the medicine may be most beneficial. Our global governance process provides the framework for ensuring a consistent, high-quality approach worldwide. Protecting participants throughout the trial process is a priority and we have strict procedures to help ensure participants are not exposed to unnecessary risks.

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

As of 31 December 2019, we shared anonymised individual patient-level data from 147 studies with 50 research teams and responded to 161 requests from external researchers using our portal, <http://www.astrazenecagroup-dt.pharmacm.com>, to request our clinical data and reports to support additional research. In 2019, we continued to participate in the industry-wide portal [www.trialssummaries.com](http://www.trialssummaries.com) where we publish Trial Result Summaries in easy-to-understand language and translate these to the local language for all sites where a study is conducted. As of 31 December 2019, we published Trial Result Summaries for 108 AstraZeneca trials.

As of 31 December 2019, we have published a total of five Clinical Study Packages, which includes hundreds of study reports, on regulatory agency web portals under EMA policy 0070 and Health Canada's PRCI process. Additional clinical study documents can be requested by researchers through our data request portal.

 For more information, see our website, [www.astrazeneca.com](http://www.astrazeneca.com), or our clinical trials website, [www.astrazenecaclinicaltrials.com](http://www.astrazenecaclinicaltrials.com).

#### Patient safety

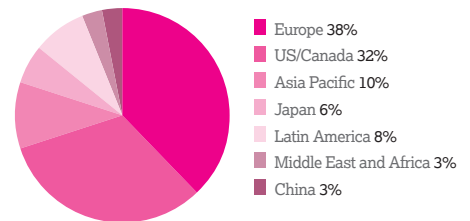
One of our Values is to put patients first and, by detecting, assessing, understanding and preventing adverse effects or any other drug-related problems, our pharmacovigilance processes and systems seek to minimise the risks and maximise the benefits of our medicines for patients.

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

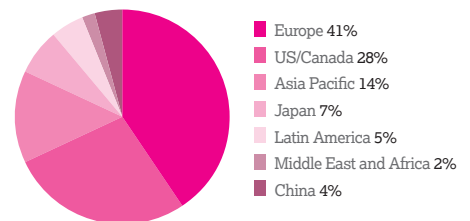
Our Chief Medical Officer is accountable for the benefit and risk profiles of our products, providing medical oversight and enforcing risk assessment processes that help us make efficient and informed decisions about patient safety. As part of our commitment to patient safety, and in order to be an industry leader in pharmacovigilance, we continue to improve the competence of the patient safety staff, and refine our processes, systems and tools. This includes exploring the use of emerging technologies, such as automation support, machine learning and digital communication interfaces which have the potential to further enhance our product safety evaluation, communication and risk mitigation capabilities.

#### Clinical trial active sites by region\*

##### BioPharmaceuticals



##### Oncology



\* Percentages have been rounded to the nearest whole number.

#### Research use of human biological samples

The use of human biological samples, such as solid tissue, biofluids and their derivatives, plays a vital role in developing a deeper understanding of human diseases and their underlying mechanisms, which helps us develop effective, new and personalised medicines.

We are committed to minimising the use of fetal tissue by exploring technological alternatives. In 2019, no additional new research proposals that include use of cells derived from human fetal tissue (hFT) were approved while three projects using hFT had progressed as at 31 December. An additional project using human embryonic stem cells (hESC) was approved in 2019, resulting in 10 projects using 21 different hESC lines or derived cells having been approved as at 31 December. Four projects are ongoing.


#### Animal research

Technology has not yet advanced to the stage where animal use can be eliminated. In addition, some animal studies are required by international regulators before medicines progress to human trials. Animal studies therefore remain a small, but necessary, part of the process of developing new drugs. We are alert to the issues around the use of animals and are working constantly to ensure our animal studies are properly justified, conducted and reported.

We are committed to helping the public understand the continuing need for animals in research, and our approach to replacing, reducing and refining our use of animals (the 3Rs). We share our 3Rs advances externally through presentations at international conferences and workshops, and contribute to the work of organisations and societies supporting the 3Rs around the world. Our Chief Veterinary Officer leads the Council for Science and Animal Welfare (C-SAW), which is the governance and oversight body for the use of animals in research and development, providing assurance to senior leaders on our responsible use of animals. C-SAW drives initiatives on the 3Rs, openness about our use of animals, and promotes a culture of care in the way we conduct our research. For example, C-SAW runs an annual global awards scheme recognising excellence in the 3Rs, achievements in openness about the use of animals and the best examples of a caring research culture. In 2019, our winning entries included a team implementing refinement in anaesthetic procedures for rats; a novel molecular biology approach allowing reduction in the number of mice needed in some studies; a collaborative project ultimately leading to changes in regulations and the replacement of some studies, which previously used fish, with non-animal alternatives. C-SAW also provides general information and education opportunities about the use of animals in research both within and outside AstraZeneca.

Animal research use varies depending on many interrelated factors, including our amount of pre-clinical research, the nature and complexity of the diseases under investigation and regulatory requirements. We believe that without our active commitment to the 3Rs, our animal use would be much greater. In 2019, animals were used for in-house studies 108,674 times (2018: 121,823<sup>1</sup>). In addition, animals were used on our behalf for CRO studies 35,210 times (2018: 29,853). In total, over 97% were rodents or fish.

<sup>1</sup> 2018 figure includes some animals used only for breeding.

 For more information, see our Sustainability Report available on our website, [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

## R&D resources

We have approximately 9,200 employees in our R&D organisation, working in various sites around the world. We currently have three strategic R&D centres: Cambridge, UK; Gaithersburg, MD, US; and Gothenburg, Sweden. Other R&D centres are located in the UK (Alderley Park and Macclesfield), the US (Waltham, MA and South San Francisco, CA), Japan (Osaka) and China (Shanghai). We also have a site in Poland (Warsaw) that focuses on late-stage development.

In November 2019, we announced the creation of a global R&D centre in Shanghai, China to carry out R&D for potential new medicines that will more than double the local R&D headcount to around 1,000. During 2019, we also opened an office in New York, NY, US with a specific focus on delivery of our Oncology pipeline, particularly in the clinical and medical space. The addition of this new office ensures that we have a presence in all four of the nationally-recognised top areas for biopharmaceutical innovation in the US.

## Cambridge

Cambridge, UK is a world-leading academic and life sciences hub. Having relocated our global corporate headquarters to Cambridge in 2016, we continue to progress the build of our new strategic R&D centre on the Cambridge Biomedical Campus (CBC) and now have 2,800 employees located in and around the city. We are already seeing the impact of significant scientific and strategic collaborations within the Cambridge cluster as a result of the relationships forged.

Construction of our R&D centre began in April 2015. During 2019, activities at the site focused on the fit-out of laboratory and scientific support spaces, interior design of the office areas and landscaping. We expect to start occupation of the building from 2020, with practical completion expected at the end of 2021. Following the review of costs by the new construction manager, the latest cost projection for the R&D centre is in the region of \$1.3 billion (c.£1.0 billion). Costs for the project have risen since our original projection due to the complexity of the build, construction cost inflation, including the impact of a weakening pound, and increased investment in new technologies and equipment (for example, genomics and screening lab) as part of our ongoing investment in R&D in the UK. The project is being funded out of operational cash flows.

Sustainability remains a key driver to our infrastructure in Cambridge. We have built Europe's largest ground source heat pump system that will generate energy for the R&D centre. We remain committed to fostering sustainable solutions within the building's operations strategy, such as harvesting rain water from the roof, and solar tracked blinds and lighting systems to maximise natural daylight.

As an integral part of the Cambridge ecosystem, we are working to co-develop future and sustainable travel solutions with the community and investing in developing scientific capability in the next generation. For example, the Energy Challenge STEM initiative fostered a community of volunteers across AstraZeneca's employees in Cambridge to bring a science challenge to more than 4,000 local primary school pupils. With its focus on scientific method and topicality around fostering awareness of the calorific value in foods, the Energy Challenge has been recognised as a contributor to health awareness in the community through recent awards.

In 2019, we also progressed the planning phase of amenities for our CBC-based employees and further consolidated our late-stage development, office-based employees across three offices in central Cambridge until our overall vision of co-location at the CBC campus is complete. This vision will enable our non-laboratory based Cambridge colleagues to be co-located on the CBC and near our key scientific, research and clinical partners. We are now updating the overall master plan for the site and the next stage will be the development of an office building opposite our R&D centre that can accommodate an additional 1,000 people.

## Investment

In 2019, R&D expenditure was \$6,059 million (2018: \$5,932 million; 2017: \$5,757 million), including Core R&D costs of \$5,320 million (2018: \$5,266 million; 2017: \$5,412 million). In addition, we spent \$1,835 million on acquiring product rights (such as in-licensing) (2018: \$476 million; 2017: \$404 million). We also invested \$10 million on the implementation of our R&D restructuring strategy (2018: \$94 million; 2017: \$201 million). The allocations of spend by early-stage and late-stage development are presented in the R&D spend analysis table below.

## R&D spend analysis

|                                       | 2019 | 2018 | 2017 |
|---------------------------------------|------|------|------|
| Discovery and early-stage development | 36%  | 37%  | 36%  |
| Late-stage development                | 64%  | 63%  | 64%  |



Link to strategy: Accelerate Innovative Science

# Next level patient experience

## Redefining clinical trials

Making clinical trials better and easier for patients.

We are developing the use of digital solutions to make clinical trials better and easier for patients. For example, once patients are on a clinical trial, we are seeking to reduce the number of visits patients need to make to clinics by:

- > enabling 70% of the data we need to be collected from home, using devices and sensors
- > using apps to help the patient know where they are in their clinical trial and share their own information with their doctor, as well as providing feedback on information collected and sharing the result of the clinical trial.

We recently won the Prix Galien award for best patient engagement technology for our work with Voluntis and the National Cancer Institute in the US developing a digital solution that supports women undergoing treatment for ovarian cancer in clinical trials of cediranib plus *Lynparza* through tolerability and management of adverse effects.

Our ambition is to develop digital health solutions to support improved patient outcomes, including digital therapeutics, across our three therapy areas.

☐ For more information see Research & Development on page 25.

>270  
global clinical trials conducted in 2019

>123,000  
patients involved within these trials each year

>19,000  
investigator sites used annually

~60  
countries involved



“Our use of innovative digital tools and technologies seeks to provide patients with an industry-leading clinical trial experience and improved patient outcomes.”

José Baselga  
EVP, Oncology R&D





# Business Review

## Delivering growth



### Delivering growth

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

#### 2019 overview

- > Product Sales grew by 12% (15% at CER) to \$24 billion
- > Emerging Markets sales increased by 18% (24% at CER), with China sales growth of 29% (35% at CER); US sales increased by 13%; Europe sales declined by 2% (up by 2% at CER); Japan sales increased by 27% (26% at CER)
- > Sales of New Medicines increased by 59% (62% at CER) to \$10 billion, representing 42% of total Product Sales
- > Working with payers to explore novel and flexible ways to assess and pay for our medicines
- > Committed to high ethical standards; 162 people removed from roles for breaches
- > 106 successful market launches
- > CDP Climate A List rating for the fourth year running
- > More than 730 collaborations around the world
- > Focus on cybersecurity with successful employee awareness training

### Putting patients first

We believe that putting patients first, or patient centricity, will make a real difference to the lives of people living with serious and life-threatening diseases. It requires us to walk as if in the shoes of patients, listen to their experiences, embed their insights and co-create with them to help us innovate and strengthen the way we work in order to deliver advances across the whole patient experience – from prevention and awareness, diagnosis, treatment and post-treatment to wellness. Our thinking extends beyond individual patients to include their caregivers, family and friends, as well as co-workers and healthcare professionals.

By understanding the people who are living with the diseases we aim to treat, considering their unique experiences and acting upon the insights we uncover, we believe we can help people in the most effective and compassionate way. Further, by working across AstraZeneca, from R&D to commercial development, and with external partners in the broader healthcare environment, we believe we can deliver the healthcare experience and outcomes that people care about most so that they can enjoy fulfilling lives.

### Sales and marketing

Our Commercial teams, which comprised around 41,000 employees at the end of 2019, are active in more than 100 countries. In most countries, we sell our medicines through wholly-owned local marketing companies. We also sell through distributors and local representative offices. We market our products largely to primary care and specialty care physicians.

Our return to Product Sales growth in 2019 was underpinned by our sales platforms. As shown on page 20 and in the Financial Review from page 78, these comprise our three main therapy areas, together with Emerging Markets and Japan. In 2019 they grew by 18% (22% at CER) and represent 90% of Total Revenue.

Sales of our New Medicines<sup>1</sup> generated incremental sales of \$9.9 billion at CER and represented 42% of total Product Sales. These New Medicines are important platforms for future growth. In Emerging Markets, they represented 23% of sales, up from 15% in 2018 and, in the US, they represented 63% of Product Sales, up from 48%. Overall, US performance reflected the success of the new Oncology medicines.

In Europe, Product Sales reflected a strong performance by our Oncology medicines, offset by a decline in *Nexium* and legacy Respiratory medicines. New Medicines represented 41% of Product Sales in Europe, up from 27% in 2018. In Established Rest of World, New Medicines represented 42% of sales in the year, up from 24% in 2018.

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

<sup>1</sup> *Tagrisso, Imfinzi, Lynparza, Calquence, Brilinta, Farxiga, Lokelma, Bevespi, Breztri and Fasenra.*



# Business Review

## Delivering growth *continued*

### Regional Product Sales

#### 1. Emerging Markets

**18%**

18% growth in the year  
(24% at CER) to  
\$8,165m

#### 2. US

**13%**

13% growth in the year  
to \$7,747m

#### 3. Europe

**(2)%**

2% decline in the year  
(2% growth at CER) to  
\$4,350m

#### 4. Established Rest of World

**17%**

17% growth in the year  
(18% at CER) to  
\$3,303m



All numbers as at 31 December 2019.

### Pricing and delivering value

Our medicines help address unmet medical need, improve health and create economic benefits. Treatments that are targeted and effective as well as innovative and personalised, can lower healthcare costs by reducing the need for more expensive care, preventing more serious and costly diseases and increasing productivity. We are committed to a pricing policy for our medicines based on four principles:

- > We determine the price of our medicines while considering their full **value** for patients, payers and society. The agreement on price involves many national, regional and local stakeholders, reflecting factors such as clinical benefit, cost-effectiveness, improvement to life expectancy and quality of life.
- > We aim to ensure the **sustainability** of both the healthcare system and our research-led business model. We believe we share a collective responsibility with healthcare providers and other stakeholders to work together to enable an efficient healthcare system for patients today and support a pipeline of new medicines for patients tomorrow.
- > We seek to ensure appropriate patient **access** to our medicines. We work closely with payers and providers to understand their priorities and requirements, and play a leading role in projects to align better the specifications of regulatory and health technology assessment (HTA) agencies or other organisations that provide value assessment of medicines. For example, we have a leading role in the European IMI ADAPT-SMART programme for exploring adaptive licensing.

> We pursue a **flexible** pricing approach that reflects the wide variation in global healthcare systems. We have developed patient access programmes that are aligned with a patient's ability to pay and a healthcare system's ability to respond. We are committed to the appropriate use of managed entry schemes and the development of real-world evidence and we are investigating innovative approaches to the pricing of medicines, such as payment for outcomes received by the patient and healthcare system.

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

More generally, we remain committed to working with payers to explore novel and flexible ways to assess and pay for medicines towards our shared goal of delivering the outcomes that matter for patients through innovative and personalised treatments. We are collaborating with payers to conclude outcomes- and value-based reimbursement that improves patient outcomes and, in 2019, entered into 44 such agreements across all three of our main therapy areas. For more information, see the case study on page 36.

We understand that our medicines will not benefit patients if they are unable to afford them which is why we offer a number of patient assistance programmes that can help increase patients' access to medicines and reduce their out-of-pocket costs. Through these programmes, we support qualifying patients in a variety of ways, including through discounts and/or product donations. Outside the US,

we generally provide these programmes in markets with limited or no public reimbursement system, no coverage beyond the most basic therapies, or where the possibility of public reimbursement is unlikely, or only after an extended period.

### US

As the fifteenth largest prescription-based pharmaceutical company in the US, we have a 2.7% market share of US pharmaceuticals by sales value. In 2019, Product Sales in the US increased by 13% to \$7,747 million (2018: \$6,876 million).

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

In 2019, the overall measurable reduction in our profit before tax for the year due to discounts on branded pharmaceuticals in the Medicare Part D Coverage Gap and an industry-wide HealthCare Reform Fee was \$547 million (2018: \$432 million; 2017: \$119 million).

In the US, there is significant pricing pressure driven by payer consolidation, restrictive reimbursement policies and cost control tools, such as exclusionary formularies and price protection clauses. Many formularies, which specify particular medicines that are approved to be prescribed in a healthcare system, or under a health insurance policy, employ 'generic first' strategies and/or require physicians to obtain prior approval for the use of a branded medicine where a generic alternative exists. These mechanisms can be used by intermediaries to limit the use of branded products and put pressure on manufacturers to reduce net prices. In 2019, 84.8% of prescriptions dispensed in the US were generic (2018: 84.8%). In addition, patients are seeing changes in the design of their health plan benefits and may experience variation, including increases, in both premiums and out-of-pocket payments for their branded medications. The patient out-of-pocket spend is generally in the form of a co-payment or co-insurance, but there is a growing trend towards high-deductible health plans which require patients to pay the full list price until they meet certain out-of-pocket thresholds.

Ongoing scrutiny of the US pharmaceutical industry, focused largely on pricing, has been the basis of multiple policy proposals in the US. Over the course of 2019, Congress and the Trump Administration have issued several proposals designed to increase generic competition, reform coverage and reimbursement of drug therapies, reduce list prices and out-of-pocket costs, limit price increases, and increase regulatory rebate liability, among other topics. Several hearings have been held in Congress on drug pricing to inform the development of specific policies. In February 2019, our CEO, Pascal Soriot, testified before the Senate Finance Committee, along with the CEOs of other pharmaceutical companies, on the topic of drug pricing. AstraZeneca is actively supporting solutions that provide access and affordability while continuing to support scientific innovation.

In addition, lawmakers at both the federal and state levels have sought increased drug pricing transparency and have proposed and implemented policies that include measures relating to the submission of proprietary manufacturer data, establishment of price parameters that are indexed to certain federal programmes, and reporting of changes in pricing beyond certain thresholds.

Though widespread adoption of a broad national price control scheme in the near future is unlikely, we continue to comply with new

state-level regulations in this area. We recognise the sustained potential for substantial changes to laws and regulations regarding drug pricing that could have a significant impact on the pharmaceutical industry.

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

□ For more information, see Community investment on page 50.

## Europe

The total European pharmaceutical market was worth \$195 billion in 2019. We are the fifteenth largest prescription-based pharmaceutical company in Europe (see Market definitions on page 268) with a 1.8% market share of pharmaceutical sales by value.

In 2019, our Product Sales in Europe decreased by 2% at actual rate of exchange (2% increase at CER) to \$4,350 million (2018: \$4,459 million). Key drivers of the decline were the ongoing impact of divestments such as *Nexium*, *Alvesco* and *Atacand*, in addition to continued competition from *Symbicort* analogues, which we expect to persist in 2020. The continued macroeconomic environment, pricing pressure from payers and parallel trade across markets also affected sales.

Despite these conditions, we continued to launch and saw sustained performance of innovative medicines, in particular with *Tagrisso*, *Imfinzi*, *Lynparza*, *Fasenra* and *Forxiga*. Reimbursement remains a key priority to unlock potential and launch new medicines. We are focused on partnering with payers to develop innovative pricing solutions that deliver value to patients. Oncology sales in Europe grew by 35% at actual rate of exchange (42% at CER), partly driven by emerging use of *Tagrisso* for the treatment of patients in the 1st-line EGFR7-mutated (EGFRm) NSCLC setting as more countries gained reimbursement, as well as continued strong levels of demand in the 2nd-line setting. *Imfinzi* sales of \$179 million (2018: \$27 million) followed recent regulatory approvals and launches. *Lynparza* sales grew by 51% (59% at CER) to \$287 million, benefiting from the increasing levels of reimbursement and BRCA-testing rates. *Fasenra* sales of \$118 million in the year represented an increase of 268% (287% at CER), accompanied by *Forxiga* sales growth of 18% (25% at CER).

## Established Rest of World (ROW)\* Japan

Japan remains an attractive market for innovative pharmaceutical companies. It is currently positioned as the second largest pharmaceutical market for R&D-driven pharmaceutical companies. However, there is continued pressure on healthcare spending. Further to that, a cost-effectiveness evaluation was introduced for certain categories of drugs from April 2019. Discussions for further drug budget restrictions are underway at the Japanese health ministry.

In 2019, our Product Sales in Japan increased by 27% at actual rate of exchange (26% at CER) to \$2,548 million (2018: \$2,004 million), positioning AstraZeneca as the seventh largest prescription-based pharmaceutical company in Japan with a 3.5% market share of pharmaceutical sales by value.

Despite price cuts in October and repricing for *Tagrisso* in November, we have outperformed market growth. Results have been driven by the strong achievement of our New Medicines, particularly Oncology brands *Tagrisso*, *Imfinzi* and *Lynparza*, together with *Fasenra* and *Forxiga*, all with double digit growth in 2019. In September, *Breztri* was launched in Japan, becoming the first country for AstraZeneca globally to provide the drug to patients. *Breztri* is still the only triple-combination therapy in a pressurised metered-dose inhaler device in Japan.

## Canada

In 2019, Product Sales in Canada decreased by 4% at actual rate of exchange (1% at CER) to \$470 million (2018: \$489 million). This was primarily due to the impact of divestments such as *Alvesco* and *Omnaris*, accompanied by continued competition in *Pulmicort* and *Onglyza*. Given the significant future potential of *Forxiga*, we continue to prioritise commercial support over *Onglyza*. There continues to be pricing pressure from both public and private payers. We remain committed to exploring innovative value-based pricing solutions that improve patient outcomes. Despite these conditions, we continued to launch and saw strong performance in innovative medicines, in particular *Tagrisso*, *Lynparza*, *Imfinzi* and *Fasenra*. Oncology sales in Canada grew by 95% at actual rate of exchange (100% at CER).

## Business Review

### Delivering growth *continued*

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# 13%

13% increase in Product Sales in the US in 2019 to \$7,747 million

# 29%

29% increase in Product Sales in China in 2019 (35% at CER) to \$4,880 million

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“AstraZeneca was the fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2019.”

#### Australia and New Zealand

Our sales in Australia and New Zealand declined by 12% at actual rate of exchange (6% at CER) in 2019. This was primarily due to continued erosion of *Symbicort* with the impact of an analogue that entered the market in 2018 and the imposition of some prescription restrictions for the LABA/ICS class of medicines as well as modest declines in some of the more mature established brands such as *Seloken*, *Pulmicort* and *Losec*. However, sales in 2019 declined at a slower rate compared with that seen in 2018. The pace of generic erosion has moderated, notably with *Crestor* and *Atacand*. Sales growth from new products such as *Tagrisso* and *Fasenra* are helping to partially offset this. However, sales in the *Forxiga* family declined. Australia remains a predominantly HTA reimbursed market with products aiming to be reimbursed needing to show a clear level of cost effectiveness and benefit to patients versus existing standard of care. Within this context, the Group's pipeline of new assets and indications provide good opportunities for future growth.

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

#### Emerging Markets

Emerging Markets, as defined in Market definitions on page 268, comprise various countries with dynamic, growing economies. As outlined in Healthcare in a changing world from page 11, these countries represent a major growth opportunity for the pharmaceutical industry due to high unmet medical need and sound economic fundamentals. Emerging Markets are not immune, however, to economic downturn. Market volatility is higher than in Established Markets, and various political and economic challenges exist. These include regulatory and government interventions. In selected markets, governments are encouraging local manufacturing and investment by offering more favourable market access conditions and pricing is increasingly controlled by payers through price referencing regulations in addition to cost effectiveness and cost minimisation approaches.

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

With revenues of \$8,165 million, AstraZeneca was the fourth largest multinational pharmaceutical company, as measured by prescription sales, and the fastest-growing top 10 multinational pharmaceutical company in Emerging Markets in 2019.

#### China

In China, AstraZeneca is the second largest pharmaceutical company by value in the hospital sector, as measured by sales. Sales in China in 2019 increased by 29% at actual rate of exchange (35% at CER) to \$4,880 million (2018: \$3,795 million). We delivered sales growth above the growth rate of the hospital market sector through strategic brand investment, systematic organisational capability improvements and long-term channel expansion programmes in our main therapy areas.

*Forxiga*, *Lynparza* and roxadustat were listed in the National Reimbursed Drug List (NRDL) and roxadustat was launched during 2019. Pricing practices remain a priority for regulators, and new national regulations, in addition to provincial and hospital tenders, continue to put increasing pricing pressures on pharmaceutical companies in China. The introduction of the Generics Quality Consistency Evaluation (GQCE) in 2018 will have an impact on pharmaceuticals' budgets and pricing through setting new standards for bioequivalence that generic products must adhere to as part of participation in a process called Value Based Procurement (VBP) that covers up to 70% of anticipated hospital volumes. This evaluation is being applied retrospectively, so several existing generic products may fail and be withdrawn which could lead to a consolidation in the sector. This would leave fewer, higher-quality generics in the market thereby putting pressure on any originator brand price premiums and driving a reduction in overall medical costs.

In 2018, the first round of VBP, which involved *Crestor* and *Iressa*, was announced with implementation from early 2019. This resulted in a level of sales decline for *Crestor* of 5% in 2019, while sales in *Iressa* grew by 5%. In 2019, a further round of VBP was completed and *Crestor* did not win any of the tender share. The next round of VBP, with implementation during 2020, may possibly involve additional AstraZeneca brands.

The industry-wide growth rate is expected to be 5.7% over the next five years, following the updates of the NRDL and expanding health insurance coverage. Nevertheless, the healthcare environment in China remains dynamic. Opportunities are arising from incremental healthcare investment, in-licensing, strong underlying demand for our more established medicines and the emergence of innovative medicines such as *Tagrisso*, *Lynparza* and *roxadustat*.

Several initiatives were announced in the latter part of 2019 to support transformation of healthcare in China. As described on page 29, these included the creation of a global R&D centre in Shanghai. A new AI Innovation Centre, also in Shanghai, will be established to capitalise on the latest digital technology in R&D, manufacturing, operations and commercialisation to help accelerate the delivery of medicines to patients in China and globally. Finally, an agreement was reached with CICC, one of China's leading investment banks, to jointly create a healthcare investment fund combining CICC's strong investment and capital management expertise with AstraZeneca's expertise in the Chinese healthcare system. The fund's target size is \$1 billion and will initially focus on domestic companies and partners.

### Emerging market healthcare <sup>BV</sup>

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

We also have a variety of patient access programmes in Emerging Markets, each tailored to meet the needs of the local community. These include patient assistance programmes, such as *Terapia Plus* in Ukraine, *Karta Zdorovia* in Russia and *FazBem* in Brazil which offer products at a discounted cost.

For information on our access to healthcare programmes in Emerging Markets and as one of our sustainability priorities, please see pages 35 and 52 and our Sustainability Report.

### Responsible sales and marketing <sup>BV</sup>

We are committed to employing high ethical standards of sales and marketing practice worldwide, in line with our Code of Ethics and supporting requirements (our policy framework). We maintain a robust compliance programme in our efforts to ensure compliance with all applicable laws, regulations and adopted industry codes. As outlined in Global

Compliance and Internal Audit Services on page 112, our compliance programme is delivered by dedicated compliance professionals who advise on and monitor adherence to our policy framework.

These professionals also support our line managers locally in ensuring that their staff meet our ethical standards. A network of nominated signatories reviews our promotional materials and activities against applicable requirements. Our Internal Audit Services department, in partnership with external audit experts, also conducts compliance audits on selected marketing companies.

□ For more information about the assurance provided by Bureau Veritas, see page 266.

Approximately 41,000 employees are engaged in our commercial activities and, in 2019, we identified eight confirmed breaches of external sales and marketing regulations or codes (2018: four). There were 2,597 instances, most of them minor, of non-compliance with our policy framework (described in the panel on the right) in our Commercial Business Units, including instances by employees and third parties (2018: 2,042). We removed a total of 162 employees and third parties from their roles as a result of these breaches (a single breach may involve more than one person). We also formally warned 713 others and provided further guidance or coaching on our policies to 2,346 more. The Audit Committee is provided with the breach statistics on a quarterly basis. Further commentary on the most serious breaches is also provided to the Audit Committee.

### Anti-bribery and anti-corruption <sup>BV</sup>

We do not tolerate bribery or any other form of corruption. We conveyed our commitment to ethical behaviour in the 2019 annual Code training, reinforced through anti-bribery/anti-corruption training materials delivered and made available to relevant employees and third parties, including mandatory training for Commercial employees in 2019 which will be followed by training for employees in other business units in 2020.

Bribery and corruption remains a business risk as we launch new medicines in markets across the globe and enter into partnerships and collaborations, and the risk is a focus of our third-party risk management process, as well as our Business Development due diligence procedures. It is also a focus of our monitoring and audit programmes. The majority of marketing company audits include anti-bribery/anti-corruption work programmes.

### Transparency reporting <sup>BV</sup>

AstraZeneca is committed to the highest standards of conduct in all our operations, including the disclosure of payments to healthcare practitioners (HCPs), healthcare organisations (HCOs) and patient organisations, with full transparency where recipients have provided consent and in accordance with all current local, state and global-level obligations covering the 45 markets with existing reporting requirements. We are progressively heading towards increased disclosure in additional markets globally and, in all locations, we are committed to ensuring payments are justified and reasonable.

#### Code of Ethics

We are committed to employing high ethical standards when carrying out all aspects of our business globally. Our Code of Ethics (the Code) is based on our Values, expected behaviours and key policy principles. It applies to all Executive and Non-Executive Directors, officers, employees and temporary staff, in all companies within our Group worldwide. It empowers employees to make decisions in the best interests of the Group and the people we serve, now and in the long term, by outlining our commitments in simple terms and focusing on why these commitments matter. The Code is at the core of our compliance programme. It has been translated into approximately 40 languages and guides employees on how to make the best day-to-day choices and how to act in a consistent, responsible way, worldwide. There are two mandatory training courses dedicated to the Code: one is for new starters; the second is the annual training for all employees, reminding them of the key commitments. In 2019, 100% of all active employees completed the annual training on the Code of Ethics.

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

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

# The Next stage



Link to strategy: Deliver Growth and Therapy Area Leadership

## ● Improving patient access

Exploring new value-based payment models.

## ● What we're doing

- > We stand behind the value of our medicines, taking on financial risk and reimbursing those who pay for our medicines if the medicine does not perform as expected.
- > We are investing in innovative value strategies, including value-based agreements, where we partner with payers to move towards reimbursement based on the value of our medicines and collecting data to measure real-world impact for patients.
- > We are working with key stakeholders to shape policies that promote the implementation of these sorts of agreements, both for our own medicines and those of others.
- > For more information, see Pricing and delivering value on page 32.

## ● 44

Globally, in 2019, we entered into 44 value-based agreements across our three main therapy areas. With these new agreements, we have now entered into more than 70 agreements in the US alone.

- For example, in the US, we entered into a groundbreaking agreement for University of Pittsburgh Medical Center (UPMC) Medicare patients prescribed *Brilinta* that reduced out-of-pocket costs for patients. What UPMC pays for *Brilinta* will vary based on patient outcomes, tying the cost of the medicine to its real-world clinical performance.



"Across our therapy areas, we are committed to exploring innovative value strategies to improve patient access and affordability. We are doing so by focusing on the value our medicines bring patients and deliver to the wider healthcare system."

**Ruud Dobber**  
EVP, BioPharmaceuticals  
Business Unit

# Business Review

## Delivering growth

### *continued*

### Operations

**Our manufacturing and supply function continues to support our growth by ensuring, through our Operations 2020 plan, that we deliver new launches on time and in full, combined with strong customer service and product lead time reductions.**

Operations 2020 was launched in 2015 to enhance supply capabilities in order to respond better to the expanding patient and market needs. It focuses on supporting the delivery of our many new product launches, strengthening our science and technology capabilities across the globe, creating a more agile and flexible supply chain, and embedding Lean principles throughout our network. We are working to ensure our new product launch capabilities successfully support AstraZeneca's promising new product pipeline. By creating robust standard launch processes for both small molecules and biologics, we have achieved a world-class new product launch platform – one that is sustainable and fit for the future. In 2019, we delivered 106 successful market launches and 12 pre-registration launches.

We remain on course to achieve the primary goals of Operations 2020 and have begun to develop our Operations plan for 2025 aligned to our refreshed strategy.

### Quality, regulation and compliance

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

To ensure compliance with global Good Manufacturing Practice regulations, the Operations Quality team continuously reviews and strengthens the Quality Systems at our manufacturing sites through internal audit programmes, external intelligence and sharing learnings between sites. In 2019, these measures helped us successfully achieve zero critical observations from 31 independent inspections. We review observations from these inspections together with the outcomes of internal audits and, where necessary, implement improvement actions.

We are committed to maintaining the highest ethical standards and compliance with internal policies, laws and regulations. We review and

comment upon evolving national and international compliance regulations through our membership of industry associations, including IFPMA, EFPIA and PhRMA.

### Supply chain management

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

As a consequence of the UK leaving the EU on 31 January 2020, we have continued to work closely with our suppliers on their readiness for the impact of the transition period ending on 31 December 2020 without an extension or trade agreement being in place between the UK and the EU, with a view to mitigating the effect on our business.

Since late 2017, we have completed a detailed assessment of approximately 400 suppliers across all areas of our supply chain, including our major and critical suppliers. We have seen a decline in the overall level of supplier-related risk due to various mitigations, including revised logistics channels, additional warehousing, the potential to move clinical trial-related activities, stock building of product and manufacturing-related goods, movement of stock locations, and assessment of the opportunity for supplier substitution. While we continue to make progress, it is possible that adverse events will impact supplier activities. Issue management may therefore play a key element in our ability to maintain safe supply of our medicines and ongoing business operations more generally.

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

### Supply chain financing

AstraZeneca has a supply chain finance programme to support the cash flow of its supply base. This programme, supported by Taulia Inc. and Greensill Capital, provides suppliers with visibility of invoices and payment dates. Suppliers can access this platform free of charge and have full optionality and flexibility on an invoice-by-invoice basis to request early payment of invoices. On election of an early payment, a charge is incurred by the supplier based on the period of acceleration, central bank interest rate, and the rate agreed between Taulia Inc. and each supplier. All early payments are paid by Greensill Capital, and AstraZeneca settles the original invoice amount with Greensill Capital at maturity of the original invoice due date.

We believe this programme offers a benefit to our suppliers, as it provides visibility and flexibility to manage their cash flow, and the rates offered can be preferential to their cost of funding. The programme is live in the US, UK, Sweden and Germany. As of December 2019, the programme had 3,032 suppliers enrolled and a potential early payment balance of \$492 million.

For more information on supply chain financing, see Note 20 on page 199.

### Responsible supply chain <sup>EV</sup>

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

We monitor compliance through assessments and improvement programmes and we will not use suppliers who are unable to meet our standards. Our Global Standard Expectation of Third Parties is published on our website, [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability). We conducted a total of 15,519 assessments in 2019 (2018: 12,967).

In 2019, we conducted 38 audits on high-risk suppliers (external manufacturing partners), seeking to ensure that they employ appropriate practices and controls. 26% of these suppliers met our expectations, with a further 68% implementing improvement plans to address minor instances of non-compliance. Through our due diligence process, no high-risk engagements were rejected.

For more information on our Responsible supply chain, see [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

# Business Review

## Delivering growth *continued*

### Manufacturing capabilities

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

In 2016, we sold our manufacturing site in Avlon, UK, to Avara Avlon Pharma Services Ltd. The company subsequently went into administration. In 2019, we decided to set aside a fund, to be administered independently, to make sure our former employees at the site receive redundancy payments should the ongoing administration of the site not generate enough funds to cover redundancy costs.

In January 2020, AstraZeneca acquired the Reims packing and distribution centre from Avara Reims Pharmaceutical Services. This transaction saw the site and former Avara Reims employees transfer to AstraZeneca. Reims will continue to pack and distribute for the French domestic and other markets currently served by the site.

For biologics, our principal commercial manufacturing facilities are in the US (Frederick, MD; Greater Philadelphia, PA), the UK (Speke) and the Netherlands (Nijmegen), with capabilities in process development, manufacturing and distribution of biologics, including global supply of mAbs and influenza vaccines. In Sweden, we are completing extensive qualification of our new biologics drug product manufacturing facility in order to commence manufacturing in 2020.

