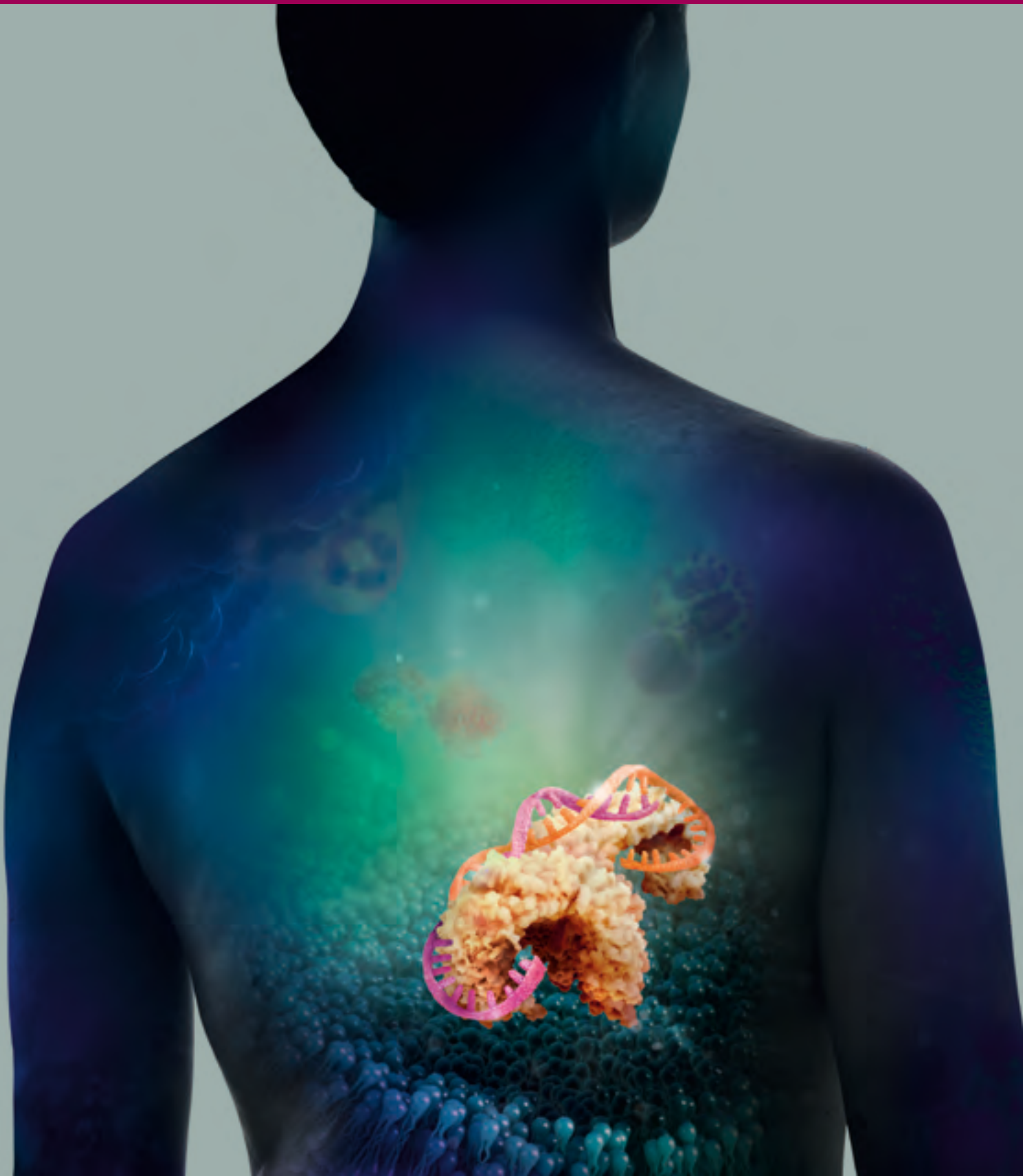


What science can do

AstraZeneca Annual Report and Form 20-F Information 2015



Marketed Products

Respiratory, Inflammation and Autoimmunity



- > **Accolate** (zafirlukast) is an oral leukotriene receptor antagonist for the treatment of asthma.
- > **Bricanyl Respules** (terbutaline) is a short-acting beta₂-agonist administered via a nebuliser for acute treatment of asthma and COPD in both children and adults.
- > **Bricanyl Turbuhaler** (terbutaline) is a short-acting beta₂-agonist for the acute treatment of bronchial-obstructive symptoms in asthma and COPD.
- > **Daliresp** (roflumilast) is an oral PDE4 (phosphodiesterase-4) inhibitor for adults with severe COPD to decrease their number of exacerbations (US only).
- > **Duaklir Genuair** (aclidinium/formoterol in a dry powder inhaler) is a fixed dose combination of a long-acting muscarinic antagonist (LAMA) and a long-acting beta₂-adrenergic receptor agonist (LABA) for the maintenance treatment of COPD.
- > **Eklira Genuair/Tudorza/Bretaris** (aclidinium in a dry powder inhaler) is a LAMA for the maintenance treatment of COPD.
- > **Oxis Turbuhaler** (formoterol) is a fast onset, long-acting beta₂-agonist for the treatment of bronchial-obstructive symptoms in asthma and COPD.
- > **Pulmicort Turbuhaler/Pulmicort Flexhaler** (budesonide) is an inhaled corticosteroid for maintenance treatment of asthma.
- > **Pulmicort Respules** (budesonide) is a corticosteroid, administered via a nebuliser, for the treatment of asthma in both children and adults.
- > **Rhinocort** (budesonide) is a nasal steroid treatment for allergic rhinitis (hay fever), perennial rhinitis and nasal polyps.
- > **Symbicort pMDI** (budesonide/formoterol in a pressurised metered-dose inhaler) is a combination of an inhaled corticosteroid and a fast onset, long-acting beta₂-agonist for maintenance treatment of asthma and COPD, including chronic bronchitis and emphysema in the US, Australia and some other markets.

- > **Symbicort Turbuhaler** (budesonide/formoterol in a dry powder inhaler) is a combination of an inhaled corticosteroid and a fast onset, long-acting beta₂-agonist for the maintenance treatment of asthma and COPD. In asthma, it is also approved for *Symbicort Maintenance And Reliever Therapy (Symbicort SMART)*. *Symbicort Turbuhaler* is approved in Europe, Japan and many other countries excluding the US.

Cardiovascular and Metabolic diseases



Cardiovascular disease

- > **Atacand¹/Atacand HCT/Atacand Plus** (candesartan cilexetil) is an angiotensin II antagonist for the 1st line treatment of hypertension and symptomatic heart failure.
- > **Brilinta/Brilique** (ticagrelor) is an oral antiplatelet for acute coronary syndromes (ACS).
- > **Crestor²** (rosuvastatin calcium) is a statin for dyslipidaemia and hypercholesterolemia.
- > **Plendil** (felodipine) is a calcium antagonist for hypertension and angina.
- > **Seloken/Toprol-XL** (metoprolol succinate) is a beta-blocker once-daily tablet for control of hypertension, heart failure and angina.
- > **Tenormin³** (atenolol) is a beta-blocker for hypertension, angina pectoris and other CV disorders.
- > **Zestril⁴** (lisinopril dihydrate) is an angiotensin converting enzyme inhibitor for a wide range of CV diseases, including hypertension.

Metabolic disease

- > **Bydureon** (exenatide extended-release for injectable suspension) is a once-weekly injectable glucagon-like peptide-1 (GLP-1) receptor agonist available as a single-dose tray or a single-dose pen indicated to improve glycaemic control, in adults with Type 2 diabetes.
- > **Byetta** (exenatide injection) is a twice-daily injectable GLP-1 receptor agonist indicated to improve glycaemic control in adults with Type 2 diabetes.

- > **Farxiga/Forxiga** (dapagliflozin) is a selective inhibitor of human sodium-glucose co-transporter 2 (SGLT2 inhibitor) indicated as an adjunct to diet and exercise to improve glycaemic control in adult patients with Type 2 diabetes.
- > **Kombiglyze XR** (saxagliptin and metformin hydrochloride extended release) combines saxagliptin (*Onglyza*) and extended release metformin (metformin XR) in a once-daily tablet for Type 2 diabetes.
- > **Komboglyze** (saxagliptin and metformin hydrochloride) combines saxagliptin (*Onglyza*) and metformin immediate release (metformin IR) in a twice-daily tablet for Type 2 diabetes.
- > **Onglyza** (saxagliptin) is an oral dipeptidyl peptidase 4 (DPP-4) inhibitor for Type 2 diabetes.
- > **Symlin** (pramlintide acetate) is an injected amylin analogue for Type 1 and Type 2 diabetes in patients with inadequate glycaemic control.
- > **Xigduo** (dapagliflozin and metformin hydrochloride) combines dapagliflozin (*Farxiga/Forxiga*), an SGLT2 inhibitor, and metformin IR, in a twice-daily tablet to improve glycaemic control in adult patients with Type 2 diabetes who are inadequately controlled by metformin alone.
- > **Xigduo XR** (dapagliflozin and metformin hydrochloride extended-release) combines dapagliflozin (*Farxiga/Forxiga*), an SGLT2 inhibitor, and metformin XR, in a once-daily tablet to improve glycaemic control in adult patients with Type 2 diabetes who are inadequately controlled by metformin alone.

¹ Licensed from Takeda Chemicals Industries Ltd.

² Licensed from Shionogi. The extension of the global licence agreement with Shionogi for *Crestor* and the modification of the royalty structure became effective 1 January 2014.

³ Divested US rights to *Tenormin* to Alvogen Pharma US Inc. effective 9 January 2015.

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

Marketed Products continued

Oncology



- > **Arimidex** (anastrozole) is an aromatase inhibitor used to treat breast cancer. It has been shown to be significantly superior to tamoxifen at preventing breast cancer recurrence during and beyond the five-year treatment course.
- > **Casodex, Cosudex** (bicalutamide) is an anti-androgen therapy used to treat prostate cancer. A 50mg tablet is used for advanced prostate cancer; a 150mg tablet is used for locally advanced prostate cancer.
- > **Faslodex** (fulvestrant) is an injectable estrogen receptor antagonist. It is used for the treatment of hormone receptor positive advanced breast cancer for post-menopausal women whose disease has progressed following treatment with prior endocrine therapy.
- > **Iressa** (gefitinib) is an epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) that acts to block signals for cancer cell growth and survival in advanced non-small cell lung cancer (NSCLC).
- > **Lynparza** (olaparib) is an oral poly ADP-ribose polymerase (PARP) inhibitor. It is approved in the EU for the treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer. It is approved in the US for the treatment of patients with germline BRCA-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.
- > **Nolvadex** (tamoxifen citrate) is a widely used breast cancer treatment outside the US.
- > **Tagrisso** (osimertinib) is an EGFR-TKI indicated for patients with metastatic EGFR T790M mutation-positive NSCLC.
- > **Zoladex** (goserelin acetate implant) in one and three month subcutaneous or intra-muscular injections, is a luteinising hormone-releasing hormone (LHRH) agonist used to treat prostate cancer, breast cancer and certain benign gynaecological disorders.

Infection, Neuroscience and Gastrointestinal



Infection

- > **Fluenz/FluMist** (influenza vaccine live, intra-nasal) is an intra-nasal, live, attenuated, trivalent influenza vaccine.
- > **Fluenz Tetra/FluMist Quadrivalent**¹ (influenza vaccine live, intra-nasal) is an intra-nasal, live, attenuated, quadrivalent influenza vaccine.
- > **Merrem/Meronem**² (meropenem) is a carbapenem anti-bacterial used to treat serious infections in hospitalised patients.
- > **Synagis**³ (palivizumab) is a humanised MAb used to prevent serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in paediatric patients at high risk of acquiring RSV disease.
- > **Zinforo**⁴ (ceftaroline fosamil) is a novel injectable cephalosporin used in community-acquired pneumonia and complicated skin and soft tissue infections.

¹ Daiichi Sankyo holds rights to *Fluenz Tetra/FluMist Quadrivalent* in Japan.

² Licensed from Dainippon Sumitomo Pharmaceuticals Co., Limited.

³ US rights only. AbbVie holds rights to *Synagis* outside the US.

⁴ Licensed from Forest (now a wholly-owned subsidiary of Allergan). AstraZeneca holds global rights, excluding the US, Canada and Japan.

Neuroscience

- > **Diprivan** (propofol) is an intravenous general anaesthetic used to induce and maintain general anaesthesia, intensive care sedation and conscious sedation for surgical and diagnostic procedures.
- > **EMLA** (lidocaine and prilocaine) is a local anaesthetic for topical application (cream and patch) to prevent pain associated with injections and minor surgical procedures, and to facilitate cleansing/debridement of leg ulcers.

- > **Movantik/Moventig** (naloxegol) is a once-daily, peripherally-acting mu-opioid receptor antagonist approved for the treatment of opioid-induced constipation (OIC) in adult patients. The indication varies by jurisdiction.
- > **Naropin** (ropivacaine) is a long-acting local anaesthetic for surgical anaesthesia and acute pain management.
- > **Seroquel IR** (an immediate release formulation of quetiapine fumarate) is an atypical anti-psychotic generally approved for the treatment of schizophrenia and bipolar disorder (mania, depression and maintenance).
- > **Seroquel XR** (an extended release formulation of quetiapine fumarate) is generally approved for the treatment of schizophrenia, bipolar disorder, major depressive disorder and, on a more limited basis, for generalised anxiety disorder.
- > **Vimovo**¹ (naproxen/esomeprazole magnesium) is generally approved for symptomatic relief in the treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis in patients at risk of developing NSAID-associated gastric and/or duodenal ulcers.
- > **Xylocaine** (lidocaine) is a short-acting local anaesthetic for topical and regional anaesthesia.
- > **Zomig** (zolmitriptan) is used for the acute treatment of migraine, plus for the acute treatment of cluster headache in the EU. *Zomig* is available in three formulations: oral tablet; orally dispersible tablet; and nasal spray.

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

Gastrointestinal

- > **Losec/Prilosec** (omeprazole) is a proton pump inhibitor used to treat acid-related diseases.
- > **Nexium** (esomeprazole magnesium) is a proton pump inhibitor used to treat acid-related diseases.

Development Pipeline

as at 31 December 2015

Includes AstraZeneca sponsored or directed studies only.

Phase III/Pivotal Phase II/Registration NMEs and significant additional indications

Regulatory submission dates shown for assets in Phase III and beyond. As disclosure of compound information is balanced by the business need to maintain confidentiality, information in relation to some compounds listed here has not been disclosed at this time.

Compound	Mechanism	Area Under Investigation	Date Commenced Phase	Estimated Regulatory Submission/Submission Acceptance [†]			
				US	EU	Japan	China
Respiratory, Inflammation and Autoimmunity							
anifrolumab* TULIP	IFN-alphaR MAb	systemic lupus erythematosus	Q3 2015	2019 (Fast Track)	2019	2019	
benralizumab* CALIMA SIROCCO ZONDA BISE BORA GREGALE	IL-5R MAb	severe asthma	Q4 2013	H2 2016	H2 2016	N/A	N/A
benralizumab* TERRANOVA GALATHEA	IL-5R MAb	COPD	Q3 2014	2018	2018	N/A	N/A
brodalumab* AMAGINE-1,2,3	IL-17R MAb	psoriasis	Q3 2012	Accepted ¹	Accepted	N/A	N/A
Zurampic (lesinurad) CLEAR 1,2 CRYSTAL	selective uric acid reabsorption inhibitor (URAT-1)	chronic treatment of hyperuricemia in patients with gout	Q4 2011	Approved	Accepted ²		
PT003 GFF PINNACLE	LABA/LAMA	COPD	Q2 2013	Accepted	H2 2016	2017	2017
PT010	LABA/LAMA/ICS	COPD	Q3 2015	2018	2018	2017	2019
tralokinumab STRATOS 1,2 TROPOS MESOS	IL-13 MAb	severe asthma	Q3 2014	2018	2018	2018	
Cardiovascular and Metabolic diseases							
Brilinta/Brilique ³	P2Y12 receptor antagonist	arterial thrombosis		Launched	Launched	Accepted	Launched
Epanova [#]	omega-3 carboxylic acids	severe hypertriglyceridemia		Approved		2018	2019
Farxiga/Forxiga ⁴	SGLT2 inhibitor	Type 2 diabetes		Launched	Launched	Launched	Accepted
roxadustat* OLYMPUS ROCKIES	hypoxia-inducible factor prolyl hydroxylase inhibitor	anaemia in CKD/ESRD	Q3 2014	2018	N/A	N/A	H2 2016 ⁵
ZS-9 (sodium zirconium cyclosilicate)	potassium binder	hyperkalaemia		Accepted	Accepted		
Oncology							
acalabrutinib ^{#6}	Bruton's tyrosine kinase (BTK) inhibitor	B-cell blood cancers		H2 2016			
cediranib ICON 6	VEGFR tyrosine kinase inhibitor	PSR ovarian cancer	Q2 2007		Accepted (Orphan Drug)		
durvalumab* PACIFIC	PD-L1 MAb	stage III NSCLC	Q2 2014	2017	2020	2020	
durvalumab* HAWK ⁸	PD-L1 MAb	2nd line SCCHN (PD-L1 positive)	Q1 2015	2017 (Fast Track)	2019	2019	
durvalumab* + tremelimumab ALPS ⁹	PD-L1 MAb + CTLA-4 MAb	metastatic pancreatic ductal carcinoma	Q4 2015	2017	2017	2017	
durvalumab* + tremelimumab ARCTIC	PD-L1 MAb + CTLA-4 MAb	3rd line NSCLC	Q2 2015	2017	2017	2017	
durvalumab* + tremelimumab CONDOR ⁹	PD-L1 MAb + CTLA-4 MAb	2nd line SCCHN (PD-L1 negative)	Q2 2015	2017	2019	2019	
durvalumab* + tremelimumab DANUBE	PD-L1 MAb + CTLA-4 MAb	1st line bladder	Q4 2015	2018	2018	2018	
durvalumab* + tremelimumab EAGLE	PD-L1 MAb + CTLA-4 MAb	2nd line SCCHN	Q4 2015	2019	2019	2019	
durvalumab* + tremelimumab KESTREL	PD-L1 MAb + CTLA-4 MAb	1st line SCCHN	Q4 2015	2018	2018	2018	
durvalumab* + tremelimumab MYSTIC	PD-L1 MAb + CTLA-4 MAb	1st line NSCLC	Q3 2015	2017	2017	2017	
durvalumab* + tremelimumab NEPTUNE	PD-L1 MAb + CTLA-4 MAb	1st line NSCLC	Q4 2015	2019	2019	2019	
moxetumomab pasudotox* PLAIT	anti-CD22 recombinant immunotoxin	hairy cell leukaemia	Q2 2013	2017 (Orphan Drug)	2018		
selumetinib* ASTRA	MEK inhibitor	differentiated thyroid cancer	Q3 2013	2018	2018		
selumetinib* SELECT-1	MEK inhibitor	2nd line KRASm NSCLC	Q4 2013	2017	2017		
Tagrisso (AZD9291) AURA, AURA 2	EGFR tyrosine kinase inhibitor	≥2nd line advanced EGFRm T790M NSCLC	Q2 2014	Launched (Breakthrough designation, Priority Review, Orphan Drug)	Approved ⁷ (Accelerated assessment)	Accepted (Priority Review)	2017

Additional Information

Development Pipeline continued

Compound	Mechanism	Area Under Investigation	Date Commenced Phase	Estimated Regulatory Submission/Submission Acceptance [†]			
				US	EU	Japan	China
Tagrisso (AZD9291) AURA 3	EGFR tyrosine kinase inhibitor	≥2nd line advanced EGFRm T790M NSCLC	Q3 2014	2017	2017	2017	
tremelimumab [‡] DETERMINE	CTLA-4 MAb	mesothelioma	Q2 2014	H2 2016 (Orphan Drug, Fast Track)	H2 2016	H2 2016	
Infection, Neuroscience and Gastrointestinal							
CAZ AVI [#]	cephalosporin/beta lactamase inhibitor	serious infections, complicated intra-abdominal infection, complicated urinary tract infection	Q1 2012	N/A	Accepted		2017
CAZ AVI [#]	cephalosporin/beta lactamase inhibitor	hospital-acquired pneumonia/ventilator-associated pneumonia	Q2 2013	N/A	Accepted		2017
MEDI-550	pandemic influenza virus vaccine	pandemic influenza prophylaxis		N/A	H1 2016 [§]	N/A	N/A
Zinforo [‡]	extended spectrum cephalosporin with affinity to penicillin-binding proteins	pneumonia/skin infections		N/A	Launched	N/A	Submitted

[†] US and EU dates correspond to anticipated acceptance of the regulatory submission.

[#] Partnered and/or in collaboration.

[‡] Registrational Phase II/III trial.

¹ US regulatory submission accepted in Q1 2016.

² CHMP Positive Opinion received December 2015.

³ Brilinta in the US; Brilique in rest of world.

⁴ Farxiga in the US; Forxiga in rest of world.

⁵ Rolling NDA submission to be initiated in H2 2016.

⁶ Completion of the agreement with Acerta Pharma Q1 2016.

⁷ CHMP Positive Opinion received December 2015. Approval received Q1 2016.

⁸ MAA submitted December 2015. Regulatory acceptance anticipated H1 2016.

