

What science can do

AstraZeneca Annual Report and Form 20-F Information 2016



Chief Executive Officer's Review



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

A transitional phase

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

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

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

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

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

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

Investing for the future

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

Achieve scientific leadership

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

2016 Strategic priorities overview



Achieve scientific leadership

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

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

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

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

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



Return to growth

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



Be a great place to work

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

Chief Executive Officer's Review continued

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

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

Prioritised and accelerated pipeline

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

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

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

Return to growth

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

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

Be a great place to work

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

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

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

Looking ahead

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

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



Pascal Soriot
Chief Executive Officer



Investing for the future: Led by science in Cambridge

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

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

As a global science-led business, we have:

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



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

As a scientific partner, we have:

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

Being committed to protecting the environment, we are:

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

To inspire the next generation of scientists, we:

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



Key facts

130

Over 130 collaborations
in Cambridge



2,000

Around 2,000 employees
in Cambridge



Watch the video at
www.astrazeneca.com