As part of our ongoing review of manufacturing capabilities and capacity, we announced changes to our network in 2019. In January, we announced our decision to discontinue operations at our Boulder and Longmont, CO manufacturing facilities to increase efficiencies in our global biologics supply chain. This consolidated our biologics drug substance manufacturing network to one large-scale drug substance facility, the Frederick Manufacturing Center, MD. The sites at Boulder and Longmont, CO were preserved for potential sale. As neither Boulder nor Longmont were licensed for commercial operations, there was no impact to supply or global availability of any of our biologics medicines.

In September 2019, we announced our intention to exit our manufacturing facility at Wedel in Germany by late 2021. This decision was taken after careful consideration of our future product demand, existing production capacity and our long-term business strategy. We are committed to treating those employees affected in a fair and respectful manner, and to ensuring the consistent supply of our products to patients during the transition period. In line with this, we are working closely with the local Works Council to provide outplacement and transition support.

At the end of 2019, approximately 12,800 people were employed at 25 Operations sites in 16 countries. The Reims packing and distribution centre acquired in January 2020 became our 26th Operations site.

### Environmental protection

We follow the science to protect the planet by managing our impact on the environment across our value chain, from R&D activities, our own operations, into our supply chain and customer use of products. Our Code of Ethics as described on page 35 is the overarching document for our environmental management system. It applies to all functions and locations and is supported by global standards and procedures that establish mandatory requirements in key risk areas. We monitor and manage performance through comprehensive assurance programmes that include performance reporting and internal auditing. Our 2019 targets (against a 2015 baseline) included:

- > reducing our operational greenhouse gas (GHG) footprint in line with our approved Science Based Target
- > limiting the increase in our energy consumption to no more than 6% to 1,916 GWh
- > limiting the increase in our waste generation to less than 19% to 36,635 tonnes
- > reducing water use by 8% to 3.98 million m<sup>3</sup>.

The tables on the right provide data on our global GHG emissions, energy use, waste production and water consumption for 2019. The data coverage includes 100% of our owned and controlled sites globally. To support the achievement of our targets, a resource efficiency capital fund has been in place since 2015 to invest in projects at sites. In 2019, \$15.5 million (2018: \$19 million) was committed to resource efficiency projects at our manufacturing and R&D sites, and a further \$14 million has been committed for 2020.

### Operational greenhouse gas footprint emissions (tonnes CO<sub>2</sub>e)<sup>1</sup>

|      |           |
|------|-----------|
| 2019 | 1,974,949 |
| 2018 | 1,852,104 |
| 2017 | 1,768,071 |
| 2016 | 1,739,046 |
| 2015 | 1,845,505 |

**1,974,949 tonnes CO<sub>2</sub>e**

### Energy consumption (MWh)<sup>1</sup>

|      |           |
|------|-----------|
| 2019 | 1,749,404 |
| 2018 | 1,863,931 |
| 2017 | 1,757,895 |
| 2016 | 1,799,669 |
| 2015 | 1,828,712 |

**1,749,404 MWh**

% total energy from renewables<sup>1</sup>

|             |
|-------------|
| 2019: 29.4% |
| 2018: 28.9% |
| 2017: 27.0% |
| 2016: 25.1% |
| 2015: 6.2%  |

### Waste production (tonnes)

|      |        |
|------|--------|
| 2019 | 34,193 |
| 2018 | 31,080 |
| 2017 | 31,199 |
| 2016 | 31,899 |
| 2015 | 30,785 |

**34,193 tonnes**

### Water use (million m<sup>3</sup>)

|      |      |
|------|------|
| 2019 | 3.55 |
| 2018 | 4.01 |
| 2017 | 3.89 |
| 2016 | 4.02 |
| 2015 | 4.32 |

**3.55 million m<sup>3</sup>**

<sup>1</sup> Regular review of the data is carried out to ensure accuracy and consistency. This has led to changes in the data from previous years. The data quoted in this Annual Report are generated from the revised data.



### Greenhouse gas emissions reduction

During 2019, our verified science-based targets for Scope 1 and Scope 2 emissions were confirmed to be in line with the most ambitious scenario of the Paris Agreement – limiting warming to under 1.5 degrees celsius. Progress towards these targets has been made through increased fuel efficiency of our sites and commercial sales fleet and procurement of electricity from certified renewable sources increasing to represent 70% of total electricity imports. Our total Scope 1 and Scope 2 emissions have been reduced by 36% from our 2015 baseline. Although our Scope 3 emissions sources continue to fluctuate, we have made progress towards our 2025 science-based targets for these emission sources through strategic developments, including committing to changing the propellants used in our inhalers, improving our switching of freighting of goods from air to sea, and engaging our key suppliers to set science-based targets and renewable energy goals. Including emissions from patient use of our inhaler therapies, our operational GHG footprint totalled 1,974,949 metric tonnes in 2019, an increase of 7% from our 2015 baseline.

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

### Energy use

Despite anticipated net increase in activity across our site network in 2019, we aimed to limit increases in total energy consumption to 6% above our 2015 baseline. Our resource efficiency capital fund committed \$14 million to energy efficiency projects in 2019, such as LED lighting and utility efficiency at our Macclesfield, UK site. In 2019, our energy use was 1,749 GWh, a decrease of 4% from our 2015 baseline. We have made further progress on our target to use 100% renewable power by 2025. In 2019, we used certified zero emission power equivalent to 62% of total power consumption, including 5,300 MWh of renewable power generated on our sites.

□ For more information on GHG emissions reporting, see Sustainability: supplementary information on page 266.

### Waste management

Due to anticipated activity growth across our site network in 2019, we aimed to limit increases in our waste volumes to a 19% increase from our 2015 baseline. In 2019, our total waste was 34,193 metric tonnes, an 11% increase on 2015. As waste generation is linked to production volumes, our waste reduction ambitions are going to be challenged as our business grows. However, we are focusing on processes to boost our operational efficiency and investing in waste reduction projects to help us reach our target to reduce waste generation by 10% by 2025. While waste prevention is an essential goal, we seek to maximise treatment by material recycling and avoiding landfill disposal when prevention is impractical.

### Water stewardship

We recognise the need to use water responsibly and, where possible, to minimise water use in our facilities. In 2019, we targeted an 8% reduction from our 2015 water use. In 2019, our water footprint was 3.55 million m<sup>3</sup>, an 18% reduction from our 2015 baseline. Water reduction and reuse projects throughout our site network have improved the efficiency of water use across our operations. Our major sites and those in water-stressed areas work to Water Conservation Plans to ensure we are managing our water risks and to facilitate sharing of best practice in water stewardship around our site network.

### Product environmental stewardship

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

Our pMDI therapies rely on hydrofluoroalkane (HFA) propellants, which are emitted during use and disposal, and contribute to our Scope 3 GHG footprint. While HFAs have no ozone depletion potential and a third or less of the global warming potential than the chlorofluorocarbons they replaced, they are still potent greenhouse gases.

During 2019, we progressed a project spanning all key functions in the business to investigate alternative low-Global Warming Potential propellant options available from an environmental, technical, regulatory, medical and commercial viewpoint.

### Pharmaceuticals in the environment

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

As part of our progress towards our 2025 environmental targets, our 2019 targets included:

- > Safe API discharges for AstraZeneca sites (100%) and globally managed first tier suppliers (>90%). Target met – at one AstraZeneca supply site there was a single measured API concentration that exceeded our API discharge limits. This followed a change implemented to reduce emissions. Subsequently, further process improvements and monitoring were implemented, which reduced emissions to below the safe API discharge limits.
- > Management of PIE through our ecopharmacovigilance programme. Target met – programme delivered and a manuscript published describing the environmental risks of more than 120 APIs resulting from patient use in 22 countries in Europe.

We conduct collaborative research to understand the fate, behaviour and impact of pharmaceuticals on the environment. In 2019, we co-authored 12 peer-reviewed publications to enhance our knowledge of the risks associated with this emerging issue. We also hosted a stakeholder workshop in Nairobi, Kenya to understand the environmental risks associated with increased patient access to medicines in emerging economies.

□ Further information on our efforts in these areas, including environmental risk assessment data for our medicines, is available on our website, [www.astrazeneca.com/sustainability/environmental-sustainability](http://www.astrazeneca.com/sustainability/environmental-sustainability).

>150

Completed more than 150 major or strategically important business development transactions in the last three years, including 29 in 2019 (2018: 80)

>730

We have more than 730 collaborations worldwide

### Business development

Business development, specifically partnering, is an important element of our business. It supplements and strengthens our pipeline and our efforts to achieve scientific leadership. We work with others around the world, including academia, governments, industry, scientific organisations and patient groups, as well as other pharmaceutical companies, to access the best science to stimulate innovation and accelerate the delivery of new medicines to target unmet medical need. We currently have more than 730 collaborations around the world.

Our business development activity takes many forms and can be broadly grouped into:

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

### Alliances, collaborations and acquisitions

We continue to assess opportunities to make strategic, value-enhancing additions to our portfolio and pipeline in our main therapy areas, including through in-licensing and acquisitions. No company acquisitions were completed in 2019.

Over the past three years, we have completed more than 150 major or strategically important business development transactions, including some 29 in 2019. Of these transactions, eight were completed on behalf of Oncology R&D and eight on behalf of BioPharmaceuticals R&D. Nine related to pre-clinical assets or programmes and 12 to precision medicine, genomics or access to genetic data<sup>1</sup>.

Collaboration activities that focus on the development and/or commercialisation of specific medicines are a component of our strategy. They have an important role to play in the delivery of our ambition as we continue to focus on developing key products within our main therapy areas. This activity can create additional value from our existing and potential medicines, and falls broadly into two categories:

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

Of particular note, we announced a global development and commercialisation collaboration agreement with Daiichi Sankyo for *Enhertu* (DS-8201), a proprietary antibody-drug conjugate (ADC) and potential new targeted medicine for cancer treatment. AstraZeneca and Daiichi Sankyo will jointly develop and commercialise *Enhertu* worldwide, except in Japan where Daiichi Sankyo will maintain exclusive rights. Daiichi Sankyo will be solely responsible for manufacturing and supply. Under the terms of the agreement, AstraZeneca agreed to pay Daiichi Sankyo an upfront payment of \$1.35 billion, half of which was settled in the second quarter of 2019 with the remainder payable 12 months later. Contingent payments of up to \$5.55 billion comprise up to \$3.8 billion for potential successful achievement of future regulatory and other milestones, as well as up to \$1.75 billion of potential sales-related milestones. AstraZeneca and Daiichi Sankyo will share equally development and commercialisation costs as well as profits from *Enhertu* worldwide, except for Japan, where Daiichi Sankyo will incur all costs and AstraZeneca will receive a royalty on sales.

We also amended the existing agreement with Ironwood in mainland China, China Hong Kong and China Macau for *Linzess*, a first-in-class new treatment for patients with irritable bowel syndrome with constipation. The amended agreement gives AstraZeneca sole responsibility for developing, manufacturing and commercialising *Linzess* in the above markets. AstraZeneca will pay Ironwood three non-contingent payments, totalling \$35 million, between 2021 and 2024. In addition, Ironwood could receive up to \$90 million in milestone payments, contingent on the achievement of certain sales targets. Ironwood will also be eligible for royalties beginning in the mid-single digit percent, based on the annual net sales of *Linzess* in the above markets, where Ironwood will no longer jointly fund the development and commercialisation of *Linzess* or share in the profit from sales.

In addition, we acquired an FDA Priority Review Voucher from a subsidiary of Sobi for a total cash consideration of \$95 million.

<sup>1</sup> Following the restructuring of R&D and the associated realignment of Business Development teams across AstraZeneca, the basis for reporting transaction activity has changed. As a result, metrics for 2019 are not directly comparable to those reported in previous years.

### Collaboration Revenue

In March 2019, we announced an update to the presentation of Total Revenue within our Statement of Comprehensive Income, effective 1 January 2019. Total Revenue now includes 'Collaboration Revenue', which comprises upfronts, milestone receipts and royalties and other income arising from transactions involving AstraZeneca's medicines along with income of a similar nature arising from transactions where AstraZeneca has acquired an interest in a medicine and entered into an active

collaboration with the seller. Collaboration Revenue replaces the category of Externalisation Revenue, which only included income arising from transactions involving AstraZeneca's medicines.

Details of significant business development transactions which give rise to Collaboration Revenue are included in the Financial Review from page 82. The change in revenue category from Externalisation Revenue to Collaboration Revenue is described within the Group Accounting Policies on page 173. The Collaboration Revenue generated in 2019 is provided in Note 1 on page 181.

### Divestments

We divest medicines that typically sit outside our main therapy areas and that can be deployed better by other companies, in order to redirect investment and resources in our main areas of focus, while ensuring continued or expanded patient access. For example, in 2019, we divested US rights to *Synagis* used for the prevention of serious lower respiratory tract infection caused by respiratory syncytial virus to Sobi. Sobi now commercialises *Synagis* in the US and around 130 AstraZeneca employees transferred to Sobi as part of the transaction. Sobi also gained the right to participate in AstraZeneca's share of US profits and losses related to potential new medicine MEDI8897. AstraZeneca will continue to develop MEDI8897 in collaboration with Sanofi. AstraZeneca received an upfront consideration of \$1.5 billion, consisting of \$1.0 billion in cash and \$500 million in ordinary shares of Sobi. AstraZeneca will also receive up to \$470 million in sales-related payments for *Synagis*: a potential \$175 million milestone following the submission of the Biologics License Application for MEDI8897; potential net payments of approximately \$110 million on achievement of other MEDI8897 profit and development-related milestones; and a total of \$60 million in non-contingent payments for MEDI8897 during 2019-2021.

In 2019, we also divested global commercial rights, excluding China, Japan, the US and Mexico, for  *Losec* and associated brands to Cheplapharm. The divestment included medicines containing omeprazole marketed by AstraZeneca or its collaborators under the *Acimax*, *Antra*, *Meptral*, *Mopral*, *Omepral* and *Zoltum* medicine names. *Losec* is a proton pump inhibitor discovered and developed by AstraZeneca, which helps reduce the amount of acid produced by the stomach in patients with gastrointestinal reflux conditions and ulcers. It has a number of approved indications and is commonly prescribed for patients with gastro-oesophageal reflux disease. Cheplapharm paid AstraZeneca \$243 million on completion in the fourth quarter and may also pay sales-contingent milestones of up to \$33 million across 2021 and 2022.

In addition, we completed the sale and licence of the commercial rights to *Seroquel* and *Seroquel XR* in Europe and Russia to Cheplapharm. *Seroquel* and *Seroquel XR*, used primarily to treat schizophrenia and bipolar disorder, have lost their compound patent protection in Europe and Russia. AstraZeneca will continue to manufacture and supply *Seroquel* and *Seroquel XR* to Cheplapharm during a transition period. Cheplapharm made an upfront payment of \$178 million to AstraZeneca and may also make future sales-contingent payments of up to \$61 million.

In a separate transaction, we completed the sale of commercial rights to *Seroquel* and *Seroquel XR* in the US and Canada to Cheplapharm. *Seroquel* and *Seroquel XR* have lost their compound patent protection in the US and Canada. Cheplapharm made an upfront payment of \$35 million to AstraZeneca and may also make future sales-contingent payments of up to \$6 million.

We also completed the divestment of commercial rights to *Arimidex* and *Casodex* in a number of European, African and certain other countries to Juvisé Pharmaceuticals. The medicines, used primarily to treat breast and prostate cancers, have lost their compound patent protection in these countries. Juvisé Pharmaceuticals made an upfront payment of \$181 million to AstraZeneca and may also make future sales-contingent payments of up to \$17 million. AstraZeneca already divested the rights to both *Arimidex* and *Casodex* in the US in 2017.

These agreements will enable us to concentrate our resources on bringing multiple new medicines to patients.

### Proceeds

The resulting revenue from these activities supports our R&D investments in our main therapy areas. A total of 11 transactions that contribute to Collaboration Revenue or generate income through divestment or out-licensing were completed in 2019.

□ More information on our partnering activity in 2019 can be found in the Financial Review from page 78 and Notes 1 and 2 to the Financial Statements from page 180.

## Intellectual Property

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

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

### Patent process

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

□ For information about third-party challenges to patents protecting our products, see Note 29 to the Financial Statements from page 221.

□ For more information on the risks relating to patent litigation and early loss and expiry of patents, see Risk from page 246.

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

# Business Review

## Delivering growth

### *continued*

#### Patent expiries

The table on pages 243 to 245 sets out certain patent expiry dates and sales for our key marketed products.

#### Other exclusivities

Regulatory data protection (RDP or 'data exclusivity') is an important additional form of exclusivity which is separate from, but runs in parallel with, patent exclusivity. RDP arises in respect of data which is required to be submitted to regulatory authorities to obtain marketing approvals for our medicines.

Significant investment is required to generate such data (for example, through conducting global clinical trials) and these proprietary data are protected from use by third parties (such as generic manufacturers) for a number of years in a limited number of countries. The period of such protection, and the extent to which it is respected, differs significantly among countries and varies depending on whether an approved drug is a small molecule or biologic compound. RDP is an important protection for our products, and we strive to enforce our rights to it, particularly as patent rights are increasingly being challenged. The RDP period starts from the date of the first marketing approval from the relevant regulatory authority and runs parallel to any patent protection. For small molecule drugs, RDP generally expires prior to patent expiry in all major markets.

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

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

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

#### Compulsory licensing and access

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.

More generally, we are committed to expanding access to healthcare through intellectual property and to providing transparency about where our patents are filed and enforced. See our Intellectual Property statement on our website [www.astrazeneca.com](http://www.astrazeneca.com) to learn more about our approach, and to view patent rights for medicines used to treat Index diseases.

#### Information technology and information services resources

**In 2019, we continued to sharpen our focus on running IT with high-quality performance – improving IT cost efficiency, systems performance and delivering higher levels of support for business priorities.**

#### Transforming the way we work

We believe the future of healthcare is one of individualised healthcare solutions focused on improved patient outcomes, driven by science and data. We are therefore embarking on a digital transformation, developing digital solutions to: enhance the delivery of our medicines; reduce inefficiencies and support patients in engaging with their own health; redefining the clinical trial experience through the use of digital tools and technologies to improve patient safety and outcomes; harnessing data science and artificial intelligence to transform the way we discover and develop new medicines; and transforming our Group operations using digital technologies. Our drive towards integrated care is dependent on building interoperable and trusted health data frameworks to be able to unlock the full potential of scientific data for patients and healthcare systems.

With our IT foundation now firmly in place and operating at high levels of efficiency, we have a growing programme portfolio to support this business transformation and which takes advantage of data and analytics, artificial intelligence, digital and the Internet of Things. In order to deliver on these commitments, IT has actively been strengthening its capabilities through recruiting key external

talent into the organisation, as the expertise to succeed in some of these technologies was not internally present at the levels needed. In addition to recruiting leaders in new technologies, the IT organisation continues to harness internal capabilities, enabling us to accelerate drug development, revenue growth and profitability.

#### Cybersecurity

The cybersecurity threat landscape continues to grow in both volume and complexity. The healthcare industry is increasingly becoming a target of cyber criminals as medical records often contain large volumes of valuable personal data, which could be used for criminal activity. Protecting our IT systems, IP and confidential information against cybercrimes continues to be a critical area of focus and investment. Our implementation of the National Institute of Standards and Technology Cybersecurity Framework (NIST CSF) allows us to understand cyber resilience and risk positioning, improving our ability to prevent attacks and minimise damage and data loss should a breach occur. We have seen success with our mandatory employee cybersecurity awareness training programme, which helps employees recognise and defend against common and high-risk cyber threats.

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

For more details, including the risks relating to information technology and cyber threats, see Risk from page 246.



Link to strategy: Deliver Growth and Therapy Area Leadership

# Next steps

## ● Improving outcomes for patients

Establishing Health Innovation Hubs to deliver patient-focused disease management solutions.

## ● What we're doing

- > Health Innovation Hubs put us at the centre of interaction between the patient, medicine, technology, healthcare professionals and policy makers to reimagine how we can improve patient outcomes through:
  - better public-private partnerships based on a shared innovation agenda
  - innovation and co-creation with start-up companies and technology partners
  - bringing innovation to AstraZeneca as we work to improve the entire patient experience with whole disease solutions.

## ● What's next?

- > We are collaborating with partners around the world to deliver integrated care and holistic disease management across all our therapy areas.
- > Our network of hubs aims to solve, showcase and scale innovative and holistic health solutions in order to optimise health management, improve patient outcomes and increase the value of our medicines – both for patients and those who pay for them.

# 10

We have 10 major Health Innovation Hubs. See page 65 for more information.



“We are investing around the world to meet the changing needs of patients. With our Health Innovation Hubs, we have brought together R&D, commercial and digital resources to reimagine how we can improve outcomes. We work with patients to identify the main challenges they face and then collaborate with them and partners within academia, medical professionals, government, technology companies and entrepreneurs to co-develop and implement solutions to those challenges.”

**Iskra Reic**  
EVP, Europe & Canada

# Business Review

## A great place to work: Employees



### Employees

We grow and prosper by recruiting, retaining and developing talented people. We do that by being a great place to work, encouraging and rewarding innovation, entrepreneurship and high performance. Our People strategy supports our strategic priorities and is built on three pillars: performing as an enterprise team, being committed to lifelong learning and being champions of inclusion and diversity.

#### 2019 overview

- > Hired 16,100 permanent employees; employees with less than two years' service now represent 36% of our global workforce
- > Voluntary employee turnover increased to 10.5%
- > High performers were promoted at twice the rate of the wider employee population
- > 'Leading Business' programme launched to develop leadership capability
- > 690 women have completed the 'Women as Leaders' programme, while the proportion of women in senior roles increased to 45.4%

- > Launched Global Standards on sexual harassment, and harassment and bullying
- > Worked to create a 'Speak Up' culture to prevent and detect any behaviour not in line with our Values, Code of Ethics and Global Standards
- > Made further progress against our safety, health and wellbeing targets
- > Performed well in the results of real earnings survey of all our employees

#### Performing as an enterprise team

We continue to develop workforce plans to ensure we can attract and develop the critical capabilities required to deliver our strategic priorities. These plans are underpinned by predictive analytics, meaning workforce decisions are data-driven. We also use workforce analytics to ensure that we manage our global workforce in an optimum way and continue to implement a significant number of automation initiatives, including more than 20 in 2019, which allow our workforce to spend a higher proportion of their time on higher-value activity.

#### Attracting key talent and critical capabilities

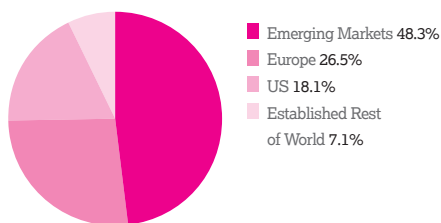
We are working to attract emerging talent, as well as investing in internships and recruitment opportunities globally. For example, we conduct a global programme to hire recent graduates for pharmaceutical technology and development, procurement, quality, engineering, IT, supply chain, and biometrics and information sciences functions. We have also implemented an MBA Development programme in our US Commercial Business, providing business rotations to give our future leaders breadth of experience.

Additionally, we offer a 12-week internship opportunity for business school students to contribute to key initiatives in our Oncology therapy area.

The talent scout model implemented in 2018 continues to be successful in enhancing our ability to attract key talent and critical capabilities into senior roles. This has been supported by an enhanced employee referral scheme, which has become an increasingly important source of hiring.

### A global business

#### Employees by reporting region



**70,600**  
employees

Co-located around three strategic R&D centres

1. Gaithersburg, MD, US  
3,200
2. Cambridge, UK  
2,800
3. Gothenburg, Sweden  
2,200

#### By geographical area



|                            |   |  |  |
|----------------------------|---|--|--|
| 1. US<br>12,800<br>18.1%   | 4. Canada<br>900<br>1.2%                      | 7. Other Europe<br>8,300<br>11.7%      | 10. China<br>18,100<br>25.6%                   |
| 2. UK<br>7,100<br>10.1%    | 5. Central and South America<br>3,000<br>4.3% | 8. Russia<br>1,200<br>1.7%             | 11. Japan<br>3,000<br>4.3%                     |
| 3. Sweden<br>6,500<br>9.1% | 6. Middle East and Africa<br>1,700<br>2.5%    | 9. Other Asia Pacific<br>6,900<br>9.8% | 12. Australia and New Zealand<br>1,100<br>1.6% |

All numbers as at 31 December 2019.

During 2019, we hired 16,100 permanent 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. Most of this hiring has been focused in our Emerging Markets, in particular China, as we continue to reshape our workforce footprint to support our strategic objectives and to position us well for the future. Our data indicates that these recent recruits are performing strongly although, in some areas of the business, retention of this population is challenging.

Voluntary employee turnover increased to 10.5% (2018: 10.1%). The voluntary employee turnover rate among our high performers increased in 2019 to 7.0% (2018: 6.0%), while the voluntary employee turnover of recent hires remained stable at 14.4% (2018: 14.4%). We seek to reduce regretted turnover through more effective hiring and induction, exit interviews, risk assessments and retention plans.

The uncertainty faced by individuals and their families following the UK's departure from the EU could have an impact on hiring and retaining staff in some business-critical areas. Consequently, we continue to provide extensive support and information to employees who might be impacted, monitor trends in recruitment and resignation closely, and guide new hires through our recruitment process.

#### **A culture of high performance**

Continuing our emphasis on high performance, in 2019 our high performers were promoted at twice the rate of the wider employee population. We require every employee to have high-quality objectives, aligned to our strategy, which we monitor closely. Managers are accountable for working with their teams to develop individual and team performance targets, and for ensuring employees understand how they contribute to our overall business objectives.

Our salary and bonus budgets are distributed in line with our principles, allowing us to clearly differentiate reward according to performance. We encourage participation in various employee share plans, some of which are described in the Directors' Remuneration Report from page 125, and in Note 28 to the Financial Statements from page 217. Additionally, in the UK, we have made changes to the way we reward, provide benefits and support our people. These changes are designed to rebalance the reward mix, improve understanding of benefits and simplify our processes.

#### **Listening to our workforce**

Employee opinion surveys help us measure employee satisfaction and engagement, and progress in our aim of being a great place to work. Comparing our most recent survey (December 2019) to the previous year (December 2018), of the 20 items common to both surveys, we improved in 19 items and remained stable for one other. We continue to score highly for 'understanding and belief of the future direction and strategy', and we saw good progress in items around senior leader communication and prioritisation, although there is still scope for improvement. We also exceeded our scorecard target for 'I would recommend AstraZeneca as a great place to work'. Although we saw a reduction in the score for the proportion of employees who felt 'comfortable to speak up' in our mid-year June survey, a significant increase in the score in our December 2019 survey meant we exceeded the score for December 2018 and our scorecard target for this item. Despite progress in the latest survey, there remains further opportunity to simplify the way we work.

#### **Developing a culture of lifelong learning**

We encourage employees to take ownership of their own development and expect leaders to spend time supporting their employees' development. To support this, we have implemented a global platform to increase the visibility and accessibility of job opportunities and received over 27,000 applications from internal candidates through this platform in 2019.

In early 2019, we took a decision to review how we support the learning and development of our people. This work involved a substantial investment to develop a culture of lifelong learning and support the up-skilling and re-skilling of our people. This included a new operating model and global team, a technology roadmap and associated technology investments, and an integrated content strategy.

#### **Developing our people**

Following the successful launch of 'Leading People' in 2017 (a social online learning platform aimed at managers) and 'Leading Self' in 2018 (aimed at employees below manager level), and after a successful pilot in 2018, in 2019, we launched our 'Leading Business' programme, connecting 512 managers from all areas and regions of AstraZeneca to develop their leadership capability. We continue to see a positive impact of these experiences in engagement and retention measures. This is supported by 'Manager Essentials', launched in April 2019 to more than 9,000 people managers across AstraZeneca, which is a curated set of digital resources that support the development of manager capability.

Our 'Women as Leaders' programme aims to encourage more women into senior roles. Approximately 690 women had completed the programme by the end of 2019, with continuing feedback that it is providing positive career outcomes for the participants. In addition, we have developed women's networks in most countries, continued to hold empowerment summits in various locations around the world and to support mentoring relationships, for example, introducing mentoring by senior women for emerging talent in Operations.

In 2018, we launched the 'Rising Leaders Experience', a development programme aimed at emerging talent who demonstrate the potential to reach senior leadership roles. The programme accelerates and supports their development through a development centre, a leadership workshop, executive coaching, an AstraZeneca mentor, and a stretch assignment.

In addition, in 2019, we launched a global mentoring programme, with the aim of pairing mentors and mentees in order to encourage personal development and to support the implementation of a culture of lifelong learning. This has been successful, with over 900 mentors registered and almost 400 mentor-mentee relationships established.

In 2019, 80% of vacancies across the top three levels of our organisation were filled internally, reflecting our long-term commitment to develop high-quality leaders and the rigour of our leadership succession planning. To ensure our senior leadership reflects our diverse geographic footprint, we track the country of origin of senior leaders and reflect this in our diversity targets. In 2019, 18.3% of employees who are either members of the SET, or their direct reports, have a country of origin that is an Emerging Market or Japan (an increase from 5% in 2012 but below our 2019 target of 20%).

# Business Review

## A great place to work: Employees *continued*

### Champions of inclusion and diversity

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. We focus on inclusive leadership at all levels, creating a culture where people feel able to speak up, as well as building and sustaining a diverse talent pipeline.

As part of our commitment to inclusion and diversity, we have implemented numerous initiatives across the globe, such as unconscious bias training, the formation of various employee resource groups (such as an LGBT+ network) and updated recruitment standards to ensure diverse candidate lists. We have also established an Inclusion and Diversity Council, chaired by the CEO, in addition to holding empowerment summits across eight sites.

### Gender diversity

Our commitments include a goal to increase the number of women on our leadership teams. As shown in the gender diversity figure on this page, women comprise 50.0% of our global workforce. There were four women on our Board (33% of the total) at the end of 2019 with Shriti Vadera retiring from the Board with effect from 1 January 2019. Below Board level, the representation of women in senior roles (i.e. roles at Career Level F or above which constitute the six highest bands of our employee population) increased to 45.4% in 2019 (2018: 44.6%), which exceeded our scorecard target of 45.0% for this measure and compares favourably to external benchmarks. Women are also currently promoted at a higher rate than men across all levels of seniority, positively impacting the gender balance. In 2019, the Board changes resulted in AstraZeneca ranking 39th in the FTSE 100 ranking for Women on Boards, and sixth place in the FTSE 100 for Women on Executive Committees and Direct Reports, as well as retaining our inclusion in the Bloomberg Gender Equality Index.

### Leadership oversight

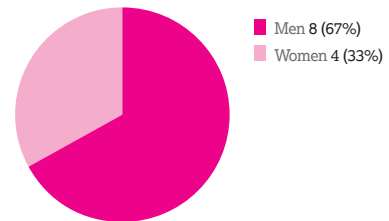
Diversity is integrated into our Code of Ethics and its associated Workforce Global Policy as described on page 35. In addition to the two diversity metrics tracked in the AstraZeneca scorecard (representation of women in senior roles and senior leadership country of origin that is an Emerging Market or Japan), on a bi-annual basis, the Senior Executive Team (SET) and Board are provided with a comprehensive overview of the AstraZeneca workforce, covering a wide range of metrics and measures (including trends around gender diversity, leadership ethnic diversity and age profile). The SET is also provided with a quarterly summary of key workforce metrics, including gender diversity and leadership ethnic diversity. Within the US, we track overall ethnic minority representation, ethnic minority representation in senior roles, and ethnic minority representation in succession plans.

We are committed to hiring and promoting talent ethically and in compliance with applicable laws. Our Code of Ethics and its supporting Standards are designed to help protect against discrimination on any grounds (including disability) and cover recruitment and selection, performance management, career development and promotion, transfer, training, retraining (including retraining, if needed, for people who have become disabled), and reward. Our Global Standard for Inclusion and Diversity sets out how we foster an inclusive and diverse workforce where everyone feels valued and respected because of their individual ability and perspective. More information on our Standards and Global Policy framework can be found on page 35 and on our website, [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

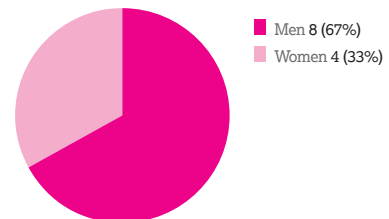
In addition to our Global Standard on Inclusion and Diversity, we launched two further Global Standards in 2019: on sexual harassment, and harassment and bullying. Drawing on our commitment to respect each other and uphold equal opportunity, we aim to build a culture where everyone feels safe to speak up. These Standards are reinforced by training and education on the importance of speaking up (which includes challenging behaviours that are inconsistent with our Values and Code of Ethics), demonstrating inclusive leadership and responding to allegations of misconduct. We have multiple channels available for reporting. Allegations are taken seriously and handled in a manner that is sensitive to the confidentiality and security of those making a report and is subject to global oversight.

### Gender diversity

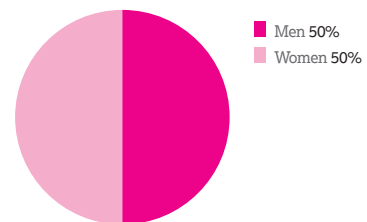
#### Board of Directors of the Company



#### Senior Executive Team



#### AstraZeneca employees



All numbers as at 31 December 2019.



## Human rights <sup>BV</sup>

Our Code of Ethics and Human Rights Statement commit us to respecting and promoting international human rights – not only in our own operations, but also in our wider spheres of influence, such as our third-party providers. To that end, we integrate human rights considerations into our processes and practices. We are also committed to ensuring that there is no modern slavery or human trafficking in our supply chains or any part of our business. Our full statement required under section 54 of the UK Modern Slavery Act is available on our website, [www.astrazeneca.com](http://www.astrazeneca.com).

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

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

In 2017, we signed up to the 'Fair Wage' database. These independently produced data were used in our end of 2018 survey to measure against the real earnings of all our employees, in which we performed well.

For more information about the assurance provided by Bureau Veritas, see page 266.

## Managing change <sup>BV</sup>

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

For more information on our restructuring programme, see the Financial Review from page 78.

## Employee relations <sup>BV</sup>

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

The purpose of this function is to build and maintain a positive work environment where every employee can feel safe, with the right terms and conditions, productive, motivated and able to speak up. The Board of Directors, in collaboration with our Global Compliance and Employee Relations functions, supports our efforts to create a 'Speak Up' culture to prevent and detect any behaviour not in line with our Values, Code of Ethics and Global Standards.

To achieve this objective, we also work to develop and maintain good relations with local workforces and work closely with our recognised national trade unions. We also regularly consult with employee representatives or, where applicable, trade unions, who share our aim of retaining key skills and mitigating job losses. According to our internal Human Rights survey carried out in 2018 and concluded in February 2019, 67% of our employees recognise and have a relationship with trade unions. Where trade unions do not exist in an area of operation, 97% of countries have established arrangements to engage similarly with their workforce.

## Safety, health and wellbeing <sup>BV</sup>

We work to promote a safe, healthy and energising work environment for our workforce and partners. Our standards apply globally and are stated in our Code of Ethics as described on page 35 and available on [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability). We have established and monitor a set of safety, health and wellbeing targets aimed at supporting our workforce and keeping AstraZeneca among the sector leaders in performance. Our performance in this area is in the Sustainability Report and Sustainability Data Summary available on [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability) and is assured by Bureau Veritas.

For more information about the assurance provided by Bureau Veritas, see page 266.

## Safety

### Vehicle collisions

| Year          | Collisions per million km | Target |
|---------------|---------------------------|--------|
| 2019          | 2.84                      | 3.39   |
| 2018          | 3.74                      | 3.58   |
| 2017          | 4.05                      | 3.76   |
| 2016          | 4.66                      | 4.00   |
| 2015 baseline | 4.13                      |        |

### Work-related injuries

| Year              | Reportable injury rate per million hours worked | Target |
|-------------------|---|--------|
| 2019              | 1.05  | 1.37   |
| 2018 <sup>†</sup> | 1.32  | 1.50   |
| 2017              | 1.48  | 1.60   |
| 2016              | 1.57  | 1.69   |
| 2015 baseline     | 1.78  |        |

<sup>†</sup> Data restated as a result of one injury case being reported late.

As shown above, we made further progress against our strategic targets in 2019, achieving a 31% reduction in vehicle collision rate and a 41% reduction in the work-related injury rate from the 2015 baseline. In addition, there were no work-related fatalities during 2019. Building on our previous success in establishing a culture of health and wellbeing, we continue to focus on active health promotion. We have programmes to address all four essential health activities – healthy eating and drinking, physical activity, tobacco cessation and mental wellbeing – at 71% of our sites.