Phases I and II NMEs and significant additional indications

Compound	Mechanism	Area Under Investigation	Phase	Date Commenced Phase
Respiratory, Inflammation and Autoimmunity				
abediterol (AZD0548)	LABA	asthma/COPD	II	Q4 2007
anifrolumab [#]	IFN-alphaR MAb	lupus nephritis	II	Q4 2015
AZD7594	inhaled SGRM	asthma/COPD	II	Q3 2015
AZD7624	inhaled P38 inhibitor	COPD	II	Q4 2014
AZD9412 [#]	inhaled interferon beta	asthma/COPD	II	Q3 2015
mavrilimumab [#]	GM-CSFR MAb	rheumatoid arthritis	II	Q1 2010
MEDI-551 [#]	CD19 MAb	neuromyelitis optica ¹	II	Q1 2015
MEDI2070 [#]	IL-23 MAb	Crohn's disease	II	Q1 2013
abrilumab [#]	alpha(4)beta(7) MAb	Crohn's disease/ulcerative colitis	II	Q4 2012
MEDI9929 [#]	TSLP MAb	asthma/atopic dermatitis	II	Q2 2014
PT010	LABA/LAMA/ICS	asthma	II	Q2 2014
RDEA3170	selective uric acid reabsorption inhibitor (URAT-1)	chronic treatment of hyperuricemia in patients with gout	II	Q3 2013
tralokinumab	IL-13 MAb	atopic dermatitis	II	Q1 2015
anifrolumab [#]	IFN-alphaR MAb	systemic lupus erythematosus (subcutaneous)	I	Q4 2015
AZD1419 [#]	TLR9 agonist	asthma	I	Q3 2013
AZD7986	DPP1	COPD	I	Q4 2014
AZD8871	MABA	COPD	I	Q4 2015
AZD8999	MABA	COPD	I	Q4 2013
AZD9567	oral SGRM	rheumatoid arthritis	I	Q4 2015
lesinurad+allopurinol	selective uric acid reabsorption inhibitor (URAT-1)+xanthine oxidase inhibitor	chronic treatment of hyperuricemia in patients with gout	I	Q4 2015
MEDI4920	anti-CD40L-Tn3 fusion protein	primary Sjögren's syndrome	I	Q2 2014
MEDI5872 [#]	B7RP1 MAb	systemic lupus erythematosus	I	Q4 2008
MEDI7836	IL-13 MAb-YTE	asthma	I	Q1 2015
Cardiovascular and Metabolic diseases				
MEDI6012	LCAT	ACS	II	Q4 2015
AZD4076	anti-miR103/107 oligonucleotide	non-alcoholic fatty liver disease/non-alcoholic steatohepatitis (NASH)	I	Q4 2015
MEDI0382	GLP-1/glucagon dual agonist	diabetes/obesity	I	Q1 2015
MEDI4166	PCSK9/GLP-1 MAb + peptide fusion	diabetes/cardiovascular	I	Q4 2015
MEDI8111	Rh-factor II	trauma/bleeding	I	Q1 2014

Compound	Mechanism	Area Under Investigation	Phase	Date Commenced Phase
Oncology				
AZD1775 [#]	WEE-1 inhibitor	ovarian cancer	II	Q4 2012
AZD2014	mTOR serine/threonine kinase inhibitor	solid tumours	II	Q1 2013
AZD3759 BLOOM	EGFR tyrosine kinase inhibitor	brain metastases in advanced	II	Q4 2015
Tagrisso (AZD9291) BLOOM	EGFR tyrosine kinase inhibitor	EGFRm NSCLC		
AZD4547	FGFR tyrosine kinase inhibitor	solid tumours	II	Q4 2011
AZD5069 + durvalumab [#]	CXCR2 + PD-L1 MAb	SCCHN	II	Q3 2015
AZD9150 [#] + durvalumab [#]	STAT3 inhibitor + PD-L1 MAb			
AZD5363 [#]	AKT kinase inhibitor	breast cancer	II	Q1 2014
durvalumab [#]	PD-L1 MAb	solid tumours	II	Q3 2014
durvalumab [#] + tremelimumab	PD-L1 MAb + CTLA-4 MAb	gastric cancer	II	Q2 2015
MEDI-551 [#]	CD19 MAb	diffuse B-cell lymphoma	II	Q1 2012
MEDI-573 [#]	IGF MAb	metastatic breast cancer	II	Q2 2012
savolitinib/volitinib [#]	MET tyrosine kinase inhibitor	papillary renal cell carcinoma	II	Q2 2014
selumetinib [#]	MEK inhibitor	2nd line KRAS wt NSCLC	II	Q1 2013
AZD0156	ATM serine/threonine kinase inhibitor	solid tumours	I	Q4 2015
AZD2811	Aurora B kinase inhibitor	solid tumours	I	Q4 2015
AZD5312 [#]	androgen receptor inhibitor	solid tumours	I	Q2 2014
AZD6738	ATR serine/threonine kinase inhibitor	solid tumours	I	Q4 2013
AZD8186	PI3 kinase beta inhibitor	solid tumours	I	Q2 2013
AZD8835	PI3 kinase alpha inhibitor	solid tumours	I	Q4 2014
AZD9150 [#]	STAT3 inhibitor	haematological malignancies	I	Q1 2012
Tagrisso (AZD9291) + (durvalumab [#] or selumetinib [#] or savolitinib [#]) TATTON	EGFR tyrosine kinase inhibitor + (PD-L1 MAb or MEK inhibitor or MET tyrosine kinase inhibitor)	advanced EGFRm NSCLC	I	Q3 2014
AZD9496	selective oestrogen receptor downregulator (SERD)	ER+ breast cancer	I	Q4 2014
durvalumab [#]	PD-L1 MAb	solid tumours	I	Q3 2014
durvalumab [#] + MEDI0680	PD-L1 MAb + PD-1 MAb	solid tumours	I	Q2 2014
durvalumab [#] + MEDI6383 [#]	OX40 agonist + PD-L1 MAb	solid tumours	I	Q2 2015
durvalumab [#] + dabrafenib + trametinib ²	PD-L1 MAb + BRAF inhibitor + MEK inhibitor	melanoma	I	Q1 2014
durvalumab [#] + tremelimumab	PD-L1 MAb + CTLA-4 MAb	solid tumours	I	Q4 2013
Iressa + durvalumab [#]	PD-L1 MAb + EGFR tyrosine kinase inhibitor	NSCLC	I	Q2 2014
MEDI0562 [#]	humanised OX40 agonist	solid tumours	I	Q1 2015
MEDI-551 [#] + rituximab	CD19 MAb + CD20 MAb	haematological malignancies	I	Q2 2014
MEDI-565 [#]	CEA BiTE MAb	solid tumours	I	Q1 2011
MEDI0639 [#]	DLL-4 MAb	solid tumours	I	Q2 2012
MEDI0680	PD-1 MAb	solid tumours	I	Q4 2013
MEDI1873	GITR agonist fusion protein	solid tumours	I	Q4 2015
MEDI3617 [#]	ANG-2 MAb	solid tumours	I	Q4 2010
MEDI4276	HER2 bispecific ADC MAb	solid tumours	I	Q4 2015
MEDI6383 [#]	OX40 agonist	solid tumours	I	Q3 2014
MEDI9197 [#]	TLR 7/8 agonist	solid tumours	I	Q4 2015
MEDI9447	CD73 MAb	solid tumours	I	Q3 2015
Infection, Neuroscience and Gastrointestinal				
AZD3241	myeloperoxidase inhibitor	multiple system atrophy	II	Q2 2015 (Orphan Drug)
AZD3293 [#]	beta-secretase inhibitor	Alzheimer's disease	II	Q4 2014
CXL [#]	beta lactamase inhibitor/cephalosporin	methicillin-resistant <i>S. aureus</i>	II	Q4 2010
MEDI7510	RSV sF+GLA-SE	prevention of RSV disease in older adults	II	Q3 2015
MEDI8852	influenza A MAb	influenza A treatment	II	Q4 2015
MEDI8897 [#]	RSV MAb-YTE	passive RSV prophylaxis	II	Q1 2015 (FDA Fast Track)
MEDI4893	MAb binding to <i>S. aureus</i> toxin	hospital-acquired pneumonia/serious <i>S. aureus</i> infection	II	Q4 2014 (FDA Fast Track)
ATM AVI [#]	monobactam/beta lactamase inhibitor	targeted serious bacterial infections	I	Q4 2012
AZD8108	NMDA antagonist	suicidal ideation	I	Q4 2014
MEDI1814	amyloid beta MAb	Alzheimer's disease	I	Q2 2014
MEDI3902	anti-Psl/PcrV	prevention of nosocomial pseudomonas pneumonia	I	Q3 2014 (FDA Fast Track)

[#] Partnered and/or in collaboration.

¹ Neuromyelitis optica: Now lead indication. Multiple sclerosis trial completed in 2015.

² MedImmune-sponsored trial in collaboration with Novartis AG.

Development Pipeline continued

Significant Life-Cycle Management

Compound	Mechanism	Area Under Investigation	Date Commenced Phase	Estimated Regulatory Submission Acceptance ¹			
				US	EU	Japan	China
Respiratory, Inflammation and Autoimmunity							
Duaklir Genuair [#]	LAMA/LABA	COPD		2018	Launched	2018	2018
Symbicort SYGMA	ICS/LABA	as-needed use in mild asthma	Q4 2014	N/A	2018		2019
Symbicort	ICS/LABA	breath actuated inhaler asthma/COPD		2018			
Cardiovascular and Metabolic diseases							
Brilinta/Brilique ¹ EUCLID	P2Y12 receptor antagonist	outcomes trial in patients with peripheral artery disease	Q4 2012	2017	2017	2017	2018
Brilinta/Brilique ¹ HESTIA	P2Y12 receptor antagonist	prevention of vaso-occlusive crises in paediatric patients with sickle cell disease	Q4 2014	2020	2020		
Brilinta/Brilique ¹ PEGASUS-TIMI 54	P2Y12 receptor antagonist	outcomes trial in patients with prior myocardial infarction	Q4 2010	Launched (Priority Review)	Accepted ²	Accepted	H2 2016
Brilinta/Brilique ¹ SOCRATES	P2Y12 receptor antagonist	outcomes trial in patients with stroke or TIA	Q1 2014	H1 2016	H1 2016	H2 2016	2017
Brilinta/Brilique ¹ THEMIS	P2Y12 receptor antagonist	outcomes trial in patients with Type 2 diabetes and CAD, but without a previous history of MI or stroke	Q1 2014	2018	2018	2018	2019
Bydureon EXSCEL	GLP-1 receptor agonist	Type 2 diabetes outcomes trial	Q2 2010	2018	2018	2018	
Bydureon weekly suspension	GLP-1 receptor agonist	Type 2 diabetes	Q1 2013	2017	2017		
Epanova STRENGTH	omega-3 carboxylic acids	outcomes trial in statin-treated patients at high CV risk, with persistent hypertriglyceridemia plus low HDL-cholesterol	Q4 2014	2020	2020	2020	2020
Epanova/Farxiga/Forxiga ³	omega-3 carboxylic acids/ SGLT2 inhibitor	non-alcoholic fatty liver disease/ non-alcoholic steatohepatitis (NASH)	Q1 2015				
Farxiga/Forxiga ³ DECLARE-TIMI 58	SGLT2 inhibitor	Type 2 diabetes outcomes trial	Q2 2013	2020	2020		
Farxiga/Forxiga ³	SGLT2 inhibitor	Type 1 diabetes	Q4 2014	2018	2017	2018	
Kombiglyze XR/Komboglyze ⁴	DPP-4 inhibitor/metformin FDC	Type 2 diabetes		Launched	Launched		Submitted
Onglyza SAVOR-TIMI 53	DPP-4 inhibitor	Type 2 diabetes outcomes trial	Q2 2010	Accepted	Launched		H2 2016 ⁵
saxagliptin/dapagliflozin FDC	DPP-4 inhibitor/SGLT2 inhibitor FDC	Type 2 diabetes	Q2 2012	Accepted ⁶	Accepted		
Xigduo XR/Xigduo ⁷	SGLT2 inhibitor/metformin FDC	Type 2 diabetes		Launched	Launched		
Oncology							
Faslodex FALCON	oestrogen receptor antagonist	1st line hormone receptor +ve advanced breast cancer	Q4 2012	H2 2016	H2 2016	H2 2016	2020
Lynparza (olaparib) SOLO-1	PARP inhibitor	1st line BRCAm ovarian cancer	Q3 2013	2017	2017	2017	
Lynparza (olaparib) SOLO-2	PARP inhibitor	2nd line or greater BRCAm PSR ovarian cancer, maintenance monotherapy	Q3 2013	H2 2016	2017	2017	
Lynparza (olaparib) SOLO-3	PARP inhibitor	gBRCA PSR ovarian cancer	Q1 2015	2018			
Lynparza (olaparib) GOLD	PARP inhibitor	2nd line gastric cancer	Q3 2013				2017
Lynparza (olaparib) OlympiA	PARP inhibitor	gBRCA adjuvant breast cancer	Q2 2014	2020	2020	2020	
Lynparza (olaparib) OlympiAD	PARP inhibitor	gBRCA metastatic breast cancer	Q2 2014	H2 2016	2017	2017	
Lynparza (olaparib) POLO	PARP inhibitor	pancreatic cancer	Q1 2015	2018	2018	2018	
Lynparza (olaparib)	PARP inhibitor	prostate cancer	Q3 2014	(Breakthrough Therapy designation) ⁸			
Tagrisso (AZD9291) ADAURA	EGFR tyrosine kinase inhibitor	adjuvant EGFRm NSCLC	Q4 2015	2022	2022		
Tagrisso (AZD9291) FLAURA	EGFR tyrosine kinase inhibitor	1st line advanced EGFRm NSCLC	Q1 2015	2017	2017	2017	2020
Tagrisso (AZD9291) + durvalumab [#] CAURAL ⁹	EGFR tyrosine kinase inhibitor + PD-L1 MAb	≥2nd line advanced EGFRm T790M NSCLC	Q3 2015				

Compound	Mechanism	Area Under Investigation	Date Commenced Phase	Estimated Regulatory Submission Acceptance†			
				US	EU	Japan	China
Infection, Neuroscience and Gastrointestinal							
Diprivan#	sedative and anaesthetic	conscious sedation		N/A	Launched	Accepted	Launched
linaclotide#	GC-C receptor peptide agonist	irritable bowel syndrome with constipation (IBS-C)		N/A	N/A	N/A	Accepted ¹⁰
Nexium	proton pump inhibitor	stress ulcer prophylaxis					H2 2016
Nexium	proton pump inhibitor	paediatrics		Launched	Launched	H2 2016	Accepted

[†] US and EU dates correspond to anticipated acceptance of the regulatory submission.

[#] Partnered and/or in collaboration.

¹ *Brilinta* in the US; *Brilique* in rest of world.

² CHMP Positive Opinion received December 2015.

³ *Farxiga* in the US; *Forxiga* in rest of world.

⁴ *Kombiglyze XR* in the US; *Komboglyze* in the EU.

⁵ Timing of China submission dependent on US regulatory approval.

⁶ CRL received October 2015.

⁷ *Xigduo XR* in the US; *Xigduo* in the EU.

⁸ Breakthrough Therapy designation granted for prostate cancer patients with BRCA1/2 or ATM gene mutated mCRPC who have received previous taxane-based chemotherapy and one newer hormonal agent (abiraterone or enzalutamide).

⁹ Temporarily closed to enrolment.

¹⁰ Submission accepted January 2016.

Terminations

NME/Line Extension	Compound	Reason for Discontinuation	Area Under Investigation
NME	AZD2115 [#]	Strategic	COPD
NME	AZD5213	Safety/efficacy	Tourette's syndrome/neuropathic pain
NME	AZD5847	Safety/efficacy	tuberculosis
NME	AZD9977	Safety/efficacy	diabetic kidney disease
NME	durvalumab [#] ATLANTIC	Strategic	3rd line NSCLC (PD-L1 positive)
NME	durvalumab [#] + MEDI6469 [#]	Strategic	solid tumours
NME	selumetinib [#] SUMIT	Safety/efficacy	uveal melanoma
NME	sifalimumab [#]	Strategic	systemic lupus erythematosus ¹
NME	tenapanor (AZD1722) [#]	Safety/efficacy	ESRD-Pi/CKD with T2DM
NME	MEDI-551 [#] + MEDI0680	Safety/efficacy	diffuse large B-cell lymphoma
NME	MEDI-559	Safety/efficacy	passive RSV prophylaxis
NME	MEDI6469 [#]	Strategic	solid tumours
NME	MEDI6469 [#] + rituximab	Strategic	solid tumours
NME	MEDI6469 [#] + tremelimumab	Strategic	solid tumours
LCM	brodalumab [#]	Lack of efficacy	asthma
LCM	durvalumab [#] after (<i>Tagrisso</i> (AZD9291) or <i>Iressa</i> or (selumetinib [#] + docetaxel) or tremelimumab)	Strategic	NSCLC
LCM	MEDI-551 [#]	Safety/efficacy	chronic lymphocytic leukaemia
LCM	moxetumomab pasudotox [#]	Safety/efficacy	paediatric acute lymphoblastic leukaemia
LCM	<i>Nexium</i>	Regulatory	refractory reflux oesophagitis (JP)
LCM	tralokinumab	Safety/efficacy	idiopathic pulmonary fibrosis

[#] Partnered and/or in collaboration.

¹ SLE project stopped but molecule under evaluation for alternative indications.

Completed Projects/Divestitures

Compound	Mechanism	Area Under Investigation	Completed/Divested	Estimated Regulatory Submission Acceptance [†]			
				US	EU	Japan	China
<i>Myalept</i>	leptin analogue	lipodystrophy	Completed	Launched			
<i>Lynparza</i> (olaparib) capsule	PARP inhibitor	BRCa/PSR ovarian cancer	Completed	Launched	Launched		
AZD0914	GyrAR	serious bacterial infections (Phase III)	Divested in Phase II				
<i>Movantik/Moventig</i> ^{#1}	oral peripherally-acting mu-opioid receptor antagonist	opioid-induced constipation	Completed	Launched	Launched		
<i>Bydureon</i> Dual Chamber Pen	GLP-1 receptor agonist	Type 2 diabetes	Completed	Launched	Launched	Launched	
brodalumab AMVISION-1,2 ²	IL-17R MAb	psoriatic arthritis	Partnered				
<i>Caprelsa</i> ³	VEGFR/EGFR tyrosine kinase inhibitor with RET kinase activity	medullary thyroid cancer	Divested	Launched	Launched	Approved ⁴	Accepted
<i>Caprelsa</i> ³	VEGFR/EGFR tyrosine kinase inhibitor with RET kinase activity	differentiated thyroid cancer	Divested				
<i>Entocort</i> ⁵	glucocorticoid steroid	Crohn's disease/ulcerative colitis	Completed/Divested	Launched	Launched	Q4 2015	N/A
<i>Iressa</i>	EGFR tyrosine kinase inhibitor	EGFRm NSCLC	Completed	Launched ⁶	Launched	Launched	Launched
AZD4901 ⁷	NK3 receptor antagonist	polycystic ovarian syndrome	Divested in Phase II				

[†] US and EU dates correspond to anticipated acceptance of the regulatory submission.

[#] Partnered and/or in collaboration.

¹ *Movantik* in the US; *Moventig* in EU.

² AstraZeneca has granted Valeant an exclusive licence to develop and commercialise brodalumab.

³ Divested to Genzyme (deal completed October 2015).

⁴ Approved in Japan in September 2015.

⁵ Global rights, outside the US, divested to Tillotts Pharma AG in July 2015. AstraZeneca continues to support the Japanese regulatory submission.

⁶ Launched in US Q3 2015.

⁷ Divested to Millendo Therapeutics, Inc. Agreement announced January 2016.

Patent Expiries

Patent expiries for our key marketed products

AstraZeneca is exposed to third party challenges of its patents and products. Generic products may be launched at risk and our patents may be revoked, circumvented or found not to be infringed. For more information, please see Risk from page 212. Many of our products are subject to challenges by third parties. Details of material challenges by third parties can be found in Note 27 to the Financial Statements from page 186. The expiry dates shown below do not include any granted SPC/PTE and/or Paediatric Exclusivity periods unless asterisked; see key in footnotes. (In Europe, the exact SPC situation may vary by country as different Patent Offices may grant SPC at different rates.) A number of our products are subject to generic competition in one or more markets. Further information can be found in the Geographical Review from page 227.