In 2019, we carried out several activities and initiatives focused on continuous improvements in key risk areas, including driver safety (our highest risk for significant injury and fatalities), travel security, health and wellbeing, potential serious incidents and fatal events. We also explored organisational cultural impact on safety, and developed and rolled out a new workforce wellbeing strategy to advance mental and physical health for our employees and extended workforce.



Link to strategy: Be a Great Place to Work

# Next up

## ● Being a great place to work

Attracting and retaining the best people.

## ● Champions of inclusion and diversity

- > Our Inclusion and Diversity Council, which was established in 2019 and is chaired by our CEO, Pascal Soriot, signed AstraZeneca up to two United Nations initiatives that aim to tackle discrimination and strive for diversity and equality in the workplace.
- > Held five Empowerment Summits across eight sites, in the US, the UK, Sweden, Poland and Brazil in 2019.

## ● Increased emphasis on 'Speak Up'

- > The global campaign built understanding of what 'Speak Up' means across the Group, and encouraged awareness and provided guidance to all employees on how to identify and challenge behaviours not aligned to our culture.
- > Increased visibility of our Employee Resource Groups, aligned them to organisational priorities and supported them with structure and funding.

## ● Building a culture of lifelong learning and development

- > Built a multi-tiered and blended Leader, Manager & Employee learning and development offering to encourage coaching and feedback, inclusive leadership, leading in digital, sustainability, and patient centricity.
- > Established multi-tiered development centres to support our goal of building a diverse pipeline of future leaders.



"To secure our current and future success, we are nurturing a culture that encourages our people to be themselves and helps each of them to be the best they can be."

**Fiona Cicconi**  
EVP, Human Resources



## Contributing to society

We aim to make a significant financial contribution to the communities in which we operate. In addition, we make a non-financial contribution to society that comprises our medicines for patients and our sustainability for people and the environment. We are committed to operating in a way that recognises the interconnection between business growth, the needs of society and the limitations of our planet.

### 2019 overview

- > 64 Healthy Lung partnerships
- > Fifth anniversary of Healthy Heart Africa
- > Tenth anniversary of Young Health Programme with new UNICEF partnership
- > Gave more than \$72 million through our community investment activities
- > Employees volunteered more than 28,000 hours on community projects globally
- > Sustainability strategy focused on access to healthcare, environmental protection, and ethics and transparency

As a science-led, patient-focused pharmaceutical company, our innovative medicines impacted more than 120 million patient lives in 2019. But our contribution to society extends beyond this to include our wider efforts to benefit people and the planet. Additionally, wherever we work in the world, we aim to make a positive impact on our communities, making financial contributions, supporting healthcare and STEM education programmes, volunteering, and through product donations.

As a major investor, employer and taxpayer, we also make a significant contribution to the economies of all the countries in which we operate. We pay corporate income taxes, customs duties, excise taxes, stamp duties, employment and many other business taxes where applicable in the jurisdictions in which we operate. In addition, we collect and pay employee taxes and indirect taxes such as value added tax.

### Access to healthcare

We recognise that providing access to healthcare for all those who need it is a significant and complex global challenge. As one of the three priorities of our Sustainability strategy (see page 52), we are working towards a future where all people have access to sustainable healthcare solutions for life-changing treatment and prevention. The economic, social and environmental factors affecting access include the affordability of medicines, the maturity of healthcare systems, the existence or lack of supportive policies and insurance coverage, and the robustness of supply chains and distribution networks. Further challenges include the availability of trained staff, such as doctors, nurses and community health workers, as well as investment in primary healthcare and public health services, such as disease prevention and screening services.

Meeting these challenges requires innovation and collaboration and we are working to make a meaningful contribution to the transformation of healthcare. Our approach recognises that there is no single solution and takes account of the varying barriers to healthcare in different parts of the world. We tailor our programmes and initiatives to meet the needs of local communities, partner with the experts on the ground, and share best practice and replicate schemes when we can. Our goal is to improve health for patients and add value to society.

Below, we highlight some of our key access to healthcare programmes and initiatives. Further examples in this Annual Report include Lung Ambition (see page 57) and Precision (see page 69). For more information, see Emerging market healthcare on page 35. More detail on our access programmes can be found in our 2019 Sustainability Report, available on our website, [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

### Healthy Lung

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

Thus far, we have initiated 64 formal partnerships and signed 23 memoranda of understanding with national and regional governments, professional organisations and NGOs to drive care improvement, which has enabled Healthy Lung to:

- > support the training of more than 53,000 healthcare professionals
- > enable diagnosis of more than 1.1 million cases of asthma and/or COPD
- > activate more than 1,300 Respiratory Centres
- > align 28 national care guidelines and care pathways to international best practice.

The programme now has a presence in Asia, Latin America, and the Middle East and Africa.

### Healthy Heart

Healthy Heart Africa (HHA) was designed to contribute to the prevention and control of hypertension and decreasing the burden of cardiovascular disease across Africa. The programme supports sustainable models by working with local health systems. Each model works independently with partners in the country of implementation to address different health challenges and health environments, with the aim of providing a sustainable means of fighting hypertension in Africa.

Since launching in Kenya five years ago and subsequently expanding to Ethiopia in 2016, Tanzania in 2018 and Ghana in 2019, HHA has:

- > conducted more than 13.5 million blood pressure screenings in the community and in healthcare facilities
- > trained more than 7,200 healthcare workers, including doctors, nurses, community health volunteers and pharmacists, to provide education and awareness, screening and treatment services for hypertension
- > activated more than 750 healthcare facilities in Africa to provide hypertension services, including, where appropriate, the establishment of a secure supply chain for low-cost, high-quality antihypertensive medicines
- > identified more than 2.4 million elevated blood pressure readings.

## Business Review

# A great place to work: Contributing to society *continued*


### Young Health Programme

In 2019, we celebrated the tenth year of our award-winning Young Health Programme (YHP). YHP is a philanthropic community investment programme which focuses on young people and non-communicable disease (NCD) prevention. Despite the fact that more than two thirds of premature deaths from NCDs can be linked to behaviours that first began in adolescence, young people and their health continues to be an under-recognised, under-served and under-researched component of the global health agenda. In 2019, we reached nearly one million young people with health information on NCDs and risk behaviours and trained more than 8,500 peer educators and healthcare workers. Working with local governmental and non-governmental groups, we launched new programmes in Mexico, Myanmar, Thailand and Vietnam. This brings the total number of active YHP initiatives to 18. We also announced a recommitment to the programme through to 2025, with a pledge of \$35 million (£28 million) from 2021 to 2025.

We continue to deliver this programme in partnership with leading non-profit organisations that include Plan International UK, NCD Child and the NCD Alliance, following a model of investment in advocacy, research and community-based programming. We support the growth and development of young people with our ongoing collaboration with One Young World. In 2019, we offered 25 scholarships to young global health leaders bringing the total number of scholarships to 75.

In January 2020, we announced that YHP was to partner with UNICEF to prevent NCDs among young people. We will support UNICEF with a \$12.5 million grant to support programming which will reach more than five million young people, train 1,000 youth advocates and positively shape public policy.

We were named Business of the Year at Third Sector's Business Charity Awards, which recognise the outstanding contribution that UK companies make to good causes.

 Further information on YHP can be found on its website, [www.younghealthprogrammehp.com](http://www.younghealthprogrammehp.com).

### Responsible R&D

Our initiatives include a responsible R&D strategy to drive global health outcomes. This includes: integrating access considerations into R&D governance to increase the speed and breadth of patient access; driving excellence in product life-cycle management through our work on product safety and product environmental stewardship; engaging in scientific collaborations to build local capacity for R&D; and investing in science and technology, such as digitalisation and precision medicine, which can help reduce infrastructure costs and ensure effective treatment.

### Community investment


Our Global Standard on External Funding encompasses community investment and provides guidance to ensure a consistent, transparent and ethical approach around the world, based on local need. Our activities are focused on healthcare in the community and supporting science education. They include financial and non-financial contributions. In 2019, we gave more than \$72 million (2018: \$57 million) through our community investment activities to more than 900 non-profit organisations in 53 countries. The increase reflects a change in practice with a number of larger contributions being transferred to our Charitable Foundations. The amount includes more than \$27.4 million (2018: \$17.5 million) for product donations that were given in support of public health needs and disaster relief. The increase reflects changes in the volume and mix of products donated. In addition to these community investments, we also donated more than \$801 million (2018: \$686 million) of medicines in connection with patient assistance programmes around the world, the largest of which is our AZ&Me programme in the US.


Our global disaster relief partner is the British Red Cross. In 2019, we continued to support humanitarian efforts to provide healthcare to people affected by armed conflict in Northern Nigeria and we also responded to appeals for support to Ebola and Cyclone Idai relief efforts. Our global product donation partners are Americares, Direct Relief International and Health Partners International of Canada.

In 2019, our Step Up! Young Health Global Grants Programme provided a total of \$151,401 to 16 organisations that are innovating to improve the health and wellbeing of young people.

We continue to support *Connections for Cardiovascular Health*<sup>SM</sup>, a programme of the AstraZeneca HealthCare Foundation that was launched in 2010 to address heart health in the US. In 2019, the AstraZeneca HealthCare Foundation provided \$775,000 in continuation grants to 11 non-profit organisations for programmes that aim to help prevent, better manage and reduce cardiovascular disease.

Making a positive impact on our communities is also about volunteering. We encourage our employees to volunteer and support their efforts with one day's leave for community service. In 2019, our employees volunteered more than 28,000 hours on community projects in countries around the world.

 For more information on the Step Up! Young Health Global Grants Programme, visit [www.younghealthprogrammehp.com](http://www.younghealthprogrammehp.com).

 For more information on the AstraZeneca HealthCare Foundation's *Connections for Cardiovascular Health*<sup>SM</sup> programme, visit [www.astrazeneca-us.com/foundation](http://www.astrazeneca-us.com/foundation).


 For more information on the AstraZeneca HealthCare Foundation, see the Glossary from page 268.

### Product donation programmes

As noted above, in some countries, our patient assistance programmes offer medicine for free to patients who cannot afford to pay. These programmes vary by country with the largest being AZ&Me in the US. AZ&Me is governed as a 501(c) (4) organisation, which categorises the activity for the purpose of social welfare and establishes specific governance requirements, which keeps it separate from our commercial business.

In 2019, we celebrated the eleventh year of our collaboration with Americares and the Sihanouk Hospital Center of Hope (SHCH) for the Cambodia Breast Cancer Initiative. The collaboration aims to strengthen existing treatment services while expanding in scale to reach additional patients. The programme screened 843 new patients; provided information on early detection and screening to more than 10,000 individuals; diagnosed 82 cases of breast cancer and continued to treat 404 patients who were previously diagnosed; and administered more than 15,000 units of free AstraZeneca medicines to post-menopausal breast cancer patients in the SHCH's treatment cohort.

 For more information about AZ&Me, see page 33.

 Learn more in our 2019 Sustainability Report on [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

### Health and the environment

During 2019, we continued with our pilot programme in respiratory health at Lake Victoria's Dunga Beach, in Western Kenya, which enables the local community to transform waste into clean energy. The goal of the programme is preventing exposure to air pollutants by offering a substitute to wood-burning cookstoves and improving the respiratory health of the nearby community with an alternative fuel source. By providing a substitute for solid fuels, it also reduces the time and effort dedicated by women and children to collecting firewood, time which is then invested in schooling and income-generating activities.

The pilot is run with the Cambridge Institute for Sustainability Leadership (CISL) who studied the environmental impact of this intervention, with base-line and end-line reports published by CISL.

## Sustainability <sup>BV</sup>

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

### Governance

Sustainability governance frames how we operate. Geneviève Berger, a Non-Executive Director, oversees the implementation of our sustainability matters on behalf of the Board of Directors. Our ambition is to be a leader in sustainability by delivering the strategy from the materiality assessment carried out in 2018 and as outlined in our Sustainability Report. Katarina Ageborg is responsible for the global strategy, and performance measures are tracked by the SET on the quarterly Company Scorecard.

Our Sustainability Advisory Board comprises five SET members and four external sustainability experts. It provided guidance on strategic direction, recommendations for opportunities, and insights and feedback twice in 2019. Throughout the year, we engaged with employees and external stakeholders, including investors, Ministries of Health, NGOs, patients and suppliers.

### Our approach

Our approach is aligned with our Purpose and business strategy, allowing us to maximise the benefit for our patients, our business, broader society and the planet. As outlined below, we have a global strategy that integrates sustainability practices throughout our operations. In 2019, we put into operation our updated approach based on a structured sustainability materiality assessment that engaged external and internal stakeholders. We measure our progress through annual and long-term targets, and sustainability-related occurrences are incorporated into publicly released quarterly results for investors.

## Benchmarking and assurance

### Recognition of our work in sustainability

#### DJSI



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

#### FTSE4Good



- > Named as a FTSE4Good Index series constituent, which is designed to measure the performance of companies demonstrating strong Environmental, Social and Governance (ESG) practices

#### CDP



- > Water A List – among the top 1.5% of companies participating in CDP's water security programme for our commitment to transparency around environmental risks and demonstration of sustainable water management
- > Climate change A List – in recognition of our strategy and actions to reduce emissions and mitigate climate change

#### ISAE3000 Assured



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

For more information, see Sustainability: supplementary information on page 266 and the letter of assurance available on [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

We recognise the connection between enterprise risk management and sustainability management. Enterprise risk management helped inform the sustainability materiality assessment and we have better aligned our risk and sustainability classifications. Sustainability is considered throughout our quarterly risk reviews.

We show performance in our Sustainability Data Summary. Expanded discussion about our sustainability journey is in our 2019 Sustainability Report.

Learn more on our website, [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

# Business Review

## A great place to work: Contributing to society

### continued

#### Our sustainability strategy

At AstraZeneca, health is our business and our contribution to society. How we operate supports sustainable ecosystems for healthcare that benefit people and our planet through science-based innovation.

Our aspiration is for the future to be healthy and that we are an active participant for a healthy society, planet and business. Our pioneering medicines touch the lives of millions of people so it is a business imperative that we are partners and activists for solutions to global health. At the heart of our sustainability approach is access to healthcare and its connection to environmental protection, and ethics and transparency.

| Our pillars                    | 1. Access to healthcare<br>Health is at the heart of our business  | 2. Environmental protection<br>The health of the planet impacts all life  | 3. Ethics and transparency<br>Equality and prosperity for all fuels healthy societies   |
|--------------------------------|--|---|---|
| Our ambitions to 2025          | Work towards a future where all people have access to sustainable healthcare solutions for life-changing treatment and prevention  | Manage our environmental impact across all our activities and our products  | Create positive societal impact and promote ethical behaviour in all markets across our value chain   |
| The connection to human health | Innovating, partnering in and transforming healthcare is essential for global health   | Supporting a healthy environment helps prevent the onset of certain diseases and improve health outcomes  | Fostering a culture of doing the right thing across our worldwide operations, including our supply chain, promotes health and wellbeing   |
| Our material issues            | Disease prevention and treatment, Responsible R&D, Investments in health systems, Environment's impact on health, and Affordability  | Product environmental stewardship, Greenhouse gas reduction, Pharmaceuticals in the environment, Water stewardship, and Waste management  | Ethical business culture, Inclusion and diversity, Talent and workforce evolution, Workforce wellbeing and safety, Responsible supply chain, and Human rights   |
| Why it matters                 | <p>Access to healthcare at AstraZeneca goes beyond our medicines. We are working towards a future where all people have access to sustainable healthcare solutions. We are transforming the future of healthcare along the continuum from prevention and awareness to diagnosis and treatment. We innovate across our therapy areas to address the challenges of diseases for patients, and the unmet medical need created by them. We recognise that healthcare delivery systems may be complex and multi-layered and we collaborate with experts to foster patient-centred quality healthcare designed to improve the health outcomes of patients. Our internal initiatives place a strong emphasis on the role of health in workforce wellbeing and safety, our supply chain and environmental stewardship.</p> <p>Information in respect of our focus areas in broadening access to healthcare can be found in this Annual Report as follows:</p> <ul style="list-style-type: none"> <li>&gt; Investments in health systems and Disease prevention and treatment – see Access to healthcare – page 49</li> <li>&gt; Affordability – see Pricing and delivering value – page 32</li> <li>&gt; The environment's impact on health – page 50</li> <li>&gt; Responsible R&amp;D – page 50</li> </ul> | <p>We are taking climate action now because we recognise the strong connection between a healthy planet and healthy people. With health at the heart of our business, we work to foster environments in which all life can thrive – seeking opportunities for environmental stewardship and mitigating climate impacts by managing natural resources and ensuring environmental safety of our products across our operations and value chain.</p> <p>Information in respect of our focus areas in protecting the environment can be found in this Annual Report as follows:</p> <ul style="list-style-type: none"> <li>&gt; Greenhouse gas emissions reduction – page 39</li> <li>&gt; Waste management – page 39</li> <li>&gt; Water stewardship – page 39</li> <li>&gt; Product environmental stewardship – page 39</li> <li>&gt; Pharmaceuticals in the environment – page 39</li> </ul> | <p>We want to be valued not only for our medicines, but also for the way we work. We believe integrity, respect and transparency comprise the foundation of a healthy business culture. We build trust by demonstrating ethical business practices and fair treatment in everything we do across our value chain and in society.</p> <p>Information in respect of our focus areas in ethics and transparency can be found in this Annual Report as follows:</p> <ul style="list-style-type: none"> <li>&gt; Ethical business culture: Our Values and norms, practices, standards and principles that guide the actions and behaviour of employees, including our Code of Ethics (see page 35), and acting in an ethical manner that goes beyond compliance with policies, laws and regulations. This applies across all our operation and our entire value chain and includes: <ul style="list-style-type: none"> <li>– Bioethics (including animal welfare) – page 28</li> <li>– Anti-bribery and anti-corruption – page 35</li> <li>– Intellectual Property – page 41</li> <li>– Responsible sales and marketing – page 35</li> <li>– Transparency reporting – page 35</li> </ul> </li> <li>&gt; Inclusion and diversity – page 46</li> <li>&gt; Talent and workforce evolution – page 44</li> <li>&gt; Workforce wellbeing and safety – page 47</li> <li>&gt; Responsible supply chain – page 37</li> <li>&gt; Human rights – page 47</li> </ul> |
| Our global development impact  |     |      |      |

For more information on our targets and performance, and contribution to the UN Sustainable Development Goals, see our 2019 Sustainability Report available on our website, [www.astrazeneca.com/sustainability](http://www.astrazeneca.com/sustainability).

#### Non-Financial Information Statement

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

- > Code of Ethics on page 35
- > Environmental matters on pages 38-39 and page 266
- > Employees on pages 44-47
- > Social matters on pages 49-50 and page 52
- > Respect for human rights on page 47
- > Anti-corruption and anti-bribery matters on page 35

Information on the Group's Principal Risks is included in Risk Overview on pages 74-77 and information on the non-financial key performance indicators relevant to our business is included in Key Performance Indicators from page 20. A description of our business model is contained in Business model and life-cycle of a medicine from page 8.



Link to strategy: Be a Great Place to Work

# Next Move

## Zero carbon emissions

### Ambition Zero Carbon

Our strategy to eliminate emissions by 2025 and be carbon negative by 2030.

### What are we doing?

Our Ambition Zero Carbon strategy is to achieve zero carbon emissions from our global operations by 2025 and ensure our entire value chain is carbon negative by 2030. It accelerates our existing science-based targets, doubling energy productivity and using renewable energy for both power and heat. Our strategy sets out to make our global operations responsible for zero carbon emissions without relying on offset schemes to reach zero emissions on aggregate.

### \$1bn

We will invest up to \$1 billion to achieve our goals and to develop the next-generation respiratory inhalers with near-zero Global Warming Potential (GWP) propellants.

### 100%

100% electric vehicle fleet five years ahead of schedule.

### 50m

AZ Forest is our 50-million tree reforestation initiative in collaboration with local governments and One Tree Planted, a non-profit organisation focused on global reforestation.

“The commitments AstraZeneca has made as part of our Ambition Zero Carbon strategy will enable us to speed up the reduction of our impact on climate, bringing forward our decarbonisation plans by more than a decade, and inspire collaboration at a global level to effect policy change.”

**Pascal Soriot**  
Chief Executive Officer



# Oncology

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

## Unmet medical need and world market

- > Cancer is the second leading cause of death globally
- > Lung cancer claims a life every 18 seconds; it has the highest cancer mortality rate, followed by colorectal, stomach, liver and breast cancer
- > With over two million new cases for each in 2018, lung cancer and breast cancer are the two most common types of cancer
- > Other common cancers include prostate and ovarian cancer

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

### Estimated annual cancer cases (m)

|      |      |
|------|------|
| 2040 | 29.5 |
| 2030 | 24.1 |
| 2020 | 19   |

## 1.8m

Lung cancer was responsible for the deaths of 1.8 million people in 2018.

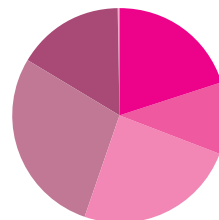
## 2.1m

Breast cancer is the most frequent cancer among women, impacting 2.1 million women each year.

### Therapy area world market (MAT/Q3/19)

## \$124.4bn

Annual worldwide market value



- Chemotherapy \$24.4bn
- Hormonal therapies \$13.1bn
- Monoclonal antibodies (mAbs) \$30.0bn
- Small molecule targeted agents \$34.7bn
- Immune checkpoint inhibitors \$20.9bn
- Other oncology therapies \$0.1bn

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





## Key marketed products and revenues 2019

Our Oncology performance in 2019 was driven by the rapid and broad market penetration of our new medicines, with several launches and new indications across our key markets.

## Oncology Product Sales

# \$8,667m

37% of total

2018: \$6,028m

2017: \$4,024m

| Product   | Disease area  | Revenue                                | Commentary  |
|---|---|--|---|
| <i>Tagrisso</i><br>(osimertinib)                | Lung cancer   | ↑ \$3,189m, up 71%<br>(74% at CER)     | Approved in 80 countries, including the US, Japan, China and the EU, for 1st-line EGFRm advanced non-small cell lung cancer (NSCLC), and more than 85 countries, including the US, Japan, China and the EU, for 2nd-line use in patients with EGFRm T790M mutation-positive advanced NSCLC.   |
| <i>Imfinzi</i><br>(durvalumab)                  | Lung cancer<br>Bladder cancer                                     | ↑ \$1,469m, up 132%<br>(133% at CER)   | Approved in the curative-intent setting of unresectable, Stage III NSCLC after chemoradiotherapy in 61 countries, including the US, Japan, China and the EU. Also approved for previously treated patients with advanced bladder cancer in 15 countries, including the US. Regulatory reviews are also underway in small cell lung cancer (SCLC).   |
| <i>Lynparza</i><br>(olaparib)                   | Ovarian cancer<br>Breast cancer<br>Pancreatic cancer              | ↑ \$1,198m, up 85%<br>(89% at CER)     | Approved in 73 countries for the maintenance treatment of platinum-sensitive relapsed ovarian cancer, regardless of BRCA status. Also approved in the US, the EU, Japan, China and several other countries as 1st-line maintenance treatment of BRCA-mutated (BRCAm) advanced ovarian cancer following response to platinum-based chemotherapy. In 58 countries, including the US and Japan, it is approved for germline BRCAm, HER2-negative, metastatic breast cancer, previously treated with chemotherapy; in the EU, this includes locally-advanced breast cancer. Approved in the US as a 1st-line maintenance treatment for germline BRCAm metastatic pancreatic cancer. |
| <i>Calquence</i><br>(acalabrutinib)             | Mantle cell lymphoma (MCL)<br>Chronic lymphocytic leukaemia (CLL) | ↑ \$164m, up 164%<br>(164% at CER)     | Approved for the treatment of adult patients with CLL in the US, Canada and Australia. Also approved for previously treated patients with MCL in 12 countries, including the US, Canada, Australia, Brazil, Qatar, the United Arab Emirates, Israel, Mexico, Argentina, Singapore, Chile and India.   |
| <i>Lumoxiti</i><br>(moxetumomab pasudotox-tdfk) | Hairy cell leukaemia (HCL)  |  | Approved in the US for ≥3rd-line relapsed or refractory HCL. In 2018, the commercialisation rights of <i>Lumoxiti</i> were licensed to Innate Pharma for the US and EU.   |
| <i>Enhertu</i><br>(trastuzumab deruxtecan)      | Breast cancer   |  | Approved in the US for HER2-positive unresectable or metastatic breast cancer following two or more prior anti-HER2 based regimens. Regulatory reviews are also underway in other jurisdictions for breast cancer.  |
| Legacy  |   |  |   |
| <i>Faslodex</i><br>(fulvestrant)                | Breast cancer   | ↓ \$892m, down 13%<br>(11% at CER)     |   |
| <i>Zoladex</i><br>(goserelin acetate implant)   | Prostate cancer<br>Breast cancer                                  | ↑ \$813m, up 8%<br>(13% at CER)        |   |
| <i>Iressa</i><br>(gefitinib)                    | Lung cancer   | ↓ \$423m, down 18%<br>(15% at CER)     |   |
| <i>Arimidex</i><br>(anastrozole)                | Breast cancer   | ↑ \$225m, up 6%<br>(11% at CER)        |   |
| <i>Casodex/Cosudex</i><br>(bicalutamide)        | Prostate cancer   | ↔ \$200m, flat at 0%<br>(up 3% at CER) |   |
| Others  |   | ↓ \$94m, down 18%<br>(17% at CER)      |   |

Full product information from page 243.

## Our strategy for Oncology

In 2019, we focused our Oncology business on six key areas that reflect both our commercial priorities and our key scientific platforms:

- > *Tagrisso* and tumour drivers and resistance (TDR) mechanisms
- > *Imfinzi* and immuno-oncology (IO)
- > *Lynparza* and DNA damage response (DDR)
- > *Calquence* and haematology
- > *Enhertu* (DS-8201) and antibody-drug conjugates (ADCs)
- > Established portfolio.

Our Oncology activities have spanned across our four strategic imperatives.

### 1. Focus research on four scientific platforms:

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

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

### 2. Focus on early stages of disease and relapsed or refractory patients:

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

### 3. Lead precision medicine in the most prevalent and deadly tumour types:

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

### 4. Leverage our global footprint:

To deliver these treatment-changing solutions to as many patients in need as possible, we are building capacity across all geographies. We are also deploying new access solutions to ensure that patients that need our medicines can get them. In addition, through our Oncology Business Unit, we are increasing focus and improving response time in key markets such as the US, UK, Italy, France, Germany, Spain, Japan and China.

# Therapy Area Review

## Oncology *continued*

### 2019 pipeline highlights

In 2019, we had more than 75 new molecular entities (NMEs) under investigation in various stages of development from Phase I through to Phase III.

Our late-stage pipeline delivered a strong flow of new clinical data across our portfolio and we continued to present our scientific progress at major medical congresses. We also continued to invest in new clinical entities through partnerships and acquisitions.

Full details are given in the Development Pipeline from page 238 and highlights from the progress our Oncology pipeline made in 2019 against our KPIs are shown below.

### Life-cycle phases – R&D

#### NME Phase II a/b starts/progressions

We have initiated Phase II clinical trials in various solid tumours with MEDI5752, our novel bispecific antibody which targets PD-1 and CTLA-4, and with AZD9833, an oral SERD in development for ER+ breast cancer. AZD4635, an A2AR antagonist and oleclumab, our IgG1 mAb against CD73, are being explored as a combination therapy in patients with prostate cancer.

| Product               | Cancer type        |
|-----------------------|--------------------|
| AZD4635 + oleclumab   | Prostate cancer    |
| AZD9833               | Breast cancer      |
| AZD9833 + palbociclib | ER + breast cancer |
| MEDI5752              | Solid tumours      |

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

| Product | Cancer type |
|---------|-------------|
| None    | –           |

Investment decisions have been made for eight projects, but clinical trials have yet to start.

#### NME and major LCM regional submissions

2019 was a landmark year with submissions for seven different medicines in 10 indications across regions.

| Product              | Cancer type   | Region        |
|----------------------|---|---------------|
| Bevacizumab (FKB238) | VEGF cancer treatment   | US, EU, Japan |
| Calquence            | Relapsed/refractory CLL (ASCEND)  | EU, US        |
| Calquence            | 1st-line CLL (ELEVATE-TN)   | EU, US        |
| Imfinzi + SoC        | 1st-line extensive-stage SCLC (CASPIAN)                                   | US, EU, Japan |
| Lumoxiti             | 3rd-line HCL  | EU            |
| Lynparza             | gBRCAm metastatic breast cancer (OlympiAD)                                | China         |
| Lynparza             | 1st-line pancreatic cancer (POLO)   | US, EU        |
| Lynparza             | Prostate cancer (PROfound)  | US, EU        |
| Lynparza + Avastin   | Ovarian cancer (PAOLA-1)  | US            |
| Selumetinib          | Neurofibromatosis type 1 (SPRINT)   | US            |
| Enhertu              | HER2-positive unresectable or metastatic breast cancer (DESTINY-Breast01) | US, Japan     |

Plus one project where submissions have been made and regulatory acceptance is pending.

### Life-cycle phases – approvals


#### NME and major LCM regional approvals

Our medicines expanded into new indications with approvals for *Calquence* in CLL and for *Lynparza* in germline BRCA-mutated (gBRCAm) pancreatic cancer, and in new regions with *Lynparza* approved in the EU for gBRCAm metastatic breast cancer and *Imfinzi* approved in China for unresectable, Stage III NSCLC. We also had the first global approval for *Enhertu* in 2019 in HER2-positive unresectable or metastatic breast cancer.

| Product   | Cancer type   | Region           |
|-----------|---|------------------|
| Calquence | Relapsed/refractory CLL (ASCEND)  | US               |
| Calquence | 1st-line CLL (ELEVATE-TN)   | US               |
| Enhertu   | HER2-positive unresectable or metastatic breast cancer (DESTINY-Breast01) | US               |
| Imfinzi   | Locally advanced (Stage III) NSCLC (PACIFIC)                              | China            |
| Lynparza  | gBRCAm metastatic breast cancer (OlympiAD)                                | EU               |
| Lynparza  | 1st-line ovarian cancer (SOLO-1)  | EU, Japan, China |
| Lynparza  | 1st-line pancreatic cancer (POLO)   | US               |
| Tagrisso  | 1st-line NSCLC (FLAURA)   | China            |

### Discontinued projects

| Product                           | Cancer type                                | Reason          |
|-----------------------------------|--|-----------------|
| AZD0156                           | Solid tumours                              | Strategic       |
| AZD4547                           | Solid tumours                              | Safety/efficacy |
| AZD4785                           | Solid tumours                              | Safety/efficacy |
| AZD8186                           | Solid tumours                              | Strategic       |
| Imfinzi + dabrafenib + trametinib | Melanoma                                   | Safety/efficacy |
| Imfinzi + Iressa                  | NSCLC                                      | Safety/efficacy |
| Imfinzi + MEDI0680                | Solid tumours                              | Safety/efficacy |
| Imfinzi + tremelimumab            | 1st-line NSCLC (NEPTUNE)                   | Safety/efficacy |
| Lynparza + AZD6738                | Gastric cancer                             | Safety/efficacy |
| MEDI3726                          | Prostate cancer                            | Safety/efficacy |
| MEDI7247                          | Haematological malignancies, solid tumours | Safety/efficacy |
| Oleclumab + AZD4635               | NSCLC                                      | Strategic       |
| Savolitinib                       | Papillary renal cell carcinoma (SAVOIR)    | Strategic       |

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

# Lung Ambition Alliance

In collaboration with the International Association for the Study of Lung Cancer (IASLC), Guardant Health and the Global Lung Cancer Coalition (GLCC), in July 2019, we announced the formation of the Lung Ambition Alliance. It has the goal of one day eliminating lung cancer as a cause of death and has identified three areas of focus that span the patient experience:

**1. Increasing lung cancer screening and early diagnosis** by raising awareness of the effectiveness of screening and addressing barriers to early detection, with continued improvements to the ease and reliability of diagnostics and contributions to better understanding of disease progression.

**2. Delivering innovative medicine** by enabling widespread paradigm shifts to earlier intervention when there is still potential for a cure.

**3. Enhancing quality care** by working with advocates and policymakers to deliver projects that address the challenges most urgent to patients on the local level and by improving coordination across the multidisciplinary team of treaters.

Through effective activation of these workstreams, the Alliance has set the goal of doubling five-year survival for lung cancer by 2025.

“Through the Lung Ambition Alliance, we are working together with top oncology minds to accelerate progress and help patients with lung cancer live longer and better lives.”

**David Fredrickson**  
EVP, Oncology Business Unit

## 2019 review – strategy in action

2019 saw stable performances from our established Oncology products, steady growth from our innovative new medicines portfolio, and a generally positive news flow from our late-stage pipeline in each of our four strategic pillars.

### **Tagrisso and tumour drivers and resistance mechanisms**

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

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

In 2019, it became our top-selling medicine as we extended its global roll-out for 1st-line NSCLC. *Tagrisso* also continues to be investigated in NSCLC in the adjuvant setting (ADAURA), in the locally-advanced unresectable setting (LAURA), in combination with chemotherapy (FLAURA2) in the metastatic setting, and with potential new medicines to address resistance to EGFR-TKIs (SAVANNAH, ORCHARD).

In September 2019, *Tagrisso* was approved as a 1st-line treatment in China for adults with locally-advanced or metastatic NSCLC. Also in September, the benefit of using *Tagrisso* in the 1st-line treatment of adult patients with locally-advanced EGFRm NSCLC was confirmed with the results of a key secondary

endpoint of the Phase III FLAURA trial. Results showed a statistically significant and clinically meaningful improvement in OS, for *Tagrisso* versus gefitinib or erlotinib, both of which were previous standard of care treatments.

Several other next-generation potential medicines from our TDR platform moved into or progressed in Phase III in 2019:

- > Selumetinib: A MEK 1/2 inhibitor, and part of a global strategic oncology collaboration with MSD, selumetinib was granted Breakthrough Therapy Designation by the FDA in April 2019 for the treatment of paediatric patients aged three years and older with neurofibromatosis type 1 (NF1) symptomatic and/or progressive, inoperable plexiform neurofibromas (PN), a rare, incurable genetic condition. In November 2019, we announced its filing acceptance by the FDA for a potential indication in NF1.
- > Savolitinib: A selective inhibitor of c-MET receptor tyrosine kinase, savolitinib is being investigated with Hutchison China MediTech Limited (Chi-Med), both as a monotherapy and in combination. It has shown promising signs of clinical efficacy in patients with MET gene alterations in lung cancer and gastric cancer with an acceptable safety profile, including promising preliminary efficacy and safety results in the ongoing China Phase II study of savolitinib monotherapy in NSCLC patients with MET mutations. It also showed promise in the TATTON Phase Ib expansion cohort when combined with *Tagrisso* in patients with EGFRm MET-amplified NSCLC; this combination has been taken into a large Phase II trial, SAVANNAH, which is ongoing.
- > Capivasertib (AZD5363): Our AKT inhibitor, capivasertib entered Phase III development in the first half of 2019 for triple negative breast cancer.

Other agents in early development include: AZD9496, a selective oestrogen receptor degrader (SERD) in Phase I development for the treatment of oestrogen receptor positive (ER+) breast cancer; AZD9833, a SERD in Phase II development for the treatment of ER+ breast cancer; AZD5153, a bromodomain-4 inhibitor in Phase I for solid tumours; and in our cell death portfolio, AZD5991 (MCL1 inhibitor) and AZD4573 (CDK9 inhibitor), which are being investigated in haematological malignancies.

### **Imfinzi and immuno-oncology**

*Imfinzi*, a human mAb that binds to PD-L1 and blocks the interaction of PD-L1 with PD-1 and CD80 continued its strong commercial performance in 2019, building on its quick adoption in the US and supported by new approvals and accelerating growth in markets outside the US.

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

### **Treating early-stage NSCLC**

*Imfinzi* is the only immunotherapy to demonstrate OS at three years in unresectable Stage III NSCLC and represents a new standard of care treatment. In 2019, three-year OS results from the Phase III PACIFIC trial showed a durable and sustained OS benefit in patients with unresectable, Stage III NSCLC who had not progressed following concurrent chemoradiation therapy (CRT), a previous standard of care treatment. In December, *Imfinzi* was approved in China for patients with unresectable Stage III NSCLC.

## Therapy Area Review Oncology *continued*

Lung cancer is a key area of focus for our IO portfolio and we announced new trials in 2019 to investigate the full potential of *Imfinzi* in early-stage NSCLC:

- > ADJUVANT BR.31, an externally-sponsored research study led by the Canadian Cancer Trials Group, will explore the benefits of treatment with *Imfinzi* following complete tumour resection.
- > PACIFIC-2 will assess efficacy and safety of *Imfinzi* given concurrently with platinum-based CRT in Stage III NSCLC patients.
- > PACIFIC-5 will assess the efficacy and safety of *Imfinzi* in patients treated with either sequential or concurrent CRT in patients with unresectable Stage III NSCLC.

### Late-stage NSCLC

Our clinical trial portfolio also explores ways to improve outcomes for patients who have relapsed or are diagnosed with metastatic disease. In this setting, *Imfinzi* is being investigated as a monotherapy and in combination with tremelimumab and/or chemotherapy in the PEARL and POSEIDON trials.

In August 2019, we announced that NEPTUNE, a Phase III trial of *Imfinzi* in combination with tremelimumab, an anti-CTLA4 antibody, versus standard of care platinum-based chemotherapy in the 1st-line treatment of patients with Stage IV (metastatic) NSCLC, failed to meet its primary endpoint. We are continuing to analyse the clinical and biomarker data from this trial to gain further insights to improve IO approaches for patients with metastatic NSCLC.

In October 2019, we announced positive PFS results from the Phase III POSEIDON trial for *Imfinzi* and tremelimumab when added to chemotherapy in previously-untreated Stage IV (metastatic) NSCLC. The trial met its primary endpoint by showing a statistically significant and clinically meaningful improvement in the final PFS analysis in patients treated with the combination of *Imfinzi* and a broad choice of five standard of care platinum-based chemotherapy options versus chemotherapy alone. The triple combination of *Imfinzi* plus tremelimumab and chemotherapy also demonstrated a statistically significant and clinically meaningful PFS improvement versus chemotherapy alone as a key secondary endpoint. OS data from this trial are now expected in 2021.

### *Imfinzi* in SCLC

SCLC, which constitutes about 15% of all lung cancer diagnoses, is a fast-growing cancer that recurs and progresses rapidly. It is the most aggressive type of lung cancer with only 6% of patients alive after five years.

In 2019, *Imfinzi* demonstrated both a significant survival benefit and improved responses in extensive-stage SCLC in the Phase III CASPIAN trial. The FDA subsequently granted Orphan Drug Designation to *Imfinzi* for the treatment of SCLC and, in November 2019, granted Priority Review for the treatment of patients with 1st-line extensive-stage SCLC.

*Imfinzi* is also being tested following concurrent CRT in limited-stage SCLC in the Phase III ADRIATIC trial.

### Exploring other indications

Beyond lung cancer, we continue to explore the potential of *Imfinzi* and tremelimumab in head and neck squamous cell carcinoma (HNSCC) (KESTREL), bladder cancer (DANUBE, NILE, POTOMAC, NIAGARA) and in hepatocellular carcinoma (HCC) (HIMALAYA, EMERALD-1, and EMERALD-2).

### Our IO pipeline

Our IO pipeline contains NMEs targeting multiple pathways, novel mechanisms to boost current immune response, and agents to modify the tumour microenvironment both alone and in combination with checkpoint inhibition. We continue to explore the adenosine pathway, which is increasingly recognised as critical to tumour suppression and represents a new frontier within IO. Some of the 2019 highlights from our IO pipeline include:

- > Monalizumab: Our first-in-class humanised anti-NKG2A antibody is being investigated in HNSCC, colorectal cancer, and haematological malignancies. Monalizumab is now transitioning to a Phase III trial in HNSCC in combination with cetuximab.
- > Oleclumab is our Immunoglobulin G1 (IgG1) mAb against CD73. It is being explored in combination with *Imfinzi* and chemotherapy in pancreatic cancer, as well as in combination with *Tagrisso*, AZD4635 or *Imfinzi* in lung cancer.
- > AZD4635: An adenosine 2A receptor (A2AR) inhibitor is being explored as monotherapy and in combination with *Imfinzi* in solid tumours in Phase II trials.
- > AZD9150: danvatirsen, a STAT3 antisense oligonucleotide (ASO) continues to be investigated in Phase II in patients with 2nd-line HNSCC and in combination with *Calquence* for haematological cancers.
- > MEDI5752: A novel bispecific antibody designed to target PD-1 and CTLA-4 checkpoints on immune cells is being studied in a range of solid tumours.
- > MEDI0457: a human papilloma virus (HPV) vaccine currently tested in combination with *Imfinzi* in HPV-positive HNSCC.
- > MEDI5083: Preclinical data on this novel fusion protein that activates the CD40 pathway were presented at the 2019 American Association for Cancer Research (AACR) meeting.

### *Lynparza* and DNA damage response

*Lynparza* is our first and best-in-class oral poly ADP-ribose polymerase (PARP) inhibitor, and the first targeted treatment to block DDR in cells/tumours harbouring a deficiency in homologous recombination repair (HRR), such as mutations in BRCA1 and/or BRCA2. We have a global strategic oncology collaboration with MSD to co-develop and co-commercialise *Lynparza*.

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

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In 2014, *Lynparza* became the world's first approved PARP inhibitor. Initially indicated for the treatment of ovarian cancer, in 2017, it became the first PARP inhibitor to demonstrate benefits in certain types of breast cancer. In 2019, *Lynparza* exceeded \$1 billion in sales worldwide, demonstrating its uptake by physicians in need of treatment options for multiple cancer types.

### Leadership in ovarian cancer

We are committed to changing the way advanced ovarian cancer is treated in the 1st-line setting. The positive SOLO-1 trial had already demonstrated the significant benefit of extending PFS much earlier, bringing the goal of long-term remission and cure in ovarian cancer closer for women with tumours that harbour a BRCA mutation. In 2019, results from the Phase III PAOLA-1 trial in the 1st-line maintenance setting in women regardless of biomarker status or surgical outcome and a broader patient group than in SOLO-1, showed that *Lynparza*, when added to the standard of care, bevacizumab, delivered a statistically significant and clinically meaningful improvement in PFS. Women taking the *Lynparza*-bevacizumab combination lived longer without disease progression or death compared with those taking bevacizumab alone. The goal of 1st-line treatment is to delay progression of the disease for as long as possible, with the intent of achieving complete remission or cure and these data have the potential to change clinical practice in how women with advanced ovarian cancer are treated.

### First PARP inhibitor to achieve positive Phase III results in four different cancer types

In 2019, *Lynparza* became the first and only PARP inhibitor with positive Phase III trial results in four different tumour types: pancreatic and prostate, as well as ovarian and breast.

The Phase III POLO trial explored the efficacy of *Lynparza* tablets as 1st-line maintenance monotherapy in patients with gBRCAm metastatic pancreatic cancer whose disease has not progressed on platinum-based chemotherapy. POLO is the first positive

Phase III trial of any PARP inhibitor in this disease where there is a critical unmet medical need.

Results from the POLO trial showed a statistically significant and clinically meaningful improvement in PFS, where *Lynparza* nearly doubled the time patients with gBRCAm metastatic pancreatic cancer lived without disease progression or death to a median of 7.4 months compared with 3.8 months on placebo. Based on these results, *Lynparza* has now been approved in the US for the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic cancer whose disease has not progressed on at least 16 weeks of a 1st-line platinum-based chemotherapy regimen.

The Phase III PROfound trial of *Lynparza* in men with metastatic castration-resistant prostate cancer (mCRPC) showed a statistically significant and clinically meaningful improvement in radiographic PFS with *Lynparza* versus enzalutamide or abiraterone in men with mCRPC whose tumours harbour mutations in one of 15 potential HRR genes, including BRCA1, BRCA2 and ATM. The potential benefits of *Lynparza* in mCRPC will continue to be tested in the Phase III PROpel trial that will assess the combination of *Lynparza* with abiraterone in 1st-line mCRPC.

#### Progress across the DDR pipeline

Our DDR pipeline continues to expand and progress:

- > AZD7648, a potent and selective DNA-PK inhibitor which could be an innovative new way to target alternative DDR dependencies.
- > Adavosertib (AZD1775), our WEE1 inhibitor continues in Phase II development for ovarian and other solid tumours in combination with *Lynparza*, in combination with chemotherapy, and as a monotherapy.
- > Ceralasertib (AZD6738), an ataxia telangiectasia and Rad3-related (ATR) serine/threonine protein kinase inhibitor is being evaluated in Phase I/II trials in solid tumours and haematological malignancies as monotherapy and in combination with other targeted therapies, including *Lynparza* in triple negative breast cancer. It is also being investigated in combination with *Calquence* in CLL, and in combination with radiation therapy and chemotherapy.
- > AZD2811 an aurora kinase B inhibitor in development as monotherapy in Phase II in SCLC and acute myeloid leukaemia.
- > AZD1390, a blood-brain barrier penetrant inhibitor of ATM is in Phase I for brain tumours.

#### Calquence and haematology

*Calquence* is our irreversible oral Bruton's tyrosine kinase (BTK) inhibitor. It was approved for the treatment of MCL in the US in 2017.

In November 2019, the FDA approved *Calquence* for adult patients with CLL or small lymphocytic lymphoma (SLL). The US approval was granted under the FDA's Real-Time Oncology Review and the newly established Project Orbis programme which provides a framework for concurrent submission and review of oncology medicines among international partners. The FDA, the Australian Therapeutic Goods Administration, and Health Canada collaborated on this review and approval for CLL in Australia and Canada followed shortly after. Approval was based on positive results from the interim analyses of two Phase III clinical trials – ASCEND and ELEVATE-TN. The ASCEND trial compared *Calquence* with rituximab combined with delalib or bendamustine in patients with relapsed or refractory CLL and the ELEVATE-TN trial evaluated the safety and efficacy of *Calquence* alone or in combination with obinutuzumab compared with chlorambucil in combination with obinutuzumab in patients with previously untreated CLL. Together, the trials showed that *Calquence* in combination with obinutuzumab or as a monotherapy significantly reduced the relative risk of disease progression or death versus the comparator arms in both 1st-line and relapsed or refractory CLL. Across both trials, the safety and tolerability of *Calquence* were consistent with its established profile.

There was also progress made in our haematology early-phase clinical programme, with AZD5991 (an MCL1 inhibitor), AZD4753 (a CDK9 inhibitor) and AZD0466 (a dual inhibitor of Bcl2 and Bcl-xL), all being investigated as part of our cell death programme, as well as ADCs, MEDI7247 and MEDI2228. In addition, the BTK and STAT3 combination is being explored in Phase I trials with *Calquence* and danvatirsen (AZD9150), a STAT3 ASO.

#### Enhertu and antibody-drug conjugates

In March 2019, we added *Enhertu* (DS-8201, trastuzumab deruxtecan), a new targeted medicine for cancer treatment to our ADC portfolio by signing a global development and commercialisation collaboration agreement with Daiichi Sankyo. The agreement enables both companies to jointly develop and commercialise the medicine worldwide, except in Japan, where Daiichi Sankyo will maintain exclusive rights.

*Enhertu* is currently in development for the treatment of multiple HER2-expressing cancers, including breast, gastric, colorectal and NSCLC. Following positive top-line results from the pivotal Phase II DESTINY-Breast01 trial in May 2019, regulatory submissions were completed in the US and Japan for previously treated patients with HER2-positive,

unresectable and/or metastatic breast cancer. In October 2019, the FDA accepted the BLA application for *Enhertu* and granted Priority Review and, in December 2019, *Enhertu* received Accelerated Approval by the FDA for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting. Detailed results of the DESTINY-Breast01 trial demonstrated an overall response rate of 60.9% and a median PFS of 16.4 months, based upon a median duration of follow-up of 11.1 months.

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

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We are also progressing with the development of our early stage ADC pipeline – MEDI7247 in haematological malignancies and solid tumours and MEDI2228 in multiple myeloma.

#### Established portfolio and biosimilars

In 2019, our established oncology brands – *Faslodex*, *Zoladex* and *Iressa* – performed well, with growth in *Zoladex* and moderate sales decreases of *Faslodex* and *Iressa*.

*Faslodex* showed a slower decline than expected, largely led by growth in combination use with CDK4/6 inhibitors and slower generic competition in the EU. Decline in the second half of the year was primarily driven by generic competition in the US.

*Iressa* sales continued to decline due to generic entries in select markets, the uptake of *Tagrisso* in 1st-line EGFRm advanced NSCLC, and the pricing impact on *Iressa* from centralised procurement in China.

*Zoladex* double-digit growth was based on increased access to medical castration and ovarian suppression, as well as earlier detection and diagnosis in prostate and breast cancers, predominantly in China and Emerging Markets.

We are partnering with Fuji Kirin Biologics and Samsung Biologics to develop two biosimilar molecules within joint venture companies. Both programmes progressed in 2019, with the more advanced biosimilar bevacizumab programme reporting positive clinical data and achieving a successful BLA submission with the US and EU regulators. Bevacizumab is a cornerstone of VEGF cancer treatment with some 15 approved indications either as monotherapy or in combination.

# Cardiovascular, Renal & Metabolism

Our mission is to protect the lives of people from the often devastating consequences of heart failure, cardiovascular, metabolic and renal diseases, and to change clinical practice to address unmet medical need. We are committed to the seamless management of diseases, improving patient outcomes and decreasing the mortality rate.

## Unmet medical need and world market

Cardiovascular, Renal & Metabolism (CVRM) diseases are the leading causes of death across the globe, killing more than 20 million people each year.

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

**425m**

Number of people living with diabetes.

**64m**

Number of people living with heart failure and cardiovascular disease which are responsible for the deaths of 17.9 million people per year.

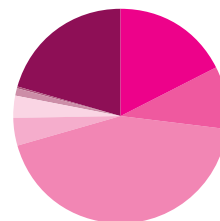
**200m**

Number of people living with chronic kidney disease.

Therapy area world market  
(MAT/Q3/19)

**\$194.4bn**

Annual worldwide market value



- High blood pressure \$34.1bn
- Abnormal levels of blood cholesterol \$17.0bn
- Diabetes \$89.9bn
- Thrombosis \$7.6bn
- CKD \$10.1bn
- CKD associated anaemia \$6.9bn
- Hyperkalaemia \$0.4bn
- Other CV \$45.3bn

Source: IQVIA.  
AstraZeneca focuses on specific segments within this overall therapy area market. Sales for CKD and CKD associated anaemia fall outside the CVRM total market. All sales for CKD associated anaemia (\$6.9bn) fall within the CKD market and should not be double-counted.



## Key marketed products and revenues 2019

*Brilinta* and *Farxiga* continued to provide a foundation for continued growth in the therapy area and our renal franchise made progress, with *Lokelma* launching in the US and progressively in Europe. Overall CVRM Product Sales were up 3% on 2018 (6% at CER).

## CVRM Product Sales

# \$6,906m

29% of total

2018: \$6,710m

2017: \$7,266m

| Product   | Disease area   | Revenue                          | Commentary   |
|---|--|----------------------------------|--|
| <i>Brilinta/Brilique</i> (ticagrelor)                                 | Acute coronary syndromes (ACS) and high-risk patients with history of myocardial infarction (MI) | ↑ \$1,581m, up 20% (23% at CER)  | Approved in more than 110 countries for ACS and more than 70 countries for high-risk patients with history of heart attack; included in major guidelines. <i>Brilinta</i> delivered consistent quarter-over-quarter growth in 2019 in all regions.   |
| <i>Farxiga/Forxiga</i> (dapagliflozin)                                | Type-2 diabetes, Type-1 diabetes   | ↑ \$1,543m, up 11% (14% at CER)  | Approved in 100 countries to improve glycaemic control in adult patients with type-2 diabetes; included in major guidelines. <i>Farxiga</i> delivered consistent, solid growth quarter-over-quarter in 2019. Approval for type-1 diabetes in EU and Japan. Complete Response Letter received from FDA for type-1 diabetes. |
| <i>Bydureon</i> (exenatide XR injectable suspension)                  | Type-2 diabetes  | ↓ \$549m, down 6% (5% at CER)    | Approved in more than 70 countries to improve glycaemic control in adults with type-2 diabetes; included in major guidelines. In 2019, <i>Bydureon</i> continued launch progress with <i>BCise</i> in a highly dynamic GLP-1 class.  |
| <i>Onglyza</i> (saxagliptin)  | Type-2 diabetes  | ↔ \$527m, down 3% (0% at CER)    | Approved in more than 85 countries for the treatment of adults with type-2 diabetes; included in guidelines. <i>Onglyza</i> maintained a strong performance in 2019 in Emerging Markets, driven by China, while facing US price pressure.  |
| <i>Byetta</i> (exenatide injection)                                   | Type-2 diabetes  | ↓ \$110m, down 13% (11% at CER)  |  |
| <i>Symlin</i> (pramlintide acetate)                                   | Type-2 diabetes  | n/m \$34m, movement n/m          |  |
| <i>Qtern</i> (metformin hydrochloride, saxagliptin and dapagliflozin) | Type-2 diabetes  | ↑ \$18m, up 261% (276% at CER)   | In 2019, our combination therapy of dapagliflozin, saxagliptin and metformin hydrochloride was approved in the US as <i>Qternmet</i> XR and in the EU as <i>Qtrimet</i> .  |
| <i>Lokelma</i> (sodium zirconium cyclosilicate (SZC))                 | Hyperkalaemia  | n/m \$14m, movement n/m          | Approved with launches under way in the US, EU, Canada and China for the treatment of adults with hyperkalaemia.   |
| Legacy  |  |                                  |  |
| <i>Crestor</i> (rosuvastatin calcium)                                 | Dyslipidaemia<br>Hyper-cholesterolaemia  | ↓ \$1,278m, down 11% (8% at CER) | Financial impact has stabilised following patent expiries in the US (2016) and EU/Japan (2017). Licensed from Shionogi. The extension of the global license agreement with Shionogi for <i>Crestor</i> became effective 1 January 2014.  |
| <i>Seloken/Toprol-XL</i> (metoprolol succinate)                       | Hypertension<br>Heart failure<br>Angina  | ↑ \$760m, up 7% (12% at CER)     | Divested rights in Europe to Recordati in May 2017. Divested US rights to Aralez effective October 2016.   |
| <i>Atacand/Atacand HCT/Atacand Plus</i> (candesartan cilexetil)       | Hypertension<br>Heart failure  | ↓ \$221m, down 15% (11% at CER)  | Divested rights to Cheplapharm in 28 European markets in July 2018. Licensed from Takeda Chemicals Industries Ltd.   |
| Others  |  | ↓ \$273m, down 9% (6% at CER)    |  |

## Our strategy for CVRM

We have divided CVRM into four distinct but interrelated disease areas: cardiovascular disease, heart failure, metabolic and renal diseases. In developing targeted medicines for these diseases, we recognise that, in addition to their differences, these four areas are interconnected. Whereas shared risk factors are often currently neither diagnosed nor addressed, science suggests that, by considering common mechanisms of CVRM diseases, we can work with healthcare practitioners (HCPs) to improve outcomes in patients with one specific diagnosis before co-morbidities emerge.

## Our ambition in CVRM

Our aim is to develop and grow a portfolio of medicines that address the multiple risk factors or co-morbidities across CVRM. Our efforts are built on global randomised clinical trials (RCTs) that are as close as possible to clinical practice and real-world evidence (RWE) research. These help us gather vital insights into patient needs and clinical practice, and develop treatments that meet the requirements of both patients and HCPs.

Our ambition is as follows:

- > **Cardiovascular:** to help eliminate CV risk factors and stop disease progression.
- > **Heart failure:** to help prevent, treat and cure this leading cause of death.
- > **Renal:** to help treat life-threatening complications and slow disease progression.
- > **Metabolism:** to treat beyond HbA1C (average blood glucose levels), prevent cardio-renal complications and explore non-alcoholic steatohepatitis (NASH).

With our existing medicines and those in late-stage development, we are already delivering life-changing results in the four CVRM disease areas and their complications.

- > **Cardiovascular:** *Brilinta*
- > **Heart failure:** *Farxiga*, *Lokelma*
- > **Renal:** *Lokelma*, roxadustat, *Farxiga*
- > **Metabolism:** *Brilinta*, *Farxiga*, *Bydureon*, *Qtern*

We additionally have a pipeline of more than 25 therapies and therapy combinations and believe we have a comprehensive portfolio of potential medicines that might combat these life-threatening conditions.

Beyond our research, we also invest in strategic partnerships to better educate stakeholders about these diseases and improve patient access to healthcare worldwide.

# Therapy Area Review Cardiovascular, Renal & Metabolism *continued*

## 2019 pipeline highlights

Our pipeline includes biologics, antisense oligonucleotides, mRNA, ProTACs and cell therapy. We are researching pioneering approaches in the field of disease regression and organ regeneration for conditions such as CKD, ACS, coronary artery disease (CAD), chronic heart failure (HF) and NASH.

Full details are given in the Development Pipeline from page 238 and highlights from the progress our CVRM pipeline made in 2019 against our KPIs are shown below.

## Life-cycle phases – R&D

### New molecular entity (NME) Phase II a/b starts/progressions

We have initiated Phase II clinical trials, exploring NASH and diabetic kidney disease (DKD).

| Product    | Disease |
|------------|---------|
| Cotadutide | NASH    |
| MEDI3506   | DKD     |
| Verinurad  | CKD     |

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

| Product | Disease |
|---------|---------|
| None    | –       |

### NME and major LCM regional submissions

*Farxiga* entered a new disease area for the treatment of heart failure and we also submitted label updates for diabetes based on results from the DECLARE trial. Our renal portfolio made regulatory filings for both *Lokelma* and roxadustat, plus data submissions for *Brilinta*.

| Product                | Disease  | Region               |
|------------------------|--|----------------------|
| <i>Brilinta</i>        | CV outcomes trial in patients with CAD and type-2 diabetes without a previous history of MI or stroke (THEMIS) | US, EU, Japan, China |
| <i>Farxiga/Forxiga</i> | Type-2 diabetes (DECLARE)  | EU, China            |
| <i>Farxiga/Forxiga</i> | Worsening heart failure or cardiovascular death in patients with chronic heart failure (DAPA-HF)               | US, EU               |
| <i>Lokelma</i>         | Hyperkalaemia  | Japan, China         |
| Roxadustat             | Anaemia in CKD/end-stage renal disease (ROCKIES/OLYMPUS)   | US                   |

## Life-cycle phases – approvals

### NME and major LCM regional approvals

We made progress in providing new medicines such as *Lokelma* and roxadustat to renal patients where significant unmet medical need remains. The breadth of *Farxiga*'s indications grew with the label updated based on positive CV and renal outcomes data from the DECLARE trial in type-2 diabetes.

| Product  | Disease   | Region    |
|--|---|-----------|
| <i>Bydureon BCise</i>  | Type-2 diabetes cardiovascular outcomes trial (CVOT) (EXSCEL) | US        |
| <i>Bydureon</i>  | Type-2 diabetes CVOT (EXSCEL)                                 | US        |
| <i>Bydureon BCise</i>  | Type-2 diabetes CVOT (DURATION programme harmonisation)       | US        |
| <i>Farxiga/Forxiga</i>                                       | Type-2 diabetes (DERIVE)                                      | US        |
| <i>Farxiga/Forxiga</i>                                       | Type-1 diabetes (DEPICT)                                      | Japan, EU |
| <i>Farxiga/Forxiga</i>                                       | Type-2 diabetes CVOT (DECLARE)                                | EU, US    |
| <i>Lokelma</i>   | Hyperkalaemia   | China     |
| <i>Qternmet XR</i> (saxagliptin + dapagliflozin + metformin) | Type-2 diabetes   | US        |
| <i>Qtrilmet</i> (saxagliptin + dapagliflozin + metformin)    | Type-2 diabetes   | EU        |
| Roxadustat <sup>1</sup>                                      | Hyperkalaemia   | Japan     |

<sup>1</sup> Development and commercialisation collaboration with FibroGen in China. FibroGen holds the NDA. Approved in 2019 in China for non-dialysis dependent patient population (2018 approval was for dialysis-dependent patient population).

## Discontinued projects

| Product        | Disease   | Reason          |
|----------------|---|-----------------|
| <i>Epanova</i> | CV outcomes study in statin-treated patients at high CV risk, with persistent hypertriglyceridaemia plus low HDL-cholesterol (STRENGTH) | Safety/efficacy |

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



# Improving Care for Cardiovascular Disease in China

Care for Cardiovascular Disease in China (CCC) is a multi-year project focused on improving compliance with evidence-based therapy for patients with acute coronary syndromes (ACS) and atrial fibrillation (AFib) in almost 200 tertiary and secondary hospitals across China. The programme is a collaborative effort between the American Heart Association, the Chinese Society of Cardiology, and it is supported by funding from an independent educational grant from AstraZeneca.

Four core pillars of the programme – data collection, analysis, feedback and process improvement – address the quality of ACS and AFib care in its entirety, from assessing gaps in guideline compliance, through recommending and training on opportunities for improvement, to recognising best-practice solutions.

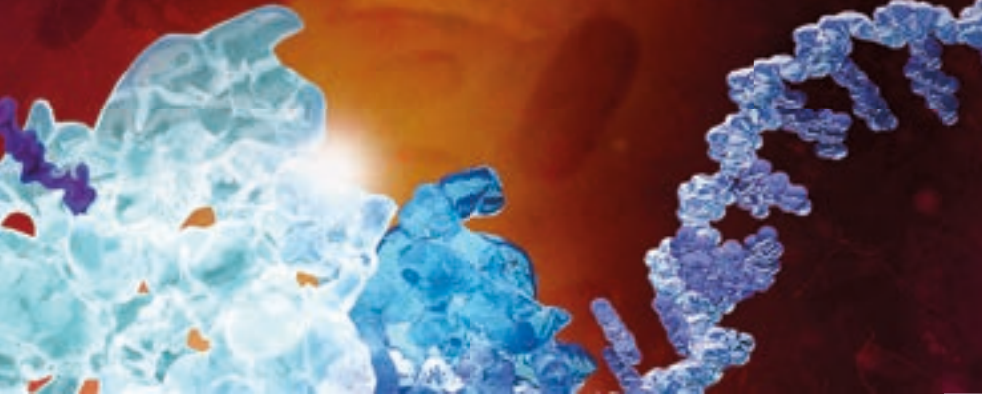
Regular data collection, which was first used to evidence the guideline compliance gap, now serves to verify the ongoing success and quality improvement achieved by the programme. For example, an 80.7% compliance rate in guideline-led care for ACS patients among those hospitals enrolled compares with 75.2% before the programme started.

## 81%

compliance rate in guideline-led care for ACS patients among hospitals enrolled

## 200

CCC projects in action in almost 200 tertiary and secondary hospitals across China



the rate of hospitalisation from HF. In the US, the FDA granted Fast Track designation for the development of *Farxiga* in HF, followed by Priority Review for patients with HFREF. It opens up the possibility of a once-daily pill changing the current treatment for HF. Our extensive clinical programme includes several more Phase III trials for the potential cardio-renal benefits of *Forxiga*, DAPA-CKD, DELIVER and DETERMINE. These will explore its effectiveness in addressing areas of high unmet medical need in HF, chronic HF and CKD.

HF patients are often prescribed life-saving renin-angiotensin-aldosterone system inhibitors (RAASi), which lead to elevated potassium levels. These patients have an increased risk of developing hyperkalaemia, which can be life-threatening if left untreated. *Lokelma* is a treatment for hyperkalaemia which was launched in the US and EU in 2019. Currently under way, the Phase II PRIORITIZE-HF trial is designed to evaluate the benefits and risks of using *Lokelma* to initiate and intensify RAASi therapy in HF patients.

We are also exploring innovative approaches, previously regarded as impossible, such as regenerating the heart by growing heart muscle back and studying novel molecules such as VEGF-A mRNA to work toward vascular regeneration and cardiac repair.

## 2019 review – strategy in action

As noted above, our CVRM strategy includes rigorous clinical programmes evaluating the use of our medicines in large patient populations:

- > **Randomised clinical trials:** More than 22,500 patients are currently participating in our R&D-led CVRM trials at more than 3,000 sites worldwide in both Established and Emerging Markets. Our focus on diabetes research includes almost 50 clinical trials worldwide, with an enrolment target of 56,000 patients. These RCTs include the DapaCare Programme, OLYMPUS and ROCKIES, and THEMIS.
- > **Real-world evidence data:** Our RWE studies have included CVD-REAL and DISCOVER, which both set out to deliver innovative data from large-scale settings.

## Metabolism

Data from the landmark Phase III DECLARE-TIMI 58 trial for *Farxiga*, part of the DapaCare clinical programme which demonstrated the effective reduction in heart failure (HF) risk in a broad range of people with type-2 diabetes, provided the basis for the label updates in both the EU and the US. The FDA approved *Farxiga* to reduce the risk of hospitalisation for HF in adult patients with type-2 diabetes and established CV disease or multiple CV risk factors, based on results from DECLARE. This was following the EMA's label update for *Forxiga* to include CV outcomes and renal data from DECLARE. *Farxiga* is also currently under regulatory review in China with a decision anticipated in the first half of 2020. Throughout 2019, additional subanalyses from

the DECLARE trial showed additional benefits for renal and metabolic health through earlier treatment. We are also working to illustrate the economic value and wider societal benefits of this integrated approach for type-2 diabetes and HF risk which, through earlier treatment, can avoid more serious outcomes for patients.

Another common metabolic disease is non-alcoholic fatty liver disease (NAFLD). With an estimated 25% of people worldwide currently living with NAFLD, we are exploring deeper into the mechanisms and complications of NASH, a subtype of NAFLD, and finding potential treatments through molecules such as cotadutide (MEDI0382) and AZD2693.

## Heart failure

As part of our efforts to prevent, treat and cure HF as a leading cause of death, we are developing treatments that include earlier intervention across interconnected conditions like type-2 diabetes. As indicated above, the DECLARE-TIMI 58 trial provided evidence of *Farxiga*'s effectiveness in the prevention of HF, and in cardio-renal protection. We are now looking beyond type-2 diabetes in trials that have enrolled patients with and without type-2 diabetes, and are moving from the prevention to the treatment of HF.

During 2019, full results from the landmark Phase III DAPA-HF trial, the first HF outcomes trial with a sodium-glucose cotransporter 2 (SGLT2) inhibitor in patients with and without type-2 diabetes, and the first to explore SGLT2 inhibitors for use outside of diabetes, showed that *Farxiga* reduced the risk of CV death and

## Therapy Area Review Cardiovascular, Renal & Metabolism *continued*

### Cardiovascular disease

In working towards our objective of eliminating CV residual risk and stopping disease progression, we believe we are already making a difference in patients with coronary artery disease (CAD), including those who previously experienced a heart attack, by reducing the risk of experiencing further life-threatening CV events. In those patients who have not experienced a heart attack or stroke, but are at a high risk of a CV event, the Phase III THEMIS trial met its primary endpoint and showed that *Brilinta* plus aspirin reduced the risk for the composite of CV death, heart attack, or stroke compared with aspirin alone, a statistically significant relative reduction of 10%, in patients with CAD and type-2 diabetes. Furthermore, in patients with CAD and type-2 diabetes who had undergone percutaneous coronary intervention, a 15% relative risk reduction was observed for *Brilinta* for CV events. We have applied to regulators in the EU, US and Japan to add a new indication to the *Brilinta* label based on the THEMIS study.

Strokes remain a significant cause of mortality and disability, and a transient ischaemic attack (TIA) can be a warning of a future stroke – these individuals are at a high risk of a subsequent CV event. High-level results from the Phase III THALES trial showed *Brilinta*, taken with aspirin for 30 days, reached a statistically significant and clinically meaningful reduction in the risk of the composite endpoint of stroke and death, compared to aspirin alone.

In January 2020, following the recommendation from an independent Data Monitoring Committee, we decided to close the Phase III STRENGTH trial for *Epanova* due to its low likelihood of demonstrating a benefit to patients with mixed dyslipidaemia.

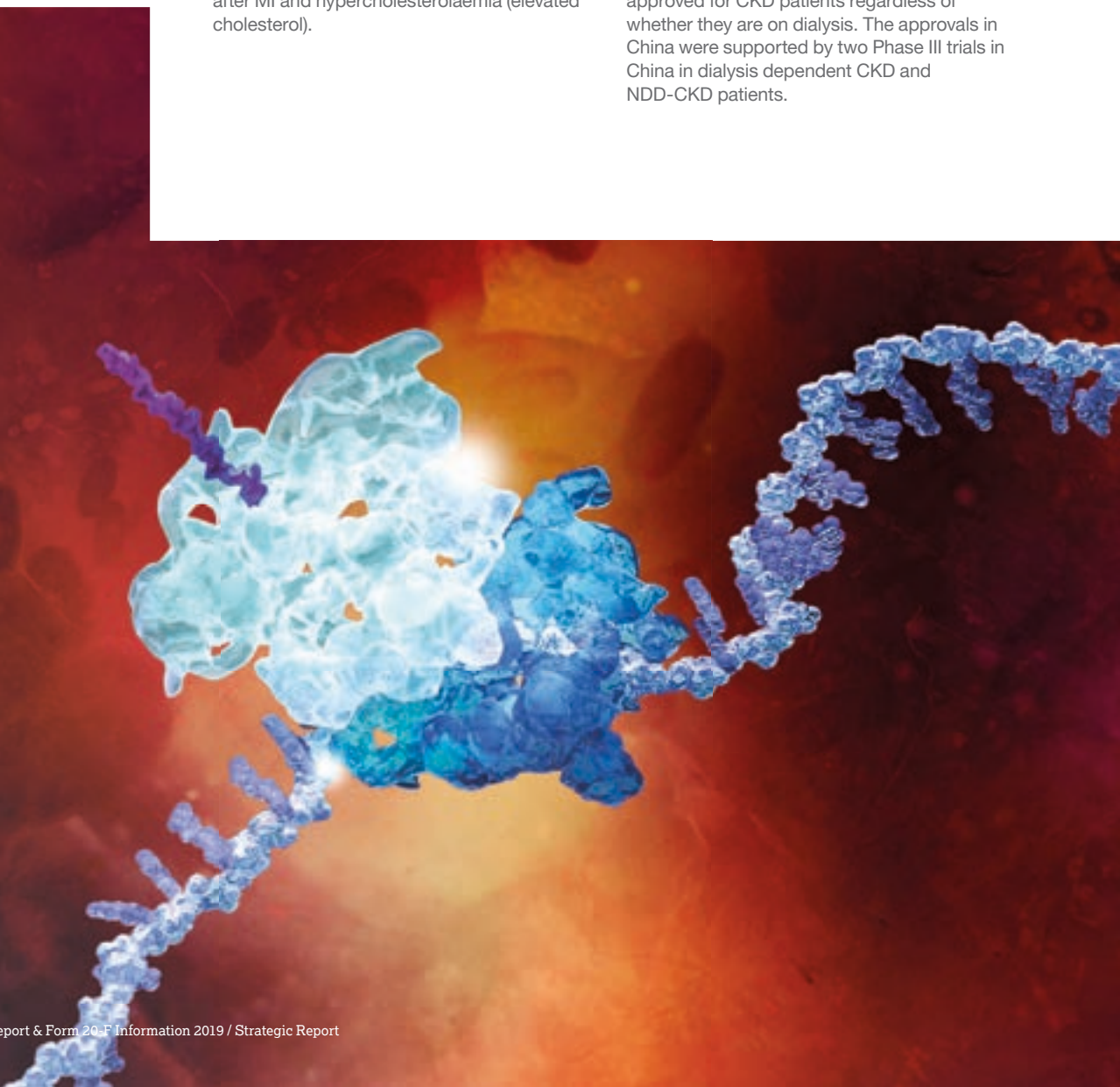
We also continue to investigate new molecules such as MEDI5884, AZD6615, AZD3366 and AZD5718 with the aim of helping to reach and transform the lives of more patients living with CV disease. We believe these molecules have the potential to prevent both primary and secondary CV events in multiple high CV risk patient groups, such as those with atherosclerosis in acute and chronic conditions after MI and hypercholesterolaemia (elevated cholesterol).

*Crestor* is approved in more than 115 countries for the treatment of dyslipidaemia and hypercholesterolaemia and the financial impact has stabilised following patent expiries in the US (2016) and EU/Japan (2017). *Crestor* is now subject to generic competition in a majority of markets.

### Renal diseases

A CKD diagnosis currently means a rapid progression towards end-stage renal disease (ESRD), with the potential for dialysis and serious life-threatening complications. To help transform the lives of more patients, we are investigating the potential of roxadustat, *Lokelma* and *Farxiga* to treat these complications and halt disease progression.