US

Key marketed products	US patent expiry		US Product Sales (\$m)		
	New Chemical Entity patent(s)	Expiry dates of other patents (such as the FDA Orange Book)	2015	2014	2013
<i>Atacand</i> ³			34	44	72
<i>Brilinta</i>	2018, 2019	2021, 2030	240	146	73
<i>Bydureon</i>		2016 ¹ , 2017, 2018, 2020, 2021, 2022, 2024, 2025, 2026, 2028	482	374	131
<i>Byetta</i>		2016 ¹ , 2017, 2018, 2020	209	199	152
<i>Crestor</i> ⁴	2016 ^{1, 2}	2018 ² , 2021 ² , 2022 ²	2,844	2,918	2,912
<i>Daliresp</i>	2020 ¹	2023, 2024	104	–	–
<i>Faslodex</i>		2021 ²	356	340	324
<i>Farxiga</i>	2020	2020, 2027, 2028, 2029, 2030	261	122	–
<i>Iressa</i>	2017 (2022 ⁵)		6	–	–
<i>Kombiglyze XR</i>	2023 ¹	2025	– ⁶	– ⁶	– ⁶
<i>Lynparza</i>	2022, 2024	2024, 2027, 2028, 2031	70	–	–
<i>Nexium</i>		2016 ² , 2018 ² , 2019 ² , 2020 ^{2,7}	902	1,876	2,123
<i>Onglyza</i>	2023 ¹	2028	420	481	265
<i>Pulmicort</i> ⁸		2018, 2019 ²	200	211	224
<i>Seloken/Toprol-XL</i>			89	91	131
<i>Seroquel XR</i> ⁹		2017	716	738	743
<i>Symbicort</i>		2017, 2018, 2021, 2023, 2024, 2026, 2028, 2029	1,520	1,511	1,233
<i>Synagis</i>		2023	285	499	617
<i>Tudorza</i>	2020	2016, 2022, 2027	103	–	–
<i>Zoladex</i>		2021, 2022	28	26	23

China, EU and Japan

Key marketed products	China patent expiry	EU patent expiry ¹¹	Japan patent expiry	China, EU and Japan combined Product Sales (\$m) ¹⁰		
				2015	2014	2013
<i>Atacand</i> Patents	12	Expired	12	91	151	200
<i>Brilique</i> NCE Patents Non-NCE Patents	2018, 2019 2021	2018, 2024 ¹ 2021 ¹³	2018, 2019 2021, 2027	255	232	155
<i>Bydureon</i> Non-NCE Patents	2020, 2021 ¹⁴ , 2025 ¹⁴	2017, 2020, 2021, 2021 ¹ , 2022, 2024, 2026, 2027 ¹⁵	2018, 2021, 2024, 2025, 2026, 2027, 2028	82	59	17
<i>Byetta</i> Non-NCE Patents	2020	2017, 2018, 2020, 2021 ^{1,15}	2018, 2020 ¹	84	105	46
<i>Crestor</i> NCE Patent Non-NCE Patents		2017 ^{1,2} 2020	2017 ¹ 2021, 2023 ¹	1,585	1,877	1,864
<i>Duaklir Genuair</i> NCE Patent Non-NCE Patents	2020 2016, 2022, 2025, 2027	2025 ¹ 2016, 2022, 2025, 2027, 2028, 2029	2025 ¹ 2016, 2022, 2025, 2027, 2028	21	–	–
<i>Eklira Genuair</i> NCE Patent Non-NCE Patents	2020 2016, 2022, 2025, 2027	2025 ¹ 2016, 2022, 2025, 2027, 2028, 2029	2025 ¹ 2016, 2022, 2025, 2027, 2028	61	12	–
<i>Faslodex</i> Non-NCE Patents	2021 ¹⁶	2021	2026 ¹	259	295	272

Key marketed products	China patent expiry	EU patent expiry ¹¹	Japan patent expiry	China, EU and Japan combined Product Sales (\$m) ¹⁰		
				2015	2014	2013
<i>Forxiga</i>				134	74	10
NCE Patent	2023	2027 ¹	2023			
Non-NCE Patents	2027, 2028	2027, 2028	2028 ¹ , 2028			
<i>Iressa</i>				389	459	489
NCE Patent	2016	2019 ¹⁷	2018			
<i>Kombiglyze XR</i>				⁶	⁶	⁶
NCE Patent	2021	2026 ¹	–			
Non-NCE Patents	2025	2025	–			
<i>Komboglyze</i>				⁶	⁶	⁶
NCE Patent	2021	2026 ¹	–			
Non-NCE Patents	2025	2025	–			
<i>Lynparza</i>				23	–	–
NCE Patent	2021, 2024	2021, 2029 ¹	2021, 2024			
Non-NCE Patents	2024, 2027	2024, 2027	2024, 2027			
<i>Nexium</i>				950	966	828
NCE Patent	Expired	Expired	2018 ¹			
Non-NCE Patents	2018, 2019	2018	2018, 2019			
<i>Onglyza</i>				168	164	62
NCE Patent	2021	2024 ¹	–			
Non-NCE Patents	2025	2025	–			
<i>Pulmicort</i> ¹⁸				653	564	481
Non-NCE Patents	2018	2018	2018			
<i>Seloken/Toprol-XL</i>				428	428	400
Non-NCE Patents	Expired	Expired	Expired			
<i>Seroquel XR</i>				176	306	381
Non-NCE Patents	2017	2017	¹⁹			
<i>Symbicort</i>				1,310	1,666	1,634
Non-NCE Patents	2018	2018, 2019	2017, 2019, 2020			
<i>Synagis</i>				377	401	443
Non-NCE Patents	–	2023	2023			
<i>Zoladex</i>				468	526	581
Non-NCE Patents	2021	2021	2021			

¹ Date represents expiry of granted PTE; or expiry of granted SPC where SPC has been granted in several or all countries.

² Date includes Paediatric Exclusivity.

³ *Atacand* HCT.

⁴ A settlement agreement permits Watson Laboratories, Inc. and Actavis, Inc. (together, Watson) to begin selling its generic version of *Crestor* and its rosuvastatin zinc product beginning 2 May 2016.

⁵ Date in brackets reflects seven years' Orphan Drug exclusivity to 13 July 2022.

⁶ *Komboglyze*/*Kombiglyze XR* Product Sales are included in the *Onglyza* Product Sales figure.

⁷ Licence agreements with Teva and Ranbaxy Pharmaceuticals Inc. and other generic companies allow each to launch a generic version in the US from May 2014, subject to regulatory approval.

⁸ A licence agreement with Teva permits their ongoing sale in the US of a generic version from December 2009. The 2018 expiry relates to the *Flexhaler* device, while the 2019 expiry relates to the formulation in the *Flexhaler* presentation and also to *Respules*.

⁹ Licence agreements with various generics companies allow launches of generic versions of *Seroquel XR* in the US from 1 November 2016 or earlier upon certain circumstances, subject to regulatory approval.

¹⁰ Aggregate revenue for China, the EU and Japan.

¹¹ Expiry in major EU markets.

¹² Takeda retained rights.

¹³ The patent was revoked during opposition proceedings at the European Patent Office. The patentee has appealed that decision.

¹⁴ Regulatory approval for the product is pending in China.

¹⁵ There is eight years' data exclusivity and two years' market exclusivity for *Byetta* and *Bydureon* to 2016.

¹⁶ Decision of the Patent Reexamination Board invalidating the patent suspended pending outcome of appeal process.

¹⁷ SPC expires 2 March 2019. There is eight years' data exclusivity and two years' market exclusivity for *Iressa* in the EU to 24 June 2019.

¹⁸ The 2018 expiry relates to the formulation in the *Turbuhaler* presentation and to a process useful for the *Respules* product.

¹⁹ Rights licensed to Astellas.

Risk

Risks and uncertainties

Operating in the pharmaceutical sector carries various inherent risks and uncertainties that may affect our business. In this section, we describe the risks and uncertainties that we consider material to our business in that they may have a significant effect on our financial condition, results of operations, and/or reputation.

These risks are not listed in any particular order of priority and have been categorised consistently with the Principal risks detailed from page 21. Other risks, unknown or not currently considered material, could have a similar effect. We believe that the forward-looking statements about AstraZeneca in this Annual Report, identified by words such as 'anticipates', 'believes', 'expects' and 'intends', and that include, among other things, Future prospects in the Financial Review on page 76, are based on reasonable assumptions. However, forward-looking statements involve inherent risks and uncertainties such as those summarised below. They relate to events that may occur in the future, that may be influenced by factors beyond our control and that may have actual outcomes materially different from our expectations.

Product pipeline and IP risks	Impact
<p>Failure to meet development targets</p> <p>The development of any pharmaceutical product candidate is a complex, risky and lengthy process involving significant financial, R&D and other resources, which may fail at any stage of the process due to various factors. These include failure to obtain the required regulatory or marketing approvals for the product candidate or its manufacturing facilities; unfavourable clinical efficacy data; safety concerns; failure of R&D to develop new product candidates; failure to demonstrate adequate cost-effective benefits to regulatory authorities and/or payers; and the emergence of competing products.</p> <p>Because our business model and strategy rely on the success of relatively few compounds, the failure of any in line production may have a significant negative effect on our business or results of operations.</p> <p>Production and release schedules for biologics may be more significantly impacted by regulatory processes than other products. This is due to more complex and stringent regulation on the manufacturing of biologics and their supply chain.</p>	<p>A succession of negative drug project results and a failure to reduce development timelines effectively, or produce new products that achieve the expected commercial success, could frustrate the achievement of development targets, adversely affect the reputation of our R&D capabilities, and is likely to materially adversely affect our business and results of operations. See also Failure to achieve strategic priorities or to meet targets or expectations on page 225.</p>
<p>Delay to new product launches</p> <p>Our continued success depends on the development and successful launch of innovative new drugs. The anticipated launch dates of major new products significantly affect our business, including investment in large clinical studies; the manufacture of pre-launch product stocks; investment in marketing materials pre-launch; sales force training; and the timing of anticipated future revenue streams from new Product Sales. Launch dates are primarily driven by our development programmes and the demands from various factors, including adverse findings in pre-clinical or clinical studies, regulatory demands, price negotiation, competitor activity and technology transfer.</p>	<p>Significant delays to anticipated launch dates of new products could have a material adverse effect on our financial condition and/or results of operations. For example, for the launch of products that are seasonal in nature, delays in regulatory approvals or manufacturing difficulties may delay launch to the next season which, in turn, may significantly reduce the return on costs incurred in preparing for the launch for that season. In addition, a delayed launch may lead to increased costs if, for example, marketing and sales efforts need to be rescheduled or performed for longer than expected.</p>

Acquisitions and strategic alliances, including licensing and collaborations, may be unsuccessful

We seek licensing arrangements and strategic collaborations to expand our product portfolio and geographical presence as part of our business strategy. Such licensing arrangements and strategic collaborations are key, enabling us to grow and strengthen the business. The success of such arrangements is largely dependent on the technology and other IP rights we acquire, and the resources, efforts and skills of our partners.

Also, under many of our licensing arrangements and strategic collaborations, we make milestone payments well in advance of the commercialisation of the products, with no assurance that we will recoup these payments.

We may also seek to acquire complementary businesses or enter into other strategic transactions. The integration of an acquired business could involve incurring significant debt and unknown or contingent liabilities, as well as having a negative effect on our reported results of operations from acquisition-related charges, amortisation of expenses related to intangibles and charges for the implementation of long-term assets. We may also experience difficulties in integrating geographically separated organisations, systems and facilities, and personnel with different organisational cultures.

Furthermore, we experience strong competition from other pharmaceutical companies in respect of licensing arrangements, strategic collaborations, and acquisition targets, and therefore, we may be unsuccessful in implementing some of our intended projects or we may have to pay a significant premium over book or market values for our acquisitions.

If we fail to complete these types of collaborative projects in a timely manner, on a cost-effective basis, or at all, this may limit our ability to access a greater portfolio of products, IP technology and shared expertise.

Additionally, disputes or difficulties in our relationship with our collaborators or partners may arise, often due to conflicting priorities or conflicts of interest between parties, which may erode or eliminate the benefits of these alliances.

The incurrence of significant debt or liabilities due to the integration of an acquired business could cause deterioration in our credit rating and result in increased borrowing costs and interest expense. We may issue additional shares to pay for acquired businesses, which would result in the dilution of our then existing shareholders.

Further, if liabilities are uncovered in an acquired business, an acquired business fails to perform in line with expectations, or a strategic transaction does not deliver the results we intended, then the Group or our shareholders may suffer losses and may not have adequate remedies against the seller or third parties. Integration processes may also result in business disruption, diversion of management resources, the loss of key employees and other issues, such as a failure to integrate IT and other systems.

Risk continued

Product pipeline and IP risks	Impact
<p>Difficulties obtaining and maintaining regulatory approvals for new products</p> <p>We are subject to strict controls on the commercialisation processes for our pharmaceutical products, including their development, manufacture, distribution and marketing. Safety, efficacy and quality must be established before a drug can be marketed for a given indication. The criteria for establishing safety, efficacy and quality may vary by country or region and the submission of an application to regulatory authorities may or may not lead to the grant of marketing approval. Regulators can refuse to grant approval or may require additional data before approval is given, even though the medicine may already be launched in other countries. Approved products are also subject to regulations, and a failure to comply can potentially result in losing regulatory approval to market our products. Regulations may require a company to conduct additional clinical trials after a drug's approval, which can result in increased costs, labelling challenges or loss of regulatory approval.</p> <p>Factors, including advances in science and technology, evolving regulatory science, and different approaches to benefit/risk tolerance by regulatory authorities, the general public, and other third party public interest groups influence the initial approvability of new drugs. Existing marketed products are also subject to these same forces, and new data and meta-analyses have the potential to drive changes in the approval status or labelling. Recent years have seen an increase in post-marketing regulatory requirements and commitments, and an increased call for third party access to regulatory and clinical trial data packages for independent analysis and interpretation, and broader data transparency.</p> <p>Unanticipated and unpredictable policy making by governments and regulators can adversely influence regulatory decision making, often leading to severe delays in regulatory approval. The predictability of the outcome and timing of review processes remains challenging due to evolving regulatory science, competing regulatory priorities, unpredictable policy making and limits placed on regulatory authority resources.</p>	<p>Delays in regulatory reviews and approvals impact patient and market access. In addition, post-approval requirements result in increased costs and may impact the labelling and approval status of currently marketed products.</p>
<p>Failure to obtain and enforce effective IP protection</p> <p>Our ability to obtain and enforce patents and other IP rights in relation to our products is an important element in protecting our investment in R&D and creating long-term value for the business. Some countries in which we operate are still developing their IP laws, others are limiting the applicability of their IP laws to certain pharmaceutical inventions. Certain countries may seek to limit or deny effective IP protection for pharmaceuticals because of adverse political perspectives around the desirability of appropriate IP protection for pharmaceuticals.</p>	<p>Limitations on the availability of patent protection or the use of compulsory licensing in certain countries in which we operate could have a material adverse effect on the pricing and sales of our products and, consequently, could materially adversely affect our revenues from those products. More information about protecting our IP, the risk of patent litigation and the early loss of IP rights is contained in the Intellectual Property section on page 60, the Effects of patent litigation in respect of IP rights risk on page 218 and the Expiry or loss of, or limitations to, IP rights and consequential pressure from generic competition risk on page 215.</p>

Expiry or loss of, or limitations to, IP rights and consequential pressure from generic competition

A pharmaceutical product is protected from being copied for the limited period of protection under patent rights and/or related IP rights such as Regulatory Data Protection or Orphan Drug status. This period of protection helps us recoup our overall R&D investment. Early loss of IP rights may threaten our ability to recoup our investment in a patent product. Expiry or loss of these rights can materially adversely affect our revenues and financial condition due to the launch of generic copies of the product in the country where the rights have expired or been lost (see the Patent Expiries section on pages 210 and 211, which contains a table of certain patent expiry dates for our key marketed products). Products protected by our IP account for a significant proportion of our revenues. For example, in 2015, US Product Sales for *Crestor* and *Seroquel XR* were \$2,844 million (2014: \$2,918 million) and \$716 million (2014: \$738 million), respectively. Additionally, the expiry or loss of patents covering other innovator companies' products may also lead to increased competition and pricing pressure for our own, still-patented, products in the same product class due to the availability of lower priced generic products in that product class. Typically, products under patent protection or within the period of Regulatory Data Protection generate significantly higher revenues than those not protected by such rights.

A pharmaceutical product competes with other products marketed by research-based pharmaceutical companies and approved for the same condition, as well as with generic drugs for that condition marketed by generic drug manufacturers. Generic versions of products are often sold at lower prices than branded products, as the manufacturer does not have to recoup the significant cost of R&D investment and market development. The majority of our patented products, including *Nexium*, *Crestor* and *Seroquel XR*, are subject to pricing pressures due to competition from generic copies of these products and from generic forms of other drugs in the same product class (for example, generic forms of *Losec/Prilosec*, *Lipitor* and *Seroquel IR*). Additionally, generic manufacturers are often able to invest more resources in the marketing of their products than we do, due to their lack of R&D expenses.

As well as facing generic competition upon expiry or loss of IP rights, we also face the risk that generic drug manufacturers seek to market generic versions of our products prior to expiries of our patents and/or the Regulatory Exclusivity periods. For example, as detailed in Note 27 to the Financial Statements from page 186, we are currently facing challenges from numerous generic drug manufacturers regarding our patents relating to key products, including *Brilinta*, *Faslodex*, *Seroquel XR*, *Byetta*, *Daliresp*, *Onglyza* and *Crestor* (which goes off-patent in the US in May 2016). Patent challenges are also discussed in the Effects of patent litigation in respect of IP rights risk on page 218. Generic manufacturers may also take advantage of the failure of certain countries to properly enforce Regulatory Data Protection and may launch generics during this protected period. This is a particular risk in some Emerging Markets where appropriate patent protection may be difficult to obtain or enforce.

If challenges to our IP by generic drug manufacturers succeed and generic products are launched, or generic products are launched 'at risk' on the expectation that challenges to our IP will be successful, this may materially adversely affect our revenues and financial condition. Furthermore, if limitations on the availability, scope or enforceability of patent protection are implemented in jurisdictions in which we operate, generic manufacturers in these countries may be increasingly able to introduce competing products to the market earlier than they would have been able to, had more robust patent protection or Regulatory Data Protection been available.

Risk continued

Commercialisation risks	Impact
<p>Abbreviated approval processes for biosimilars</p> <p>While no application for a biosimilar has been made in relation to an AstraZeneca biologic, various regulatory authorities are implementing or considering abbreviated approval processes for biosimilars that would compete with patented biologics.</p> <p>For example, in 2010, the US enacted the Biologics Price Competition and Innovation Act within the ACA, which contains general directives for biosimilar applications. The FDA issued final guidance in April 2015 on implementing an abbreviated biosimilar approval pathway. In March 2015, the FDA approved the first biosimilar product submitted under the abbreviated biosimilar pathway. However, significant questions remain, including standards for designation of interchangeability and data collection requirements to support extrapolation of indications. In addition, due to the recent submissions and approvals of abbreviated biosimilar applications, a number of legal challenges constraining the requirements of the abbreviated biosimilar pathway are under review. For example, in July 2015, the US Court of Appeals for the Federal Circuit held that biosimilar applicants were not required to provide copies of the biosimilar application or manufacturing information but needed to provide 180-day commercial marketing notice to the reference sponsor. Although this decision and other ongoing legal challenges do not directly impact an AstraZeneca biologic, uncertainty regarding the abbreviated biosimilar approval pathway may remain until these initial legal challenges reach final conclusion.</p> <p>In Europe, the EMA published final guidelines on similar biologics containing MABs and in May 2012, the first MAB biosimilar application was submitted with recommendation for approval made by the EMA. Notably, various jurisdictions have adopted either the EMA guidelines or those set forth by WHO to enable biosimilars to enter the market after discrete periods of data exclusivity.</p>	<p>The extent to which biosimilars would differ from patented biologics on price is unclear. However, due to their complex nature, it is uncertain whether biosimilars would have the same impact on patented biologics that generic products have had on patented small molecule products.</p> <p>In addition, it is uncertain when any such abbreviated approval processes may be fully realised, particularly for more complex protein molecules such as MABs. Such processes may materially and adversely affect the future commercial prospects for patented biologics, such as the ones that we produce.</p>
<p>Political and socio-economic conditions</p> <p>We operate in over 100 countries around the world, some of which may be subject to political and social instability. There may be disruption to our business if there is instability in a particular geographic region, including as a result of war, terrorism, riot, unstable governments, civil insurrection or social unrest. For instance, our operational risks in Ukraine have increased due to growing political and economic uncertainty in the region.</p>	<p>Deterioration of, or failure to improve, socio-economic conditions, and situations and/or resulting events, depending on their severity, could adversely affect our supply and/or distribution chain in the affected countries and the ability of customers or ultimate payers to purchase our medicines. This could adversely affect our business or results of operations. Broader economic developments, such as potential international sanctions and global oil price developments, could exacerbate this effect in the Ukrainian and Russian markets.</p>

Developing our business in Emerging Markets

The development of our business in Emerging Markets is a critical factor in determining our future ability to sustain or increase our global Product Sales. This poses various challenges including: more volatile economic conditions and/or political environments; competition from multinational and local companies with existing market presence; the need to identify and to leverage appropriate opportunities for sales and marketing; poor IP protection; inadequate protection against crime (including counterfeiting, corruption and fraud); inadequate infrastructure to address disease outbreaks (such as the Ebola virus); the need to impose developed market compliance standards; the need to meet a more diverse range of national regulatory, clinical and manufacturing requirements; inadvertent breaches of local and international law; not being able to recruit appropriately skilled and experienced personnel; identification of the most effective sales and marketing channels and route to market; and interventions by national governments or regulators restricting market access and/or introducing adverse price controls.

The failure to exploit potential opportunities appropriately in Emerging Markets or materialisation of the risks and challenges of doing business in such markets, including inadequate protection against crime (including counterfeiting, corruption and fraud) or inadvertent breaches of local and international law may materially adversely affect our reputation, business or results of operations.

Challenges to achieving commercial success of new products

The successful launch of a new pharmaceutical product involves substantial investment in sales and marketing activities, launch stocks and other items. The commercial success of our new medicines is particularly important to replace lost Product Sales following patent expiry. We may ultimately be unable to achieve commercial success for any number of reasons. These include difficulties in manufacturing sufficient quantities of the product candidate for development or commercialisation in a timely manner, the impact of price control measures imposed by governments and healthcare authorities, the outcome of negotiations with third party payers, erosion of IP rights, including infringement by third parties, failure to show a differentiated product profile and changes in prescribing habits.

As a result, we cannot be certain that compounds currently under development will achieve success, and our ability to accurately assess, prior to launch, the eventual efficacy or safety of a new product once in broader clinical use can only be based on data available at that time, which is inherently limited due to relatively short periods of product testing and relatively small clinical study patient samples.

The commercialisation of biologics is often more complex than for small molecule pharmaceutical products, primarily due to differences in the mode of administration, technical aspects of the product, and rapidly changing distribution and reimbursement environments.

Our products are subject to competition by other products approved for the same or similar indication, and the approval of a competitive product that is considered superior, or equivalent to, one of our products may result in immediate and significant decreases in our revenues.

If a new product does not succeed as anticipated or its rate of sales growth is slower than anticipated, there is a risk that we may be unable to fully recoup the costs incurred in launching it, which could materially adversely affect our business or results of operations.

Due to the complexity of the commercialisation process for biologics, the methods of distributing and marketing biologics could materially adversely impact our revenues from the sales of biologics medicines, such as *Synagis* and *FluMist/Fluenz*.