Roxadustat is a first-in-class, oral hypoxia inducible factor prolyl hydroxylase inhibitor (HIF-PHI) that has the potential to transform the lives of people living with anaemia in CKD, both those on dialysis and not on dialysis. In August 2019, roxadustat was approved in China for the treatment of anaemia in non-dialysis dependent (NDD) patients, making China the first and only country where roxadustat is approved for CKD patients regardless of whether they are on dialysis. The approvals in China were supported by two Phase III trials in China in dialysis dependent CKD and NDD-CKD patients.



In May 2019, we announced positive top-line results from the pooled CV safety analyses of the global Phase III programme for roxadustat, the largest clinical programme in the world to investigate a HIF-PHI. Results from the Phase III OLYMPUS and ROCKIES trials and detailed results from the pooled efficacy and CV safety analyses showed positive efficacy and no increased CV risk in NDD, dialysis dependant and incident dialysis patients with anaemia in CKD versus placebo, epoetin alfa, and epoetin alfa, respectively. Further analyses informed the NDA filing in the US, which we submitted in December 2019 with our partner FibroGen. A regulatory decision is anticipated in the second half of 2020.

People living with CKD are at an increased risk of developing hyperkalaemia and, in addition to the launch of *Lokelma* referred to above, in June 2019, we announced results from DIALIZE, the first ever randomised, placebo-controlled Phase IIIb trial to evaluate *Lokelma* in patients on stable haemodialysis. Label updates for *Lokelma* have been submitted in the US and EU and decisions are expected in the first half of 2020. *Lokelma* was approved in China and is also under regulatory review in Japan with a decision expected in the first half of 2020.

In order to help meet the unmet medical need in CKD, we are exploring the clinical science behind our medicines with DAPA-CKD and DELIGHT, an exploratory Phase II/III trial, also part of the DapaCare programme. The two trials evaluate the potential benefits of *Farxiga* in the treatment of CKD, renal or CV death in CKD patients with and without albuminuria. DAPA-CKD will be the first trial evaluating *Farxiga*, an antidiabetic SGLT2 inhibitor by origin, in CKD patients without type-2 diabetes.

We are also progressing verinurad, a novel renal urate transporter (URAT1) inhibitor currently in Phase IIb development for the treatment of CKD. Results from the Phase IIa CITRINE trial demonstrated that treatment with verinurad plus febuxostat decreased albuminuria and serum urate in patients with type-2 diabetes mellitus, potentially slowing progression of CKD. In August 2019, the first subject was dosed in the Phase IIb SAPPHIRE trial for verinurad.

Our ambition is to transform the standard of care for CKD from day-to-day management to one that can identify and address root causes to aggressively prevent, treat, manage, modify and even halt progression of the disease. We also continue to investigate new molecules such as MEDI8367, MEDI3506 (IL33) and AZD2373 (APOL1) with the aim of stopping the progression of ESRD, treating patients with DKD and developing the first precision medicine in CKD.

### Beyond research

We invest in programmes to educate stakeholders about CVRM and improve patient access to healthcare.

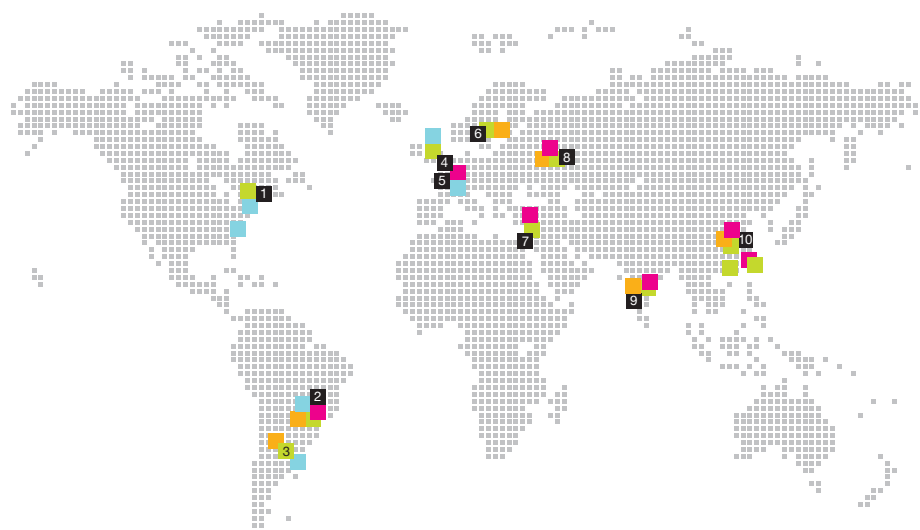
Some of our most notable programmes include Healthy Heart, which addresses hypertension and the increasing burden of CV disease (see page 49 for more information); Improving Cardiovascular Care in China (see page 63); and One Brave Idea, which aims to understand the molecular events surrounding the earliest transition from wellness to disease in coronary heart disease.

In 2019, we launched Accelerate Change Together (ACT), a cross-functional programme in diabetes, HF and CKD to drive policy and healthcare system change to better manage cardio-renal complications in type-2 diabetes, reduce incidence of HF and support earlier diagnosis of CKD.

We have taken this thinking one step further by reimagining how we can improve outcomes for patients across their personal health experience. We have created Health Innovation Hubs and a network comprising both structural locations and virtual partnerships to deliver patient-centric disease management solutions across all our therapy areas. The map below shows the 10 major hubs that form the foundation of our global Health Innovation Hub network. For more information, see page 43.

## The Health Innovation Hub network

### By geographical area



|                             |                            |                                  |                           |                        |
|-----------------------------|----------------------------|----------------------------------|---------------------------|------------------------|
| 1. US Hub<br>Boston         | 2. Brazil Hub<br>Sao Paulo | 3. Argentina Hub<br>Buenos Aires | 4. UK Hub<br>Cambridge    | 5. France Hub<br>Paris |
| 6. Sweden Hub<br>Gothenburg | 7. Israel Hub<br>Tel-Aviv  | 8. Russia Hub<br>Moscow          | 9. India Hub<br>Bangalore | 10. China Hub<br>Wuxi  |

### Health Innovation Hubs

#### Public-Private Partnerships

AstraZeneca + technology/start-up companies + government/health system in a physical location

#### System Partnership

AstraZeneca + government/health system

### Start-up Hubs

#### Start-up Hubs/Models

Incubator/accelerator models whereby we work with start-up companies to identify and solve challenges, and scale ideas

### Experience Design Centres

#### Internal (AstraZeneca Teams/Brands)

Bring innovation to AstraZeneca to redefine how we take products, services and experiences to market

#### External (HCP/patient)

Work with HCPs/patients to observe and design solutions, and test innovation

# Respiratory

We aim to transform the treatment of respiratory diseases with our growing portfolio of inhaled combinations at the core of care, biologics for the unmet medical needs of specific patient populations and scientific advancements in disease modification with the ambition of achieving remission or even cures for patients.

## Unmet medical need and world market

Today, more than 700 million people have asthma or chronic obstructive pulmonary disease (COPD). Of the 250 million people who are in our eight largest commercial markets, more than 65 million of those with asthma and 124 million with COPD do not receive maintenance treatment for these chronic diseases. Despite currently available medicines, therapeutic advances are needed to reduce morbidity and mortality.

We estimate that new medicines and Emerging Markets will drive 6% annual growth over the next decade, reaching \$47 billion by 2028.

Antibody that binds to upstream epithelial cytokines to prevent a range of inflammatory responses.

### 339m

339 million individuals worldwide have asthma, with prevalence expected to rise.

### 50%

Severe asthma accounts for about 10% of asthma patients but 50% of the physical and socio-economic burden of asthma.

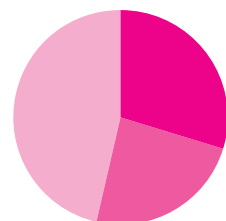
### 384m

Globally, 384 million people have COPD, and it is the third leading cause of death worldwide. COPD exacerbations represent a significant burden for patients, carers and society. COPD costs are estimated to exceed \$100 billion per year globally.

Therapy area world market  
(MAT/Q3/19)

### \$69.9bn

Annual worldwide market value



■ Asthma \$20.9bn  
■ COPD \$16.7bn  
■ Other \$32.0bn

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

## Key marketed products and revenues 2019

Our Respiratory business strengthened its growth in 2019, with sales up 10% (13% at CER). *Symbicort* continued volume market leadership and became the value leader in 2019 in the inhaled corticosteroid (ICS)/long-acting beta2-agonist (LABA) class. *Pulmicort* continued to deliver strong revenue growth, led by Emerging Markets in which China stood out. *Breztri Aerosphere* (PT010) was approved and launched in Japan, and approved in China. In biologics, *Fasenra* has been approved in 53 countries for severe eosinophilic asthma and is currently reimbursed in 36 countries.

## Respiratory Product Sales

# \$5,391m

23% of total

2018: \$4,911m

2017: \$4,706m

| Product  | Disease area   | Revenue                         | Commentary  |
|--|----------------|---------------------------------|---|
| <i>Symbicort</i> (budesonide/formoterol)                         | Asthma<br>COPD | ↔ \$2,495m, down 3% (0% at CER) | Continued volume market leadership and became the value leader of the ICS/LABA class led by strong growth in Emerging Markets.  |
| <i>Pulmicort</i> (budesonide)                                    | Asthma         | ↑ \$1,466m, up 14% (18% at CER) | Brand growth led by Emerging Markets with leadership in China. Growth in China due to increased medical access supported by nebulisation room expansion and improved coverage of emerging/county hospitals. |
| <i>Fasenra</i> (benralizumab)                                    | Severe asthma  | ↑ \$704m, up 137% (139% at CER) | <i>Fasenra</i> leads the IL-5 class in new prescriptions in the US, Japan, Germany and France.  |
| <i>Daliresp/Daxas</i> (roflumilast)                              | COPD           | ↑ \$215m, up 14% (15% at CER)   | Growth driven by favourable affordability-programme changes and inventory movements in the US.  |
| <i>Duaklir</i> (aclidinium/formoterol)                           | COPD           | ↓ \$77m, down 19% (15% at CER)  | Growth in Europe is in line with expectations. <i>Duaklir</i> was approved in the US and launched by Circassia in October 2019. AstraZeneca will continue to supply the medicine.                           |
| <i>Tudorza/Ekira</i> (aclidinium)                                | COPD           | ↓ \$72m, down 35% (32% at CER)  | Reflects the flat long-acting muscarinic antagonist (LAMA) market. Sales in the US are now booked by Circassia following its acquisition of the product in January 2019.                                    |
| <i>Bevespi Aerosphere</i> (glycopyrrolate/formoterol)            | COPD           | ↑ \$42m, up 26% (26% at CER)    | <i>Bevespi Aerosphere</i> revenue and growth is in line with other long-acting muscarinic antagonists/LABA launches.  |
| <i>Breztri Aerosphere</i> (budesonide/glycopyrrolate/formoterol) | COPD           | n/m \$2m, movement n/m          | <i>Breztri Aerosphere</i> revenue is in line with other launches in COPD under Japan's Ryotanki restriction.  |
| Others   | Asthma<br>COPD | ↓ \$390m, down 13% (9% at CER)  |   |

## Our strategy for Respiratory

Our respiratory medicines reached more than 53 million patients receiving acute and maintenance therapy in 2019. We have a strong pipeline with more than 10,300 patients actively participating in Phase I-IV respiratory clinical trials across the world.

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

1. Our strength in inhaled combination medicines.
2. A leading biologics portfolio.
3. An exciting early- and mid-stage pipeline.

## Inhaled medicines

In inhaled medicine, our focus is on two key areas of clinical care. In asthma, we are working to prevent attacks by reducing over-reliance on short-acting beta2-agonist (SABA) reliever monotherapy and advancing anti-inflammatory reliever therapy, evidenced by the approvals of *Symbicort Turbuhaler* as an anti-inflammatory reliever as-needed in mild asthma in multiple countries in 2019. *Symbicort* continued its leadership in the ICS/LABA class, and remains a cornerstone of current asthma and COPD care. We expect to be one of only two key global players to offer the leading inhaled combination therapy classes for COPD in all major regions. Based on the full Phase III data results, *Breztri Aerosphere* has a highly competitive clinical profile across a broad range of patients and at two doses of ICS.

## Biologics

In biologics, we aim to transform outcomes among patients with the greatest unmet medical need and relegate chronic oral steroid use to last resort, given its association with adverse events. Our first respiratory biologic, *Fasenra*, is approved for severe eosinophilic asthma and is also being investigated for other eosinophil-driven diseases. In the future,

tezepelumab, a potential first-in-class anti-thymic stromal lymphopoietin (TSLP) mAb that blocks a key upstream driver of inflammation in asthma, has the potential to treat a broad population of severe asthma patients, including those patients who are ineligible for biologic therapies today, if the Phase III programme reflects the positive Phase IIb data.

## In the pipeline

Our mid-stage and early portfolios include novel and inhaled biologics, early biology-led treatment, lung repair and regeneration. Beyond *Fasenra* and tezepelumab programmes, we have one new molecular entity in Phase III, six new molecular entities in Phase II, four new molecular entities in Phase I, two life-cycle management projects and a robust pre-clinical pipeline. In addition to asthma and COPD we are also investigating other respiratory opportunities in idiopathic pulmonary fibrosis (IPF) and chronic cough.

Our respiratory market leadership in China positions us well to support improvements in acute treatment using our leading nebulisation portfolio, which is supported with more than 17,500 nebulisation centres, and establishing maintenance inhaled treatment as the standard of care (SoC) in asthma and COPD.

# Therapy Area Review

## Respiratory *continued*

### 2019 pipeline highlights

The progress of our pipeline in 2019 reflects our commitment to transforming critical areas of care in respiratory.

In inhaled medicine, we reported Phase III trial results in COPD for *Breztri Aerosphere* (PT010), our triple-combination therapy and it was approved for COPD in Japan and China. We also advanced *Symbicort Turbuhaler* and PT027 (ICS/SABA combination) as anti-inflammatory reliever therapies in asthma,

with the approval of *Symbicort Turbuhaler* as an anti-inflammatory reliever therapy in 11 countries and the continuation of the Phase III clinical trial programme for PT027 by our co-development partner, Avillion.

In line with our strategy to transform outcomes with respiratory biologics, *Fasenra* was granted additional regulatory approvals and is now approved in 50 countries around the world for severe eosinophilic asthma.

Full details of our pipeline are given in the Development Pipeline from page 238 and highlights from the progress of our Respiratory pipeline made against our KPIs in 2019 are shown below.

### Life-cycle phases – R&D

#### New molecular entity (NME) Phase IIa/b starts/progressions

| Product | Disease |
|---------|---------|
| AZD7594 | Asthma  |

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

In 2019, the first patients were enrolled in the Phase III RESOLUTE trial of *Fasenra* in COPD.

| Product        | Disease                                       |
|----------------|---|
| <i>Fasenra</i> | COPD (RESOLUTE)                               |
| <i>Fasenra</i> | Eosinophilic granulomatosis with polyangiitis |
| <i>Fasenra</i> | Nasal polyps (China, Japan)                   |

Plus two projects where an investment decision was made, but the clinical trial is yet to start.

#### NME and major LCM regional submissions

In the second half of 2019, *Symbicort* received regulatory filing acceptance by the National Medical Products Administration (NMPA) in China for use in mild asthma.

| Product                   | Disease       | Region               |
|---------------------------|---------------|----------------------|
| <i>Breztri Aerosphere</i> | COPD (KRONOS) | US <sup>1</sup> , EU |
| <i>Symbicort</i>          | Mild asthma   | China                |

<sup>1</sup> CRL issued by the FDA relating to the NDA. See page 70.

### Life-cycle phases – approvals

#### NME and major LCM regional approvals

*Breztri Aerosphere* received the first global approval for the treatment of COPD in Japan, with subsequent approval in China. *Bevespi Aerosphere* was also approved for COPD in Japan.

| Product  | Disease       | Region       |
|--|---------------|--------------|
| <i>Breztri Aerosphere</i> (budesonide/glycopyrronium/formoterol fumarate) <sup>1</sup> | COPD          | Japan, China |
| <i>Bevespi Aerosphere</i>  | COPD          | Japan        |
| <i>Fasenra</i> self-administration auto-injector                                       | Severe asthma | US, EU       |

<sup>1</sup> Known as budesonide/glycopyrronium/formoterol fumarate in China.

### Discontinued projects

| Product | Disease | Reason          |
|---------|---------|-----------------|
| AZD1419 | Asthma  | Safety/efficacy |

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

# Redefining care for severe asthma patients

Severe asthma affects approximately 34 million people worldwide and, for many, can mean a life of frequent, severe attacks, with reduced lung function and a poor quality of life. There are significant challenges to managing severe asthma as standard treatments alone often do not work sufficiently. Contributing to the problem, in many countries, patients can spend years in primary care without getting referred to a specialist for proper diagnosis and care.

We have made a long-term investment to improve severe asthma patient care through a multi-disciplinary programme called PRECISION. PRECISION brings together leading experts in asthma and healthcare policy to ensure severe asthma patients routinely receive the right care, at the right time, in the most appropriate setting. Our efforts are focused on accelerating appropriate referrals to specialists, building capability and capacity, and improving healthcare system policies and access.

PRECISION is already operating across 45 countries and, with the involvement of more than 100,000 healthcare professionals, transforming clinical standards and patient referral pathways and identifying patients most at risk based on potential over-reliance on oral corticosteroids.

## 34m

people affected worldwide by severe asthma

## 45 countries

in which PRECISION is already operating

### 2019 review – strategy in action

#### Strength in inhaled combination medicines

In 2019, the strength of our inhaled combination medicines was reflected with the performance of *Symbicort*, which continued its volume market leadership as the number one ICS/LABA combination globally and became the value leader within the ICS/LABA class globally – a major achievement for a medicine 19 years after launch.

This performance has been driven by growth in Emerging Markets in response to high unmet medical need and rapid adoption of better medical treatment, offset by continued pricing pressure in established markets in line with expectations as prices rebase through generic entries. Growth has been particularly strong in China, where there is increased government intervention to address the unmet medical need in respiratory diseases, including, for example, the Pulmonary and Critical Care Medicine initiative to improve quality standards and COPD being listed in the China 2030 state plan. In addition, *Symbicort* has been included in the Essential Drugs List, had its 2nd-line restriction removed in the National Reimbursement Drug List (NRDL) and has preferred positioning within updated national guidelines versus other treatments.

In 2019, positive results were reported from two key trials, which were designed to reflect real-world practice and assess the effectiveness of *Symbicort Turbuhaler* taken as-needed, as anti-inflammatory reliever therapy in adults with mild or mild-to-

moderate asthma. Data from the Novel START open-label trial showed a 51% reduction in the rate of annual asthma exacerbations with *Symbicort Turbuhaler* compared with albuterol. There was no difference in the exacerbation rate between *Symbicort Turbuhaler* and twice-daily maintenance budesonide plus albuterol, despite a 52% reduction in the mean steroid dose with *Symbicort Turbuhaler*. Results from PRACTICAL, a peer-reviewed trial that was independently funded by the Health Research Council of New Zealand, showed that *Symbicort Turbuhaler* used as an anti-inflammatory reliever in mild-to-moderate asthma reduced the rate of severe exacerbations versus maintenance budesonide plus terbutaline taken as-needed, a comparator regimen representative of usual care in this patient population. The safety and tolerability for *Symbicort Turbuhaler* as-needed, in both trials, was consistent with the known profile of the medicine. These data build on the results from our Phase III SYGMA trials of *Symbicort Turbuhaler* and add to the body of evidence which demonstrate the potential of *Symbicort Turbuhaler*, used as-needed, as an important treatment option for patients with mild disease at risk of asthma attacks. The trials follow on from previous studies which demonstrated the ability of *Symbicort Turbuhaler* to reduce severe exacerbations, when used as-needed for moderate-to-severe patients prescribed maintenance and reliever therapy.

In 2019, the Global Initiative for Asthma published its latest report on asthma management, calling it the most significant change in asthma management in over 30 years. The report recommended low dose ICS-formoterol combination therapy (the molecules in *Symbicort*) as-needed as the preferred reliever therapy across all asthma severities and the preferred controller and reliever therapy in mild asthma. SABA monotherapy is no longer the preferred reliever recommended for patients with mild asthma, due to increased airway inflammation and risk of serious asthma attacks, specifically the risk of serious attacks in those receiving three or more SABA canisters per year. The changes in preferred reliever therapy reflect evidence gathered during many years of our research, including more than 25 trials. In 2019, *Symbicort Turbuhaler* was approved as an anti-inflammatory reliever as-needed in mild asthma in Australia, New Zealand, Brazil, Canada, Chile, Haiti, Russia, Singapore, South Korea, Egypt and Iran. Regulatory reviews are ongoing to extend the indication in additional countries. In July 2019, the regulatory submission in the EU for *Symbicort Turbuhaler* in mild asthma was withdrawn and a new submission is anticipated during the first half of 2020. In the fourth quarter of 2019, *Symbicort* received regulatory filing acceptance by the National Medical Products Administration (NMPA) in China for use in mild asthma.

Our commitment to working to prevent attacks by reducing over-reliance on reliever monotherapy and advancing anti-inflammatory reliever therapy continues with the development of PT027. PT027 is an investigational fixed-dose combination of budesonide, an ICS and albuterol, a SABA. In 2019, our co-development partner, Avillion, initiated the second Phase III trial of PT027 in patients with mild-to-moderate asthma. Results from both the MANDALA and DENALI trials are expected to read out in 2020.

## Therapy Area Review Respiratory *continued*

In August 2019, top-line results from the Phase III ETHOS trial of PT010, our triple-combination therapy showed a significant reduction in the rate of moderate and severe exacerbations, compared with dual-combination therapies. The trial also showed, for the first time, the benefit of fixed-dose triple-combination therapy at two inhaled corticosteroid (ICS) doses, which could transform treatment practice by allowing physicians to select the optimal dose for individual patients. Safety and tolerability of PT010 were consistent with the known profiles of the dual comparators in the trial. We also received the first approvals for the treatment of COPD in Japan and China, as *Breztri Aerosphere*. In the US, the FDA issued a CRL regarding the NDA in September, and we are now working closely with the FDA regarding next steps, including submitting for review results from the positive Phase III ETHOS trial, which was not completed at the time the NDA was originally submitted.

*Bevespi Aerosphere*'s progress also continued in 2019 with regulatory approval in Japan.

Our medicines in the US partnered with Circassia also made progress. In October 2019, *Duaklir* was launched in the US for the maintenance treatment of COPD. *Duaklir* was approved based on a broad clinical database, including data from three Phase III studies, ACLIFORM, AUGMENT and AMPLIFY, and the label includes data on exacerbation reduction from the Phase IV ASCENT study. In April, the FDA approved an sNDA for *Tudorza* which includes unique positive safety language related to COPD patients with cardiovascular disease or risk factors.

### Biologic medicines

Our first respiratory biologic, *Fasenra*, continued rapid market expansion in 2019 and saw the total number of patients treated reach 50,000. It was also approved for self-administration in the EU (via a pre-filled syringe and new auto-injector device, the *Fasenra Pen*) and in the US (via *Fasenra Pen*).

The main factors driving biologic treatment rates in severe uncontrolled asthma include:

- > access to approved biologics
- > patient self-administration (which could capture approximately two-thirds of patients and frees up capacity in clinics to treat more patients)
- > improved clinical capabilities and confidence in treating severe asthma
- > evidence enabling the reduction or discontinuation of maintenance OCS use.

AstraZeneca is investing in accelerating these drivers in respiratory disease 'beyond the medicine' which should support biologics having the kind of impact that they have had in other inflammatory diseases.

For example, we recently launched Connect 360, a new, comprehensive global patient support programme designed to provide best-in-class education and support to *Fasenra* patients around the world.

In 2019, we completed enrolment of patients into our Phase IIIb PONENTE trial that is designed to further investigate the potential of *Fasenra* to eliminate maintenance oral corticosteroid use in patients with severe refractory eosinophilic asthma. PONENTE is the largest steroid-sparing trial undertaken in severe asthma to date and results are expected in 2020.

Beyond asthma, we are following the science and investing in *Fasenra*'s potential in other diseases where eosinophils are a direct cause or thought to play a critical role. This includes nasal polyps, COPD, eosinophilic esophagitis (EOE), eosinophilic granulomatosis with polyangiitis (EGPA) and hypereosinophilic syndrome (HES).

The OSTRO Phase III trial to investigate *Fasenra* in nasal polyps completed enrolment in 2019 and the first patient was enrolled in our Phase III MANDARA trial for *Fasenra* in EGPA.

In September 2019, further analysis of data from the two Phase III trials, GALATHEA and TERRANOVA, for *Fasenra* in patients with moderate-to-very-severe COPD were presented at the European Respiratory Society International Congress 2019 and published in *The Lancet Respiratory Medicine*. Building on these analyses, the first patients were enrolled in the Phase III RESOLUTE trial that will investigate the efficacy and safety of *Fasenra* 100mg in patients with moderate-to-very-severe COPD who are treated with triple inhaled therapy, have a history of frequent exacerbations and have elevated peripheral blood eosinophils. We previously reported that the GALATHEA and TERRANOVA trials did not meet their respective primary efficacy endpoints.

In April 2019, positive results from a Phase II trial, showed that *Fasenra* can achieve near-complete depletion of eosinophils and improve clinical outcomes in HES. In August 2019, the FDA granted Orphan Drug Designation for *Fasenra* for the treatment of EOE.

Positive results from the *Fasenra* Phase IIIb ANDHI trial in patients with severe eosinophilic asthma were also reported. In ANDHI, *Fasenra* on top of standard of care, demonstrated a statistically significant reduction in the annual rate of asthma exacerbations compared with placebo in patients with baseline blood eosinophil counts greater than or equal to 150 cells per microlitre (the primary endpoint). The safety and tolerability of *Fasenra* were consistent with the known profile of the medicine.

### Early science

In line with our aim to develop biologics that treat the remaining unmet medical needs of severe asthma patients, we continued to progress the development of tezepelumab through the ongoing Phase III PATHFINDER programme, with our partner Amgen, and presented further results of the biomarker analysis from the Phase IIb PATHWAY trial at the American Thoracic Society 2019 International Conference in May. In the first quarter of 2019, the FDA granted saracatinib Orphan Drug Designation for the potential treatment of idiopathic pulmonary fibrosis. Saracatinib is a small molecule, highly-potent and selective inhibitor of src tyrosine kinase previously in clinical development in oncology which has completed Phase I development.

Other compounds in early-stage development include: MEDI3506 (Phase I in COPD; Phase II in atopic dermatitis), an anti-IL-33 mAb that inhibits IL-33, a key upstream epithelial cytokine that is functionally distinct from TSLP; AZD0449 (Phase I), a potential first-in-class inhaled JAK-inhibitor being developed for a broad population of asthma patients, intended as a step-through therapy between ICS therapy and biologics; and AZD8154 (Phase I), a potent selective, dual phosphoinositide 3-kinase delta-gamma inhibitor which has the potential to be the first inhaled treatment to affect lung function through targeting mixed T2/T1/T17-cell phenotypes.



# Other Disease Areas

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

## Unmet medical need and world market

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

Nanoparticles circulating in blood stream.

### Key marketed products and revenues 2019

*Nexium* is continuing to perform strongly in China, while sales for the rest of the world are in line with expectations, given pressures from generic competition. *Fluenz Tetra/FluMist* Quadrivalent continues to be licensed in multiple markets, including the US, Canada, EU, Israel and Hong Kong, and it remains a central part of the UK and Finnish paediatric national influenza vaccination programmes.

### Other Product Sales

## \$2,601m

11% of total

2018: \$3,400m

2017: \$4,156m

| Product  | Disease area   | Revenue                           | Commentary   |
|--|--|-----------------------------------|--|
| <b>Infection</b>   |  |                                   |  |
| <i>Synagis</i> (palivizumab)   | Respiratory syncytial virus (RSV)                    | ↓ \$358m, down 46% (46% at CER)   | Divested US rights to Sobi. AbbVie holds rights to <i>Synagis</i> outside the US.  |
| <i>Fluenz Tetra/FluMist</i> Quadrivalent (live attenuated influenza vaccine) | Influenza  | ↑ \$113m, up 3% (5% at CER)       | Approved in the US, EU, Canada, Israel and Hong Kong. Daiichi Sankyo holds rights to <i>Fluenz Tetra/FluMist</i> Quadrivalent in Japan.  |
| <b>Neuroscience</b>  |  |                                   |  |
| <i>Seroquel IR/Seroquel XR</i> (quetiapine fumarate)                         | Schizophrenia<br>Bipolar disease                     | ↓ \$191m, down 47% (46% at CER)   | Divested rights in Europe and Russia in October 2019 and in US and Canada in December 2019 to Cheplapharm. Luye Pharma holds rights to <i>Seroquel</i> and <i>Seroquel XR</i> in the UK, China and other international markets. The rights to <i>Seroquel</i> and <i>Seroquel XR</i> in Japan are partnered with Astellas. |
| <i>Movantik/Moventig</i> (naloxegol)   | Opioid-induced constipation                          | ↓ \$98m, down 10% (10% at CER)    | Licensed from Nektar Therapeutics. Kyowa Kirin has held rights in the EU since March 2016. Knight Therapeutics Inc. has held rights in Canada and Israel since December 2016. Co-commercialisation in the US with Daiichi Sankyo.  |
| <i>Vimovo</i> (naproxen and esomeprazole)                                    | Osteoarthritic pain                                  | ↓ \$37m, down 47% (44% at CER)    | Licensed from Pozen and divested worldwide rights (ex-US) to Grünenthal in October 2018. Divested US rights to Horizon Pharma Inc. since November 2013.  |
| <b>Gastroenterology</b>  |  |                                   |  |
| <i>Nexium</i> (esomeprazole)   | Proton pump inhibitor to treat acid-related diseases | ↓ \$1,483m, down 13% (11% at CER) | Divested European rights to Grünenthal in October 2018.  |
| <i>Losec/Prilosec</i> (omeprazole)   | Proton pump inhibitor to treat acid-related diseases | ↔ \$263m, down 3% (up 1% at CER)  | In October 2019, divested global commercial rights, excluding China, Japan, the US and Mexico to Cheplapharm.  |

# Therapy Area Review

## Other Disease Areas




### *continued*

#### Our strategy for Other Disease Areas and 2019 pipeline highlights

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

Full details of our pipeline are given in the Development Pipeline from page 238 and highlights from the progress of our Other Disease Areas pipeline made in 2019 against our KPIs are shown below.

#### Life-cycle phases – R&D

|  | Product    | Disease                  | Region |
|--|------------|--------------------------|--------|
|  New molecular entity (NME) Phase II starts/progressions                           | None       | –                        | –      |
|  NME and major life-cycle management (LCM) positive Phase III investment decisions | Nirsevimab | Passive RSV immunisation | –      |
|  NME and major LCM regional submissions  | None       | –                        | –      |

#### Life-cycle phases – approvals

|   | Product        | Disease                                    | Region |
|---|----------------|--|--------|
|  NME and major LCM regional approvals | <i>Linzess</i> | Irritable bowel syndrome with constipation | China  |

#### Discontinued projects

| Product    | Disease                      | Reason          |
|------------|------------------------------|-----------------|
| MEDI0700   | Systemic lupus erythematosus | Strategic       |
| MEDI8852   | Influenza A treatment        | Economic        |
| Prezalumab | Primary Sjögren's syndrome   | Safety/efficacy |

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

#### 2019 review – strategy in action

##### Infection

Seasonal influenza is a serious public health problem that causes severe illness and death in high-risk populations. For the 2019-20 influenza season, *FluMist* Quadrivalent/*Fluenz* Tetra continues to be licensed in multiple markets, including the US, Canada, EU, Israel and Hong Kong, and it remains a central part of the UK and Finnish paediatric national influenza vaccination programmes. Over five million doses were delivered to support the childhood vaccinations through the UK's national immunisation programme during the 2019-20 season, and the programme is scheduled to continue during the 2020-21 season. In addition, we participate in both the Centers for Disease Control and Prevention Vaccine for Children programme and adult vaccine programme, which are federally funded programmes that ensure under or uninsured children and adults have access to vaccines at little or no cost. We also have an ongoing agreement with the WHO to donate and supply stock at reduced prices in the event of an influenza pandemic.

In May 2019, Public Health England published provisional end of season vaccine effectiveness (VE) data for the 2018-19 season in the UK. In children two to 17 years old, adjusted VE with *Fluenz* was 48.6% against all circulating strains, 49.9% against circulating A/H1N1pdm09, and 27.1% against circulating A/H3N2 strains. These latest data support the real-world effectiveness demonstrated by *Fluenz* Tetra and reinforce the public health importance of influenza vaccination as the most effective way to prevent influenza disease.

Respiratory syncytial virus (RSV) is a common seasonal virus and the most prevalent cause of lower respiratory tract infections (LRTI) among infants and young children. It is the leading cause of hospitalisations and admissions to paediatric intensive care units and leads to nearly 150,000 deaths globally in children under five years of age, with most deaths occurring in developing countries. Since its initial approval in 1998, *Synagis* has become the global standard of care for RSV

prevention and helps protect at-risk babies against RSV. *Synagis* is approved in more than 80 countries and we continue to work with our worldwide partner, AbbVie, outside the US, to protect vulnerable infants.

Nirsevimab, formerly MEDI8897, an extended half-life RSV mAb being investigated for the prevention of LRTI caused by RSV in all infants, is progressing in collaboration with Sanofi. It is being developed for use among a broad population of infants, so that they may only require one dose during an RSV season. In July 2019, we initiated pivotal Phase III and Phase II/III trials to measure the safety and efficacy of nirsevimab to prevent LRTI caused by RSV in full-term, healthy late pre-term and high-risk babies.

The pivotal Phase III (MELODY) study will determine if nirsevimab will prevent medically attended RSV-confirmed LRTIs in healthy infants born at 35 weeks or older, entering their first RSV season. This study will also confirm the safety of nirsevimab. The pivotal Phase II/III (MEDLEY) trial is a randomised, double-blind, palivizumab-controlled study to evaluate the safety, pharmacokinetics (PK), anti-drug antibody (ADA) response, and descriptive efficacy for nirsevimab in high-risk infants (pre-term or with chronic lung disease or congenital heart disease) eligible to receive *Synagis* when entering their first or second RSV season. The full results of both trials are anticipated in 2023.

### Neuroscience

We are progressing MEDI7352, a bispecific molecule which targets both nerve growth factor and tumour necrosis factor alpha, in both painful diabetic neuropathy in Phase II and osteoarthritis pain in Phase I. Also in Phase I is MEDI0618, an anti-PAR2 (protease-activated receptor 2) antibody which we are also developing for osteoarthritis pain and AZD4041, a selective orexin 1 receptor antagonist, which is being developed for substance use disorder in a collaborative effort between AstraZeneca, Eolas Therapeutics and NIH.

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

In April 2019, alongside our alliance partner Lilly, we announced the termination of the collaboration on lanabecestat, an oral beta secretase-cleaving enzyme inhibitor. We collaborate with Lilly on MEDI1814, an antibody selective for amyloid-beta 1-42 that is currently in Phase I trials as a potential disease-modifying treatment for Alzheimer's disease.

### Autoimmunity and inflammation

In August 2019, we announced that anifrolumab, a developmental mAb that inhibits the activity of all type I interferons (IFN), met the primary endpoint in the TULIP 2 Phase III trial in systemic lupus erythematosus (SLE). The results from TULIP 2 were presented in a late-breaking oral presentation at the American College of Rheumatology Congress (ACR) 2019, and published in *The New England Journal of Medicine* in December.

Results from the previous Phase III trial, TULIP 1, which did not meet the primary endpoint, were also presented at ACR 2019, and simultaneously published in *The Lancet Rheumatology*. The safety and tolerability findings in TULIP 1 and TULIP 2 were consistent with the known profile of anifrolumab.

In January 2020, it was announced that the Group will recover the global rights to brazikumab (formerly MEDI2070), a monoclonal antibody targeting IL23, from Allergan. Brazikumab is currently in a Phase IIb/III programme in Crohn's disease (CD) and a Phase IIb trial in ulcerative colitis (UC). Brazikumab adds to the growing presence in immunology where AstraZeneca has longstanding research and development capabilities. With our return to growth we are now in a strong position to competitively commercialise an immunology biologic like brazikumab, in addition to anifrolumab, *Fasenra*, tezepelumab and MEDI3506.

Given the increasing number of potential new medicines in development in immunology and the shared pathways and disease drivers across respiratory and immunology, in 2020, AstraZeneca plans to rename the therapy area of 'Respiratory' to 'Respiratory & Immunology'.

### Gastrointestinal

In October 2019, we announced an agreement to sell the global commercial rights, excluding China, Japan, the US and Mexico, for *Losec* and associated brands to Cheplapharm. The divestment includes medicines containing omeprazole marketed by AstraZeneca or its collaborators under the *Acimax*, *Antra*, *Mepral*, *Mopral*, *Omepral* and *Zoltum* medicine names.

Use of *Nexium* continued to grow in a limited number of markets such as China and Japan in 2019. This growth is expected to continue into 2020. *Nexium* is subject to generic competition globally, except for Japan.

In January 2019, Ironwood announced they had received marketing authorisation from the NMPA in China for *Linzess* for the treatment of patients with irritable bowel syndrome with constipation. In September 2019, AstraZeneca amended its collaboration agreement with Ironwood in China mainland, China Hong Kong and China Macau for *Linzess*. The amended agreement gives AstraZeneca sole responsibility for developing, manufacturing and commercialising *Linzess* in China mainland, China Hong Kong and China Macau. Ironwood will no longer be involved in the research and development or the commercialisation of *Linzess* in China; it will also transfer manufacturing responsibility to AstraZeneca. The two companies first entered into a collaboration to co-develop and co-commercialise *Linzess* in 2012.

### Our products

While this Therapy Area Review concentrates on our key marketed products, many of our other products are crucial to our business in certain countries in Emerging Markets.

For more information on our potential new products and product life-cycle developments, please see the Therapy Area pipeline tables on pages 56, 61 and 67 and the Development Pipeline table from page 238. For information on Patent Expiries of our Key Marketed Products, see from page 243.

Indications for each product described in this Therapy Area Review may vary among countries. Please see local prescribing information for country-specific indications for any particular product.

For those of our products subject to litigation, information about material legal proceedings can be found in Note 29 to the Financial Statements from page 220.

Details of relevant risks are set out in Risk from page 246.

We face a diverse range of risks and uncertainties. Those risks which have the potential to have a material impact on our business or results of operations are our Principal Risks.

The Board has carried out a robust assessment of the Principal and Emerging risks facing the Group. The table overleaf provides insight into the ongoing Principal Risks, outlining why effective management of these risks is important and relevant to the business, how we are managing them and which risks are rising, falling or have remained static during the past 12 months. The procedures in place to identify emerging risks are explained below.

### Managing risk

Our approach to risk management is designed to encourage clear decision making on which risks we take and how we manage these risks. 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. The Board believes that existing processes provide it with adequate information on the risks and uncertainties we face. Further information on our key risk management and assurance processes can be found in Risk from pages 246 to 257, 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.

### Emerging risks

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

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

### Risk management embedded in business processes

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

The Board defines the Group's risk appetite, enabling the Group, in both quantitative and qualitative terms, to judge the level of risk it is prepared to take in achieving its overall objectives. The Board expresses the acceptable levels of risk for the Group using three key dimensions. These are: (i) earnings and cash flow; (ii) return on investment; and (iii) ethics and reputation. Annually, the Group develops a detailed three-year bottom-up business plan and 10-year long-range projection to support the delivery of its strategy. The Board considers these in the context of the Group's risk appetite. Adjustments are made to the plan or risk appetite to ensure they remain aligned. Our risk management approach is aligned to our strategy and business planning processes. We cross-check financial risks and opportunities identified through the business planning process and integrate our findings into the overall risk management reporting. Line managers are accountable for identifying and managing risks and for delivering business objectives in accordance with the Group's risk appetite.

The SET is required by the Board to oversee and monitor the effectiveness of the risk management processes implemented by management. Within each SET function, leadership teams discuss the risks the business faces. This process provides a Group-wide assessment for the Board, Audit Committee and SET. Quarterly, each SET function assesses changes to these risks, new and emerging risks, and mitigation plans. These are assimilated into a Group Risk Report for the Board, Audit Committee and SET. Supporting tools are in place to assist risk leaders and managers in managing, monitoring and planning for risk. We continue to work on developing our risk management standards and guidelines. Global Compliance, Finance and Internal Audit Services support SET by advising on policy and standard setting, monitoring and auditing, and communication and training, as well as reporting on the adequacy of line management processes as they apply to risk management.

We have a business resilience framework which governs our ability to prevent or quickly adapt to situations while maintaining continuous business operations and safeguarding our people, processes and reputation. Within this we have business continuity plans to address situations in which specific risks have the potential to severely impact our business. These plans include training and crisis simulation activities for business managers.

□ More information about our Global Compliance function and the Code of Ethics can be found in the Corporate Governance Report on page 112 and the Business Review on page 35.

### Viability statement

In accordance with provision 31 of the 2018 UK Corporate Governance Code, the Board has determined that a three-year period to 31 December 2022 constitutes an appropriate period over which to provide its viability statement.

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

The three-year detailed business plan captures risks to the sales and cost forecasts at a market and SET function level. The plan is used to perform central net debt and headroom profile analysis. The following scenarios have been applied to this analysis to create a severe downside reflecting some of the Principal Risks detailed on pages 76 and 77.

- > **Scenario 1** Principal Risks: pricing, affordability, access and competitive pressures; failures or delays in the quality and execution of commercial strategies; failure to obtain, defend and enforce effective IP protection. Lower than anticipated growth rates, adverse impact of generic competition and greater than anticipated pressure on pricing across multiple products and markets.
- > **Scenario 2** Principal Risk: failure or delay in the delivery of our pipeline or launch of new products. Assumes no launches of new products.
- > **Scenario 3** Principal Risk: failure to maintain supply of compliant, quality product. Major equipment failure or significant regulatory observation at one of our major manufacturing sites results in a 12-month supply interruption for one of our key oncology products.

- > **Scenario 4** Principal Risk: failure to achieve strategic plans or meet targets and expectations. Income from divestment of core assets reinvested into core therapy areas and new products reduced by half in 2020.
- > **Scenario 5** Principal Risk: pricing, affordability, access and competitive pressures. An uncontrolled exit of the UK from the EU with associated disruption to supply and distribution channels leads to inability to supply a key product from the UK for six months following a 'no deal Brexit' outcome.
- > **Scenario 6** Principal Risks: pricing, affordability, access and competitive pressures; failures or delays in the quality and execution of commercial strategies. A significant incident leads to ongoing reputational damage in a key market resulting in an ongoing reduction in market share.
- > **Scenario 7** Principal Risks: failure in information technology, data protection or cyber crime; failure to meet regulatory and ethical expectations on commercial practices and scientific exchanges. Legal or regulatory non-compliance results in the levy of a significant fine.

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

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

### Brexit

On 23 June 2016, the UK held a referendum on the UK's continuing membership of the EU, the outcome of which was a decision for the UK to leave the EU (Brexit). Following Royal Assent of the European Union (Withdrawal Agreement) Act on 23 January 2020 and ratification of the Withdrawal Agreement by the European Parliament on 24 January 2020, the UK left the EU on 31 January 2020 and became a third country with a transition period running to 31 December 2020. The progress of current negotiations between the UK Government and the EU on their future relationship and the ratification of the outcome of those negotiations will likely determine the future terms of the UK's relationship with the

EU following the end of the transition period. Until these negotiations and parliamentary ratification processes are completed, it is difficult to anticipate the potential impact on AstraZeneca's market share, sales, profitability and results of operations.

The Group operates from a global footprint and retains flexibility to adapt to changing circumstances. The uncertainty during and after the period of negotiation is expected to increase volatility and may have an economic impact, particularly in the UK and Eurozone. Since the time of the referendum in 2016, the Group has responded by engaging proactively with key external stakeholders and establishing a cross-functional internal steering and implementation committee to understand, assess, plan and implement operational actions that may be required. The vast majority of these actions have already been implemented based on an assumption that the UK would have left the EU without a deal in 2019 (hard Brexit/no deal) such that the Group has been able to mitigate the risks arising from variable external outcomes. In January 2020, the assumption was updated to assume no extension to the transition period beyond 31 December 2020/no trade deal between the EU and UK agreed and ratified at that time, the effect of which would be similar to the previous hard Brexit/no deal assumption. Currently, the vast majority of the operational actions necessary to respond to this scenario have been implemented including, but not limited to: engagement with government and regulators; duplication of release testing and procedures for products for the EU27 and the UK markets; transfer of regulatory licences, redesign of packaging and labelling, additional inventory builds and changes to logistics plans and shipping routes; customs and duties set up for introduction or amendment of existing tariffs or processes; associated IT systems reconfigurations; and banking arrangement changes.

The Board reviews the potential impact of Brexit regularly as an integral part of its Principal Risks (as outlined overleaf) rather than as a standalone risk. The Board most recently reviewed the Group's Brexit readiness plans at its meeting in July 2019 and continues to assess its impact.

# Risk Overview

## continued

### Principal Risks

#### Strategy key

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

#### Trend key

- Increasing risk
- Decreasing risk
- Unchanged

| Risk category and Principal Risks | Context/potential impact | Management actions | Trend versus prior year |
|-----------------------------------|--------------------------|--------------------|-------------------------|
|-----------------------------------|--------------------------|--------------------|-------------------------|

### Product pipeline and intellectual property

|   |  |   |  |
|---|--|---|--|
| <p><b>Failure or delay in delivery of pipeline or launch of new products</b></p>                              | <p> The development of any pharmaceutical product candidate is a complex, risky and lengthy process involving significant financial, R&amp;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</p>   | <ul style="list-style-type: none"> <li>&gt; Prioritise and accelerate our pipeline</li> <li>&gt; Strengthen pipeline through acquisitions, licensing and collaborations</li> <li>&gt; Focus on innovative science in three main therapy areas</li> </ul>  |  |
| <p><b>Failure to meet regulatory or ethical requirements for drug development or approval</b></p>             | <p> Our pharmaceutical products and commercialisation processes are subject to extensive regulation. Delays in regulatory reviews and approvals impact patients and market access, and can materially affect our business or financial results</p>   | <ul style="list-style-type: none"> <li>&gt; Quality management systems incorporating monitoring, training and assurance activities</li> <li>&gt; Collaborating with regulatory bodies and advocacy groups to monitor and respond to changes in the regulatory environment, including revised process, timelines and guidance</li> </ul> |  |
| <p><b>Failure to obtain, defend and enforce effective IP protection or IP challenges by third parties</b></p> | <p> Discovering and developing medicines requires a significant investment of resources. For this to be a viable investment, new medicines must be safeguarded from being copied for a reasonable amount of time. If we are not successful in obtaining, maintaining, defending or enforcing our IP rights, and face competition from generic or biosimilar products, our revenues could be materially adversely affected</p> <p>Third parties may allege infringement of their IP, and may seek injunctions and/or damages, which, if ultimately awarded, could adversely impact our commercial and financial performance</p> | <ul style="list-style-type: none"> <li>&gt; Active management of IP rights and IP litigation</li> </ul>   |  |

### Commercialisation

|  |  |  |  |   |
|--|--|--|--|---|
| <p><b>Pricing, affordability, access and competitive pressures</b></p>               | <p> Operating in more than 100 countries, we are subject to political, socioeconomic and financial factors, both globally and in individual countries. There can be additional pressure from governments and other healthcare payers on medicine prices and sales in response to recessionary pressures, which may lead to a reduction in our revenue, profits and cash flow</p> | <ul style="list-style-type: none"> <li>&gt; Focus on sales platforms</li> <li>&gt; Demonstrating value of medicines/health economics</li> <li>&gt; Global footprint</li> <li>&gt; Diversified portfolio</li> </ul> |  | <p>Global economic and political conditions placing downward pressure on healthcare pricing and spending, and therefore on revenue</p>                      |
| <p><b>Failure or delays in the quality or execution of commercial strategies</b></p> | <p> 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 related launch costs</p>  | <ul style="list-style-type: none"> <li>&gt; Focus on sales platforms</li> <li>&gt; Accelerate and risk share through business development and strategic collaborations and alliances</li> </ul>                    |  | <p>Maximising the commercial potential of our new products underpins the success of our strategy and the delivery of our short- and medium-term targets</p> |

### Supply chain and business execution

|   |   |   |  |
|---|---|---|--|
| <p><b>Failure to maintain supply of compliant, quality products</b></p> | <p> Delays or interruptions in supply can lead to recalls, product shortages, regulatory action, reputational harm and lost sales revenue</p> | <ul style="list-style-type: none"> <li>&gt; Establishment of new manufacturing facilities, creating capacity and technical capability to support new product launches</li> <li>&gt; Contingency plans including dual sourcing, multiple suppliers, and close monitoring and maintenance of stock levels</li> <li>&gt; Business continuity and resilience initiatives, disaster and data recovery and emergency response plans</li> <li>&gt; Quality management systems</li> </ul> |  |
|---|---|---|--|

| Risk category and Principal Risks   | Context/potential impact   | Management actions   | Trend versus prior year  |
|---|--|--|--|
| <b>Supply chain and business execution <i>continued</i></b>   |  |  |  |
| <b>Failure in information technology, data protection or cybercrime</b>                                     |  Significant disruption to our IT systems, cybersecurity incidents including breaches of data security, or data privacy failure, could harm our reputation and materially affect our financial condition or results of operations. This could lead to regulatory penalties or non-compliance with laws and regulations  | <ul style="list-style-type: none"> <li>&gt; Cybersecurity framework and dashboard</li> <li>&gt; Privacy office oversees compliance with data privacy legislation</li> <li>&gt; Disaster and data recovery plans</li> <li>&gt; Strategies to secure critical systems and processes</li> <li>&gt; Regular cybersecurity and privacy training for employees</li> </ul>                      |  Growing multi-faceted cyber threat. Tougher legislative environment governs data protection  |
| <b>Failure to attract, develop, engage and retain a diverse, talented and capable workforce</b>             |  Failure to attract and retain highly skilled personnel may weaken our succession plans for critical positions in the medium term. Employee uncertainty as a result of, for example, Brexit or organisational change may result in a lower level of employee engagement which could impact productivity and turnover. Both could adversely affect the achievement of our strategic objectives | <ul style="list-style-type: none"> <li>&gt; Targeted recruitment and retention strategies deployed</li> <li>&gt; Identification and active support of staff potentially impacted by Brexit</li> <li>&gt; Development of our employees</li> <li>&gt; Evolve our culture</li> </ul>  |   |
| <b>Legal, regulatory and compliance</b>   |  |  |  |
| <b>Safety and efficacy of marketed products is questioned</b>   |  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  | <ul style="list-style-type: none"> <li>&gt; 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</li> </ul>                                    |   |
| <b>Adverse outcome of litigation and/or governmental investigations</b>                                     |  Investigations or legal proceedings could be costly, divert management attention and/or damage our reputation and demand for our products. Unfavourable resolutions could subject us to criminal liability, fines, penalties or other monetary or non-monetary remedies, adversely affecting our financial results   | <ul style="list-style-type: none"> <li>&gt; Combined internal and external counsel management</li> </ul>   |   |
| <b>Failure to meet regulatory and ethical expectations on commercial practices and scientific exchanges</b> |  Any failure to comply with applicable laws, rules and regulations, including bribery and corruption legislation, may result in civil and/or criminal legal proceedings and/or regulatory sanctions, fines or penalties, impacting financial results  | <ul style="list-style-type: none"> <li>&gt; Strong ethical and compliance culture</li> <li>&gt; Established compliance framework including annual Code of Ethics training for all employees</li> <li>&gt; Focus on due diligence and oversight of third-party engagements</li> </ul>   |  Increasing government and regulatory scrutiny and evolving compliance challenges as complexity of business relationships increases |
| <b>Economic and financial</b>   |  |  |  |
| <b>Failure to achieve strategic plans or meet targets or expectations</b>                                   |  Failure to implement successfully 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  | <ul style="list-style-type: none"> <li>&gt; Focus on sales platforms and innovative science in three main therapy areas</li> <li>&gt; Strengthen pipeline through acquisitions, licensing and collaborations</li> <li>&gt; Appropriate capital structure and balance sheet</li> <li>&gt; Portfolio-driven decision making process governed by senior executive-led committees</li> </ul> |   |

2019 generated accelerating Product Sales growth from outstanding New Medicine uptake, driving an increase to Core Operating profit.



“2019 delivered Product Sales growth of 12% (CER: 15%) to \$23.6 billion, with growth across all three main Therapy Areas and markets and outstanding performances by New Medicines with growth of 59% (CER: 62%)...”

### Accelerating Product Sales growth

2019 delivered Product Sales growth of 12% (CER: 15%) to \$23.6 billion, with growth across all three main Therapy Areas and markets and outstanding performances by New Medicines with growth of 59% (CER: 62%), led by *Tagrisso*, *Brilinta* and *Farxiga*, with *Lynparza* and *Imfinzi* also each delivering Product Sales of more than \$1 billion in the year. New Medicine sales represented 42% of Product Sales in 2019. Emerging Markets sales continued to grow at pace, increasing by 18% (CER: 24%), with China growth of 29% (CER: 35%) underpinned by encouraging New Medicine sales, which represented 19% of China Product Sales. New CVRM increased by 9% (CER: 12%) to \$4.4 billion with *Farxiga* and *Brilinta* continuing to demonstrate strong demand, achieving sales growth of 11% (CER: 14%) and 20% (CER: 23%), respectively, and delivering combined sales in excess of \$3 billion for 2019.

Collaboration Revenue declined by 21% (CER: 20%) to \$819 million. In spite of the anticipated reduction in collaboration activity, ongoing Collaboration Revenue from the MSD arrangement on *Lynparza* and selumetinib continues to contribute significantly, with \$610 million in 2019 (2018: \$790 million).

### Investing in future growth

Reported R&D expenses increased by 2% (CER: 5%) and Core R&D expenses increased by 1% (CER: 4%), both of which were partly driven by the promising investment in the development of *Enhertu* with Daiichi Sankyo. Reported SG&A expenses increased by 16% (CER: 20%) and Core SG&A expenses increased by 5% (CER: 8%), primarily due to the investment in additional personnel to support the China expansion strategy.

### Divestment activity

2019 Reported Other operating income was \$1.5 billion and included income from various disposal transactions, including the sale of the US rights to *Synagis* to Sobi and the sale of the global rights to *Losec* (excluding China, Japan, US and Mexico) to Cheplapharm.

Reported Operating profit declined by 14% (CER: 16%) to \$2.9 billion due to higher intangible asset impairments. Core Operating profit grew by 13% (CER: 13%) to \$6.4 billion in the year, driven by the growth of Product Sales. Reported EPS was \$1.03 and Core EPS was \$3.50.

### Share issuance generated \$3.5 billion

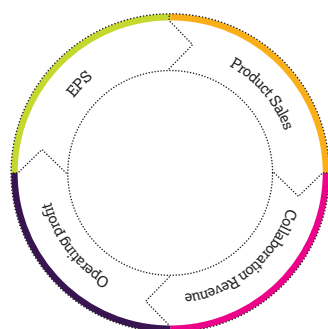
We generated a Net cash inflow from operating activities of \$3.0 billion in the year. In April 2019, we completed a placing of new Ordinary Shares, which generated proceeds of \$3.5 billion to fund the initial commitments arising from the Daiichi Sankyo collaboration as well as to support a reduction in Net debt. We ended the year with total gross debt of \$18.2 billion: \$6.3 billion of cash, investments and derivatives; with Net debt of \$11.9 billion down from \$13.0 billion in 2018.

Marc Dunoyer  
Chief Financial Officer



## Highlights

### Financial performance



#### Product Sales

**\$23.6bn**

Reported and Core  
(2018: \$21.0bn)

#### Collaboration Revenue

**\$0.8bn**

Reported and Core  
(2018: \$1.0bn)

#### Operating profit

**\$2.9bn**

14% decline – Reported  
(CER: 16%)

#### EPS

**\$1.03**

40% decline – Reported  
(CER: 44%)

**\$6.4bn**

13% growth – Core  
(CER: 13%)

**\$3.50**

1% growth – Core  
(CER: 0%)

### Sales platforms

#### Emerging Markets

**18%**

Growth  
(CER: 24%)

#### Respiratory

**10%**

Growth  
(CER: 13%)

#### New CVRM

**9%**

Growth  
(CER: 12%)

#### Japan

**27%**

Growth  
(CER: 26%)

#### Oncology

**44%**

Growth  
(CER: 47%)

### Summary performance in 2019

|  | Reported      |               |             | CER                               |  |             | Core          |               |           |
|--|---------------|---------------|-------------|-----------------------------------|--|-------------|---------------|---------------|-----------|
|  | 2019<br>\$m   | 2018<br>\$m   | % change    | CER<br>growth <sup>1</sup><br>\$m | Growth<br>due to<br>exchange<br>effects<br>\$m | % change    | 2019<br>\$m   | 2018<br>\$m   | % change  |
| Product Sales  | 23,565        | 21,049        | 12          | 3,155                             | (639)  | 15          | 23,565        | 21,049        | 12        |
| Collaboration Revenue                                      | 819           | 1,041         | (21)        | (210)                             | (12)   | (20)        | 819           | 1,041         | (21)      |
| <b>Total Revenue</b>                                       | <b>24,384</b> | <b>22,090</b> | <b>10</b>   | <b>2,945</b>                      | <b>(651)</b>                                   | <b>13</b>   | <b>24,384</b> | <b>22,090</b> | <b>10</b> |
| Cost of Sales  | (4,921)       | (4,936)       | –           | (226)                             | 241  | 5           | (4,761)       | (4,317)       | 10        |
| <b>Gross profit</b>  | <b>19,463</b> | <b>17,154</b> | <b>13</b>   | <b>2,719</b>                      | <b>(410)</b>                                   | <b>16</b>   | <b>19,623</b> | <b>17,773</b> | <b>10</b> |
| Operating expenses   | (18,080)      | (16,294)      | 11          | (2,295)                           | 509  | 14          | (14,748)      | (14,248)      | 4         |
| Other operating income and expense                         | 1,541         | 2,527         | (39)        | (969)                             | (17)   | (38)        | 1,561         | 2,147         | (27)      |
| <b>Operating profit</b>                                    | <b>2,924</b>  | <b>3,387</b>  | <b>(14)</b> | <b>(545)</b>                      | <b>82</b>                                      | <b>(16)</b> | <b>6,436</b>  | <b>5,672</b>  | <b>13</b> |
| Net finance expense  | (1,260)       | (1,281)       | (2)         | (55)                              | 76   |             | (765)         | (736)         | 4         |
| Share of after tax losses of joint ventures and associates | (116)         | (113)         | 3           | (5)                               | 2  |             | (116)         | (113)         | 3         |
| <b>Profit before tax</b>                                   | <b>1,548</b>  | <b>1,993</b>  | <b>(22)</b> | <b>(605)</b>                      | <b>160</b>                                     | <b>(29)</b> | <b>5,555</b>  | <b>4,823</b>  | <b>15</b> |
| Taxation   | (321)         | 57            | (663)       | (370)                             | (8)  |             | (1,109)       | (540)         | 105       |
| <b>Profit after tax</b>                                    | <b>1,227</b>  | <b>2,050</b>  | <b>(40)</b> | <b>(975)</b>                      | <b>152</b>                                     |             | <b>4,446</b>  | <b>4,283</b>  | <b>4</b>  |
| <b>Basic earnings per share (\$)</b>                       | <b>1.03</b>   | <b>1.70</b>   | <b>(40)</b> | <b>(0.79)</b>                     | <b>0.12</b>                                    | <b>(44)</b> | <b>3.50</b>   | <b>3.46</b>   | <b>1</b>  |

<sup>1</sup> As detailed on page 81, CER growth is calculated using prior year actual results adjusted for certain exchange rate effects including hedging.

# Financial Review

## *continued*

### **Business background and results overview**

The business background is covered in the Healthcare in a changing world section from page 11 and the Therapy Area Review from page 54, which describe in detail the developments in our products.

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

- > The risk of competition from generics following loss of patent protection or patent expiry of one of our products, or an 'at risk' launch by a competitor, or the launch of a competitive product in the same class as one of our products, with potential adverse effects on sales volumes and prices. Details of patent expiries for our key marketed products are included in Patent Expiries of Key Marketed Products from page 243.
- > The adverse impact on pharmaceutical prices as a result of the macroeconomic and regulatory environment. For instance, in the US, political leadership has continued to consider drug pricing controls and transparency measures at national and local levels. In other parts of the world, governments have continued to implement and expand price control measures, including reference pricing.
- > The timings of new product launches, which can be influenced by national regulators, the speed to market relative to competitor products and the risk that such new products do not succeed as anticipated, together with the rate of sales growth and costs following new product launches.
- > Currency fluctuations. Our functional and reporting currency is the US dollar, but we have substantial exposures to other currencies, in particular the Chinese renminbi, euro, Japanese yen, pound sterling and Swedish krona.
- > Macro factors such as greater demand from an ageing population and increasing requirements of Emerging Markets.
- > Supply chain risks including the failure of third parties to supply timely quality products, such as raw materials and the risk of catastrophic failure of critical internal processes leading to an inability to research, manufacture or supply products to patients.

Further details of the risks faced by the business are given in Risk Overview from page 74 and Risk from page 246.

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

### **Measuring performance**

The following measures are referred to in this Financial Review when reporting on our performance both in absolute terms, but more often in comparison to earlier years:

- > **Reported performance:** Reported performance takes into account all the factors (including those which we cannot influence, such as currency exchange rates) that have affected the results of our business, as reflected in our Group Financial Statements prepared in accordance with IFRSs as issued by the IASB (IFRS) and as adopted by the EU.
- > **Core performance:** Core financial measures are adjusted to exclude certain significant items, using a set of established principles. Readers should refer to our explanation of Core measures on page 81 for a detailed definition of this measure.

### **Use of non-GAAP performance measures**

Non-GAAP financial measures: Core financial measures, EBITDA, Net debt, Ongoing Collaboration Revenue and Initial Collaboration Revenue are non-GAAP financial measures because they cannot be derived directly from the Financial Statements.

Management believes that these non-GAAP financial measures, when provided in combination with Reported results, will provide investors with helpful supplementary information to better understand the financial performance and position of the Group on a comparable basis from period to period. These non-GAAP financial measures are not a substitute for, or superior to, financial measures prepared in accordance with GAAP.

By disclosing non-GAAP financial and growth measures, in addition to our Reported financial information, we are enhancing investors' ability to evaluate and analyse the financial performance and trends of our ongoing business and the related key business drivers. The adjustments are made to our Reported financial information in order to show non-GAAP financial measures that illustrate clearly, on a year-on-year or period-by-period basis, the impact on our performance caused by factors such as changes in revenues and expenses driven by volume, prices and cost levels relative to such prior years or periods.

As shown in the 2019 Reconciliation of Reported results to Core results table on page 84 our reconciliation of Reported financial information to Core financial measures includes a breakdown of the items for which our Reported financial information is adjusted, and a further breakdown by specific line item as such items are reflected in our Reported income statement. This illustrates the significant items that are excluded from Core financial measures and their impact on our Reported financial information, both as a whole and in respect of specific line items.

Management presents these results externally to meet investors' requirements for transparency and clarity. Core financial measures are also used internally in the management of our business performance, in our budgeting process and when determining compensation. As a result, Core financial measures merely allow investors to differentiate between different kinds of costs and they should not be used in isolation. Readers should also refer to our Reported financial information in the Summary performance in 2019 table, our reconciliation of Core financial measures to Reported financial information in the 2019 Reconciliation of Reported results to Core results table and the Excluded from Core results table on page 84 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.

### **Non-GAAP measures: definitions**

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

We strongly encourage readers of 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.

Definitions of non-GAAP measures are described on the next page.

## Non-GAAP measures: definitions

### Revenue

#### Constant exchange rate (CER) growth rates

□ Reconciliation, see page 84

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

**Why we use them:** CER measures allow us to focus on the changes in revenues and expenses driven by volume, prices and cost levels relative to the prior period. Revenues and cost growth expressed in CER allow management to understand the true local movement in revenues and costs, in order to compare recent trends and relative return on investment. CER growth rates can be used to analyse revenues in a number of ways but, most often, we consider CER growth by products and groups of products, and by countries and regions. CER revenue growth can be further analysed into the impact of revenue volumes and selling price. Similarly, CER cost growth helps us to focus on the real local change in costs so that we can manage the cost base effectively.

#### Ongoing Collaboration Revenue

□ Reconciliation, see page 83

**Definition:** Ongoing Collaboration Revenue is defined as Collaboration Revenue excluding Initial Collaboration Revenue (which is defined as Collaboration Revenue that is recognised at the point in time control is transferred). Ongoing Collaboration Revenue comprises, among other items, milestones, profit sharing and royalties. The updated category of Collaboration Revenue includes all income previously included within Externalisation Revenue. For more information please see Group Accounting Policies from page 172.

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

### Profitability

#### Core measures

□ Reconciliation, see page 84

**Core financial measures** are adjusted to exclude certain significant items. In determining the adjustments to arrive at the Core result, we use a set of established principles relating to the nature and materiality of individual items or groups of items, excluding, for example, events which are (i) outside the normal course of business, (ii) incurred in a pattern that is unrelated to the trends in the underlying financial performance of our ongoing business, or (iii) related to major acquisitions, to ensure that investors' ability to evaluate and analyse the underlying financial performance of our ongoing business is enhanced. See the 2019 Reconciliation of Reported results to Core results table on page 84 for a reconciliation of Reported to Core performance, as well as further details of the adjustments.

Core financial measures merely allow investors to differentiate between different kinds of cost and they should not be used in isolation.

**Restructuring costs**, including charges that relate to the impact of our global restructuring programmes on our capitalised manufacturing facilities and IT assets. These can take place over a significant period of time, given the long life-cycle of our business. We adjust for these charges and provisions because they primarily reflect the financial impact of change to legacy arrangements, rather than the underlying performance of our ongoing business. However, our Core results do reflect the benefits of such restructuring initiatives.

**Intangible amortisation and impairments**, including impairment reversals but excluding any charges relating to IT assets. These generally arise from business combinations and individual licence acquisitions. We adjust for these charges because their pattern of recognition is largely uncorrelated with the underlying performance of the business. However, a significant part of our revenues could not be generated without owning the associated acquired intangible assets.

**Other items**, principally comprising acquisition-related costs and credits, which include fair value adjustments and the imputed finance charge relating to contingent consideration on business combinations and legal settlements. It should 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 settlements costs, along with other acquisition-related costs, may recur in the future.

#### Gross margin percentage

□ Reconciliation, see page 84

**Definition:** The margin, as a percentage, by which Product Sales exceed the Cost of sales, calculated by dividing the difference between the two by the sales figure.

**Why we use it:** This measure sets out the progression of key performance margins and illustrates the overall quality of the business.

#### EBITDA

□ Reconciliation, see page 85

**Definition:** Reported Profit before tax plus Net finance expense, Share of after-tax losses of joint ventures and associates and charges for depreciation, amortisation and impairment.

**Why we use it:** EBITDA allows us to understand our baseline profitability, removing any 'non-operational' expenses that are not considered by management to be reflective of the underlying performance of the Group.

### Cash flow and liquidity

#### Net debt

□ Reconciliation, see page 87

**Definition:** Interest-bearing loans and borrowings net of Cash and cash equivalents, Other investments and Net derivative financial instruments.

**Why we use it:** Net debt is a measure that provides valuable additional information regarding the Group's net financial liabilities and is a measure commonly used by investors and rating agencies. It facilitates the tracking of one of our key financial priorities: deleveraging.

# Financial Review

## continued

### Revenue

Total Revenue for the year was up 10% (CER: 13%) to \$24,384 million, comprising Product Sales of \$23,565 million up 12% (CER: 15%) and Collaboration Revenue of \$819 million; a decrease of 21% (CER: 20%).

### Product Sales

#### By Geography

Product Sales in Emerging Markets continued to increase with growth of 18% (CER: 24%) to \$8,165 million in 2019. China Product Sales comprised 60% of Emerging Markets in the year, increasing by 29% (CER: 35%) to \$4,880 million. New Medicine sales, primarily driven by *Tagrisso* and *Lynparza* in Oncology and *Brilinta* and *Farxiga* in New CVRM represented 19% of China Product Sales. US Product Sales were up 13% to \$7,747 million, reflecting the success of the new Oncology medicines. In Europe, Product Sales declined by 2% (CER: increased by 2%) to \$4,349 million, reflecting a strong performance in Oncology, offset by a decline in *Nexium* of 73% (CER: 72%) and legacy Respiratory of 10% (CER: 5%) in the year. Established Rest of World Product Sales increased by 17% (CER: 18%) to \$3,305 million with sales in Japan up 27% (CER: 26%) to \$2,548 million.

#### By Product

Our largest selling products in 2019 were *Tagrisso* (\$3,189 million), *Symbicort* (\$2,495 million), *Brilinta* (\$1,581 million) and *Farxiga* (\$1,543 million). *Tagrisso* sales grew by 71% (CER: 74%) reflecting strong penetration across all markets. Global sales of *Symbicort* declined by 3% (CER: stable) with 11% growth in Emerging Markets (CER: 17%) being more than offset by declines in the US and Europe due to the impact of continued pricing pressure and managed market rebates. *Brilinta* Product Sales grew by 20% (CER: 23%), demonstrating continued strong patient uptake. *Farxiga* sales increased by 11% (CER: 14%), with growth of 40% in Emerging Markets (CER: 48%), offset by a 9% decline in the US (CER: 9%), where despite strong underlying demand, sales growth was adversely impacted by gross to net adjustments. There were also strong performances in the year from *Imfinzi* and *Lynparza*, with *Imfinzi* growing by 132% (CER: 133%) to \$1,469 million and *Lynparza* by 85% (CER: 89%) to \$1,198 million.

### Sales platforms

Our sales platforms include products in our three main Therapy Areas, and a focus on Emerging Markets and Japan. Sales platforms grew by 19% (CER: 22%), representing 90% of Total Revenue after removing the effect of certain Product Sales which are included in more than one sales platform.

#### Oncology

Product Sales of Oncology medicines increased to \$8,667 million in 2019 (2018: \$6,028 million), \$3,189 million of which came from *Tagrisso* (2018: \$1,860 million), which continues to be our leading medicine for the

### Sales platforms

|   | 2019<br>Product<br>Sales<br>\$m | 2018<br>Product<br>Sales<br>\$m | Actual<br>growth<br>% | CER<br>growth<br>% |
|---|---------------------------------|---------------------------------|-----------------------|--------------------|
| <b>Total sales platform Product Sales</b>   | <b>21,894</b>                   | 18,464                          | <b>19</b>             | <b>22</b>          |
| Individual sales platform Product Sales: (Certain Product Sales are included in more than one sales platform) |                                 |                                 |                       |                    |
| Oncology (total Oncology Product Sales)   | 8,667                           | 6,028                           | 44                    | 47                 |
| Emerging Markets  | 8,165                           | 6,891                           | 18                    | 24                 |
| Respiratory   | 5,391                           | 4,911                           | 10                    | 13                 |
| New CVRM (incorporating <i>Brilinta</i> and Diabetes)   | 4,376                           | 4,004                           | 9                     | 12                 |
| Japan   | 2,548                           | 2,004                           | 27                    | 26                 |
| <i>Reconciliation to Note 1 Revenue (page 180) as follows:</i>  |                                 |                                 |                       |                    |
| Sum of individual sales platforms   | 29,147                          | 23,838                          |                       |                    |
| Add: Product Sales not included in sales platforms  | 1,672                           | 2,585                           |                       |                    |
| Less: Product Sales double counted for Emerging Markets   |                                 |                                 |                       |                    |
| Oncology  | (2,211)                         | (1,528)                         |                       |                    |
| Respiratory   | (1,987)                         | (1,644)                         |                       |                    |
| New CVRM  | (1,133)                         | (850)                           |                       |                    |
| Less: Product Sales double counted for Japan  |                                 |                                 |                       |                    |
| Oncology  | (1,436)                         | (934)                           |                       |                    |
| Respiratory   | (377)                           | (318)                           |                       |                    |
| New CVRM  | (110)                           | (100)                           |                       |                    |
| <b>Total Product Sales</b>  | <b>23,565</b>                   | 21,049                          |                       |                    |

treatment of lung cancer and had received regulatory approval in more than 80 countries by the end of 2019.

#### Emerging Markets

Product Sales in Emerging Markets grew by 18% compared with 2018 (CER: 24%) to \$8,165 million partly driven by strong performances from New Medicines. Product Sales in China increased by 29% in 2019 (CER: 35%), representing 60% of Emerging Markets Product Sales in the year.

#### Respiratory

Product Sales of Respiratory medicines increased by 10% (CER: 13%) to \$5,391 million, with the impact of pricing pressure in the US for *Symbicort* being more than offset by a strong performance by Respiratory in Emerging Markets and higher demand for *Pulmicort* in China.