Risk continued

Commercialisation risks	Impact
<p>Effects of patent litigation in respect of IP rights</p> <p>Any of the IP rights protecting our products may be asserted or challenged in IP litigation and/or patent office proceedings initiated against or by external parties. We expect our most valuable products to receive the greatest number of challenges. Despite our efforts to establish and defend robust patent protection for our products, we may not succeed in protecting or enforcing our patents in such litigation or other challenges.</p> <p>We bear the risk that courts may decide that third parties do not infringe our asserted IP rights. This may result in AstraZeneca losing exclusivity and/or erosion of revenues.</p> <p>Where we assert our IP rights but are ultimately unsuccessful, third parties may seek damages, alleging, for example, that they have been inappropriately restrained from entering the market. In such cases, we bear the risk that we incur liabilities to those third parties.</p> <p>We also bear the risk that we may be found to infringe patents owned or licensed exclusively by third parties, including research-based and generic pharmaceutical companies and individuals. Third parties may seek damages for alleged patent infringement. In the US, they may also seek enhanced (ie up to treble) damages for alleged wilful infringement of their patents.</p> <p>Details of material patent litigation matters can be found in Note 27 to the Financial Statements from page 186.</p>	<p>Managing or litigating infringement disputes over so-called ‘freedom to operate’ can be costly. We may be subject to injunctions against our products or processes and be liable for damages or royalties. We may need to obtain costly licences. These risks may be greater in relation to biologics and vaccines, where patent infringement claims may relate to discovery or research tools, and manufacturing methods and/or biological materials. While we seek to manage such risks by, for example, acquiring licences, forgoing certain activities or uses, or modifying processes to avoid infringement claims and permit commercialisation of our products, such steps can entail significant cost and there is no guarantee that they will be successful.</p> <p>If we are not successful in maintaining exclusive rights to market one or more of our major products, particularly in the US where we achieve our highest Product Sales, our revenue and margins could be materially adversely affected.</p> <p>Unfavourable resolution of such current and similar future patent litigation matters could subject us to damages (including enhanced damages), require us to make significant provisions in our accounts relating to legal proceedings and/or could materially adversely affect our financial condition or results of operations.</p>
<p>Price controls and reductions</p> <p>Most of our key markets have experienced the implementation of various cost control or reimbursement mechanisms for pharmaceutical products.</p> <p>For example, in the US, prices are being depressed through restrictive reimbursement policies and cost control tools such as restricted lists and formularies, which 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 payers to limit the use of branded products and put pressure on manufacturers to reduce net prices. In addition, payers are shifting a greater proportion of the cost of branded medicines to the patient via out-of-pocket payments at the pharmacy counter. The patient out-of-pocket spend is generally in the form of a co-payment or, in some cases, a co-insurance, which is designed, principally, to encourage patients to use generic medicines.</p> <p>In Emerging Markets, governments are increasingly controlling pricing in the self-pay sector and favouring locally manufactured drugs.</p> <p>A summary of the principal aspects of price regulation and how pricing pressures are affecting our business in our most important markets is set out in Pricing of medicines in the Marketplace section on page 14 and overleaf in the following risk factor.</p>	<p>Due to these pricing pressures, there can be no certainty that we will be able to charge prices for a product that, in a particular country or in the aggregate, enable us to earn an adequate return on our product investment. These pressures, including the increasingly restrictive reimbursement policies to which we are subject, as well as potential legislation that expands the commercial importation of medicines into the US, could materially adversely affect our business or results of operations.</p> <p>We expect these pricing pressures will continue, and may increase.</p>

Economic, regulatory and political pressures

We face continued economic, regulatory and political pressures to limit or reduce the cost of our products.

In 2010, the US enacted the ACA, a comprehensive health reform law that expands insurance coverage, implements delivery system reforms and places a renewed focus on cost and quality. In terms of specific provisions impacting our industry, the law mandates higher rebates and discounts on branded drugs for certain Medicare and Medicaid patients as well as an industry-wide excise fee. Implementation of several health system delivery reforms included in the ACA has commenced and will continue through 2018. The ACA expands the patient population eligible for Medicaid and provides new insurance coverage for individuals through state and federally operated health insurance exchanges. In general, patients enrolled in the exchanges are subject to higher cost sharing obligations and may not have as robust access to prescription drugs as compared to patients enrolled in Medicare Part D or commercial plans. Based, in part, on the impact of ACA to other healthcare sectors, there is ongoing scrutiny of the US pharmaceutical industry that could result in further government intervention and financial constraint. Many stakeholders, including some in Congress and others in the broader healthcare system, such as health plans, have dramatically increased their criticism over the value of medicines in the US and have placed a stronger emphasis on innovative therapies. Such criticism and focus on the value of medicines has resulted in proposed policy and legislative changes at the state and federal levels aimed at imposing price controls on medicines and increasing price transparency. For more information, please see Regulatory requirements and Pricing of medicines in the Marketplace section from page 13 and page 14, respectively.

In the EU, efforts by the EC to reduce inconsistencies and improve standards in the disparate national pricing and reimbursement systems met with little immediate success as Member States guard their right to make healthcare budget decisions. The industry continues to be exposed in Europe to various *ad hoc* cost-containment measures and reference pricing mechanisms, which impact prices. There is a trend towards increasing transparency and comparison of prices among EU Member States. Recent controversy regarding the high price of a drug marketed by one of our competitors for chronic hepatitis C may provoke further EU collaboration and may eventually lead to a change in the overall pricing and reimbursement landscape.

Concurrently, many markets are adopting the use of Health Technology Assessment (HTA) to provide a rigorous evaluation of the clinical efficacy of a product, at, or post, launch. HTA evaluations are also increasingly being used to assess the clinical effect, as well as cost-effectiveness, of products in a particular health system. This comes as payers and policymakers attempt to increase efficiencies in the use and choice of pharmaceutical products.

Further information regarding these pressures is contained in Regulatory requirements and Pricing of medicines in the Marketplace section from page 13 and page 14, respectively.

While new patients entering the US healthcare system due to the ACA may lead to a slight increase in prescription drug utilisation, we expect that our financial and other costs resulting from the ACA, many of which we are unable to accurately estimate, will far outweigh any increase in Product Sales.

The continued disparities in EU and US pricing systems could lead to marked price differentials between markets, which, by way of the implementation of existing or new reference pricing mechanisms, increases the pricing pressure affecting the industry. The importation of pharmaceutical products from countries where prices are low due to government price controls, or other market dynamics, to countries where prices for those products are higher, is already prevalent and may increase. Increased transparency of net prices and strengthened collaboration by governments may accelerate the development of further cost containment policies (such as procurement or the comparison of net prices etc).

Illegal trade in our products

The illegal trade in pharmaceutical products is widely recognised by industry, non-governmental organisations and governmental authorities to be increasing. Illegal trade includes counterfeiting, theft and illegal diversion (that is, when our products are found in a market where we did not send them and where they are not approved or not permitted/allowed to be sold). There is a risk to public health when illegally traded products enter the supply chain, as well as associated financial risk. Authorities and the public expect us to help reduce opportunities for illegal trade in our products through securing the integrity of our supply chain, surveillance, investigation and supporting legal action against those found to be engaged in illegal trade.

Public loss of confidence in the integrity of pharmaceutical products as a result of illegal trade could materially adversely affect our reputation and financial performance. In addition, undue or misplaced concern about this issue may cause some patients to stop taking their medicines, with consequential risks to their health. Authorities may take action, financial or otherwise, if they believe we are liable for breaches in our own supply chains.

There is also a direct financial loss when counterfeit and/or illegally diverted products replace sales of genuine products; or genuine products are recalled following discovery of counterfeit products; or products which have been the subject of theft or illegal diversion are recalled; or illegally diverted products replace sales of products which are approved/allowed for sale in a market.

Risk continued

Commercialisation risks	Impact
<p>Increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation</p> <p>There is an increasing global focus on the implementation and enforcement of anti-bribery and anti-corruption legislation.</p> <p>For example, in the UK, the Bribery Act 2010 has extensive extra-territorial application, and imposes organisational liability for any bribe paid by persons or entities associated with an organisation where the organisation failed to have adequate preventative controls in place at the time of the offence. In the US, there has been significant enforcement activity in respect of the Foreign Corrupt Practices Act by the SEC and DOJ against US companies and non-US companies listed in the US. China and other countries are also enforcing their own anti-bribery laws more aggressively and/or adopting tougher new measures.</p> <p>We are the subject of current anti-corruption investigations and there can be no assurance that we will not, from time to time, continue to be subject to informal inquiries and formal investigations from governmental agencies. In the context of our business, governmental officials interact with us in various roles that are important to our operations, such as in the capacity of a regulator, partner or healthcare payer, reimbursor or prescriber, among others. Details of these matters are included in Note 27 to the Financial Statements from page 186.</p>	<p>Despite taking measures to prevent breaches of applicable anti-bribery and anti-corruption laws by our personnel and associated third parties, breaches may still occur, potentially resulting in the imposition of significant penalties, such as fines, the requirement to comply with monitoring or self-reporting obligations, or debarment or exclusion from government sales or reimbursement programmes, any of which could materially adversely affect our reputation, business or results of operations.</p>
<p>Failure to adhere to applicable laws, rules and regulations</p> <p>Any failure to comply with applicable laws, rules and regulations may result in civil and/or criminal legal proceedings being filed against us, or in us becoming subject to regulatory sanctions. Regulatory authorities have wide-ranging administrative powers to deal with any failure to comply with continuing regulatory oversight and this could affect us, whether such failure is our own or that of our contractors or external partners.</p>	<p>Failure to comply with applicable laws, including ongoing control and regulation, could materially adversely affect our business or results of operations. For example, once a product has been approved for marketing by the regulatory authorities, it is subject to continuing control and regulation, such as the manner of its manufacture, distribution, marketing and safety surveillance. For example, if regulatory issues concerning compliance with current Good Manufacturing Practice or safety monitoring regulations for pharmaceutical products (often referred to as pharmacovigilance) arise, this could lead to loss of product approvals, product recalls and seizures, and interruption of production, which could create product shortages and delays in new product approvals, and negatively impact patient access and our reputation.</p>
<p>Failure of information technology and cybercrime</p> <p>We are dependent on effective IT systems. These systems support key business functions such as our R&D, manufacturing, supply chain and sales capabilities and are an important means of safeguarding and communicating data, including critical or sensitive information, the confidentiality and integrity of which we rely on.</p> <p>Examples of sensitive information that we protect include loss of clinical trial records (patient names and treatments), personal information (employee bank details, home address), intellectual property of manufacturing process and compliance, key research science techniques, AstraZeneca property (theft) and privileged access (rights to perform IT tasks).</p> <p>The size and complexity of our IT systems, and those of our third party vendors (including outsource providers) with whom we contract, have significantly increased over the past decade and makes such systems potentially vulnerable to service interruptions and security breaches from attacks by malicious third parties, or from intentional or inadvertent actions by our employees or vendors.</p>	<p>Any significant disruption to these IT systems, including breaches of data security or cybersecurity, or failure to integrate new and existing IT systems, could harm our reputation and materially adversely affect our financial condition or results of operations.</p> <p>While we have invested heavily in the protection of our data and IT, we may be unable to prevent breakdowns or breaches in our systems that could result in disclosure of confidential information, damage to our reputation, regulatory penalties, financial losses and/or other costs.</p> <p>Significant changes in the business footprint and the implementation of the IT strategy, including the creation and use of captive offshore Global Technology Centres, could lead to temporary loss of capability.</p> <p>The inability to effectively backup and restore data could lead to permanent loss of data that could result in non-compliance with applicable laws and regulations.</p> <p>We and our vendors could be susceptible to third party attacks on our information security systems. Such attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including criminal groups, 'hacktivists' and others. From time to time we experience intrusions, including as a result of computer-related malware.</p>

Commercialisation risks	Impact
<p>Any expected gains from productivity initiatives are uncertain</p> <p>We continue to implement various productivity initiatives and restructuring programmes with the aim of enhancing the long-term efficiency of the business. However, anticipated cost savings and other benefits from these programmes are based on estimates and the actual savings may vary significantly. In particular, these cost-reduction measures are often based on current conditions and cannot always take into account any future changes to the pharmaceutical industry or our operations, including new business developments or wage or price increases.</p>	<p>If inappropriately managed, the expected value of these initiatives could be lost through low employee engagement and hence productivity, increased absence and attrition levels, and industrial action.</p> <p>Our failure to successfully implement these planned cost-reduction measures, either through the successful conclusion of employee relations processes (including consultation, engagement, talent management, recruitment and retention), or the possibility that these efforts do not generate the level of cost savings we anticipate, could materially adversely affect our business or results of operations.</p>
<p>Failure of outsourcing</p> <p>We have outsourced various business-critical operations to third party providers. This includes certain R&D processes, IT systems, HR and finance, tax and accounting services.</p>	<p>The failure of outsource providers to deliver timely services, and to the required level of quality, and the failure of outsource providers to co-operate with each other, could materially adversely affect our financial condition or results of operations. In addition, such failures could adversely impact our ability to meet business targets, maintain a good reputation within the industry and with stakeholders, and result in non-compliance with applicable laws and regulations.</p> <p>A failure to successfully manage and implement the integration of IT infrastructure services provided by our outsource providers could create disruption, which could materially adversely affect our business or results of operations.</p> <p>In addition, failure to manage outsourcing or insourcing transition processes may disrupt our business. For instance, as we transition services that previously were outsourced to our service centre in Chennai (India), incumbent outsource providers may cease to continue to provide the same level of resources and quality of service.</p>
<p>Failure to attract and retain key personnel and failure to successfully engage with our employees</p> <p>We rely heavily on recruiting and retaining talented employees with a diverse range of skills and capabilities to meet our strategic objectives. For example, the success of our science activities depends largely on our ability to attract and retain sufficient numbers of high-quality researchers and development specialists. We face intense competition for well-qualified individuals, as the supply of people with specific skills and significant leadership potential or in specific geographic regions may be limited.</p> <p>Our ability to achieve high levels of employee engagement in the workforce, and hence benefit from strong commitment and motivation, is key to the successful delivery of our business objectives.</p>	<p>The inability to attract and retain highly skilled personnel, in particular those in key scientific and leadership positions and those in our talent pools, may weaken our succession plans for critical positions in the medium term, may materially adversely affect the implementation of our strategic objectives and could ultimately impact our business or results of operations.</p> <p>Failure to engage effectively with our employees could lead to business disruption in our day-to-day operations, reduce levels of productivity and/or increase levels of voluntary turnover, all of which could ultimately adversely impact our business or results of operations.</p> <p>While we are committed to working on improving drivers of engagement, such as increasing our employees' understanding of our strategy and our ongoing efforts to reduce organisational complexity, our efforts may be unsuccessful.</p>

Risk continued

Supply chain and business execution risks	Impact
Difficulties and delays in the manufacturing, distribution and sale of our products <p>We may experience difficulties and delays in manufacturing our products, such as:</p> <ul style="list-style-type: none"> > Supply shortages associated with gaps between forecasted and actual demand for products. > Supply chain disruptions, including those due to natural or man-made disasters at one of our facilities or at a critical supplier or vendor. > Delays related to the construction of new facilities or the expansion of existing facilities, including those intended to support future demand for our products. > Inability to supply products due to a product quality failure or regulatory agency compliance action such as licence withdrawal, product recall or product seizure. > Other manufacturing or distribution problems, including changes in manufacturing production sites, limits to manufacturing capacity due to regulatory requirements, changes in the types of products produced, or physical limitations or other business interruptions that could impact continuous supply. 	
Reliance on third party goods and services <p>We increasingly rely on third parties for the timely supply of goods, such as raw materials (for example, the API in some of our medicines), equipment, formulated drugs and packaging, and services, all of which are key to our operations. Many of these goods are difficult to substitute in a timely manner or at all.</p> <p>Unexpected events and/or events beyond our control could result in the failure of the supply of goods and services. For example, suppliers of key goods may cease to trade or experience supply chain failures such as those described under the risk above. In addition, we may experience limited supply of biological materials, such as cells, animal products or by-products. Furthermore, government regulations could result in restricted access to, use or transport of such materials.</p>	<p>Manufacturing, forecasting, distribution and sales difficulties may result in product shortages and significant delays, which may lead to lost Product Sales and materially adversely affect our business, financial condition or results of operations.</p> <p>Third party supply failure could lead to significant delays and/or difficulties in obtaining goods and services on commercially acceptable terms and/or adversely affect AstraZeneca's reputation. This may materially adversely affect our business, financial condition or results of operations.</p> <p>Loss of access to sufficient sources of key goods and biological materials or services may interrupt or prevent planned research activities and/or increase our costs. Further information is contained in Working with suppliers in Manufacturing and Supply on page 47.</p>
Manufacturing biologics <p>Manufacturing biologics, especially in large quantities, is complex and may require the use of innovative technologies to handle living micro-organisms and facilities specifically designed and validated for this purpose, with sophisticated quality assurance and control procedures.</p> <p>Final market release of a biologic depends on a number of in-process manufacturing and supply chain parameters to ensure the product conforms with its safety, identity and strength requirements and meets its quality and purity characteristics.</p> <p>Biologics production facilities, especially for drug substance manufacture, are very specialised and can take years to develop and bring on line as licensed facilities. Predicting demand for certain classes of biologics, especially prior to launch, can be challenging. We expect that external capacity for biologics drug substance production will remain constrained for the next several years and, accordingly, may not be readily available for supplementary production in the event that we experience unforeseen need for such capacity.</p>	<p>Slight variations in any part of the manufacturing process or components may lead to a product that does not meet its stringent design specifications. Failure to meet these specifications may lead to recalls, spoilage, drug product shortages, regulatory action and/or reputational harm.</p>

Legal; regulatory and compliance risks	Impact
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Adverse outcome of litigation and/or governmental investigations

We may be subject to various product liability, consumer commercial, anti-trust, environmental, employment or tax litigation or other legal proceedings and governmental investigations. Litigation, particularly in the US, is inherently unpredictable and unexpectedly high awards for damages can result from an adverse verdict. In many cases, plaintiffs may claim enhanced damages in extremely high amounts. In particular, the marketing, promotional, clinical and pricing practices of pharmaceutical manufacturers, as well as the manner in which manufacturers interact with purchasers, prescribers and patients, are subject to extensive regulation, litigation and governmental investigation. Many companies, including AstraZeneca, have been subject to claims related to these practices asserted by federal and state governmental authorities and private payers and consumers, which have resulted in substantial expense and other significant consequences. Note 27 to the Financial Statements from page 186 describes the material legal proceedings in which we are currently involved.

Governmental investigations for example, under the Foreign Corrupt Practices Act or federal or state False Claims Acts or legal proceedings, regardless of their outcome, could be costly, divert management attention, or damage our reputation and demand for our products. Unfavourable resolution of current and similar future proceedings against us could subject us to criminal liability, fines, penalties or other monetary or non-monetary remedies, including enhanced damages, require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business or results of operations.

Failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour

Any failure to comply with laws, rules and regulations relating to anti-competitive behaviour may expose us to regulatory sanctions and/or lawsuits from governmental authorities and private, non-governmental entities.

Certain of our commercial arrangements with generics companies, which have sought to settle patent challenges on terms acceptable to both innovator and generics manufacturer, may be subject to challenge by competition authorities.

Details of material litigation matters which raise allegations of anti-competitive behaviour can be found in Note 27 to the Financial Statements from page 186.

Where a government authority investigates our adherence to competition laws, or we become subject to private party lawsuits, this may result in inspections of our sites or requests for documents and other information. Competition investigations or legal proceedings could be costly, divert management attention or damage our reputation and demand for our products.

Unfavourable resolution of such current and similar future proceedings against us could subject us to fines and penalties, including enhanced (ie up to treble) damages, require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business results of operations, including, by requiring us to change our commercial practice.

Substantial product liability claims

Any failure to comply with laws, rules and regulations relating to the manufacturing, design, and provision of appropriate warnings concerning the dangers and risks of our medicines that result in injuries allegedly caused by the use of our medicines could expose us to large product liability damages claims, settlements and awards, particularly in the US. Adverse publicity relating to the safety of a product or of other competing products may increase the risk of product liability claims.

Details of material product liability litigation matters can be found in Note 27 to the Financial Statements from page 186.

Significant product liability claims can result in requests for documents and other information. These legal proceedings could be costly, divert management attention or damage our reputation and demand for our products.

Unfavourable resolution of such current and similar future product liability claims could subject us to enhanced damages, require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our financial condition or results of operations, particularly where such circumstances are not covered by insurance. For more information, see the Limited third party insurance coverage risk on page 226.

Risk continued

Legal; regulatory and compliance risks	Impact
<p>Failure to adhere to applicable laws, rules and regulations relating to environment, health and safety; environmental and occupational health and safety liabilities</p> <p>Any failure to comply with laws, rules and regulations relating to the environment or occupational health or safety may expose us to regulatory sanctions and/or lawsuits from governmental authorities and private, non-governmental entities. Additionally, the failure to adequately anticipate and proactively manage emerging policy and legal developments associated with the environment, health and safety could adversely affect our licence to operate and/or reputation.</p> <p>We have environmental and/or occupational health and safety-related liabilities at some currently and formerly owned, leased and third party sites, the most significant of which are detailed in Note 27 to the Financial Statements from page 186.</p>	
<p>Misuse of social media platforms and new technology</p> <p>We increasingly use the internet, digital content, social media, mobile applications and other forms of new technology to communicate internally and externally. The accessibility and instantaneous nature of interactions with such media may facilitate or exacerbate the risk of data leakages from within AstraZeneca or false or misleading statements being made about AstraZeneca, which may damage our reputation. As existing social media platforms expand and evolve, and new social media platforms emerge, it becomes increasingly challenging to identify new points of entry and to put structures in place to secure and protect information.</p>	
	<p>While we carefully manage compliance and any known liabilities, and work to stay ahead of policy and legislative developments, if a significant compliance issue, environmental, occupational health or safety incident or legal requirement for which we are responsible were to arise, this could result in us being responsible for fines and penalties, damages, and other costs. In some circumstances, such liability could materially adversely affect our business or results of operations. In addition, our financial provisions for any obligations that we may have relating to environmental or occupational health and safety liabilities may be insufficient if the assumptions underlying the provisions, including for example our assumptions regarding the portion of waste at a site for which we are responsible, prove incorrect or if we are held responsible for additional contamination or occupational health and safety-related claims.</p> <p>Inappropriate use of certain media vehicles could lead to the unauthorised or unintentional public disclosure of sensitive information (such as personally identifiable information on employees, healthcare professionals or patients, for example, those enrolled in our clinical trials), which may damage our reputation, adversely affect our business or results of operations and expose us to legal risks, as well as additional legal obligations. Similarly, the involuntary public disclosure of commercially sensitive information, such as trade secrets through external media channels, or an information loss could adversely affect our business or results of operations. In addition, negative posts or comments on social media websites or other digital channels or new forms of technology about us or, for example, the safety of our products, could harm our reputation.</p>

Economic and financial risks	Impact
<p>Failure to achieve strategic priorities or to meet targets or expectations</p> <p>We may from time to time communicate our business strategy or our targets or expectations regarding our future financial or other performance (for example, the expectations described in Future prospects in the Financial Review on page 76). All such statements are of a forward-looking nature and are based on assumptions and judgements we make, all of which are subject to significant inherent risks and uncertainties, including risks and uncertainties that we are unaware of and/or that are beyond our control.</p> <p>Any failure to successfully implement our business strategy may frustrate the achievement of our financial or other targets or expectations and, in turn, materially damage our brand and materially adversely affect our business, financial position or results of operations.</p>	<p>There can be no guarantee that our financial targets or expectations will materialise on the expected timeline or at all. Actual results may deviate materially and adversely from any such target or expectation, including if one or more of the assumptions or judgements underlying any such target or expectation proves to be incorrect in whole or in part.</p>
<p>Adverse impact of a sustained economic downturn</p> <p>A variety of significant risks may arise from a sustained global economic downturn including for example the economic slowdown in China, our second largest market. Additional pressure from governments and other healthcare payers on medicine prices and volumes of sales in response to recessionary pressures on budgets may cause a slowdown or a decline in growth in some markets. In some cases, those governments most severely impacted by the economic downturn may seek alternative ways to settle their debts through, for example, the issuance of government bonds which might trade at a discount to the face value of the debt.</p> <p>In addition, our customers may cease to trade, which may result in losses from writing off debts, or the sustained economic downturn may unfavourably affect the spending patterns of the consumers of our products.</p> <p>We are highly dependent on being able to access a sustainable flow of liquid funds due to the high fixed costs of operating our business and the long and uncertain development cycles of our products. In a sustained economic downturn, financial institutions with whom we deal may cease to trade and there can be no guarantee that we will be able to access monies owed to us without a protracted, expensive and uncertain process, if at all.</p> <p>More than 95% of our cash investments are managed centrally and are invested in collateralised bank deposits or AAA credit rated institutional money market funds. Money market funds are backed by institutions in the US and the EU, which, in turn, invest in other funds, including sovereign funds. This means our credit exposure is a mix of US and EU sovereign default risk and financial institution default risk.</p>	<p>While we have adopted cash management and treasury policies to manage this risk (see the Financial risk management policies section of the Financial Review on page 76), we cannot be certain that these will be as effective as they are intended to be, in particular in the event of a global liquidity crisis. In addition, open positions where we are owed money and investments we have made in financial institutions or money market funds cannot be guaranteed to be recoverable. Additionally, if we need access to external sources of financing to sustain and/or grow our business, such as the debt or equity capital financial markets, this may not be available on commercially acceptable terms, if at all, in the event of a severe and/or sustained economic downturn. This may, for instance, be the case in the event of any default by the Group on its debt obligations, which may materially adversely affect our ability to secure debt funding in the future or our financial condition in general. Further information on debt funding arrangements is contained in the Financial risk management policies section of the Financial Review on page 76.</p>
<p>Fluctuations in exchange rates</p> <p>As a global business, currency fluctuations can significantly affect our results of operations, which are reported in US dollars. Approximately 40% of our global 2015 Product Sales were in the US, which is expected to remain our largest single market for the foreseeable future. Product Sales in other countries are predominantly in currencies other than the US dollar, including the euro, Japanese yen, Chinese renminbi, Australian dollar and Canadian dollar. We have a growing exposure to Emerging Market currencies, some of which are subject to exchange controls, and these currencies, such as that of Venezuela, may be subject to material devaluations against the US dollar. Major components of our cost base are located in the UK and Sweden, where an aggregate of approximately 20% of our employees are based.</p>	<p>Movements in the exchange rates used to translate foreign currencies into US dollars may materially adversely affect our financial condition or results of operations. Additionally, some of our subsidiaries import and export goods and services in currencies other than their own functional currency, and so the financial results of such subsidiaries could be affected by currency fluctuations arising between the transaction dates and the settlement dates for these transactions. In addition, there are foreign exchange differences arising on the translation of equity investments in subsidiaries.</p>

Risk continued

Economic and financial risks	Impact
<p>Limited third party insurance coverage</p> <p>In recent years, the costs associated with product liability litigation have increased the cost of, and narrowed the coverage afforded by, pharmaceutical companies' product liability insurance. To contain insurance costs in recent years, we have continued to adjust our coverage profile, accepting a greater degree of uninsured exposure. The Group has not held any material product liability insurance since February 2006. In addition, where claims are made under insurance policies, insurers may reserve the right to deny coverage on various grounds. For example, product liability litigation cases relating to <i>Crestor</i> and <i>Nexium</i> in the US are not covered by third party product liability insurance. See Note 27 to the Financial Statements from page 186 for details.</p>	<p>If we are found to have a financial liability due to product liability or other litigation, in respect of which we do not have insurance coverage, or if an insurer's denial of coverage is ultimately upheld, this could require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business or results of operations.</p> <p>For more information, please see the Substantial product liability claims risk on page 223.</p>
<p>Taxation</p> <p>The integrated nature of our worldwide operations can produce conflicting claims from revenue authorities as to the profits to be taxed in individual countries. The majority of the jurisdictions in which we operate have double tax treaties with other foreign jurisdictions, which provide a framework for mitigating the incidence of double taxation on our revenues and capital gains.</p> <p>AstraZeneca's worldwide operations are taxed under laws in the jurisdictions in which they operate. International standards governing the global tax environment regularly change. The Organisation for Economic Co-operation and Development (OECD) has proposed a number of changes under the Base Erosion and Profit Shifting (BEPS) Action Plans.</p>	<p>The resolution of these disputes can result in a reallocation of profits between jurisdictions and an increase or decrease in related tax costs, and has the potential to affect our cash flows and EPS. Claims, regardless of their merits or their outcome, are costly, divert management attention and may adversely affect our reputation.</p> <p>If any of these double tax treaties should be withdrawn or amended, especially in a territory where a member of the Group is involved in a taxation dispute with a tax authority in relation to cross-border transactions, such withdrawal or amendment could materially adversely affect our business or results of operations, as could a negative outcome of a tax dispute or a failure by the tax authorities to agree through competent authority proceedings. See the Financial risk management policies section of the Financial Review on page 76 for tax risk management policies and Note 27 to the Financial Statements on page 186 for details of current tax disputes.</p> <p>Changes in tax regimes could result in a material impact on the Group's cash tax liabilities and tax charge, resulting in either an increase or a reduction in financial results depending upon the nature of the change. We represent views to OECD, governments and tax authorities through public consultations to ensure international institutions and governments understand the business implications of law changes. Specific OECD BEPS recommendations that we expect to impact the Group include changes to patent box regimes, restrictions of interest deductibility and revised transfer pricing guidelines.</p>
<p>Pensions</p> <p>Our pension obligations are largely backed by assets invested across the broad investment market. Our most significant obligations relate to the UK pension fund.</p>	<p>Sustained falls in these asset values could reduce pension fund solvency levels, which may result in requirements for additional cash, restricting the cash available for business growth. Similarly, if the present value of the liabilities increase due to a sustained low interest rate environment, an increase in expectations of future inflation, or an improvement in member longevity (above that already assumed), this could also reduce pension fund solvency ratios. The likely increase in the IAS 19 accounting deficit generated by any of these factors may cause the credit rating agencies to review our credit rating, with the potential to negatively affect our ability to raise debt. See Note 20 to the Financial Statements from page 166 for further details of the Group's pension obligations.</p>

Geographical Review

This section contains further information about the performance of our products within the geographical areas in which our sales and marketing efforts are focused. Sales relates to Product Sales.

Our financial performance – Product Sales

	2015			2014			2013
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m
US	9,474	(6)	(6)	10,120	4	4	9,691
Europe	5,323	(20)	(6)	6,638	–	(1)	6,658
Established ROW	3,022	(14)	–	3,510	(12)	(4)	3,973
Emerging Markets	5,822	–	12	5,827	8	12	5,389
Total	23,641	(9)	(1)	26,095	1	3	25,711

Respiratory, Inflammation and Autoimmunity

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2015															
Symbicort	3,394	(11)	(3)	1,520	1	1,076	(26)	(14)	404	(12)	2	394	6	22	3,801
Pulmicort	1,014	7	15	200	(5)	117	(28)	(13)	88	(9)	4	609	28	35	946
Tudorza/Eklira	190	n/m	n/m	103	n/m	76	n/m	n/m	9	n/m	n/m	2	n/m	n/m	13
Daliresp	104	n/m	n/m	104	n/m	–	–	–	–	–	–	–	–	–	–
Duaklir	27	n/m	n/m	–	–	26	n/m	n/m	1	n/m	n/m	–	–	–	–
Others	258	(15)	(5)	18	(31)	88	(20)	(6)	25	(7)	4	127	(9)	(1)	303
Total	4,987	(2)	7	1,945	11	1,383	(21)	(7)	527	(9)	5	1,132	15	25	5,063

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2014															
Symbicort	3,801	9	10	1,511	23	1,462	(3)	(4)	458	8	17	370	14	22	3,483
Pulmicort	946	9	11	211	(6)	162	(5)	(6)	97	(13)	(6)	476	32	35	867
Tudorza/Eklira	13	n/m	n/m	–	–	13	n/m	n/m	–	–	–	–	–	–	–
Others	303	(7)	(6)	26	(55)	110	(4)	(5)	27	(18)	(15)	140	16	19	327
Total	5,063	8	10	1,748	15	1,747	(2)	(4)	582	2	11	986	22	27	4,677

Geographical Review continued

Cardiovascular and Metabolic diseases

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2015															
<i>Crestor</i>	5,017	(9)	(3)	2,844	(3)	916	(24)	(9)	571	(14)	(1)	686	(6)	2	5,512
<i>Onglyza/Kombiglyze XR/ Komboglyze</i>	786	(4)	2	420	(13)	141	(9)	8	66	12	27	159	27	41	820
<i>Seloken/Toprol-XL</i>	710	(6)	4	89	(2)	97	(22)	(6)	12	(37)	(26)	512	(2)	9	758
<i>Brilinta/Brilique</i>	619	30	44	240	64	230	–	18	37	12	33	112	70	91	476
<i>Bydureon</i>	580	32	35	482	29	81	42	65	8	60	80	9	125	150	440
<i>Farxiga/Forxiga</i>	492	119	137	261	114	126	91	126	32	88	124	73	n/m	n/m	225
<i>Atacand</i>	358	(29)	(15)	34	(23)	105	(38)	(26)	26	(40)	(30)	193	(21)	(4)	501
<i>Byetta</i>	316	(3)	2	209	5	62	(23)	(11)	22	(19)	(7)	23	15	30	327
<i>Plendil</i>	233	(6)	(2)	–	–	13	(32)	(16)	7	(22)	(11)	213	(4)	–	249
<i>Tenormin</i>	118	(27)	(15)	1	(88)	37	(23)	(8)	40	(26)	(15)	40	(22)	(10)	161
Others	260	(22)	(14)	54	(21)	93	(30)	(17)	13	(28)	(17)	100	(12)	(5)	333
Total	9,489	(3)	4	4,634	4	1,901	(17)	(1)	834	(12)	1	2,120	–	11	9,802

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2014															
<i>Crestor</i>	5,512	(2)	(1)	2,918	–	1,200	(2)	(3)	667	(17)	(10)	727	7	11	5,622
<i>Onglyza/Kombiglyze XR/ Komboglyze</i>	820	117	119	481	82	155	177	175	59	195	210	125	238	251	378
<i>Seloken/Toprol-XL</i>	758	1	4	91	(31)	124	(5)	(4)	19	(21)	(13)	524	13	17	750
<i>Brilinta/Brilique</i>	476	68	70	146	100	231	42	40	33	94	106	66	120	133	283
<i>Bydureon</i>	440	191	191	374	185	57	235	235	5	n/m	n/m	4	100	100	151
<i>Farxiga/Forxiga</i>	225	n/m	n/m	122	100	66	n/m	n/m	17	n/m	n/m	20	n/m	n/m	10
<i>Atacand</i>	501	(18)	(16)	44	(39)	169	(25)	(26)	43	(39)	(35)	245	1	5	611
<i>Byetta</i>	327	59	59	199	31	81	125	119	27	145	164	20	186	200	206
<i>Plendil</i>	249	(4)	(4)	–	–	19	(10)	(10)	9	(10)	(10)	221	(3)	(3)	260
<i>Tenormin</i>	161	(18)	(15)	8	(47)	48	(6)	(6)	54	(30)	(23)	51	(6)	(4)	197
Others	333	(8)	(7)	68	36	133	(19)	(19)	18	(28)	(24)	114	(7)	(5)	362
Total	9,802	11	12	4,451	17	2,283	9	8	951	(11)	(3)	2,117	13	17	8,830

Oncology

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2015															
<i>Zoladex</i>	816	(12)	7	28	8	171	(24)	(12)	272	(16)	(2)	345	(2)	27	924
<i>Faslodex</i>	704	(2)	9	356	5	207	(15)	2	54	(8)	5	87	14	49	720
<i>Iressa</i>	543	(13)	(2)	6	n/m	128	(22)	(8)	137	(23)	(10)	272	(3)	4	623
<i>Casodex</i>	267	(17)	(6)	1	(80)	30	(29)	(14)	131	(22)	(11)	105	1	9	320
<i>Arimidex</i>	250	(16)	(5)	19	27	49	(36)	(24)	79	(27)	(17)	103	4	16	298
<i>Lynparza</i>	94	n/m	n/m	70	n/m	23	n/m	n/m	–	–	–	1	n/m	n/m	–
<i>Tagrisso</i>	19	n/m	n/m	15	n/m	4	n/m	n/m	–	–	–	–	–	–	–
Others	132	(7)	6	19	(24)	23	(30)	(18)	60	25	44	30	(17)	–	142
Total	2,825	(7)	7	514	25	635	(19)	(4)	733	(17)	(4)	943	–	18	3,027

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2014															
<i>Zoladex</i>	924	(7)	(4)	26	13	226	(10)	(12)	322	(13)	(6)	350	–	4	996
<i>Faslodex</i>	720	6	7	340	5	245	11	10	59	(5)	3	76	3	14	681
<i>Iressa</i>	623	(4)	(1)	–	–	166	(6)	(7)	177	(12)	(4)	280	4	6	647
<i>Casodex</i>	320	(15)	(10)	5	–	42	(21)	(21)	169	(25)	(18)	104	12	14	376
<i>Arimidex</i>	298	(15)	(12)	15	150	76	(18)	(19)	108	(30)	(24)	99	1	5	351
Others	142	–	4	25	–	33	14	14	48	(20)	(13)	36	29	36	142
Total	3,027	(5)	(2)	411	7	788	(4)	(6)	883	(18)	(11)	945	4	8	3,193

Infection, Neuroscience and Gastrointestinal Infection

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2015															
Synagis	662	(26)	(26)	285	(43)	377	(6)	(6)	–	–	–	–	–	–	900
FluMist/Fluenz	288	(2)	–	206	(6)	76	9	16	7	–	14	(1)	(100)	(100)	295
Merrem/Meronem	241	(5)	11	16	167	24	(23)	(10)	2	(50)	(50)	199	(6)	10	253
Others	59	(24)	(17)	24	(41)	6	(25)	(25)	3	(67)	(22)	26	13	40	78
Total	1,250	(18)	(15)	531	(30)	483	(5)	(4)	12	(40)	(15)	224	(4)	13	1,526

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2014															
Synagis	900	(15)	(15)	499	(19)	401	(9)	(9)	–	–	–	–	–	–	1,060
FluMist/Fluenz	295	20	20	218	10	70	67	64	7	75	100	–	–	–	245
Merrem/Meronem	253	(14)	(10)	6	(45)	32	(35)	(35)	4	(20)	(20)	211	(7)	(3)	293
Others	78	(13)	(10)	41	(27)	5	–	(20)	9	(31)	(8)	23	64	50	89
Total	1,526	(10)	(9)	764	(13)	508	(6)	(6)	20	(9)	9	234	(4)	–	1,687

Neuroscience

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2015															
Seroquel XR	1,025	(16)	(12)	716	(3)	202	(41)	(30)	25	(43)	(34)	82	(18)	(1)	1,224
Seroquel IR	250	40	56	46	n/m	63	(29)	(18)	34	(6)	8	107	(14)	(5)	178
Local Anaesthetics	392	(20)	(6)	–	–	136	(31)	(17)	142	(15)	(1)	114	(7)	6	488
Vimovo	84	(13)	2	1	(90)	35	6	27	24	4	22	24	(20)	(10)	96
Movantik/Moventig	29	n/m	n/m	28	n/m	1	n/m	n/m	–	–	–	–	–	–	–
Others	332	(21)	(10)	22	(12)	84	(24)	(10)	65	(22)	(11)	161	(20)	(10)	420
Total	2,112	(12)	(3)	813	16	521	(32)	(20)	290	(18)	(5)	488	(16)	(4)	2,406

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2014															
Seroquel XR	1,224	(9)	(8)	738	(1)	343	(18)	(18)	44	(39)	(35)	99	(7)	–	1,337
Seroquel IR	178	(48)	(46)	(72)	n/m	89	(15)	(16)	36	(66)	(63)	125	(17)	(13)	345
Local Anaesthetics	488	(4)	–	–	–	197	(4)	(5)	168	(8)	(1)	123	1	9	510
Vimovo	96	5	9	10	(50)	33	3	3	23	15	25	30	58	63	91
Others	420	(7)	(4)	25	(24)	110	(4)	(5)	84	(14)	(7)	201	(3)	1	452
Total	2,406	(12)	(10)	701	(10)	772	(12)	(12)	355	(26)	(20)	578	(5)	1	2,735

Gastrointestinal

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2015															
Nexium	2,496	(32)	(26)	902	(52)	284	(23)	(7)	549	(9)	5	761	(6)	3	3,655
Losec/Prilosec	340	(19)	(10)	18	(32)	97	(25)	(10)	74	(30)	(19)	151	(5)	(1)	422
Others	142	(27)	(24)	117	(17)	19	(56)	(47)	3	(57)	(57)	3	–	33	194
Total	2,978	(30)	(24)	1,037	(49)	400	(26)	(11)	626	(13)	1	915	(5)	2	4,271

	World			US		Europe			Established ROW			Emerging Markets			Prior year
	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	Sales \$m	Actual growth %	CER growth %	World sales \$m
2014															
Nexium	3,655	(6)	(4)	1,876	(12)	368	2	2	606	2	9	805	2	5	3,872
Losec/Prilosec	422	(13)	(11)	28	(7)	129	(2)	(2)	106	(36)	(30)	159	(1)	1	486
Others	194	(16)	(16)	141	(21)	43	–	–	7	–	–	3	–	33	231
Total	4,271	(7)	(5)	2,045	(12)	540	1	1	719	(7)	1	967	1	5	4,589

Additional Information

Geographical Review continued

Growth rates in this Geographical Review are expressed at CER unless otherwise stated. All commentary in this section relates to Product Sales.

2015 in brief

- > AstraZeneca is the sixth largest prescription-based pharmaceutical company in the US, with a 4.5% market share of US pharmaceuticals by sales value.
- > AstraZeneca is the twelfth largest prescription-based pharmaceutical company in Europe, with a 2.5% market share of sales by value.
- > In 2015, sales in the US decreased by 6% to \$9,474 million (2014: \$10,120 million; 2013: \$9,691 million). Declines in revenue from *Nexium*, *Crestor* and *Synagis* were partially offset by strong performance of our Growth Platforms, including *Farxiga*, *Bydureon* and *Brilinta*, the launches of *Lynparza* and *Tagrisso* as well as the impact of completing the acquisition of Actavis's rights to *Tudorza* and *Daliresp* in the US.
- > Sales in Europe declined by 6% to \$5,323 million in the year (2014: \$6,638 million; 2013: \$6,658 million). Strong growth from the Diabetes portfolio was more than offset by pricing pressure and continued generic competition facing *Crestor*, *Nexium* and *Seroquel XR*. A 14% decline in *Symbicort* sales to \$1,076 million (2014: \$1,462 million; 2013: \$1,502 million) reflected adverse pricing movements driven by competition from analogues in key markets. *Duaklir* more than doubled its first-half sales in the final quarter and *Lynparza* was launched in Europe in 2015.
- > Sales in the Established Rest of World (ROW) were stable in the year at \$3,022 million (2014: \$3,510 million; 2013: \$3,973 million). Japan sales increased 4% at CER to \$2,020 million (2014: \$2,227 million; 2013: \$2,485 million) driven by strong growth of *Crestor* and *Nexium*, though there was a decline in the sales of *Symbicort*. Canada sales grew by 4% to \$533 million at CER (2014: \$590 million; 2013: \$637 million) in the year driven by increased sales of *Onglyza* and *Symbicort*.
- > Emerging Markets sales in the year increased by 12% to \$5,822 million (2014: \$5,827 million; 2013: \$5,389 million) with contributions to growth emanating from across the region. Around 60% of Emerging Markets sales were derived outside of China in the year.

- > China sales in the year increased by 15% to \$2,530 million (2014: \$2,242 million; 2013: \$1,840 million), while Brazil sales grew by 16% at CER to \$381 million (2014: \$451 million; 2013: \$447 million) and Russia sales grew by 21% at CER to \$231 million (2014: \$312 million; 2013: \$310 million).