#### New CVRM

New CVRM grew by 9% (CER: 12%) with revenue of \$4,376 million. Within New CVRM, sales of *Brilinta* in the year were \$1,581 million, an increase of 20% (CER: 23%). *Brilinta* sales in the US were up 21% to \$710 million, as it remained the branded oral anti-platelet market leader. Diabetes Product Sales were 4% (CER: 6%) higher than in 2018, driven primarily by growth of 11% in *Farxiga* (CER: 14%) with global sales of \$1,543 million as it continued to be our largest-selling Diabetes medicine.

#### Japan

Japan Product Sales grew by 27% (CER: 26%) to \$2,548 million with *Tagrisso* growing by 100% (CER: 97%) and *Forxiga* by 16% (CER: 14%).

### Collaboration Revenue

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

#### MEDI8897 (Sanofi)

- > In March 2017, AstraZeneca announced an agreement to develop and commercialise MEDI8897 jointly with Sanofi. Under the terms of the global agreement, Sanofi made an upfront payment of €120 million and will pay up to €495 million upon achievement of certain development and sales-related milestones. All costs and profits are shared equally. The US element of this collaboration is subject to a participation agreement with Sobi, entered into in November 2018, effective 23 January 2019.
- > In July 2019, AstraZeneca received notification that the Phase III clinical milestone had been triggered, resulting in Collaboration Revenue of \$33 million being recognised in 2019.

#### Zoladex (TerSera)

- > In March 2017, AstraZeneca entered into an agreement with TerSera for the commercial rights to *Zoladex* in the US and Canada. TerSera paid \$250 million upon completion of the transaction. The Group will also receive sales-related income through milestones totalling up to \$70 million, as well as recurring quarterly sales-based payments at a mid-teen percent of Product Sales. AstraZeneca will also manufacture and supply *Zoladex* to TerSera, providing a further source of ongoing income from *Zoladex* in the US and Canada.
- > In December 2018, TerSera paid a sales-related milestone of \$35 million to AstraZeneca.

### Lynparza/selumetinib (MSD)

- > In July 2017, the Group announced a global strategic oncology collaboration with MSD to co-develop and co-commercialise AstraZeneca's *Lynparza* for multiple cancer types. Under the collaboration, the companies will develop and commercialise *Lynparza* jointly, both as monotherapy and in combination with other potential medicines. AstraZeneca and MSD will also jointly develop and commercialise AstraZeneca's selumetinib, currently being developed for multiple indications including thyroid cancer. Independently, AstraZeneca and MSD will develop and commercialise *Lynparza* in combination with their respective PD-L1 and PD-1 medicines, *Imfinzi* and *Keytruda*. Under the terms of the agreement, the two companies will share the development and commercialisation costs for *Lynparza* and selumetinib monotherapy and non-PD-L1/PD-1 combination therapy opportunities. Gross profits from *Lynparza* and selumetinib Product Sales generated through monotherapies or combination therapies will be shared equally. MSD will fund all development and commercialisation costs of *Keytruda* in combination with *Lynparza* or selumetinib. AstraZeneca will fund all development and commercialisation costs of *Imfinzi* in combination with *Lynparza* or selumetinib. AstraZeneca will continue to manufacture *Lynparza* and selumetinib. As part of the agreement, MSD will pay AstraZeneca up to \$8.5 billion in total consideration, including \$1.6 billion upfront, \$750 million for certain licence options and up to \$6.2 billion contingent upon successful achievement of future regulatory and sales milestones. Of the upfront payment of \$1.6 billion, \$1.0 billion was recognised as Collaboration Revenue on deal completion in 2017, with the remaining \$0.6 billion deferred to the balance sheet.
- > AstraZeneca will book all Product Sales of *Lynparza* and selumetinib; gross profits due to MSD under the collaboration will be recorded under Cost of sales.
- > In November 2017, MSD exercised the first licence option resulting in Collaboration Revenue of \$250 million.
- > In January 2018, the FDA expanded the approved use of *Lynparza* to include the treatment of patients with certain types of breast cancer. The approval triggered a \$70 million milestone payment from MSD to AstraZeneca.
- > In June 2018, net sales of *Lynparza* reached \$250 million cumulative sales threshold, triggering a sales-related milestone of \$100 million to fall due to AstraZeneca.
- > In November 2018, MSD exercised the second licence option resulting in Collaboration Revenue of \$400 million. In addition to the exercise of this option, net sales of *Lynparza* reached the \$500 million cumulative sales threshold, triggering a sales-related milestone of \$150 million to fall due to AstraZeneca.

### Collaboration Revenue<sup>1</sup>

|  | 2019<br>\$m | 2018<br>\$m |
|--|-------------|-------------|
| <b>Initial Collaboration Revenue</b>                 |             |             |
| <i>Crestor</i> (Almirall) – milestone                | –           | 61          |
| Other  | –           | 51          |
| <b>Total Initial Collaboration Revenue</b>           | <b>–</b>    | <b>112</b>  |
| <b>Ongoing Collaboration Revenue</b>                 |             |             |
| <i>Lynparza/selumetinib</i> (MSD) – option exercised | <b>100</b>  | 400         |
| <i>Lynparza/selumetinib</i> (MSD) – milestone        | <b>510</b>  | 390         |
| <i>Zoladex</i> (TerSera) – milestone                 | –           | 35          |
| <i>Crestor</i> (Almirall) – milestone                | <b>39</b>   | –           |
| MEDI8897 (Sanofi) – milestone                        | <b>33</b>   | –           |
| Royalties  | <b>62</b>   | 49          |
| Other  | <b>75</b>   | 55          |
| <b>Total Ongoing Collaboration Revenue</b>           | <b>819</b>  | 929         |
| <b>Total Collaboration Revenue</b>                   | <b>819</b>  | 1,041       |

<sup>1</sup> The updated category of Collaboration Revenue includes all income previously included within Externalisation Revenue. For more information please see Group Accounting Policies on page 173.

- > In December 2018, AstraZeneca was notified of an FDA approval of *Lynparza*, which triggered the SOLO-1 \$70 million milestone payment to AstraZeneca.
- > In April 2019, AstraZeneca was notified that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency had adopted a positive opinion recommending *Lynparza* as a 1st-line maintenance treatment of BRCA-mutated advanced ovarian cancer, which triggered an approval milestone, resulting in Collaboration Revenue of \$30 million.
- > In June 2019, AstraZeneca was notified that *Lynparza* had been approved in the EU as a maintenance treatment after 1st-line chemotherapy in patients with BRCA-mutated advanced ovarian cancer. This triggered an approval milestone, resulting in Collaboration Revenue of \$30 million.
- > In September 2019, AstraZeneca was notified that net sales of *Lynparza* had reached the \$750 million cumulative sales threshold, triggering a sales-related milestone, resulting in Collaboration Revenue of \$200 million.
- > In October 2019, MSD notified AstraZeneca of its intention to exercise the third and final licence option of the agreement. The payment of \$100 million was received in November 2019 and was recognised as Collaboration Revenue for 2019.
- > In November 2019, AstraZeneca received notification that net sales of *Lynparza* had reached the \$1 billion cumulative sales threshold triggering a sales-related payment of \$250 million, which has been recognised as Collaboration Revenue for 2019.

### *Crestor* (Almirall)

- > In December 2017, AstraZeneca entered into an agreement effective January 2018 with Almirall, under which Almirall is granted an exclusive and perpetual licence to distribute and undertake certain manufacturing activities related to *Crestor* and *Provisacor* in Spain. Almirall made an upfront payment of €51 million on completion of the deal and will pay additional sales-related milestones of up to €55 million plus a royalty for 10 years.
- > In 2019, AstraZeneca received notification that the three sales-related milestones had been met, triggering a payment of €35 million. Collaboration Revenue of \$39 million has been recognised in respect of these payments.

# Financial Review

## continued

### Income Statement

#### 2019 Reconciliation of Reported results to Core results

|   | 2019<br>Reported<br>\$m | Restructuring<br>costs<br>\$m | Intangible<br>amortisation<br>and<br>impairments<br>\$m | Diabetes<br>Alliance <sup>1</sup><br>\$m | Other <sup>2</sup><br>\$m | 2019<br>Core <sup>3</sup><br>\$m | Core 2019 compared with<br>Core 2018 <sup>3</sup> |                    |
|---|-------------------------|-------------------------------|---|--|---------------------------|----------------------------------|---|--------------------|
|   |                         |                               |   |  |                           |                                  | Actual<br>growth<br>%                             | CER<br>growth<br>% |
| <b>Gross profit</b>                             | 19,463                  | 73                            | 87  | –  | –                         | 19,623                           | 10  | 13                 |
| <i>Product Sales gross margin %<sup>4</sup></i> | 79.1                    |                               |   |  |                           | 79.8                             |   |                    |
| Distribution expenses                           | (339)                   | –                             | –   | –  | –                         | (339)                            | 2   | 7                  |
| Research and development expenses               | (6,059)                 | 101                           | 638   | –  | –                         | (5,320)                          | 1   | 4                  |
| Selling, general and administrative expenses    | (11,682)                | 173                           | 1,771   | (126)                                    | 775                       | (9,089)                          | 5   | 8                  |
| Other operating income and expense              | 1,541                   | –                             | 1   | –  | 19                        | 1,561                            | (27)  | (26)               |
| <b>Operating profit</b>                         | 2,924                   | 347                           | 2,497   | (126)                                    | 794                       | 6,436                            | 13  | 13                 |
| Operating margin as a % of Total Revenue        | 12.0                    |                               |   |  |                           | 26.4                             |   |                    |
| Net finance expense                             | (1,260)                 | –                             | –   | 287                                      | 208                       | (765)                            |   |                    |
| Taxation  | (321)                   | (66)                          | (519)   | (54)                                     | (149)                     | (1,109)                          |   |                    |
| Basic earnings per share (\$)                   | 1.03                    | 0.22                          | 1.52  | 0.08                                     | 0.65                      | 3.50                             | 1   | –                  |

#### 2018 Reconciliation of Reported results to Core results

|   | 2018<br>Reported<br>\$m | Restructuring<br>costs<br>\$m | Intangible<br>amortisation<br>and<br>impairments<br>\$m | Diabetes<br>Alliance <sup>1</sup><br>\$m | Other <sup>2</sup><br>\$m | 2018<br>Core <sup>3</sup><br>\$m | Core 2018 compared with<br>Core 2017 <sup>3</sup> |                    |
|---|-------------------------|-------------------------------|---|--|---------------------------|----------------------------------|---|--------------------|
|   |                         |                               |   |  |                           |                                  | Actual<br>growth<br>%                             | CER<br>growth<br>% |
| <b>Gross profit</b>                             | 17,154                  | 432                           | 187   | –  | –                         | 17,773                           | (4)   | (4)                |
| <i>Product Sales gross margin %<sup>4</sup></i> | 76.6                    |                               |   |  |                           | 79.5                             |   |                    |
| Distribution expenses                           | (331)                   | –                             | –   | –  | –                         | (331)                            | 7   | 6                  |
| Research and development expenses               | (5,932)                 | 94                            | 572   | –  | –                         | (5,266)                          | (3)   | (3)                |
| Selling, general and administrative expenses    | (10,031)                | 181                           | 1,582   | (60)                                     | (323)                     | (8,651)                          | 10  | 9                  |
| Other operating income and expense              | 2,527                   | (10)                          | 4   | –  | (374)                     | 2,147                            | 10  | 10                 |
| <b>Operating profit</b>                         | 3,387                   | 697                           | 2,345   | (60)                                     | (697)                     | 5,672                            | (17)  | (17)               |
| Operating margin as a % of Total Revenue        | 15.3                    |                               |   |  |                           | 25.7                             |   |                    |
| Net finance expense                             | (1,281)                 | –                             | –   | 337                                      | 208                       | (736)                            |   |                    |
| Taxation  | 57                      | (146)                         | (487)   | (73)                                     | 109                       | (540)                            |   |                    |
| Basic earnings per share (\$)                   | 1.70                    | 0.43                          | 1.47  | 0.16                                     | (0.30)                    | 3.46                             | (19)  | (19)               |

<sup>1</sup> Relating to the 2014 acquisition of BMS's share of Global Diabetes Alliance.

<sup>2</sup> See page 81 for further details of other adjustments.

<sup>3</sup> Each of the measures in the Core column in the above table is a non-GAAP measure.

<sup>4</sup> Gross margin as a % of Product Sales reflects Gross profit derived from Product Sales, divided by Product Sales.

#### Excluded from Core results

|  |  |
|--|--|
| <b>Restructuring costs</b>                     | > Restructuring expenses totalling \$347 million (2018: \$697 million) were driven by the Wedel site closure (\$62 million) and Finance Transformation (\$92 million), offset by a reversal of the 2018 impairment resulting from the announcement of the US Biologics site closures in Longmont and Boulder, CO (\$93 million).   |
| <b>Intangible amortisation and impairments</b> | > Amortisation totalling \$1,466 million (2018: \$1,663 million) relating to intangible assets, except those related to IT and to our acquisition of BMS's share of our Global Diabetes Alliance (which are separately detailed below). Further information on our intangible assets is contained in Note 10 to the Financial Statements from page 190.<br>> Intangible impairment charges of \$1,031 million (2018: \$683 million) excluding those related to IT. 2019 charges include \$533 million relating to the write down of the <i>Epanova</i> intangible asset. Further details relating to intangible asset impairments are included in Note 10 to the Financial Statements from page 190. |
| <b>Diabetes Alliance</b>                       | > Costs associated with our acquisition of BMS's share of our Global Diabetes Alliance in February 2014 amounting to \$161 million (2018: \$277 million), including a fair value credit of \$516 million, amortisation charges of \$390 million and discount unwind in Sweden and the US of \$287 million.   |
| <b>Other</b>                                   | > Other charges which include net legal provisions amounted to \$1,002 million (2018: credit of \$489 million). Further details of legal proceedings in which we are currently involved are contained within Note 29 to the Financial Statements from page 220.<br>> Also included in other charges are a \$208 million discount unwind charge (2018: \$208 million) and a \$69 million charge (2018: credit of \$126 million) for net fair value adjustments relating to contingent consideration and the Acerta Pharma put option arising on our other business combinations as detailed in Note 20 to the Financial Statements from page 199.   |

## Gross profit

Reported Gross profit increased by 13% (CER: 16%) to \$19,463 million. Core Gross profit increased by 10% (CER: 13%) to \$19,623 million. These increases reflected the growth in Product Sales.

## Operating expenses

Reported R&D expenses increased by 2% (CER: 5%) to \$6,059 million and Core R&D expenses increased by 1% (CER: 4%) to \$5,320 million. The increase of both Reported and Core R&D expenses in the year was partly as a result of investment in the development of *Enhertu*.

Reported SG&A expenses increased by 16% (CER: 20%) to \$11,682 million and Core SG&A expenses increased by 5% (CER: 8%) to \$9,089 million. The increase of both Reported and Core SG&A expenses was primarily driven by investment in headcount to support the China expansion strategy, as well as support for New Medicines. The difference between growth of Reported and Core SG&A expenses partly reflected the fair value adjustments arising on acquisition-related liabilities recognised in 2019, an increase in legal provisions and higher intangible impairment charges.

## Other operating income and expense

Reported Other operating income and expense in the year was down 39% (CER: 38%) at \$1,541 million and includes \$515 million on the sale of the US rights to *Synagis* to Sobi, \$243 million from the sale of the global rights to *Losec*, excluding the US, Japan, China and Mexico to Cheplapharm, \$213 million from the sale of the rights to *Seroquel* and *Seroquel XR* in the US, Canada, Europe and Russia to Cheplapharm and \$181 million on the sale of the rights to *Arimidex* and *Casodex* to Juvisé.

As these elements of our income arose from product divestments, where we no longer retain significant ongoing economic interest, in accordance with our Collaboration Revenue definition in the Accounting Policy note on page 173 and the requirements of IFRS 15 'Revenue from Contracts with Customers', proceeds from these divestments are recorded as Other operating income and expense.

## Operating profit

Reported Operating profit declined by 14% (CER: 16%) to \$2,924 million in the year. The Reported Operating margin declined by three percentage points (CER: four percentage points) to 12% of Total Revenue. Core Operating profit grew 13% (CER: 13%) in the year to \$6,436 million. The Core Operating profit margin increased by one percentage point to 26% of Total Revenue, as a result of operating leverage offset by a reduction in Other operating income and expense.

## Reconciliation of Reported Profit before tax to EBITDA

|  | 2019<br>\$m  | 2018<br>\$m  | Actual<br>growth<br>% | CER<br>growth<br>% |
|--|--------------|--------------|-----------------------|--------------------|
| Reported Profit before tax                                 | 1,548        | 1,993        | (22)                  | (29)               |
| Net finance expense  | 1,260        | 1,281        | (2)                   | 4                  |
| Share of after tax losses of joint ventures and associates | 116          | 113          | 3                     | 5                  |
| Depreciation, amortisation and impairment                  | 3,762        | 3,753        | -                     | 3                  |
| <b>EBITDA</b>  | <b>6,686</b> | <b>7,140</b> | <b>(6)</b>            | <b>(6)</b>         |

## Net finance expense

Reported Net finance expense decreased by 2% (CER: increased by 4%) in the year to \$1,260 million (2018: \$1,281 million). Core Net finance expense increased by 4% (CER: 10%) in the year to \$765 million. The increase to Reported and Core Net finance expense at CER partly reflected an adverse movement in loan interest, as well as the effect of the adoption of IFRS 16.

## Profit before tax

Reported Profit before tax declined by 22% (CER: 29%) in the year to \$1,548 million (2018: \$1,993 million), reflecting the increase in Operating expenses and the decrease in Other operating income and expense. Pre-tax adjustments to arrive at Core Profit before tax amounted to \$4,007 million in 2019 (2018: \$2,830 million), comprising \$3,512 million adjustments to Operating profit (2018: \$2,285 million) and \$495 million to Net finance expense (2018: \$545 million). EBITDA decreased by 6% (CER: 6%) to \$6,686 million.

## Taxation

The Reported tax rate in the year was 21% and the Core tax rate was 20%. These tax rates were higher than the UK Corporation Tax Rate due to the impact of the geographical mix of profits.

The income tax paid for the year was \$1,118 million (72% of Reported Profit before tax). This was \$797 million higher than the Reported tax charge for the year, which benefited from a net deferred tax credit of \$988 million (2018: \$806 million), relating to the elimination of unrealised profit on inventory, intangible amortisation and impairment, other deferred tax items and \$218 million provision releases following the expiry of the statute of limitations or the conclusion of tax authority review, partially offset by net increases in provisions for tax contingencies.

Additional information on these items is contained in Note 4 from page 183 to the Financial Statements.

We pay corporate income taxes, customs duties, excise taxes, stamp duties, employment and many other business taxes in all jurisdictions where applicable. In addition, we collect and pay employee taxes and indirect taxes such as value-added tax.

## Total comprehensive income

Total comprehensive income decreased by \$375 million from the prior year, resulting in net income of \$616 million for 2019. The decrease in Other comprehensive income was primarily driven by the Remeasurement of the defined benefit pension liability of \$364 million (2018: \$46 million), Foreign exchange losses arising on designating borrowings in net investment hedges of \$252 million (2018: \$520 million) and Fair value movements on cash flow hedges of \$101 million (2018: \$37 million).

## EPS

Reported EPS of \$1.03 in the year represented a decline of 40% (CER: 44%). The performance was driven by a decline in Collaboration Revenue and Other operating income and expense and increased Operating expenses. Core EPS in the year grew by 1% (CER: stable) to \$3.50. The difference between the Reported and Core performance in 2019 was due to an increase in legal provisions, revaluation movements on acquisition-related liabilities and higher intangible impairment charges.

## Restructuring

Since 2007, we have undertaken significant efforts to restructure and reshape our business to improve our long-term competitiveness. The first phases of this restructuring, involving the integration of MedImmune, efficiencies within the R&D function and a reduction in SG&A expenses, were completed in 2011. The targeted commercial restructuring announced in 2015 has also been successfully completed with a total cost of \$151 million.

In 2016, we announced plans to advance our strategy through sharper focus by streamlining operations, primarily in Commercial and Manufacturing, to redeploy investment to key Therapy Areas, particularly Oncology. Restructuring costs associated with this programme were initially forecast to be \$1.5 billion by the end of 2017 and generate net annualised benefits of \$1.1 billion by 2018. The total cost estimate is now \$1.3 billion to be incurred by the end of 2020, with benefits expected to be \$1.1 billion in 2020. In addition to the 2016 plan, there are two further active programmes. The first is the continuation of the Phase 3 restructuring that was announced in 2012, superseded by Phase 4 in 2013 and subsequently expanded in 2014. This initiative consists of centralisation of our global R&D footprint into three strategic centres,

## Financial Review *continued*

transformation of the IT organisation, closure of a number of manufacturing facilities and other activities to simplify and streamline the organisation. At the time of the announcement, the Phase 4 programme was estimated to incur \$3.2 billion of costs and deliver \$1.1 billion of annualised benefits by 2016. By the end of 2019, the Phase 4 programme had incurred costs of \$3.6 billion, creating headroom for investment in our pipeline and launch capability. The Phase 4 programme is now expected to complete in 2022 with total programme costs estimated to be \$3.8 billion and annualised benefits of \$1.2 billion.

The second step was initiated in 2016 and relates to multi-year transformation programmes within our SG&A functions (principally Finance and HR) with anticipated costs by the end of 2018 of \$270 million. At the time of the announcement, we expected these transformation programmes to deliver annualised benefits of \$111 million by 2020. By the end of 2019, these programmes had incurred costs of \$398 million with total expected costs rising to \$441 million.

The aggregate restructuring charge incurred in 2019 across all our restructuring programmes was \$347 million (2018: \$697 million), net of a \$93 million credit relating to the impairment reversal on Longmont and Boulder, CO, and including the ongoing integration of other acquired assets. Final estimates for programme costs, benefits and headcount impact in all functions are subject to completion of the requisite consultation in the various areas.

Our priority as we undertake these restructuring initiatives is to work with our affected employees on the proposed changes, acting in accordance with relevant local consultation requirements and employment law.

### **Brexit readiness preparations and planning**

Following the UK referendum outcome in June 2016 for the UK to leave the EU, the UK Government and European Commission negotiated the terms on which the UK would leave the EU and the framework for the future relationship. In January 2020, Royal Assent of the European Union (Withdrawal Agreement) Act by the UK Parliament was granted and the Withdrawal Agreement was ratified by the European Parliament. The UK left the EU on 31 January 2020 with a transition period running to 31 December 2020. Immediately after the UK left the EU, the UK Government and European Commission began the process of negotiating the future relationship which, if the negotiations are successfully concluded and ratified in the UK and EU, would apply after the end of the transition period. At this time, it remains unclear whether an agreement will be reached on the future relationship before the end of the transition

period and if it would be ratified by the UK Parliament and the European Parliament. In the absence of a ratified future relationship agreement at the end of the transition period, it is unclear what trading relationships the UK will have with the EU and other significant trading partners after 31 December 2020 given the range of political and legal options. Until the future relationship negotiation process is completed, it is difficult to anticipate the potential impact on our market share, sales, profitability, cash flows and results of operations.

In response to the UK referendum outcome and in light of the UK parliamentary impasse on Brexit since the date of the referendum until the UK general election on 12 December 2019, the Group took the decision to implement appropriate actions to mitigate where possible the potential risk of disruption to the supply of medicines (including potential new medicines currently undergoing clinical trials), including duplication of release testing and procedures for products based in the EU27 and the UK, transfer of regulatory licences, customs and duties set up for the introduction or amendment of existing tariffs or processes and associated IT systems reconfiguration. In addition, the Group engaged with its major suppliers to assess their readiness and continues to work with them to mitigate the risk of disruption to supply chains which could arise at the end of the transition period.

The costs associated with this and certain other actions directly related to Brexit will be charged as restructuring, with the majority of such costs expected to be cash costs. The current estimate of these costs is approximately \$40 million. However, until the process to determine the future relationship is concluded by the UK and EU parliaments and the impacts of transition to any new arrangement between them are known with clarity, it is difficult to anticipate the overall potential impact on the Group's operations and hence the final expected costs to be incurred.

### **Cash flow and liquidity – for the year ended 31 December 2019**

Net cash generated from operating activities was \$2,969 million for 2019 (2018: \$2,618 million). The increase to Operating cash inflows reflected the underlying improvement in business performance, combined with favourable working capital movements, partly offset by an increase in Tax paid, reflecting the phasing of tax payments between periods and the impact of 2018 refunds.

Net investment cash outflows were \$1,130 million (2018: inflow of \$443 million).

Investment cash outflows for 2019 include \$709 million (2018: \$349 million) of Payments of contingent consideration arising on business combinations and \$1,481 million (2018: \$328 million) for the purchase of other intangible assets, including the first of two \$675 million

upfront payments to Daiichi Sankyo, as part of the strategic collaboration on *Enhertu* and the impact of a final true up net payment of \$413 million to MSD.

Investment cash inflows include \$2,076 million (2018: \$2,338 million) from the sale of intangible assets, including \$821 million on the sale of the US rights to *Synagis* to Sobi, \$243 million from the sale of the global rights to *Losec* excluding the US, Japan, China and Mexico to Cheplapharm, \$181 million on the sale of the rights to *Arimidex* and *Casodex* to Juvisé and \$178 million from the sale of the rights to *Seroquel* and *Seroquel XR* in Europe and Russia to Cheplapharm. The comparative period in 2018 included \$700 million on the sale of *Nexium* rights in Europe to Grünenthal, \$482 million relating to the 2017 sale of our remaining anaesthetic portfolio to Aspen, \$354 million on the sale of *Alvesco*, *Omnaris* and *Zetonna* rights outside the US to Covis Pharma, \$275 million from the sale of UK, China and other international regions' rights to *Seroquel XR* and *Seroquel* IR to Luye Pharma and \$205 million from the sale of European rights to *Atacand* to Cheplapharm.

Net cash distributions to shareholders were \$67 million (2018: \$3,450 million), including proceeds from the issue of Share capital of \$3,525 million (2018: \$nil) and the proceeds from the exercise of share options of \$32 million (2018: \$34 million) less dividends paid of \$3,592 million (2018: \$3,484 million).

### **Bonds**

In 2019, AstraZeneca repaid a \$1.0 billion 1.95% bond, which matured in September 2019. There were no bonds issued in 2019. In August 2018, AstraZeneca issued \$3.0 billion of bonds in the US dollar debt capital markets with maturities of five, 10 and 30 years and repaid a \$1.0 billion 1.75% bond and a \$0.4 billion floating rate bond, both of which matured in November 2018.

### **Debt**

At 31 December 2019, outstanding gross debt (interest-bearing loans and borrowings) was \$18,227 million (2018: \$19,113 million). Of the gross debt outstanding \$2,010 million is due within one year (2018: \$1,754 million). On 1 January 2019, the Group adopted IFRS 16, which eliminates the classification of leases as either operating or finance leases. The adoption of the new standard has resulted in the initial recognition of Lease liabilities of \$720 million at 1 January 2019. Net debt at 31 December 2019 was \$11,904 million, compared with \$13,003 million at the beginning of the year, as a result of the cash flows and Lease liabilities as described above. At 31 December 2019, Cash and cash equivalents and liquid investments totalled \$6,280 million (2018: \$5,726 million) and undrawn committed cash facilities totalled \$4,125 million (2018: \$4,125 million).



## Summary cash flows

|   | 2019<br>\$m     | 2018<br>\$m | 2017<br>\$m |
|---|-----------------|-------------|-------------|
| <b>Net debt brought forward at 1 January</b>  | <b>(13,003)</b> | (12,679)    | (10,657)    |
| Profit before tax   | 1,548           | 1,993       | 2,227       |
| Sum of changes in interest, depreciation, amortisation, impairment and share of after tax losses on joint ventures and associates | 5,138           | 5,147       | 4,486       |
| Movement in working capital and short-term provisions   | (346)           | (639)       | (50)        |
| Tax paid  | (1,118)         | (537)       | (454)       |
| Interest paid   | (774)           | (676)       | (698)       |
| Gains on disposal of intangible assets  | (1,243)         | (1,885)     | (1,518)     |
| Fair value movements on contingent consideration arising from business combinations   | (614)           | (495)       | 109         |
| Non-cash and other movements  | 378             | (290)       | (524)       |
| <b>Net cash available from operating activities</b>   | <b>2,969</b>    | 2,618       | 3,578       |
| Disposal of intangibles (net of purchases)  | 595             | 2,010       | 1,082       |
| Non-contingent payments on business combinations  | –               | –           | (1,450)     |
| Payment of contingent consideration from business combinations  | (709)           | (349)       | (434)       |
| Other capital expenditure (net)   | (1,016)         | (1,218)     | (1,319)     |
| <b>Investments</b>  | <b>(1,130)</b>  | 443         | (2,121)     |
| Dividends   | (3,592)         | (3,484)     | (3,519)     |
| Share proceeds  | 3,525           | 34          | 43          |
| <b>Distributions</b>  | <b>(67)</b>     | (3,450)     | (3,476)     |
| Lease liabilities: IFRS 16 <sup>3</sup>   | (675)           | –           | –           |
| Other movements   | 2               | 65          | (3)         |
| <b>Net debt carried forward at 31 December</b>  | <b>(11,904)</b> | (13,003)    | (12,679)    |

## Bonds issued in 2019 and 2018

|                              | Repayment dates | Face value of bond \$m | Net book value of bond at 31 December 2019 \$m |
|------------------------------|-----------------|------------------------|--|
| <b>Bonds issued in 2019:</b> |                 |                        |  |
| <b>Total 2019</b>            |                 | –                      | –  |
| <b>Bonds issued in 2018:</b> |                 |                        |  |
| 3.5% USD bond                | 2023            | 850                    | 845  |
| Floating rate USD notes      | 2023            | 400                    | 400  |
| 4% USD bond                  | 2029            | 1,000                  | 992  |
| 4.375% USD bond              | 2048            | 750                    | 736  |
| <b>Total 2018</b>            |                 | 3,000                  | 2,973  |

## Net debt reconciliation

|                                      | 2019<br>\$m        | 2018<br>\$m | 2017<br>\$m |
|--------------------------------------|--------------------|-------------|-------------|
| Cash and cash equivalents            | 5,369              | 4,831       | 3,324       |
| Other investments <sup>1,2</sup>     | 911                | 895         | 1,300       |
| <b>Cash and investments</b>          | <b>6,280</b>       | 5,726       | 4,624       |
| Overdraft and short-term borrowings  | (225)              | (755)       | (845)       |
| Lease liabilities                    | (675) <sup>3</sup> | –           | (5)         |
| Current instalments of loans         | (1,597)            | (999)       | (1,397)     |
| Loans due after one year             | (15,730)           | (17,359)    | (15,560)    |
| <b>Loans and borrowings</b>          | <b>(18,227)</b>    | (19,113)    | (17,807)    |
| Net derivative financial instruments | 43                 | 384         | 504         |
| <b>Net debt</b>                      | <b>(11,904)</b>    | (13,003)    | (12,679)    |

<sup>1</sup> Other investments in 2019 include \$62 million (2018: \$46 million) of non-current Treasury investments.

<sup>2</sup> Other investments include non-current investments, which are included within the balance of \$1,401 million (2018: \$833 million) in the Statement of Financial Position on page 169. The equivalent GAAP measure to Net debt is 'liabilities arising from financing activities', which excludes the amounts for cash and overdrafts, other investments and non-financing derivatives shown above and includes the Acerta Pharma put option of \$2,146 million (2018: \$1,838 million) shown in non-current other payables.

<sup>3</sup> Included in the Net debt reconciliation for 2019 are Lease liabilities of \$675 million, which arose on the adoption of IFRS 16 on 1 January 2019. Please see 'Group Accounting Policies' from page 172 and Note 8 'Leases' on page 189 for more information.

## Financial position – 31 December 2019

All data in this section is on a Reported basis.

## Property, plant and equipment

In 2019, Property, plant and equipment increased by \$267 million to \$7,688 million with additions of \$996 million (2018: \$1,034 million), impairments of \$53 million (2018: charge of \$291 million) and exchange adjustments of \$3 million (2018: credit of \$301 million) offset by depreciation of \$647 million (2018: \$614 million) and disposals and other movements of \$138 million (2018: \$22 million).

## Right-of-use assets

Following the adoption of IFRS 16 on 1 January 2019, the Group have recognised Lease liabilities and corresponding Right-of-use assets for arrangements that were previously classified as Operating leases. Right-of-use assets at 31 December 2019 were \$647 million (2018: \$nil).

## Business combinations

No business acquisitions were made in 2019, 2018 or 2017.

## Goodwill and intangible assets

Our goodwill of \$11,668 million (2018: \$11,707 million) principally arose on the acquisition of MedImmune in 2007, the restructuring of our US joint venture with MSD in 1998 and the acquisition of BMS's share of the Global Diabetes Alliance.

Intangible assets amounted to \$20,833 million at 31 December 2019 (2018: \$21,959 million). The decrease was mainly driven by amortisation in the year of \$1,928 million (2018: \$2,165 million). Intangible asset additions were \$2,001 million in 2019 (2018: \$513 million), \$1.7 billion of which arose from the strategic collaboration with Daiichi Sankyo on *Enherthu*. Impairment charges in the year were \$1,033 million (2018: \$683 million) including impairments on *Epanova*, *Bydureon*, *Qtern*, *Eklira* and *FluMist*. Disposals of intangible assets totalled \$10 million in the year (2018: \$339 million).

Further details of our additions to Intangible assets, and impairments recorded, are included in Note 10 to the Financial Statements from page 190.

## Assets held for sale

Assets held for sale of \$70 million comprise tangible assets relating to the Boulder manufacturing site. In 2018, Assets held for sale of \$982 million comprised mainly tangible assets relating to the US rights to *Synagis* arising from the acquisition of MedImmune.

## Receivables, payables and provisions

Total current and non-current Trade and other receivables increased by \$412 million with current Trade and other receivables increasing by \$187 million to \$5,761 million as a result of higher invoiced sales in China and a reduction in debt factoring in the US.

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Trade and other payables increased by \$667 million in 2019 to \$20,278 million. The increase was due to the recognition of payables in relation to the strategic collaboration, entered into during the year, with Daiichi Sankyo on *Enhertu*, offset by reductions in contingent consideration liabilities arising on business combinations.

The increase to Provisions of \$673 million in 2019 was primarily driven by a \$444 million increase to legal provisions. Further details of the charges made against provisions are contained in Notes 21 and 29 to the Financial Statements from pages 200 and 220 respectively.

The divestment of the US rights to *Synagis*, which completed in 2019, included \$150 million held as a financial liability. AstraZeneca will also receive \$175 million following the submission of the Biologics License Application (BLA) for MEDI8897, potential net payments of \$110 million for other MEDI8897 profit-related milestones and \$60 million in non-contingent payments for MEDI8897 during the period from 2019 to 2021.

#### Contingent consideration

The majority of our business acquisitions have included elements of consideration that are contingent on future development and/or sales milestones, with both the Diabetes and Respiratory acquisitions in 2014 also including royalty payments linked to future revenues. The acquisitions of ZS Pharma in 2015 and Acerta Pharma in 2016 had no contingent consideration element and there were no relevant acquisitions in 2017, 2018 and 2019.

Our agreement with BMS provides for various sales-related royalty payments up until 2025. Our transaction with Almirall includes further payments of up to \$0.6 billion for future development, launch, and various other sales-related milestone payments, and sales-related royalty payments as detailed in Note 20 to the Financial Statements from page 199.

All these future payments are treated as contingent consideration liabilities, and are fair valued using decision-tree analyses, with key assumptions, including the probability of success, the potential for delays and the expected levels of future revenues. The fair value is updated at each reporting date to reflect our latest estimate of the probabilities of these key assumptions. Given the long-term nature of the liabilities, the fair value calculation includes the discounting of future potential payments to their present value using discount rates appropriate to the period over which payments are likely to be made. Over time, as the target date of a consideration payment approaches, the discount in absolute terms of such future potential payment to its present value decreases. Therefore, in each period we take a corresponding charge reflecting the passage of time. We refer to this charge as 'Discount unwind'. The calculation of the fair value is considered to be a key estimate.