2014 in brief

- > AstraZeneca was the fourth largest prescription-based pharmaceutical company in the US, with a 5.2% market share of US pharmaceuticals by sales value.
- > AstraZeneca was the tenth largest prescription-based pharmaceutical company in Europe, with a 2.8% market share of sales by value.
- > In the US, sales increased by 4% to \$10,120 million (2013: \$9,691 million; 2012: \$10,655 million), driven by an increase in Diabetes franchise sales, aided by the acquisition of BMS's 50% interest in the diabetes alliance, as well as strong performance across our Growth Platforms, including *Symbicort* and *Brilinta*, offset by declines in revenue from *Nexium*, *Seroquel IR* and *Synagis*. Sales from our Diabetes franchise increased by \$644 million or 109% to \$1,234 million.
- > Sales in Europe decreased by 1% to \$6,638 million (2013: \$6,658 million; 2012: \$7,143 million). Key drivers of the decline were the ongoing volume erosion on *Atacand* and *Seroquel XR* following generic entry and the negative price and volume impacts primarily related to government pricing interventions. *Crestor* volumes declined 3% due to increased pressure from generic statins in a number of markets. *Symbicort* sales decreased to \$1,462 million (2013: \$1,502 million; 2012: \$1,465 million) due to pricing pressure and the impact of *Symbicort* analogues. These challenges were partially offset by our Growth Platforms, including *Brilinta* growth and the expansion of our Diabetes portfolio following the acquisition of BMS's interest in the joint diabetes alliance plus continued strong demand for *Fuenz* (2014: \$70 million; 2013: \$42 million; 2012: \$3 million).
- > Established Rest of World sales decreased by 4% to \$3,510 million (2013: \$3,973 million; 2012: \$5,080 million). Canada continued to be negatively impacted by erosion of *Crestor* and *Nexium* sales due to generic competition, with total sales down 1%. Sales in Australia were also lower due to generic

competition to *Crestor* and *Atacand*. Sales growth in Japan declined by 3% to \$2,227 million (2013: \$2,485 million; 2012: \$2,904 million), as a result of generic pressure on oncology products, *Casodex* and *Arimidex*, and the impact of the April 2014 mandated biennial price cut. Strong demand in Japan continued for *Nexium* and *Crestor*, with sales increasing to \$860 million (2013: \$815 million; 2012: \$665 million).

> Emerging Markets sales increased by 12% to \$5,827 million (2013: \$5,389 million; 2012: \$5,095 million), with sales growth in China of 22%. Volume growth on *Brilinta*, our Diabetes and Respiratory franchises, *Nexium* and *Crestor*, was partially offset by pricing pressure, predominantly in China and Asia Pacific.

US

In 2015, sales in the US decreased by 6% to \$9,474 million (2014: \$10,120 million; 2013: \$9,691 million). Declines in revenue from *Nexium*, *Crestor* and *Synagis* were partially offset by strong performance of our Growth Platforms, including *Farxiga*, *Bydureon* and *Brilinta*, the launches of *Lynparza* and *Tagrisso* as well as the impact of completing the acquisition of Actavis's rights to *Tudorza* and *Daliresp* in the US. Sales from our Diabetes franchise increased by \$187 million or 15% to \$1,421 million (2014: \$1,234 million; 2013: \$590 million).

Brilinta sales of \$240 million (2014: \$146 million; 2013: \$73 million) increased 64% in 2015. *Brilinta* continued its strong momentum with significant 2015 growth in hospital units purchased volume (+58% November 2015), new-to-brand prescriptions (39%) and total prescriptions (48%), supported with our expanded indication to include long-term use in patients with a history of heart attack. The new label nearly doubles the number of patients indicated for *Brilinta* in the US and is highlighted with language that demonstrates *Brilinta*'s superiority over *Plavix*. *Brilinta* grew its US branded leadership in oral antiplatelet (OAP) new-to-brand retail prescription share which increased by 2.7 percentage points over 2014 to 10.9% in 2015, and *Brilinta* also achieved US branded market leadership in share of all OAP new prescriptions for the first time in 2015.

Crestor continued to demonstrate resilience in the highly competitive statin market, 89.0% of which is generic. In 2015, *Crestor* was the highest branded retail prescription

pill in the US and more than a million new patients started therapy on *Crestor* in 2015. *Crestor* achieved sales of \$2,844 million (2014: \$2,918 million; 2013: \$2,912 million) and a total prescription share within the statin market of 8.9% in December 2015. *Crestor* sales in 2015 were 3% below 2014 sales, with a decrease in volume of 6% partially offset by higher average net prices (+3%). *Crestor* continued to maintain its strong formulary access, with Commercial/Medicare preferred access of 85% at the end of 2015 (2014: 84%; 2013: 84%).

Symbicort pMDI sales at \$1,520 million were in line with 2014 (2014: \$1,511 million; 2013: \$1,233 million), with volume increases of 10% and prescription growth of 14.0% versus 2014 offset by pricing pressures. *Symbicort* achieved a 34.0% total prescription share in the month of December 2015, up 1.08 percentage points over the month of December 2014 in the ICS/LABA market.

In March 2015, we completed our acquisition of *Daliresp* and *Tudorza* from Forest Laboratories Holdings Ltd (owned by Actavis). The acquisition granted AstraZeneca US rights for manufacturing and commercialisation of these products. *Daliresp* achieved sales of \$104 million and *Tudorza* achieved sales of \$103 million for the 10 months of ownership in 2015.

In February 2014, we completed our acquisition of BMS's 50% interest in our joint diabetes alliance. The acquisition gave us ownership of the IP and global rights for the development, manufacturing and commercialisation of the diabetes business, which includes *Onglyza*, *Komboglyze*, *Kombiglyze XR*, *Farxiga/Forxiga*, *Xigduo*, *Xigduo XR*, *Byetta*, *Bydureon* and *Symmlin*. *Onglyza/Kombiglyze XR* sales in the US declined by 13% to \$420 million (2014: \$481 million; 2013: \$265 million) primarily driven by lower average net price.

Bydureon sales in the US were \$482 million (2014: \$374 million; 2013: \$131 million). *Bydureon* prescription market share remained static in 2015, with a total prescription market share of 19.4% of the rapidly growing GLP-1 market in December 2015. *Byetta* achieved sales of \$209 million (2014: \$199 million; 2013: \$152 million).

Farxiga (launched February 2014) and *Xigduo XR* (launched November 2014) accelerated the overall growth of the SGLT2

class of medicines by 79% post-launch¹ and by the end of December 2015, over 407,000 patients were on *Farxiga* or *Xigduo XR* since launch and the *Farxiga* family captured nearly one in four new SGLT2 patient treatment decisions. Our SGLT2 franchise sales grew by 114% from 2014 to 2015.

Lynparza reached \$70 million (2014: \$nil) following the launch of the medicine at the end of 2014. Growth was driven by the pool of eligible patients awaiting treatment as well as patients newly tested for BRCA mutation.

Tagrisso, the only approved medicine indicated for patients with metastatic EGFR T790M mutation-positive NSCLC, had sales of \$15 million following the launch in November 2015.

In 2015, sales of *Synagis* were down 43% to \$285 million (2014: \$499 million; 2013: \$617 million). A key driver of the decline was the continued adoption of guidelines from the American Academy of Pediatrics Committee on Infectious Disease that restricted patients eligible for preventive therapy with *Synagis*. *FluMist* Quadrivalent launched in the US in 2013 as the first and only FDA-approved nasal spray flu vaccine to help protect against four strains of influenza. *FluMist* revenues in the US were down 6% to \$206 million (2014: \$218 million; 2013: \$199 million) driven by delays in supply.

Nexium was the seventh most prescribed branded pharmaceutical in the US. *Nexium* sales in the US declined 52% to \$902 million (2014: \$1,876 million; 2013: \$2,123 million) due primarily to volume erosion, pricing pressure, and recognition of an unfavourable returns provision following loss of exclusivity. Despite the entrance of multiple generic competitors, *Nexium* remains the branded market leader retaining significant prescription market share and volume within the proton pump inhibitor class, and maintains greater than 65% share of the esomeprazole molecule market.

Seroquel IR 2015 sales were \$46 million (2014: negative \$72 million; 2013: negative \$17 million). The loss of exclusivity for *Seroquel* IR in March 2012 and unfavourable reserve adjustments for Medicaid liabilities and provisions taken on channel inventories resulted in negative sales in 2014 and 2013. No further adjustments were required in 2015. The presence of generic competition has also impacted the prescription volume of *Seroquel XR*. Sales of *Seroquel XR* were

down 3% to \$716 million (2014: \$738 million; 2013: \$743 million) driven by lower volume.

Movantik launched in March 2015 and achieved US sales of \$28 million. In March 2015, the Company announced a co-commercialisation agreement with Daiichi Sankyo for *Movantik* in the US. *Movantik* share among chronic opioid patients starting a new branded Rx laxative (NBRx) in the final quarter of 2015 was 29%.

The Affordable Care Act (ACA), which was enacted in March 2010, has had, and is expected to continue to have, a significant impact on our US sales and the US healthcare industry as a whole. In 2015, the overall measurable reduction in our profit before tax for the year due to discounts on branded pharmaceutical sales to Medicare Part D beneficiaries and an industry-wide excise fee was \$786 million (2014: \$714 million; 2013: \$557 million). This amount reflects only those effects of the ACA that we know have had or will have a direct impact on our financial condition or results of operations and which we are therefore able to quantify based on known and isolatable resulting changes in individual financial items within our Financial Statements. There are other potential indirect or associated consequences of the implementation of the ACA, which continue to evolve and which cannot be estimated but could have similar impacts. These include broader changes in access to, or eligibility for, coverage under Medicare, Medicaid or similar government programmes. These could indirectly impact our pricing or sales of prescription products within the private sector. By their nature and the fact that these potentially numerous consequences are not directly linked to a corresponding and quantifiable impact on our Financial Statements, it is not possible to accurately estimate the financial impact of these potential consequences of the ACA or related legislative changes when taken together with the number of other market; and industry-related factors that can also result in similar impacts. Further details on the impact of the ACA are contained in Pricing of medicines from page 14 and in Risk from page 212.

Currently, there is no direct governmental control of prices for commercial prescription drug sales in the US. However, some publicly funded programmes, such as Medicaid and TRICARE (Department of Defense), have statutorily mandated rebates

Geographical Review continued

and discounts that have the effect of price controls for these programmes. Additionally, pressure on pricing, availability and use of prescription drugs for both commercial and public payers continues to increase. This is driven by, among other things, an increased focus on generic alternatives. Budgetary policies within healthcare systems and providers, including the use of generics only formularies, and increases in patient co-insurance or co-payments, are the primary drivers of increased generics use. In 2015, 84.0% of prescriptions dispensed in the US were generic. While widespread adoption of a broad national price-control scheme in the near future is unlikely, increased focus on pharmaceutical prices and their impact on healthcare costs is likely to continue for the foreseeable future.

Rest of World

Sales of \$14,167 million (2014: \$15,975 million; 2013: \$16,020 million) outside the US in 2015 was up by 2% at CER but negatively impacted on a Reported basis by movements in underlying currencies. Emerging Markets delivered a strong performance, up 12% with sales of \$5,822 million (2014: \$5,827 million; 2013: \$5,389 million), with Japan and Canada also generating increased sales at CER. Europe and Other Established ROW sales were down at 6% and 19% respectively reflecting the competition from generic products and the continuing challenging economic environment, partially offset by the performance of Growth Platforms.

Europe

AstraZeneca is the twelfth largest pharmaceutical company in Europe, with a 2.5% market share of prescription sales by value.

Despite a slight improvement in conditions, the macroeconomic environment remains challenging, with the ongoing impact of austerity measures leading to increased pressure on healthcare budgets. Many governments in Europe intervene directly to control the price, volume and reimbursement of medicines. Several governments have imposed price reductions and increased the use of generic medicines as part of healthcare expenditure controls. A number of countries are applying strict criteria for cost-effectiveness evaluations of medicines, which contributes

to a difficult environment for branded pharmaceuticals in Europe.

Total sales in Europe were down 6% to \$5,323 million (2014: \$6,638 million; 2013: \$6,658 million). Volume erosion on *Seroquel XR* and *Atacand* following generic entries resulted in a decrease in sales of 29% to \$307 million (2014: \$512 million; 2013: \$641 million). *Crestor* sales declined 9%, with a 7% reduction in volumes and 2% reduction in prices as a result of increased competition from generic statins in a number of countries, including France and Italy. Government interventions continue to impact both price and volume negatively.

Our Growth Platform sales partially offset these trends. *Brilique* sales increased 18% at CER to \$230 million (2014: \$231 million; 2013: \$163 million). Our Diabetes franchise generated sales of \$410 million (2014: \$359 million; 2013: \$119 million). Respiratory sales were negatively impacted by pricing pressure on *Symbicort* and the impact of *Symbicort* analogues, with sales declining to \$1,076 million (2014: \$1,462 million; 2013: \$1,502 million), as volumes fell by 3% and prices fell by 11%.

In Germany, sales increased by 4% to \$601 million (2014: \$693 million; 2013: \$657 million), driven by strong growth across the Diabetes portfolio and continued growth with *Brilique*. Total Diabetes sales reached \$126 million in 2015 (2014: \$108 million; 2013: \$32 million). Overall growth was partly offset by the ongoing impact of pricing and generic versions of *Atacand* and *Seroquel XR*.

In the UK and Ireland, sales decreased by 18% to \$633 million (2014: \$832 million; 2013: \$766 million), driven by ongoing volume erosion on *Seroquel XR* following generic entries and a decline in *Zoladex* sales to \$58 million (2014: \$83 million; 2013: \$94 million). Diabetes sales decreased to \$61 million in 2015 (2014: \$68 million; 2013: \$27 million) and *Brilique* sales marginally decreased to \$28 million (2014: \$30 million; 2013: \$18 million).

Sales in France decreased by 9% to \$922 million (2014: \$1,213 million; 2013: \$1,212 million), driven by price and volume erosion on *Atacand* and *Zoladex*, following generic entries and subsequent government pricing interventions. Increased pressure from

generic statins has adversely affected *Crestor*, with sales down 12% to \$298 million (2014: \$404 million; 2013: \$428 million). At constant exchange rates, France experienced growth of *Brilique* with \$29 million of sales (2014: \$30 million; 2013: \$18 million) and Diabetes with \$50 million of sales (2014: \$52 million; 2013: \$20 million).

Sales in Italy decreased by 5% to \$544 million (2014: \$688 million; 2013: \$737 million), mainly driven by generic entries, pricing intervention and the implementation of volume prescription controls associated with existing and new austerity measures.

Sales in Spain increased by 3% at CER to \$426 million (2014: \$497 million; 2013: \$507 million), mainly driven by strong growth across the Growth Platforms.

Established ROW²

Established ROW sales of \$3,022 million were flat at CER (2014: \$3,510 million; 2013: \$3,973 million). The key products with sales growth in Established ROW in 2015 were *Nexium*, *Symbicort*, *Brilinta*, and *Onglyza*.

Japan

Sales in Japan were \$2,020 million, increasing by 4% at CER but negatively impacted on a Reported basis by the revaluation of the Japanese yen (2014: \$2,227 million; 2013: \$2,485 million).

Nexium achieved sales of \$405 million (2014: \$358 million; 2013: \$278 million).

Crestor sales grew by 8% at CER to \$468 million (2014: \$502 million; 2013: \$537 million), retaining its position as the number one brand in the statin market in Japan. *Symbicort* sales at \$176 million (2014: \$207 million; 2013: \$175 million) decreased by 2%, achieving a market share of 39.4%.

Sales were also negatively impacted by generic competition for our non-promoted oncology products.

Canada

Canada returned to growth in 2015 driven by the strong performance of *Symbicort* and the Diabetes portfolio (including the launch of *Forxiga* in January 2015). Canadian sales increased by 4% at CER to \$533 million (2014: \$590 million; 2013: \$637 million).

Other Established ROW³

Sales in Other Established ROW declined by 19% to \$469 million (2014: \$693 million; 2013: \$851 million). Sales in Australia declined by 21% to \$435 million (2014: \$658 million; 2013: \$817 million) due to continued volume erosion on *Crestor* and *Atacand* following generic entries in 2013 and pricing pressure on other mature brands (*Seroquel* and *Arimidex*). *Nexium* sales in Australia declined following the loss of exclusivity in Australia in August 2014.

Emerging Markets

In Emerging Markets, sales increased by 12% to \$5,822 million (2014: \$5,827 million; 2013: \$5,389 million), which was principally driven by growth in China, Russia, Brazil and Argentina, and growth across a broad range of markets in our strategic Growth Platforms – *Brilinta*, and our Diabetes and Respiratory franchises.

In many of the larger markets, such as Brazil and Mexico, patients tend to pay directly for prescription medicines and consequently, these markets are at less risk of direct government interventions on pricing and reimbursement. In other markets, such as South Korea, Taiwan and Turkey, where governments pay for medicines, we are seeing continued efforts to reduce the cost of prescriptions in line with the efforts in Europe, Canada and Australia.

China

Sales in China (excluding Hong Kong) grew by 15% to \$2,530 million (2014: \$2,242 million; 2013: \$1,840 million). AstraZeneca remained the second largest multinational pharmaceutical company in China during 2015. Despite the market slowdown, we saw continued strong sales of Oncology and Respiratory in particular, with sales growth of 17% and 38% respectively. We have continued to make strong progress on the listing of *Brilinta*, *Byetta* and *Onglyza* into key hospitals. *Brilinta* has reached \$38 million in sales. We continue to have the largest sales force among multinational pharmaceutical companies in China. The number of hospitals covered grew by 34%.

Other Emerging Markets⁴

We continued to build our presence in Russia, with sales growing by 21% to \$231 million (2014: \$312 million; 2013: \$310 million) from strong performance in the retail segment. To increase access to our medicines, we established patient affordability programmes in 50 regions of

the Russian Federation. The Russian market grew by 12% during 2015. AstraZeneca's growth came from *Iressa*, *Pulmicort* and *Brilinta*. We have 559 clinical trial sites in 46 cities. Our new production facility in Vorsino is expected to commence commercial production in early 2016.

The Latin American pharmaceutical market continues to grow. However, in many countries, growth is being predominantly captured by generics, branded generics and private label product offerings. Sales were up 15% to \$1,024 million (2014: \$1,181 million; 2013: \$1,188 million) driven principally by Brazil, which grew by 16% to \$381 million (2014: \$451 million; 2013: \$447 million), following successful launch of *Forxiga* and continued strong uptake of *Brilinta*. Sales in Argentina also grew rapidly by 37% driven by strong growth in Diabetes, *Brilinta* and Respiratory. The Mexico prescription drug market continues to grow. Sales grew by 11% at CER to \$195 million (2014: \$210 million; 2013: \$206 million), driven by the Diabetes and Respiratory Growth Platforms.

In the Middle East and Africa, despite political challenges arising from geopolitical and broader political conflict, sales grew by 13%, driven by strong growth in Egypt, Saudi Arabia, the Gulf States, and several Emerging Markets in Africa as well as steady growth in Turkey. Sales in South Africa were flat and declined by 13% in Tunisia reflecting local market conditions. Sales of \$889 million in Asia were in line with 2014 at CER (2014: \$948 million; 2013: \$900 million). Double digit growth in Vietnam, Indonesia, Malaysia and India were offset by sales decreases due to price erosions incurred by loss of exclusivity in Taiwan and Korea.

Launches in Emerging Markets in 2015 included: *Forxiga* in India, Colombia, Ecuador, and Taiwan; *Bydureon* in Mexico; and *Zinforo* in Mexico.

¹ Growth based on Invokana trend pre *Farxiga* launch, and the composition of *Farxiga* and Invokana to 18 December 2015 (excluding holidays) to derive the impact on SGLT2 class.

² Canada, Japan, Australia and New Zealand.

³ Australia and New Zealand.

⁴ Emerging Markets excluding China.

Sustainability: supplementary information

Summary information about our commitment and performance in key areas is integrated into the relevant sections of this Annual Report. Further information about these and other areas is available on our website, www.astrazeneca.com.

The Strategy section from page 8 describes how we create value across the life-cycle of a medicine and highlights our distinctive capabilities and our strategy. Our commitment to operating responsibly underpins all of these efforts. This helps to ensure the future sustainability of the Group in a way that adds value for our stakeholders. The Sustainability section from page 57 reviews our sustainability governance and commitments. These encompass:

- > Environmental sustainability: managing our impact on the environment, across all our operations, with a particular focus on carbon emissions, waste and water use (see page 57).
- > Access to healthcare: as we expand our geographic footprint, exploring ways of increasing access to healthcare for more people, tailored locally to different patient needs (see page 50).
- > Responsible research: underpinning our accelerated drive for innovation with sound bioethics worldwide and maintaining a strong focus on patient safety in everything we do, minimising the risks and maximising the benefits of all our medicines throughout R&D, and after launch (see page 44).
- > Ethical business practices:
 - Working to consistent global standards of ethical sales and marketing practices in all our markets as we work to restore growth (see page 50).
 - Working only with suppliers who have standards consistent with our own as we increase our outsourcing to drive business efficiency (see page 47).
 - Making a positive contribution to our local communities around the world, through community support programmes consistent with improving health and promoting science (see page 58).
- > Being a great place to work:
 - Ensuring that diversity in its broadest sense is reflected in our leadership and people strategies (see pages 52 and 53).

- Continuing to develop and embed a consistent approach to human rights across our worldwide activities (see page 54).
- Promoting the safety, health and wellbeing of all our people worldwide as we continue to drive a high-performance culture and the achievement of our business goals (see page 57).

A core element of our business strategy is value-creating business development activity that strengthens our pipeline and accelerates growth. This includes targeted acquisitions. When we acquire companies we aim to align standards of responsible business and incorporate the companies in the setting of targets and measurement of performance.

Benchmarking

As expectations of stakeholders evolve, we continue to engage with them and use the feedback to inform the development of our sustainability strategy and risk management planning.

We also use the insights gained from external surveys to develop our approach in line with global best practice. A member of the Dow Jones Sustainability Index (DJSI) since 2001, we were once again listed in the 2015 World Index (the top 10% of the largest 2,500 companies). We also retained our listing on the DJSI STOXX – European Index (the top 20% of the 600 largest European companies) for the eighth year running (one of four pharmaceutical companies to do so out of 14 assessed). We achieved a total score of 84% (2014: 79%) compared with a sector best score of 88% (2014: 87%). We increased individual scores for 14 out of 24 criteria for 2015 (compared to seven out of 24 criteria in 2014). These included corporate governance, code of conduct, marketing practices, supply chain management, customer relationship management, innovation management, environmental policy management system, climate strategy, labour practice indicators and human rights, human capital development, talent attraction and retention, occupational health and safety, bioethics and health outcomes contribution. While these scores are encouraging, we lost ground in some areas, including risk and crisis management, social reporting,

environmental reporting and operational eco-efficiency, strategy to improve access to drugs or products, and addressing cost burden. To understand these lower scores better, we commissioned an in-depth external benchmark survey. We will use the analysis to plan ways to improve in these areas.