#### Summary statement of financial position – 31 December

All data in this section are on a Reported basis

|   | 2019<br>\$m   | Movement<br>\$m | 2018<br>\$m   | Movement<br>\$m | 2017<br>\$m   |
|---|---------------|-----------------|---------------|-----------------|---------------|
| Property, plant and equipment   | 7,688         | 267             | 7,421         | (194)           | 7,615         |
| Right-of-use assets   | 647           | 647             | –             | –               | –             |
| Goodwill and intangible assets  | 32,501        | (1,165)         | 33,666        | (4,347)         | 38,013        |
| Assets held for sale  | 70            | (912)           | 982           | 982             | –             |
| Inventories   | 3,193         | 303             | 2,890         | (145)           | 3,035         |
| Trade and other receivables   | 6,501         | 412             | 6,089         | 233             | 5,856         |
| Net deferred tax assets   | 228           | 1,135           | (907)         | 899             | (1,806)       |
| Trade and other payables  | (20,278)      | (667)           | (19,611)      | (130)           | (19,481)      |
| Provisions  | (1,564)       | (673)           | (891)         | 577             | (1,468)       |
| Net income tax payable  | (1,076)       | (119)           | (957)         | (131)           | (826)         |
| Retirement benefit obligations  | (2,807)       | (296)           | (2,511)       | 72              | (2,583)       |
| Non-current other investments<br>(excluding Treasury investments of<br>\$62m in 2019 (2018: \$46m)) | 1,339         | 552             | 787           | (76)            | 863           |
| Investments in associates and joint<br>ventures   | 58            | (31)            | 89            | (14)            | 103           |
| Net debt  | (11,904)      | 1,099           | (13,003)      | (324)           | (12,679)      |
| <b>Net assets</b>   | <b>14,596</b> | <b>552</b>      | <b>14,044</b> | <b>(2,598)</b>  | <b>16,642</b> |

#### Contingent consideration arising on business combinations

|                        | 2019  |  |                      | 2018  |  |                      |
|------------------------|---|--|----------------------|---|--|----------------------|
|                        | Acquisition of<br>BMS's share<br>of Diabetes<br>Alliance<br>\$m | Other<br>business<br>combinations<br>\$m | Total<br>2019<br>\$m | Acquisition of<br>BMS's share<br>of Diabetes<br>Alliance<br>\$m | Other<br>business<br>combinations<br>\$m | Total<br>2018<br>\$m |
| At 1 January           | 3,983   | 1,123                                    | 5,106                | 4,477   | 1,057                                    | 5,534                |
| Settlements            | (454)   | (255)                                    | (709)                | (349)   | –  | (349)                |
| Fair value adjustments | (516)   | (98)                                     | (614)                | (482)   | (13)                                     | (495)                |
| Discount unwind        | 287   | 69                                       | 356                  | 337   | 79                                       | 416                  |
| <b>At 31 December</b>  | <b>3,300</b>  | <b>839</b>                               | <b>4,139</b>         | <b>3,983</b>  | <b>1,123</b>                             | <b>5,106</b>         |

#### Payments due by period

|   | Less than<br>1 year<br>\$m | 1-3 years<br>\$m | 3-5 years<br>\$m | Over<br>5 years<br>\$m | Total<br>2019<br>\$m | Total<br>2018<br>\$m |
|---|----------------------------|------------------|------------------|------------------------|----------------------|----------------------|
| Bank loans and<br>other borrowings <sup>1</sup> | 2,441                      | 3,794            | 3,547            | 15,906                 | 25,688               | 27,923               |
| Lease liabilities <sup>2</sup>                  | 205                        | 275              | 129              | 128                    | 737                  | –                    |
| Operating leases                                | –                          | –                | –                | –                      | –                    | 684                  |
| Contracted capital<br>expenditure               | –                          | –                | –                | 396                    | 396                  | 625                  |
| <b>Total</b>                                    | <b>2,646</b>               | <b>4,069</b>     | <b>3,676</b>     | <b>16,430</b>          | <b>26,821</b>        | <b>29,232</b>        |

<sup>1</sup> Bank loans and other borrowings include interest charges payable in the period, as detailed in Note 27 to the Financial Statements from page 210.

<sup>2</sup> Lease liabilities arose on the adoption of IFRS 16 on 1 January 2019. Please see Note 8 "Leases" on page 189 for more information.

#### Dividends for 2019

|                         | \$          | Pence        | SEK          | Payment date     |
|-------------------------|-------------|--------------|--------------|------------------|
| First interim dividend  | 0.90        | 71.9         | 8.49         | 9 September 2019 |
| Second interim dividend | 1.90        | 146.4        | 18.32        | 30 March 2020    |
| <b>Total</b>            | <b>2.80</b> | <b>218.3</b> | <b>26.81</b> |                  |

Both the Discount unwind and any movements on the fair value of the underlying future payments can result in significant income statement movements. As detailed in the Excluded from Core section on page 84, these movements are treated as non-Core items in our Reconciliation of Reported results to Core results. In 2019, we recorded an interest charge of \$356 million on the Discount unwind on contingent consideration arising on our business combinations, and a net fair value decrease on contingent consideration of \$614 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, particularly relating to *Faxiga*, due to the competitiveness of the diabetes market. At 31 December 2019, our contingent consideration liability was \$4,139 million (2018: \$5,106 million) with the movements of the balance detailed in the table on page 88.

#### Tax payable and receivable

Net income tax payable has increased by \$119 million (2018: \$131 million) to \$1,076 million, principally due to cash tax timing differences. The tax receivable balance of \$285 million (2018: \$207 million) principally relates to cash tax timing differences.

Net deferred tax liabilities reduced by \$1,135 million (2018: \$899 million) in the year, resulting in a Net deferred tax asset of \$228 million, due to movements in deferred tax arising on the elimination of unrealised profit on inventory and associated with intangible amortisation and impairment.

Additional information on the movement in deferred tax balances is contained in Note 4 to the Financial Statements from page 183.

#### Retirement benefit obligations

In terms of the Group's major defined benefit plans, approximately 91% of our total retirement defined benefit obligations (or around 80% of net obligations) are concentrated in the UK, the US and Sweden. In the UK and US, we have now largely legacy arrangements as they have been closed to new entrants since 2000. In line with local regulations, the collectively bargained Swedish plan is still open to employees born before 1979.

Retirement benefit obligations increased by \$296 million in 2019 (2018: decrease of \$72 million) to \$2,807 million. Net remeasurement adjustments of \$364 million arose principally from lower discount rate assumptions in the UK, US and Sweden driven by falls in long-term bond yields, which increased the present value of the liabilities, partially offset by higher than expected investment performance. Employer contributions to the pension schemes of \$175 million helped offset the increase in the net obligations. Benefits paid amounted to \$512 million (2018: \$620 million).

In the UK, a High Court judgment was issued on 26 October 2018 relating to an element of pension benefits known as Guaranteed Minimum Pensions (GMPs). The ruling requires the equalisation of member benefits to address gender inequality in instances where GMP benefits are currently unequal. The Group made a provision in 2018 of £17 million (\$23 million) in past service costs for the estimated financial impact of this ruling on the UK pension fund. Discussions between the Trustee and the Company are ongoing to determine the exact impact.

Separate from this, following a review of the UK Pension Fund's administrative practice and Fund Rules, a decision was made in July 2019 to change the way in which GMP is calculated. This change applies to all future pension payments from November 2019. A past service net credit of £38 million (\$49 million) has been recognised in respect of these changes for the year ended 31 December 2019.

The Group has undertaken several initiatives to reduce our net defined benefit pension obligation exposure and manage the associated long-term financial risks. As well as paying cash contributions when required, in the UK, a freeze on pensionable pay has been in effect from 30 June 2010. In the US, both the qualified and non-qualified US pension plans were closed to future accrual in December 2017. Furthermore, liability management exercises have been carried out in the UK, including a Pension Increase Exchange exercise in 2016/2017 along with improvements to the 'at retirement' process to better support members in their retirement decisions.

Further details of our accounting for post-retirement benefit plans are included in Note 22 to the Financial Statements from page 201.

#### Commitments and contingencies

We have commitments and contingencies which are accounted for in accordance with the accounting policies described in the Financial Statements in the Group Accounting Policies section from page 172.

We also have taxation contingencies. These are described in the Taxation section in the Critical accounting policies and estimates section from page 91 and in Note 29 to the Financial Statements from page 220.

#### Off-balance sheet transactions and commitments

We have no off-balance sheet arrangements and our derivative activities are non-speculative. The table on page 88 sets out our minimum contractual obligations at the year end.

#### Research and development collaboration payments

Details of future potential R&D collaboration payments are also included in Note 29 to the Financial Statements on page 220. As detailed in Note 29, payments to our collaboration partners may not become payable due to the inherent uncertainty in achieving the development and revenue milestones linked to the future payments. We may enter into further collaboration projects in the future that may include milestone payments and, therefore, as certain milestone payments fail to crystallise due to, for example, development not proceeding, they may be replaced by potential payments under new collaborations.

#### Investments, divestments and capital expenditure

We have completed over 150 major or strategically important business development transactions over the past three years.

In addition to the business development transactions detailed under Collaboration Revenue from page 82 of this Financial Review, the following significant collaborations remain in the development phase:

#### Daiichi Sankyo

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

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#### Innate Pharma

- > In April 2015, we entered into two oncology agreements with Innate Pharma: firstly, a licence which provides us with exclusive global rights to co-develop and commercialise IPH2201 in combination with *Imfinzi* and, secondly, an option to license exclusive global rights to co-develop and commercialise IPH2201 in monotherapy and other combinations in certain treatment areas. Under the terms of the combination licence, we assumed exclusive global rights to research, develop and commercialise IPH2201 in combination with *Imfinzi*. We jointly fund Phase II studies with Innate Pharma and we lead the execution of these studies. Under the terms of the agreements, we made an initial payment to Innate Pharma of \$250 million, which included the consideration for exclusive global rights to co-develop and commercialise IPH2201 in combination with *Imfinzi*, as well as access to IPH2201 in monotherapy and other combinations in certain treatment areas. The agreement includes a Phase III initiation milestone of \$100 million, as well as additional regulatory and sales-related milestones. We record all sales and will pay Innate Pharma double-digit royalties on net sales. The arrangement includes the right for Innate Pharma to co-promote in Europe for a 50% profit share in the territory.
- > In October 2018, we exercised our option over IPH2201, and simultaneously entered into a further multi-element transaction with Innate Pharma. Under the agreement, we paid \$50 million to collaborate on, and acquire an option to license, IPH5201, a first-in-class anti-CD39 mAb. Additionally, we paid \$20 million to acquire options over four future programmes currently being developed by Innate Pharma, and paid €62.6 million to acquire a 9.8% stake in Innate Pharma. The \$100 million option fee and \$50 million and the premium paid over market price for the investment in Innate Pharma have been capitalised as intangible assets. The payment for future programmes will be expensed as research and development expenditure over four years. At the same time, we licensed the EU and US rights to *Lumoxiti* to Innate Pharma for \$50 million upfront plus future milestone payments of up to \$25 million.

#### FibroGen

- > In July 2013, we entered into a strategic collaboration with FibroGen to develop and commercialise roxadustat (FG-4592), a first-in-class oral compound in late-stage development for the treatment of anaemia from chronic kidney disease and end-stage renal disease (ESRD). This broad collaboration focuses on the US, China and all major markets excluding Japan, Europe, the CIS, the Middle East and South Africa, which are covered by an existing agreement between FibroGen and Astellas. Under the arrangement, we agreed to pay FibroGen

upfront and subsequent non-contingent payments totalling \$350 million, as well as potential development-related milestone payments of up to \$465 million, and potential future sales-related milestone payments, in addition to tiered royalty payments on future sales of roxadustat in the low 20% range. Additional development milestones will be payable for any subsequent indications which the companies choose to pursue. We will be responsible for the US commercialisation of roxadustat, with FibroGen undertaking specified promotional activities in the ESRD segment in this market. The companies will also co-commercialise roxadustat in China where FibroGen will be responsible for clinical trials, regulatory matters, manufacturing and medical affairs, and we will oversee promotional activities and commercial distribution.

#### Moderna

- > In March 2013, we signed an exclusive agreement with Moderna to discover, develop and commercialise pioneering medicines based on *messenger RNA Therapeutics* for the treatment of serious cardiovascular, metabolic and renal diseases, as well as cancer. Under the terms of the agreement, we made an upfront payment of \$240 million. We will have exclusive access to select any target of our choice in cardiometabolic and renal diseases, as well as selected targets in oncology, over a period of up to five years for subsequent development of *messenger RNA Therapeutics*. In addition, Moderna is entitled to an additional \$180 million for the achievement of three technical milestones. Through this agreement, we have the option to select up to 40 drug products for clinical development and Moderna will be entitled to development and commercial milestone payments as well as royalties on drug sales. We will lead the pre-clinical, clinical development and commercialisation of therapies resulting from the agreement and Moderna will be responsible for designing and manufacturing the *messenger RNA Therapeutics* against selected targets. We are currently progressing 19 projects across CVRM and Oncology. Utilising both companies' expertise, significant progress has also been made with the technology platform, with the focus on formulation, safety, and drug metabolism and pharmacokinetics.

We determine the above business development transactions to be significant using a range of factors. We look at the specific circumstances of the individual arrangement and apply several quantitative and qualitative criteria. Because we consider business development transactions to be an extension of our R&D strategy, the expected total value of development payments under the transaction and its proportion of our annual R&D spend, both of which are proxies for

overall R&D effort and cost, are important elements of the determination of the significance. Other quantitative criteria we apply include, without limitation, expected levels of future sales, the possible value of milestone payments and the resources used for commercialisation activities (for example, the number of staff). Qualitative factors we consider include, without limitation, new market developments, new territories, new areas of research and strategic implications.

#### Capitalisation and shareholder return

##### Capitalisation

The total number of shares in issue at 31 December 2019 was 1,312 million (2018: 1,267 million). In April 2019, AstraZeneca completed an issuance of 44,386,214 new Ordinary Shares of \$0.25 each at a price of £60.50 per share, resulting in an increase in share capital of \$11 million and an increase in share premium of \$3,479 million, net of transaction costs of \$22 million. In addition, 0.7 million Ordinary Shares were issued upon share option exercises for total proceeds of \$32 million. Shareholders' equity increased by \$659 million to \$13,127 million at the year end. Non-controlling interests were \$1,469 million (2018: \$1,576 million), with the decrease in the year as a result of the losses attributable to shareholders of the non-controlling interest in Acerta Pharma.

##### Dividend and share repurchases

The Board has recommended a second interim dividend of \$1.90 (146.4 pence, 18.32 SEK) to be paid on 30 March 2020. This brings the full-year dividend to \$2.80 (218.3 pence, 26.81 SEK). Against Reported Earnings per share, the Group had a dividend cover ratio of 0.4:1 in 2019 (2018: 0.6:1). Against Core Earnings per share, the Group had a dividend cover ratio of 1.25:1 in 2019 (2018: 1.2:1). This dividend is consistent with the progressive dividend policy, by which the Board intends to maintain or grow the dividend each year.

The Board regularly reviews its distribution policy and its overall financial strategy to continue to strike a balance between the interests of the business, our financial creditors and our shareholders. Having regard for business investment, funding the progressive dividend policy and meeting our debt service obligations, the Board currently believes it is appropriate to continue the suspension of the share repurchase programme which was announced in 2012.

The Board reviews the level of distributable reserves of the Parent Company annually and aims to maintain distributable reserves that provide adequate cover for dividend payments. As at 31 December 2019, the overwhelming majority of the profit and loss reserve of the Parent Company (2019: \$11,998 million, 2018: \$11,602 million) was available for distribution subject to the filing of these Financial Statements with the UK Companies House, details are included in the Parent Company's Statement of Changes in Equity on page 232.

The distributable reserves are sufficient to pay dividends for a number of years, as, when required, the Company can receive dividends from its subsidiaries to increase distributable reserves.

### Future prospects

As outlined earlier in this Annual Report, our strategy is focused on innovation, returning to growth and building a sustainable, durable and more profitable business.

In support of this, we made certain choices around our three strategic priorities:

- > Deliver Growth and Therapy Area Leadership
- > Accelerate Innovative Science
- > Be a Great Place to Work.

□ For more information, see Our strategic priorities from page 18.

### Full year 2020: additional commentary

The Group has conducted an assessment of the impact of the recent novel coronavirus (Covid-19) outbreak in China. All guidance and indications take account of scenario analyses that assume an unfavourable impact in China on Total Revenue and Core EPS lasting up to a few months. Depending on the impact of the epidemic, Total Revenue in 2020 is expected to increase by a high single-digit to a low double-digit percentage and Core EPS is expected to increase by a mid- to high-teens percentage. The Group is focused on improving operating leverage in 2020. Capital Expenditure is expected to be broadly stable versus 2019 and a Core Tax Rate of 18% to 22% is expected for 2020.

These targets represent management's current estimates and are subject to change. Please see the Cautionary statement regarding forward-looking statements on page 272.

### Financial risk management

#### Financial risk management policies

##### Insurance

Our risk management processes are described in Risk Overview from page 74. These processes enable us to identify risks that can be partly or entirely mitigated through the use of insurance. We negotiate the best available premium rates with insurance providers on the basis of our extensive risk management procedures. We focus our insurance resources on the most critical areas, or where there is a legal requirement, and where we can get best value for money. We purchase an external multi-line insurance programme to mitigate against significant financial loss arising from business risks, including liability, business interruption, property damage, and directors' and officers' liability. In order to contain insurance costs, as of February 2006, we adjusted our product liability coverage profile, accepting uninsured exposure above \$100 million.

### Taxation

Our approach to managing tax risk is integrated with our broader business risk management and compliance framework. Our approach is to manage tax risks and tax costs in a manner consistent with applicable regulatory requirements and with shareholders' best long-term interests, taking into account operational, economic and reputational factors. We manage tax risks in the context of substantive business transactions.

### Treasury

The principal financial risks to which we are exposed are those arising from liquidity, interest rate, foreign currency and credit. We have a centralised treasury function to manage these risks in accordance with Board-approved policies. Specifically, liquidity risk is managed through maintaining access to a number of sources of funding to meet anticipated funding requirements, including committed bank facilities, cash resources and use of debt factoring. We also use supply chain financing. For further information on our supply chain financing arrangements, please refer to the Business Review on page 37.

Interest rate risk is managed through maintaining a debt portfolio that is weighted towards fixed rates of interest. Accordingly, our net interest charge is not significantly affected by movements in floating rates of interest. We monitor the impact of currency on a portfolio basis (to recognise correlation effect), and may hedge to protect against significant adverse impacts on cash flow over the short to medium term. We aim to hedge the currency exposure that arises between the booking and settlement dates on material non-local currency purchases and sales by subsidiaries and the external dividend. Significant intra-Group loans that give rise to foreign exchange movements are also hedged.

Credit risk is managed through setting and monitoring credit limits appropriate for the assessed risk of the counterparty. The Group utilises factoring arrangements for selected trade receivables. These factoring arrangements qualify for full derecognition of the associated trade receivables under IFRS 9 'Financial Instruments'.

Our capital and risk management objectives and policies are described in further detail in Note 27 to the Financial Statements from page 212 and in Risk Overview from page 74. Sensitivity analysis of the Group's exposure to exchange rate and interest rate movements is also detailed in Note 27 to the Financial Statements from page 215.

### Critical accounting policies and estimates

Our Financial Statements are prepared in accordance with IFRS as issued by the IASB and as adopted by the EU (adopted IFRS), and the accounting policies employed are set out in the Group Accounting Policies section in the Financial Statements from page 172. In applying these policies, we make estimates and assumptions that affect the Reported amounts of assets and liabilities and disclosure of contingent assets and liabilities. The actual outcome could differ from those estimates. Some of these policies require a high level of judgement because the areas are especially subjective or complex. We believe that the most critical accounting policies and significant areas of judgement and estimation are in the following areas and align with the accounting policies containing our key accounting judgements and significant accounting estimates as disclosed in the Financial Statements on page 173: **KJ SE**

- > revenue recognition – see Revenue Accounting Policy on page 174 **KJ** and Note 1 on page 180 **SE**.
- > expensing of internal development expenses – see Research and Development Policy on page 174 **KJ**.
- > impairment review of Intangible assets – see Note 10 on page 191 **SE**.
- > useful economic life of Intangible assets – see Research and Development Policy on page 175 **KJ** and Note 10 on page 192 **SE**.
- > business combinations and Goodwill (and Contingent Consideration arising from business combinations) – see Business Combinations and Goodwill Policy on page 177 **KJ** and Note 20 on page 200 **SE**.
- > litigation liabilities – see Litigation and Environmental liabilities within Note 29 on page 221 **KJ**.
- > operating segments – see Note 6 on page 186 **KJ**.
- > employee benefits – see Note 22 on page 207 **SE**.
- > taxation – see Taxation Accounting Policies on page 175, Note 29 on page 225 **KJ** and Note 29 on page 224 **SE**.

### Revenue recognition

Product Sales are recorded at the invoiced amount (excluding inter-company sales and value-added taxes) less movements in estimated accruals for rebates and chargebacks given to managed-care and other customers and product returns, which are a particular feature in the US and are considered to be key estimates. It is the Group's policy to offer a credit note for all returns and to destroy all returned stock in all markets. Cash discounts for prompt payments are also discounted from sales. Sales are recognised when the control of the goods has been transferred to a third party, which is usually when title passes to the customer, either on shipment or on the receipt of goods by the customer, depending on local trading terms.

## Financial Review

### continued

#### Rebates, chargebacks and returns in the US

When invoicing Product Sales in the US, we estimate the rebates and chargebacks that we expect to pay, which are considered to be estimates. These rebates typically arise from sales contracts with third-party managed-care organisations, hospitals, long-term care facilities, group purchasing organisations and various federal or state programmes (Medicaid contracts, supplemental rebates, etc.). They can be classified as follows:

- > Chargebacks, where we enter into arrangements under which certain parties, typically hospitals, long-term care facilities, group purchasing organisations, the Department of Veterans Affairs, Public Health Service Covered Entities and the Department of Defense, are able to buy products from wholesalers at the lower prices we have contracted with them. The chargeback is the difference between the price we invoice to the wholesaler and the contracted price charged by the wholesaler to the other party. Chargebacks are credited directly to the wholesalers.
- > Regulatory, including Medicaid and other federal and state programmes, where we pay rebates based on the specific terms of agreements with the US Department of Health and Human Services and with individual states, which include product usage and information on best prices and average market prices benchmarks.
- > Contractual, under which entities such as third-party managed-care organisations are entitled to rebates depending on specified performance provisions, which vary from contract to contract.

The effects of these deductions on our US pharmaceuticals revenue and the movements on US pharmaceuticals revenue provisions are set out to the right.

Accrual assumptions are built up on a product-by-product and customer-by-customer basis, taking into account specific contract provisions coupled with expected performance, and are then aggregated into a weighted average rebate accrual rate for each of our products. Accrual rates are reviewed and adjusted on an as needed basis. There may be further adjustments when actual rebates are invoiced based on utilisation information submitted to us (in the case of contractual rebates) and claims/invoices are received (in the case of regulatory rebates and chargebacks). We believe that we have made reasonable estimates for future rebates using a similar methodology to that of previous years. Inevitably, however, such estimates involve judgements on aggregate future sales levels, segment mix and the customers' contractual performance.

#### Gross to Net Product Sales US pharmaceuticals

|  | 2019<br>\$m  | 2018<br>\$m  | 2017<br>\$m  |
|--|--------------|--------------|--------------|
| Gross Product Sales                        | 18,354       | 16,538       | 14,637       |
| Chargebacks                                | (2,429)      | (2,224)      | (2,299)      |
| Regulatory – Medicaid and state programmes | (1,380)      | (1,304)      | (1,462)      |
| Contractual – Managed-care and Medicare    | (5,467)      | (4,600)      | (3,598)      |
| Cash and other discounts                   | (303)        | (286)        | (30)         |
| Customer returns                           | (44)         | (119)        | (37)         |
| US Branded Pharmaceutical Fee              | (105)        | (140)        | 3            |
| Other                                      | (879)        | (989)        | (1,045)      |
| <b>Net Product Sales</b>                   | <b>7,747</b> | <b>6,876</b> | <b>6,169</b> |

#### Movements in accruals US pharmaceuticals

|   | Brought forward<br>at<br>1 January 2019<br>\$m | Provision for<br>current year<br>\$m | Adjustment in<br>respect of<br>prior years<br>\$m | Returns and<br>payments<br>\$m | Carried forward<br>at<br>31 December<br>2019<br>\$m |
|---|--|--------------------------------------|---|--------------------------------|---|
| Chargebacks                                   | 271  | 2,458                                | (29)  | (2,455)                        | 245   |
| Regulatory – Medicaid<br>and state programmes | 892  | 1,477                                | (97)  | (1,541)                        | 731   |
| Contractual – Managed-<br>care and Medicare   | 1,542  | 5,613                                | (146)   | (5,070)                        | 1,939   |
| Cash and other discounts                      | 4  | 303                                  | –   | (288)                          | 19  |
| Customer returns                              | 361  | 44                                   | –   | (225)                          | 180   |
| US Branded<br>Pharmaceutical Fee              | 52   | 111                                  | (6)   | (31)                           | 126   |
| Other   | 144  | 879                                  | –   | (878)                          | 145   |
| <b>Total</b>                                  | <b>3,266</b>                                   | <b>10,885</b>                        | <b>(278)</b>                                      | <b>(10,488)</b>                | <b>3,385</b>  |

|   | Brought forward<br>at<br>1 January 2018<br>\$m | Provision for<br>current year<br>\$m | Adjustment in<br>respect of<br>prior years<br>\$m | Returns and<br>payments<br>\$m | Carried forward<br>at<br>31 December<br>2018<br>\$m |
|---|--|--------------------------------------|---|--------------------------------|---|
| Chargebacks                                   | 206  | 2,220                                | 4   | (2,159)                        | 271   |
| Regulatory – Medicaid<br>and state programmes | 749  | 1,482                                | (178)   | (1,161)                        | 892   |
| Contractual – Managed-<br>care and Medicare   | 1,267  | 4,685                                | (85)  | (4,325)                        | 1,542   |
| Cash and other discounts                      | 4  | 286                                  | –   | (286)                          | 4   |
| Customer returns                              | 386  | 119                                  | –   | (144)                          | 361   |
| US Branded<br>Pharmaceutical Fee              | 63   | 99                                   | 41  | (151)                          | 52  |
| Other   | 151  | 989                                  | –   | (996)                          | 144   |
| <b>Total</b>                                  | <b>2,826</b>                                   | <b>9,880</b>                         | <b>(218)</b>                                      | <b>(9,222)</b>                 | <b>3,266</b>  |

|   | Brought forward<br>at<br>1 January 2017<br>\$m | Provision for<br>current year<br>\$m | Adjustment in<br>respect of<br>prior years<br>\$m | Returns and<br>payments<br>\$m | Carried forward<br>at<br>31 December<br>2017<br>\$m |
|---|--|--------------------------------------|---|--------------------------------|---|
| Chargebacks                                   | 562  | 2,432                                | (133)   | (2,655)                        | 206   |
| Regulatory – Medicaid<br>and state programmes | 807  | 1,568                                | (106)   | (1,520)                        | 749   |
| Contractual – Managed-<br>care and Medicare   | 1,443  | 3,815                                | (217)   | (3,774)                        | 1,267   |
| Cash and other discounts                      | 6  | 29                                   | 1   | (32)                           | 4   |
| Customer returns                              | 473  | 36                                   | 1   | (124)                          | 386   |
| US Branded<br>Pharmaceutical Fee              | 260  | 105                                  | (108)   | (194)                          | 63  |
| Other   | 161  | 1,030                                | 15  | (1,055)                        | 151   |
| <b>Total</b>                                  | <b>3,712</b>                                   | <b>9,015</b>                         | <b>(547)</b>                                      | <b>(9,354)</b>                 | <b>2,826</b>  |

Overall adjustments between gross and net US Product Sales amounted to \$10,374 million in 2019 (2018: \$9,662 million) with the increase driven by an overall increase in our US Product Sales and changes in product mix.

Cash discounts are offered to customers to encourage prompt payment. Accruals are calculated based on historical experience and are adjusted to reflect actual experience. Our revenue recognition policy is described within Group Accounting Policies from page 173.

Industry practice in the US allows wholesalers and pharmacies to return unused stocks within six months of, and up to 12 months after, shelf-life expiry. The customer is credited for the returned product by the issuance of a credit note. Returned products are not exchanged for products from inventory and once a return claim has been determined to be valid and a credit note has been issued to the customer, the returned products are destroyed. At the point of sale in the US, we estimate the quantity and value of products which may ultimately be returned. Our returns accruals in the US are based on actual experience. Our estimate is based on the historical sales and returns information for established products together with market-related information, such as estimated shelf life, product recalls, and estimated stock levels at wholesalers, which we receive via third-party information services. For newly launched products, we use rates based on our experience with similar products or a pre-determined percentage.

#### **Business combinations and goodwill (and contingent consideration arising from business combinations)**

Our business model includes investment in targeted business developments to strengthen our portfolio, pipeline and capabilities. These business development transactions include collaborations, asset in-licences and business acquisitions.

Each transaction is considered to establish whether it qualifies as a business combination by applying the criteria assessment detailed in IFRS 3 'Business Combinations'. The determination of a transaction being a business combination or asset acquisition is considered to be a key judgement as detailed in the accounting policy on page 177.

On the acquisition of a business, fair values are attributed to the identifiable assets and liabilities and contingent liabilities unless the fair value cannot be measured reliably, in which case the value is subsumed into goodwill.

Attributing fair values is a key judgement. Goodwill is the difference between the fair value of the consideration and the fair value of net assets acquired. Fair value is the price that would be received to sell an asset or pay for a liability in an orderly transaction at the date of acquisition. The price may be directly observable but, in most cases, is estimated using valuation techniques which normally involve predicting future cash flows and applying a market participant discount rate. No business combinations were made in 2017, 2018 or 2019.

Future contingent elements of consideration, which may include development and launch milestones, revenue threshold milestones and revenue-based royalties, are fair valued at the date of acquisition using decision-tree analysis with key inputs including probability of success, consideration of potential delays and revenue projections based on the Group's internal forecasts. Unsettled amounts of consideration are held at fair value within payables with changes in fair value recognised immediately in profit. Several of our business combinations have included significant amounts of contingent consideration. Details of the movements in the fair value of the contingent consideration in the year, and the range of possible contingent consideration amounts that may eventually become payable are contained in Note 20 to the Financial Statements from page 199. Where not all the equity of a subsidiary is acquired, the non-controlling interest is recognised either at fair value or at the non-controlling interest's proportionate share of the net assets of the subsidiary, on a case-by-case basis. Put options over non-controlling interests are recognised as a financial liability measured at amortised cost, with a corresponding entry in either retained earnings or against non-controlling interest reserves on a case-by-case basis.

As detailed above, we have significant investments in goodwill and intangible assets as a result of acquisitions of businesses and purchases of assets, such as product development and marketing rights.

Details of the estimates and assumptions we make in our annual impairment testing of goodwill are included in Note 9 to the Financial Statements on page 190. The Group, including acquisitions, is considered a single operating segment for impairment purposes. No impairment of Goodwill was identified. A significant portion of our investments in Intangible assets and Goodwill arose from the restructuring of the joint venture with MSD which commenced in 1998, the acquisition of MedImmune in 2007 and our 2014 acquisition of BMS's interest in the Group's Diabetes Alliance. We are satisfied that the carrying values of our Intangible assets as at 31 December 2019 are fully justified by estimated future cash flows. The accounting

for our Intangible assets is fully explained in Note 10 to the Financial Statements from page 190, including details of the estimates and assumptions we make in impairment testing of Intangible assets.

#### **Litigation and environmental liabilities**

In the normal course of business, contingent liabilities may arise from product-specific and general legal proceedings, from guarantees or from environmental liabilities connected with our current or former sites. Where we believe that potential liabilities have a less than 50% probability of crystallising, or where we are unable to make a reasonable estimate of the liability, we treat them as contingent liabilities. These are not provided for, but are disclosed in Note 29 to the Financial Statements from page 220.

In cases that have been settled or adjudicated, or where quantifiable fines and penalties have been assessed and which are not subject to appeal (or other similar forms of relief), or where a loss is probable (more than 50% assessed probability) and we are able to make a reasonable estimate of the loss, we indicate the loss absorbed or the amount of the provision accrued.

Where it is considered that the Group is more likely than not to prevail, or in the rare circumstances where the amount of the legal liability cannot be estimated reliably, legal costs involved in defending the claim are charged to profit as they are incurred. Where it is considered that we have a valid contract which provides the right to reimbursement (from insurance or otherwise) of legal costs and/or all or part of any loss incurred or for which a provision has been established and we consider recovery to be virtually certain, then the best estimate of the amount expected to be received is recognised as an asset.

Assessments as to whether or not to recognise provisions or assets and of the amounts concerned usually involve a series of complex judgements about future events and can rely heavily on estimates and assumptions. We believe that the provisions recorded are adequate based on currently available information and that the insurance recoveries recorded will be received.

However, given the inherent uncertainties involved in assessing the outcomes of these cases and in estimating the amount of the potential losses and the associated insurance recoveries, we could in future periods incur judgments or insurance settlements that could have a material adverse effect on our results in any particular period.

## Financial Review

### *continued*

The position could change over time, and there can, therefore, be no assurance that any losses that result from the outcome of any legal proceedings will not exceed the amount of the provisions that have been booked in the accounts.

Although there can be no assurance regarding the outcome of legal proceedings, we do not currently expect them to have a material adverse effect on our financial position, but they could significantly affect our financial results in any particular period.

#### **Sarbanes-Oxley Act Section 404**

As a consequence of our NYSE listing, we are required to comply with those provisions of the Sarbanes-Oxley Act applicable to foreign issuers. Section 404 of the Sarbanes-Oxley Act requires companies annually to assess and make public statements about the quality and effectiveness of their internal control over financial reporting. As regards Sarbanes-Oxley Act Section 404, our approach is based on the Committee of Sponsoring Organizations (COSO) 2013 framework.

Our approach to the assessment has been to select key transaction and financial reporting processes in our largest operating units and a number of specialist areas (e.g. financial consolidation and reporting, treasury operations and taxation etc.), so that, in aggregate, we have covered a significant proportion of the key lines in our Financial Statements. Each of these operating units and specialist areas has ensured that its relevant processes and controls are documented to appropriate standards, taking into account, in particular, the guidance provided by the SEC. We have also reviewed the structure and operation of our 'entity level' control environment. This refers to the overarching control environment, including structure of reviews, checks and balances that are essential to the management of a well-controlled business.

#### **Section 172(1) statement**

When making decisions, the Directors of AstraZeneca PLC must act in the way they consider, in good faith, is most likely to promote the success of the Company for the benefit of its members as a whole, while also considering the broad range of stakeholders who interact with and are impacted by our business. Throughout the year, while discharging their duties, section 172(1) (s.172(1)) requires a director to have regard, amongst other matters, to the:

- > likely consequences of any decisions in the long term
- > interests of the company's employees
- > need to foster the company's business relationships with suppliers, customers and others
- > impact of the company's operations on the community and environment
- > desirability of the company maintaining a reputation for high standards of business conduct and
- > need to act fairly as between members of the company.

In discharging their s.172(1) duties the Directors have had regard to the factors set out above, as well as other factors relevant to the decision being made. The Board acknowledges that every decision made will not necessarily result in a positive outcome for all stakeholders. By considering our Purpose and Values, together with our strategic priorities, the Board aims to ensure that the decisions made are consistent and intended to promote the Company's long-term success.

The Group engaged with key stakeholders throughout the year to understand the issues and factors that are significant for these stakeholders, and a number of actions were taken as a result of this engagement. The interaction with stakeholders, and the impact of these interactions, is set out in the Connecting with our stakeholders section from page 104 and throughout the Strategic Report. The consideration and impact of the Group's operations on the environment are contained throughout the Strategic Report, including on pages 38-39 and Ambition Zero Carbon on page 53. Information on how the Group has considered other factors, such as Communities, are also set out in Contributing to society, from page 49 and Connecting with our stakeholders on page 104.

Details of how the Board operates and matters considered by the Board are set out in the Corporate Governance Report from page 102. Examples of how Directors discharged their s.172(1) duties when making Principal Decisions during 2019 are set out on page 106. Principal Decisions are decisions and discussions which are material or strategic to the Group, but also those that are significant to any of our stakeholder groups.

#### **Strategic Report**

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

- > AstraZeneca at a glance
- > Chairman's Statement
- > Chief Executive Officer's Review
- > Business model and life-cycle of a medicine
- > Healthcare in a changing world
- > Strategy
- > Key Performance Indicators
- > Business Review
- > Therapy Area Review
- > Risk Overview
- > Financial Review

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

**A C N Kemp**

Company Secretary

14 February 2020