External assurance

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

- > Patient safety, page 44
- > Clinical trials and transparency, page 45
- > Research use of human biological samples, page 45
- > Animal research, page 45
- > Increasing access to healthcare, page 50
- > Healthy Heart Africa, page 51
- > Sales and marketing ethics, page 50
- > Working with suppliers, page 47
- > Natural resource efficiency, page 57
- > Develop a strong and diverse pipeline of leaders, page 53
- > Human rights, page 54
- > Managing change, page 54
- > Employee relations, page 54
- > Safety, health and wellbeing, page 57
- > Community investment, page 58
- > Sustainability, page 57
- > Sustainability framework, page 56.

Based on the evidence provided and subject to the scope, objectives and limitations defined in the full assurance statement, nothing has come to the attention of Bureau Veritas causing us to believe that the sustainability information contained within this Annual Report is materially misstated. Bureau Veritas is a professional services company that has a long history of providing independent assurance services in environmental, health, safety, social and ethical management and disclosure.

The full assurance statement, which includes Bureau Veritas's scope of work, methodology, overall opinion, and limitations and exclusions, is available on our website, www.astrazeneca.com.

Carbon reporting

Global greenhouse gas emissions data for the period 1 January 2015 to 31 December 2015

	Tonnes of CO ₂ e			
	2015	2014	2013 ¹	2012
Emissions from:				
Combustion of fuel and operation of facilities ²	324,300	328,700	318,600	318,700
Electricity, heat, steam and cooling purchased for own use ³	273,500	290,300	274,400	277,100
Company's chosen intensity measurement:				
Emissions reported above normalised to million US dollar revenue	24.2	23.7	23.1	21.3
<i>Supplemental information:</i>				
<i>Net electricity, heat, steam and cooling emissions, after write down due to voluntary purchase of electricity supplied under certified low carbon supply contracts or carbon certificates⁴</i>	223,700	238,600	238,200	250,800
<i>Supply chain emissions:</i>				
<i>Upstream emissions from personnel air travel, goods transport and waste incineration</i>	156,000	167,900	155,400	169,800
<i>Downstream emissions from HFA propellants released during patient use of our inhaled medicines</i>	508,800	448,900	352,000	299,600

¹ Regular review of the data is carried out to ensure accuracy and consistency. This has led to slight changes in the data for previous years. None of the changes are statistically significant. The data quoted in this Annual Report are generated from the revised data.

² Included in this section are greenhouse gases from direct fuel combustion, process and engineering emissions at our sites and from fuel use in our vehicle fleet.

³ Greenhouse gases from electricity are calculated using a location-based approach as described in GHG Protocol Scope 2 Guidance (January 2015). Market instruments (US Renewable Energy Certificates, UK Renewable Energy Guarantees of Origin) are then discounted. This approach is consistent with previous years. In future years Scope 2 emissions reporting will follow the dual reporting approach.

⁴ Some electricity supplied to our UK sites has been provided under a green power contract and is backed up with an equivalent quantity of Renewable Energy Guarantees of Origin and some of the electricity consumed at our US sites is covered by purchase of Renewable Energy Certificates.

The above table provides data on our global greenhouse gas emissions for 2015.

We have reported on all of the emission sources required under the Quoted Companies Greenhouse Gas Emissions (Directors' Reports) Regulations 2013.

These sources fall within our consolidated Financial Statements. We do not have responsibility for any emission sources that are not included in our consolidated Financial Statements.

We have used the GHG Protocol Corporate Accounting and Reporting Standard (revised edition). Emission factors for electricity have been derived from the International Energy Agency and USEPA eGRID databases and for all other fuels and emission sources from the 2006 IPCC Guidelines for National Greenhouse Gas Inventories.

Bureau Veritas has undertaken a limited assurance on the 2015 GHG emissions data. The assurance statement, including scope, methodology, overall opinion, and limitations and exclusions, is available on our website, www.astrazeneca.com.

Financials (Prior year)

Results of operations – summary analysis of year ended 31 December 2014

2014 Reported operating profit – restated

	2014 Restated ¹			2013 Restated ¹	Percentage of Total Revenue		2014 ¹ compared with 2013 ¹	
	Reported \$m	CER growth \$m	Growth due to exchange effects \$m	Reported \$m	Reported 2014 %	Reported 2013 %	CER growth ² %	Actual growth %
Product Sales	26,095	833	(449)	25,711			3	1
Externalisation Revenue	452	354	3	95			375	378
Total Revenue	26,547	1,187	(446)	25,806			5	3
Cost of sales	(5,842)	(572)	(9)	(5,261)	(22.0)	(20.4)	11	11
Gross profit	20,705	615	(455)	20,545	78.0	79.6	3	1
Distribution costs	(324)	(23)	5	(306)	(1.2)	(1.2)	7	6
Research and development expense	(5,579)	(716)	(42)	(4,821)	(21.0)	(18.7)	15	16
Selling, general and administrative costs	(13,000)	(896)	102	(12,206)	(49.0)	(47.3)	7	7
Other operating income and expense	335	(136)	(29)	500	1.2	2.0	(27)	(33)
Operating profit	2,137	(1,156)	(419)	3,712	8.0	14.4	(31)	(42)
Net finance expense	(885)			(445)				
Share of after tax losses of joint ventures	(6)			–				
Profit before tax	1,246			3,267				
Taxation	(11)			(696)				
Profit for the period	1,235			2,571				
Basic earnings per share (\$)	0.98			2.04				

¹ 2014 and 2013 results have been restated to reflect the reclassification of Externalisation Revenue from other operating income and expense as detailed in Group Accounting Policies from page 144.

² CER growth is calculated using prior year actual results adjusted for certain exchange effects including hedging.

2014 Reconciliation of Reported results to Core results

	2014 Reported \$m	Restructuring costs \$m	Intangible amortisation and impairments \$m	Acquisition of BMS's share of diabetes alliance \$m	Legal provisions and other \$m	2014 Core ² \$m	Core ² 2014 ¹ compared with 2013 ¹	
							CER growth %	Actual growth %
Gross profit	20,705	107	701	146	–	21,659	4	2
<i>Product Sales gross margin %³</i>	<i>77.6%</i>					<i>81.3%</i>		
<i>Total Revenue gross margin %</i>	<i>78.0%</i>					<i>81.6%</i>		
Distribution costs	(324)	–	–	–	–	(324)	7	6
Research and development	(5,579)	497	141	–	–	(4,941)	15	16
Selling, general and administrative costs	(13,000)	662	811	932	379	(10,216)	16	15
Other operating income and expense	335	292	230	–	(98)	759	19	15
Operating profit	2,137	1,558	1,883	1,078	281	6,937	(13)	(17)
<i>Operating margin as a % of Total Revenue</i>	<i>8.0%</i>					<i>26.1%</i>		
Net finance expense	(885)	–	–	345	47	(493)		
Taxation	(11)	(255)	(376)	(356)	(42)	(1,040)		
Basic earnings per share (\$)	0.98	1.03	1.19	0.85	0.23	4.28		

¹ 2014 and 2013 results have been restated to reflect the reclassification of Externalisation Revenue from other operating income and expense as detailed in Group Accounting Policies from page 144.

² Each of the measures in the Core column in the above table is a non-GAAP measure.

³ Gross margin as a % of Product Sales reflects gross profit derived from Product Sales, divided by Product Sales.

All growth rates in this section are expressed at CER unless otherwise stated.

2014 Product Sales increased 3% compared with 2013. Accelerating performance of the Group's Growth Platforms more than offset the impact of volume erosion on mature brands including *Nexium* in the US and pricing pressures in Established Markets. 2014 Product Sales in the US were up 4% with Europe down 1%. Established ROW Product Sales were down 4%. Emerging Markets Product Sales were up 12%, mainly driven by growth in China of 22%. China became our second largest market in 2014. Further details of our sales performance are contained in the Geographical Review from page 227.

Externalisation Revenue

As detailed in the Financial Review from page 66, the Group has updated its revenue accounting policy. Reflecting the increased level of externalisation activity, Externalisation Revenue, alongside Product Sales, are now included in Total Revenue. 2014 and 2013 results have been restated to reflect this change, resulting in \$452 million of income being reclassified from other operating income to Externalisation Revenue in 2014 (2013: \$95 million).

In mid-2014, the US Internal Revenue Service issued final regulations that affected how the annual US Branded Pharmaceutical Fee, imposed by the health care reform legislation in 2010, is recognised. Under the new regulations, the fee is based on actual sales in the current year which necessitated an additional year's charge to be recognised in 2014. In line with other pharmaceutical industry peers, we previously accrued for this charge based on prior year's sales and recorded the charge as a cost in SG&A. The final regulation had two impacts on the Group's results in 2014:

> As the fee is now calculated on actual sales in the current year, AstraZeneca considers it more appropriate to account for the fee as a deduction from revenue rather than a charge to SG&A. The new legislation was effective from July 2014 and, therefore, AstraZeneca treated the charge for the period since July 2014 as a deduction from revenue rather than as a cost in SG&A. In 2014 this had the effect of reducing revenue by \$113 million. This presentational change to the income statement had no impact on earnings for 2014.

> We recorded a catch-up full annual charge to SG&A, reflecting this new basis, in 2014. The additional year's charge was excluded from Core financial measures as detailed below.

Core gross margin as a percentage of Product Sales in 2014 was 81.3%, 0.4 percentage points lower than 2013 at CER as the effect of an unfavourable product mix, including additional costs associated with the Diabetes brands, more than offset the benefit of a lower *Crestor* royalty.

Core R&D expense in 2014 was up 15% reflecting increased spend on our late-stage pipeline.

Expenditures in core SG&A in 2014 were 16% higher than 2013, driven by investments in sales and marketing dedicated to the Group's Growth Platforms. The acquisitions of BMS's share of the diabetes alliance and the rights to Almirall's respiratory franchise in 2014 added approximately 4,100 employees. The selective investment in our Growth Platforms was partially funded by a decline in G&A costs during 2014.

Core other income in 2014 was up 19% which included royalty income of \$533 million.

The 2014 Core operating profit was down 13%. Core operating margin in 2014 was 26.1% of Total Revenue, down 6.4 percentage points from 2013. The decline in Core operating profit was greater than the decline in Total Revenue primarily due to expenditure associated with the Group's key Growth Platforms and strengthened pipeline.

Core EPS was \$4.28 in 2014, down 8% compared with 2013. The smaller decline in Core EPS compared with Core operating profit was largely due to a lower tax rate. This favourable tax effect was partially offset by an increase in the number of shares outstanding and a marginally higher Core finance expense in 2014 compared with 2013.

Pre-tax adjustments in 2014 to arrive at Core profit before tax amounted to \$5,192 million in 2014 (2013: \$4,678 million). Excluded from Core results were:

- > Restructuring costs totalling \$1,558 million (2013: \$1,421 million), incurred as the Group continued the fourth phase of restructuring announced in March 2013. Restructuring costs included in 2014 included a \$292 million loss on disposal of our Alderley Park site.
- > Amortisation totalling \$1,784 million (2013: \$1,591 million) relating to intangible assets, except those related to IT and to our acquisition of BMS's share of our Global Diabetes Alliance (which are separately detailed below). The increase was driven by amortisation charges in connection with payments in respect of our final Merck exit arrangements.
- > Intangible impairment charges of \$99 million (2013: net \$1,712 million, including a \$1,758 million impairment relating to *Bydureon*). Further details relating to intangible asset impairments are included in Note 9 to the Financial Statements from page 158.
- > Costs associated with our acquisition of BMS's share of our Global Diabetes Alliance amounting to \$1,423 million. Included within this are \$407 million of amortisation charges, a contingent consideration fair value uplift charge of \$529 million reflecting higher expected Diabetes portfolio revenues following the successful integration of the newly acquired elements, and \$345 million of interest charges relating to a discount unwind on contingent consideration arising on the acquisition (as detailed in Note 18 to the Financial Statements from page 164).
- > Net legal provisions and other charges of \$328 million (2013: income of \$46 million), including a \$201 million charge for the additional year's US Branded Pharmaceutical Fee and \$47 million discount unwind charges relating to contingent consideration arising on our other business combinations as detailed in Note 18 to the Financial Statements from page 164).

2014 Reported operating profit was down 31% at CER to \$2,137 million. The larger declines compared with the respective Core financial measures are mainly the result of our enhanced business acquisition activities including our acquisition of BMS's share of our Global Diabetes Alliance, offset by reduced impairment charges in 2014.

Financials (Prior year) continued

Net finance expense in 2014 was \$885 million (2013: \$445 million). The increase was driven by \$453 million (2013: \$nil) related to the discount unwind on both contingent consideration arising on business combinations (\$391 million) and other long-term liabilities (\$62 million).

The 2014 Reported taxation charge of \$11 million (2013: \$696 million), consisted of a current tax charge of \$872 million (2013: \$1,398 million) and a credit arising from movements on deferred tax of \$861 million (2013: \$702 million). The current tax charge in 2014 included a prior period current tax credit of \$109 million (2013: charge of \$46 million).

The tax paid in 2014 was \$1,201 million, which was 96% of Reported profit and 19% of Core profit.

The Reported tax rate for 2014 was 0.9% compared with 21.3% for 2013. The Reported tax rate of 0.9% was impacted by a one-off benefit of \$117 million in respect of the inter-governmental agreement of a transfer pricing matter, the non-Core impact of the revaluation of the fair value of contingent consideration arising on business combinations (charge of \$512 million with related tax credit of \$157 million), and the benefit of the UK Patent Box legislation (\$35 million). Excluding these effects, the Reported tax rate for 2014 would have been 18.2%. The Core tax rate for 2014 was 16.2%. Excluding the benefit from the transfer pricing agreement and Patent Box, the Core tax rate would have been 18.5%. Further details relating to movements in our taxation balances are included in Note 4 to the Financial Statements from page 151.

Reported post tax profit for 2014 was \$1,235 million, a decrease of 34%. Reported EPS was down 34% to \$0.98.

Total comprehensive income in 2014 decreased by \$2,729 million from the prior year, resulting in a loss of \$271 million. This was driven by the decrease in profit of \$1,336 million, and a decrease of \$1,393 million in other comprehensive income driven by movements in exchange rates in our consolidated results of \$1,352 million, principally due to the strengthening of the

US dollar against sterling, the euro and krona, and losses on the remeasurement of our defined benefit pension liability of \$766 million in accordance with the requirements of IAS 19 'Employee Benefits' (driven by a reduction in the discount rate applied to our pension liabilities partially offset by actuarial gains on our scheme assets).

Cash flow and liquidity – 2014

All data in this section is on a Reported basis.

Net cash generated from operating activities was \$7,058 million in the year ended 31 December 2014, compared with \$7,400 million in 2013. Reductions in working capital partially offset the lower operating profit and higher tax payments.

Working capital movements in 2014 were principally driven by general increases in trade payables and accruals, as a result of our increased R&D and SG&A spend, an increase in the US Managed Markets liabilities, an additional year's Branded Pharmaceutical levy and a reduction in trade receivables principally in Japan and the US.

Non-cash and other movements included \$512 million relating to fair value adjustments on contingent consideration arising on business combinations.

Investment cash outflows in 2014 of \$7,125 million (2013: \$3,112 million) included \$3,804 million (2013: \$1,158 million) on completion of business acquisitions, inclusive of BMS's share of our Global Diabetes Alliance (\$2,703 million), the rights to Almirall's respiratory franchise (\$876 million) and the acquisition of Definiens (\$150 million). The 2013 comparative period included payments on the completion of the acquisitions of Pearl Therapeutics, Omthera, Amplimmune and Spirogen. Investment cash outflows in 2014 also include \$657 million (2013: \$nil) of payments against contingent consideration arising on business combinations and \$1,740 million (2013: \$1,316 million) for the purchase of other intangible assets, which included a \$409 million payment to Merck on the consummation of our Second Option and \$310 million on the settlement of pre-existing launch- and sales-related milestones with BMS.

Net cash distributions to shareholders in 2014 were \$3,242 million (2013: \$2,979 million), through dividends of \$3,521 million (2013: \$3,461 million) partially offset by proceeds from the issue of shares of \$279 million (2013: \$482 million) due to the exercise of share options.

At 31 December 2014, outstanding gross debt (interest-bearing loans and borrowings) was \$10,843 million (2013: \$10,376 million). Of the gross debt outstanding at 31 December 2014, \$2,446 million was due within one year (2013: \$1,788 million).

Net debt at 31 December 2014 was \$3,223 million, compared to a net funds position of \$39 million at the beginning of 2014, as a result of the net cash outflow as described above.

Financial position – 2014

All data in this section is on a Reported basis.

In 2014, net assets decreased by \$3,607 million to \$19,646 million. The decrease in net assets was broadly as a result of dividends of \$3,532 million and adverse movements on exchange taken to reserves of \$1,352 million, partially offset by the 2014 Group profit of \$1,235 million.

Property, plant and equipment

Property, plant and equipment increased by \$192 million to \$6,010 million in 2014. Additions of \$1,607 million (2013: \$816 million), including \$515 million (2013: \$8 million) arising on business combinations, were offset by depreciation of \$776 million (2013: \$906 million) and disposals of \$582 million (2013: \$82 million). Property, plant and equipment also increased due to the transfer of a prepayment balance of \$350 million, which related to amounts paid to BMS for fixed assets under our previous joint operation with BMS; with the acquisition of BMS's interest in the diabetes franchise we acquired the underlying property, plant and equipment to which this prepayment related.

Goodwill and intangible assets

The Group's goodwill of \$11,550 million as at 31 December 2014 (2013: \$9,981 million) principally arose on the acquisition of MedImmune in 2007 and the restructuring of our US joint venture with Merck in 1998. Goodwill of \$1,841 million arising on our acquisitions of BMS's share of our Global Diabetes Alliance (\$1,530 million) and the rights to Almirall's respiratory franchise (\$311 million) was capitalised in 2014.

Intangible assets amounted to \$20,981 million at 31 December 2014 (2013: \$16,047 million). Intangible asset additions were \$8,548 million in 2014 (2013: \$3,217 million), including product rights acquired in our acquisitions of \$7,501 million (2013: \$2,416 million). Amortisation in 2014 was \$2,384 million (2013: \$1,779 million). Impairment charges in the year amounted to \$122 million (2013: \$2,082 million).

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

Receivables, payables and provisions

Trade receivables decreased by \$752 million to \$4,762 million principally in Japan and the US.

In 2014, prepayments and accrued income decreased by \$928 million. As detailed in our 2013 Annual Report, in 2013, we modified the royalty structure under our global licence agreement for *Crestor*, which was amended to include fixed minimum and maximum annual royalty payments to Shionogi. These future royalties were recognised within payables and as a prepayment. The reduction in prepayments in 2014 was driven by the payment of one year's royalties under this revised agreement, along with a transfer of \$350 million from prepayments to property, plant and equipment as detailed above.

Trade and other payables increased by \$7,163 million in 2014 to \$19,877 million, with increases of \$993 million in trade payables, \$677 million of rebates and chargebacks, and \$5,781 million in other payables, including \$6,385 million in contingent consideration offset by a

reduction of one year's Shionogi royalty payments. The increase in trade payables was driven by our increased in year R&D and SG&A spend in the later part of 2014. The rebates and chargebacks balance includes an additional year's US Branded Pharmaceutical levy.

The decrease in provisions of \$282 million in 2014 included \$633 million of cash payments, partially offset by \$434 million of additional charges recorded in 2014. Included within the \$434 million of charges for 2014 were \$254 million for our global restructuring initiative and \$91 million in respect of legal charges. Cash payments in 2014 included \$472 million for our global restructuring programme.

Tax payable and receivable

Net income tax payable decreased by \$557 million in 2014 to \$2,025 million, principally due to cash tax timing differences, foreign exchange and a \$117 million adjustment in respect of prior periods following the settlement of the inter-governmental agreement of a transfer pricing matter. The 31 December 2014 tax receivable balance of \$329 million comprised tax owing to AstraZeneca from certain governments expected to be received on settlements of transfer pricing audits and disputes and cash tax timing differences. Net deferred tax liabilities increased by \$1,045 million in 2014, mainly due to a reversal of taxable temporary differences.

Retirement benefit obligations

Net retirement benefit obligations decreased by \$690 million in 2014. Employer contributions to the pension scheme of \$184 million and beneficial exchange movements of \$268 million were offset by service cost charges of \$221 million, net financing costs of \$92 million and net remeasurement adjustments of \$766 million.

Shareholder Information

AstraZeneca PLC share listings and prices

	2011	2012	2013	2014	2015
Ordinary Shares in issue – millions					
At year end	1,292	1,247	1,257	1,263	1,264
Weighted average for year	1,361	1,261	1,252	1,262	1,264
Stock market price – per Ordinary Share					
Highest (pence)	3194.0	3111.5	3612.0	4823.5	4863.0
Lowest (pence)	2543.5	2591.0	2909.5	3549.5	3903.5
At year end (pence)	2975.0	2909.5	3574.5	4555.5	4616.5

Percentage analysis of issued share capital at 31 December

By size of account Number of Ordinary Shares	2011 %	2012 %	2013 %	2014 %	2015 %
1 – 250	0.6	0.6	0.5	0.5	0.5
251 – 500	0.7	0.7	0.6	0.6	0.6
501 – 1,000	0.8	0.8	0.8	0.7	0.7
1,001 – 5,000	1.2	1.1	1.1	1.0	0.9
5,001 – 10,000	0.2	0.2	0.2	0.2	0.2
10,001 – 50,000	1.0	1.0	1.0	1.0	0.9
50,001 – 1,000,000	13.8	12.6	12.3	13.3	13.0
Over 1,000,000 ¹	81.7	83.0	83.5	82.7	83.2

¹ Includes Euroclear and ADR holdings.

At 31 December 2015, the Company had 97,260 registered holders of 1,264,122,670 Ordinary Shares. There were 104,150 holders of Ordinary Shares held under the Euroclear Services Agreement, representing 10.8% of the issued share capital of the Company and approximately 172,000 holders of ADSs, representing 10.8% of the issued share capital of the Company. With effect from 27 July 2015, the Company's ADS ratio changed to two ADSs per one Ordinary Share. The former ratio was one ADS per one Ordinary Share. With effect from 6 February 2015, Citibank, N.A. (Citibank) succeeded JPMorgan Chase Bank (JPMorgan) as depositary of the ADSs.

In 1999, in connection with the merger between Astra and Zeneca through which the Company was formed, the Company's share capital was redenominated in US dollars. On 6 April 1999, Zeneca shares were cancelled and US dollar shares issued, credited as fully paid on the basis of one dollar share for each Zeneca share then held. This was achieved by a reduction of

capital under section 135 of the Companies Act 1985. Upon the reduction of capital becoming effective, all issued and unissued Zeneca shares were cancelled and the sum arising as a result of the share cancellation credited to a special reserve, which was converted into US dollars at the rate of exchange prevailing on the record date. This US dollar reserve was then applied in paying up, at par, newly created US dollar shares.

At the same time as the US dollar shares were issued, the Company issued 50,000 Redeemable Preference Shares for cash, at par. The Redeemable Preference Shares carry limited class voting rights, no dividend rights and are capable of redemption, at par, at the option of the Company on the giving of seven days' written notice to the registered holder of the Redeemable Preference Shares.

A total of 826 million Ordinary Shares were issued to Astra shareholders who accepted the merger offer before the final closing date, 21 May 1999. The Company received acceptances from Astra shareholders

representing 99.6% of Astra's shares and the remaining 0.4% was acquired in 2000, for cash.

Since April 1999, following the merger of Astra and Zeneca, the principal markets for trading in the shares of the Company are the LSE, the SSE and the NYSE. The table overleaf sets out, for 2014 and 2015, the reported high and low share prices of the Company, on the following bases:

- > For shares listed on the LSE, the reported high and low middle market closing quotations are derived from the Daily Official List.
- > For shares listed on the SSE, the high and low closing sales prices are as stated in the Official List.
- > For ADSs listed on the NYSE, the reported high and low sales prices are as reported by Dow Jones (ADR quotations).

		Ordinary LSE		Ordinary SSE		ADS	
		High (pence)	Low (pence)	High (SEK)	Low (SEK)	High (US\$)	Low (US\$)
2014	– Quarter 1	4103.0	3549.5	446.3	380.5	68.38	58.51
	– Quarter 2	4823.5	3723.0	532.5	409.7	81.09	62.45
	– Quarter 3	4597.0	4092.5	536.0	467.3	76.31	68.49
	– Quarter 4	4780.0	4169.5	558.5	484.5	75.38	67.15
2015	– Quarter 1	4847.0	4272.0	625.0	538.0	72.22	64.44
	– Quarter 2	4863.0	4019.0	638.0	522.5	73.35	63.71
	– Quarter 3	4424.5	3903.5	603.0	508.5	34.54 ¹	30.28 ¹
	– Quarter 4	4627.5	3947.0	597.5	509.0	34.77	30.47
	– July	4347.5	4120.5	584.5	538.0	67.89 ¹	64.33 ¹
	– August	4424.5	3903.5	603.0	508.5	34.54	30.28
	– September	4379.0	4033.5	567.0	523.5	34.37	30.69
	– October	4247.5	3947.0	548.0	509.0	32.39	30.47
	– November	4520.0	4075.0	597.5	538.0	34.11	30.85
	– December	4627.5	4285.5	597.0	550.5	34.77	32.80

¹ With effect from 27 July 2015, the Company's ADS ratio was changed to two ADSs per one Ordinary Share. The former ratio was one ADS per one Ordinary Share.

Major shareholdings

At 31 December 2015, the following had disclosed an interest in the issued Ordinary Share capital of the Company in accordance with the requirements of rules 5.1.2 or 5.1.5 of the UK Listing Authority's Disclosure and Transparency Rules:

Shareholder	Number of Ordinary Shares	Date of disclosure to Company ¹	Percentage of issued share capital
BlackRock, Inc.	100,885,181	8 December 2009	7.98
Investor AB	51,587,810	2 February 2012	4.08
The Capital Group Companies, Inc.	37,925,813	17 July 2015	3.00

¹ Since the date of disclosure to the Company, the interest of any person listed above in Ordinary Shares may have increased or decreased. No requirement to notify the Company of any increase or decrease would have arisen unless the holding moved up or down through a whole number percentage level. The percentage level may increase (on the cancellation of shares following a repurchase of shares under the Company's share repurchase programme) or decrease (on the issue of new shares under any of the Company's share plans).

So far as the Company is aware, no other person held a notifiable interest in the issued Ordinary Share capital of the Company.

No changes to major shareholdings were disclosed to the Company between 31 December 2015 and 31 January 2016. Any changes between 31 January 2016 and 29 February 2016 will be set out in the Notice of Annual General Meeting 2016 and Shareholders' Circular.

Changes in the percentage ownership held by major shareholders during the past three years are set out below. Major shareholders do not have different voting rights.

Shareholder	31 January 2016	31 January 2015	31 January 2014	2 February 2013
BlackRock, Inc.	7.98	7.99	8.01	8.08
Investor AB	4.08	4.08	4.09	4.13
The Capital Group Companies, Inc.	3.00	< 3.00	3.01	< 3.00
Invesco Limited	< 5.00	< 5.00	5.78	5.83
Axa SA	< 3.00	< 3.00	4.52	4.57
Legal & General Investment Management Limited	< 3.00	< 3.00	< 3.00	4.62

ADSs evidenced by ADRs issued by Citibank, as depositary, are listed on the NYSE. At 31 January 2016, the proportion of Ordinary Shares represented by ADSs was 11.07% of the Ordinary Shares outstanding.

Number of registered holders of Ordinary Shares at 31 January 2016:

- > In the US: 712
- > Total: 97,256

Number of record holders of ADRs at 31 January 2016:

- > In the US: 1,889
- > Total: 1,912

Shareholder Information continued

So far as the Company is aware, it is neither directly nor indirectly owned or controlled by one or more corporations or by any government.

The Company does not know of any arrangements, the operation of which might result in a change in the control of the Company.

At 31 January 2016, the total amount of the Company's voting securities owned by Directors and officers of the Company was:

Title of class	Amount owned	Percentage of class
Ordinary Shares	500,191	0.04

Related party transactions

During the period 1 January 2015 to 31 January 2016, there were no transactions, loans, or proposed transactions between the Company and any related parties which were material to either the Company or the related party, or which were unusual in their nature or conditions (see also Note 29 to the Financial Statements from page 192).

Options to purchase securities from registrant or subsidiaries

(a) At 31 January 2016, options outstanding to subscribe for Ordinary Shares were:

Number of shares	Subscription price (pence)	Normal expiry date
3,725,301	1882 – 3599	2016 – 2021

The weighted average subscription price of options outstanding at 31 January 2016 was 2713 pence. All options were granted under Company employee share schemes.

(b) Included in paragraph (a) are options granted to officers of the Company as follows:

Number of shares	Subscription price (pence)	Normal expiry date
40,343	2280 – 3599	2017 – 2021

(c) At 31 January 2016, none of the Directors of the Company held options to subscribe for Ordinary Shares.

During the period 1 January 2015 to 31 January 2016, no Director exercised any options.

Dividend payments

For Ordinary Shares listed on the LSE and the SSE, the record date for the second interim dividend for 2015, payable on 21 March 2016, is 19 February 2016 and the ex-dividend date is 18 February 2016. For ADRs listed on the NYSE, the record date is 19 February 2016 and the ex-dividend date is 17 February 2016.

The record date for the first interim dividend for 2016, payable on 12 September 2016, is 12 August 2016.

Future dividends will normally be paid as follows:

- > **First interim:** Announced in July/August and paid in September.
- > **Second interim:** Announced in January/February and paid in March.

Shareview

The Company's shareholders with internet access may visit the website, www.shareview.co.uk, and register their details to create a portfolio. Shareview is a free and secure online service from the Company's registrar, Equiniti Limited, which gives access to shareholdings, including balance movements, indicative share prices and information about recent dividends.

ShareGift

The Company welcomes and values all of its shareholders, no matter how many or how few shares they own. However, shareholders who have only a small number of shares whose value makes it uneconomic to sell them, either now or at some stage in the future, may wish to consider donating them to charity through ShareGift, an independent charity share donation scheme. One feature of the scheme is that there is no gain or loss for UK capital gains tax purposes on gifts of shares through ShareGift, and it may now also be possible to obtain UK income tax relief on the donation. Further information about ShareGift can be found on its website, www.sharegift.org, or by contacting ShareGift on 020 7930 3737 or at 17 Carlton House Terrace, London SW1Y 5AH. ShareGift is administered by The Orr Mackintosh Foundation, registered charity number 1052686. More information about the UK tax position on gifts of shares to ShareGift can be obtained from HM Revenue & Customs on its website, www.hmrc.gov.uk.

The Unclaimed Assets Register

The Company supplies unclaimed dividend data to the Unclaimed Assets Register (UAR), which provides investors who have lost track of shareholdings with an opportunity to search the UAR's database of unclaimed financial assets on payment of a small fixed fee. The UAR donates part of the search fee to charity. The UAR can be contacted on 0844 481 8180 or at uarenquiries@uk.experian.com.

Results

Unaudited trading results of AstraZeneca in respect of the first three months of 2016 will be published on 29 April 2016 and results in respect of the first six months of 2016 will be published on 28 July 2016.

Documents on display

The Articles and other documents concerning the Company which are referred to in this Annual Report may be inspected at the Company's registered office at 2 Kingdom Street, London W2 6BD.

Taxation for US persons

The following summary of material UK and US federal income tax consequences of ownership of Ordinary Shares or ADRs held as capital assets by the US holders described below is based on current UK and US federal income tax law, including the US/UK double taxation convention relating to income and capital gains, which entered into force on 31 March 2003 (the Convention). This summary does not describe all of the tax consequences that may be relevant in light of the US holders' particular circumstances and tax consequences applicable to US holders subject to special rules (such as certain financial institutions, entities treated as partnerships for US federal income tax purposes, persons whose functional currency for US federal income tax purposes is not the US dollar, tax-exempt entities, persons subject to alternative minimum tax, persons subject to the Medicare contribution tax on 'net investment income', or persons holding Ordinary Shares or ADRs in connection with a trade or business conducted outside of the US). US holders are urged to consult their tax advisers regarding the UK and US federal income tax consequences of the ownership and disposition of Ordinary Shares or ADRs in their particular circumstances.

This summary is based in part on representations of Citibank as depositary for ADRs and assumes that each obligation in the deposit agreement among the Company and the depositary and the holders from time to time of ADRs and any related agreements will be performed in accordance with its terms. The US Treasury has expressed concerns that parties to whom American depositary shares are released before shares are delivered to the depositary (pre-release), or intermediaries in the chain of ownership between holders and the issuer of the security underlying the American depositary shares, may be taking actions that are inconsistent with the claiming, by US holders of American depositary shares, of foreign tax credits for US federal income tax purposes. Such actions would also be inconsistent with the claiming of the reduced tax rates, described below, applicable to dividends received by certain non-corporate US holders. Accordingly, the availability of the reduced tax rates for dividends received by certain non-corporate US holders could be affected by actions that may be taken by parties to whom ADRs are pre-released.

For the purposes of this summary, the term 'US holder' means a beneficial owner of Ordinary Shares or ADRs that is, for US federal income tax purposes, a citizen or resident of the US, a corporation (or other entity taxable as a corporation) created or organised in or under the laws of the US, any state in the US or the District of Columbia, or an estate or trust, the income of which is subject to US federal income taxation regardless of its source.

This summary assumes that we are not, and will not become, a passive foreign investment company, as discussed below.

UK and US income taxation of dividends

The UK does not currently impose a withholding tax on dividends paid by a UK company, such as the Company.

For US federal income tax purposes, distributions paid by the Company to a US holder are included in gross income as foreign source ordinary dividend income to the extent paid out of the Company's current or accumulated earnings and profits, calculated in accordance with US federal income tax principles. The Company does

not maintain calculations of its earnings and profits under US federal income tax principles and so it is expected that distributions generally will be reported to US holders as dividends. The amount of the dividend will be the US dollar amount received by the depositary for US holders of ADRs (or, in the case of Ordinary Shares, the US dollar value of the foreign currency payment, determined at the spot rate of the relevant foreign currency on the date the dividend is received by the US holders, regardless of whether the dividend is converted into US dollars), and it will not be eligible for the dividends received deduction generally available to US corporations. If the dividend is converted into US dollars on the date of receipt, US holders of Ordinary Shares generally should not be required to recognise foreign currency gains or losses in respect of the dividend income. They may have foreign currency gain or loss (taxable at the rates applicable to ordinary income) if the amount of such dividend is converted into US dollars after the date of its receipt.

Subject to applicable limitations and the discussion above regarding concerns expressed by the US Treasury, dividends received by certain non-corporate US holders of Ordinary Shares or ADRs may be taxable at favourable US federal income tax rates. US holders should consult their own tax advisers to determine whether they are subject to any special rules which may limit their ability to be taxed at these favourable rates.

Taxation on capital gains

Under present English law, individuals who are neither resident nor ordinarily resident in the UK, and companies which are not resident in the UK, will not be liable for UK tax on capital gains made on the disposal of their Ordinary Shares or ADRs, unless such Ordinary Shares or ADRs are held in connection with a trade, profession or vocation carried on in the UK through a branch or agency or other permanent establishment.

A US holder will generally recognise US source capital gains or losses for US federal income tax purposes on the sale or exchange of Ordinary Shares or ADRs in an amount equal to the difference between the US dollar amount realised and such holder's US dollar tax basis in the Ordinary Shares or ADRs. US holders should consult their own

tax advisers about the treatment of capital gains, which may be taxed at lower rates than ordinary income for non-corporate US holders and capital losses, the deductibility of which may be subject to limitations.

Passive Foreign Investment Company (PFIC) rules

We believe that we were not a PFIC for US federal income tax purposes for the year ended 31 December 2015. However, since PFIC status depends on the composition of our income and assets, and the market value of our assets (including, among others, less than 25% owned equity investments), from time to time, there can be no assurance that we will not be considered a PFIC for any taxable year. If we were treated as a PFIC for any taxable year during which Ordinary Shares or ADRs were held, certain adverse tax consequences could apply to US holders.

Information reporting and backup withholding

Payments of dividends and sales proceeds that are made within the US or through certain US-related financial intermediaries may be subject to information reporting and backup withholding, unless: (i) the US holder is a corporation or other exempt recipient; or (ii) in the case of backup withholding, the US holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding. The amount of any backup withholding from a payment to a US holder will be allowed as a credit against the holder's US federal income tax liability and may entitle the holder to a refund, provided that the required information is timely supplied to the US Internal Revenue Service (IRS).

Certain US holders who are individuals (and under proposed US Treasury regulations, certain entities), may be required to report information relating to securities issued by non-US persons (or foreign accounts through which the securities are held), generally on IRS Form 8938, subject to certain exceptions (including an exception for securities held in accounts maintained by US financial institutions). US holders should consult their tax advisers regarding their reporting obligations with respect to the Ordinary Shares or ADRs.

Shareholder Information continued

UK inheritance tax

Under the current Double Taxation (Estates) Convention (the Estate Tax Convention) between the US and the UK, Ordinary Shares or ADRs held by an individual shareholder who is domiciled for the purposes of the Estate Tax Convention in the US, and is not for the purposes of the Estate Tax Convention a national of the UK, will generally not be subject to UK inheritance tax on the individual's death or on a chargeable gift of the Ordinary Shares or ADRs during the individual's lifetime, provided that any applicable US federal gift or estate tax liability is paid, unless the Ordinary Shares or ADRs are part of the business property of a permanent establishment of the individual in the UK or, in the case of a shareholder who performs independent personal services, pertain to a fixed base situated in the UK. Where the Ordinary Shares or ADRs have been placed in trust by a settlor who, at the time of settlement, was a US domiciled shareholder, the Ordinary Shares or ADRs will generally not be subject to UK inheritance tax unless the settlor, at the time of settlement, was a UK national, or the Ordinary Shares or ADRs are part of the business property of a permanent establishment of the individual in the UK or, in the case of a shareholder who performs independent personal services, pertain to a fixed base situated in the UK. In the exceptional case where the Ordinary Shares or ADRs are subject to both UK inheritance tax and US federal gift or estate tax, the Estate Tax Convention generally provides for double taxation to be relieved by means of credit relief.

UK stamp duty reserve tax and stamp duty

A charge to UK stamp duty or UK stamp duty reserve tax (SDRT) may arise on the deposit of Ordinary Shares in connection with the creation of ADRs. The rate of stamp duty or SDRT will generally be 1.5% of the value of the consideration or, in some circumstances, the value of the Ordinary Shares. There is no 1.5% SDRT charge on the issue of Ordinary Shares (or, where it is integral to the raising of new capital, the transfer of Ordinary Shares) into the ADR arrangement.

No UK stamp duty will be payable on the acquisition or transfer of existing ADRs provided that any instrument of transfer or written agreement to transfer is executed outside the UK and remains at all times outside the UK. An agreement for the transfer of ADRs will not give rise to a liability for SDRT.

A transfer of, or an agreement to, transfer Ordinary Shares will generally be subject to UK stamp duty or SDRT at 0.5% of the amount or value of any consideration, provided, in the case of stamp duty, it is rounded to the nearest £5.

Transfers of Ordinary Shares into CREST will generally not be subject to stamp duty or SDRT, unless such a transfer is made for a consideration in money or money's worth, in which case a liability to SDRT will arise,

usually at the rate of 0.5% of the value of the consideration. Paperless transfers of Ordinary Shares within CREST are generally liable to SDRT at the rate of 0.5% of the value of the consideration. CREST is obliged to collect SDRT from the purchaser on relevant transactions settled within the system.

Exchange controls and other limitations affecting security holders

There are no governmental laws, decrees or regulations in the UK restricting the import or export of capital or affecting the remittance of dividends, interest or other payments to non-resident holders of Ordinary Shares or ADRs.

There are no limitations under English law or the Articles on the right of non-resident or foreign owners to be the registered holders of, or to exercise voting rights in relation to, Ordinary Shares or ADRs or to be registered holders of notes or debentures of Zeneca Wilmington Inc. or the Company.

Exchange rates

The following information relating to average and spot exchange rates used by AstraZeneca is provided for convenience:

	SEK/US\$	US\$/GBP
Average rates (statement of comprehensive income, statement of cash flows)		
2013	6.5089	1.5621
2014	6.7901	1.6532
2015	8.395033	1.53567
End of year spot rates (statement of financial position)		
2013	6.4233	1.6502
2014	7.7451	1.5559
2015	8.41140	1.48165

Compliance requirements under Listing Rule 9.8.4

Other than as set out below, the Company has nothing to report under Listing Rule 9.8.4

Item	Location of details in Annual Report
Details of any long-term incentive schemes	Note 26 of the Financial Statements and Directors' Remuneration Report
Shareholder waiver of dividends	Page 96 in the Corporate Governance Report

Corporate Information

History and development of the Company

AstraZeneca PLC was incorporated in England and Wales on 17 June 1992 under the Companies Act 1985. It is a public limited company domiciled in the UK. The Company's registered number is 2723534 and its registered office is at 2 Kingdom Street, London W2 6BD (telephone +44 (0)20 7604 8000). From February 1993 until April 1999, the Company was called Zeneca Group PLC. On 6 April 1999, the Company changed its name to AstraZeneca PLC.

The Company was formed when the pharmaceutical, agrochemical and specialty chemical businesses of Imperial Chemical Industries PLC were demerged in 1993. In 1999, the Company sold the specialty chemical business. Also in 1999, the Company merged with Astra of Sweden. In 2000, it demerged the agrochemical business and merged it with the similar business of Novartis to form a new company called Syngenta AG.

In 2007, the Group acquired MedImmune, a biologics and vaccines business based in the US.

The Group's corporate office is at 2 Kingdom Street, London W2 6BD.

Articles

The current Articles were adopted by shareholders at the Company's AGM held on 24 April 2015.

Objects

The Company's objects are unrestricted.

Any amendment to the Articles requires the approval of shareholders by a special resolution at a general meeting of the Company.

Directors

The Board has the authority to manage the business of the Company, for example, through powers to allot and repurchase its shares, subject where required to shareholder resolutions. Subject to certain exceptions, Directors do not have power to vote at Board meetings on matters in which they have a material interest.

The quorum for meetings of the Board is a majority of the full Board, of whom at least four must be Non-Executive Directors. In the absence of a quorum, the Directors do not have power to determine compensation arrangements for themselves or any member of the Board.

The Board may exercise all the powers of the Company to borrow money. Variation of these borrowing powers would require the passing of a special resolution of the Company's shareholders.

All Directors must retire from office at the Company's AGM each year and may present themselves for election or re-election. Directors are not prohibited, upon reaching a particular age, from submitting themselves for election or re-election.

Within two months of the date of their appointment, Directors are required to beneficially own Ordinary Shares of an aggregate nominal amount of at least \$125, which currently represents 500 shares.

Rights, preferences and restrictions attaching to shares

As at 31 December 2015, the Company had 1,264,122,670 Ordinary Shares and 50,000 Redeemable Preference Shares in issue. The Ordinary Shares represent 99.98% and the Redeemable Preference Shares represent 0.02% of the Company's total share capital (these percentages have been calculated by reference to the closing mid-point US\$/GBP exchange rate on 31 December 2015 as published in the London edition of the Financial Times newspaper).

As agreed by the shareholders at the Company's AGM held on 29 April 2010, the Articles were amended with immediate effect to remove the requirement for the Company to have an authorised share capital, the concept of which was abolished under the Companies Act 2006. Each Ordinary Share carries the right to vote at general meetings of the Company. The rights and restrictions attaching to the Redeemable Preference Shares differ from those attaching to Ordinary Shares as follows:

- > The Redeemable Preference Shares carry no rights to receive dividends.
- > The holders of Redeemable Preference Shares have no rights to receive notices of, attend or vote at general meetings except in certain limited circumstances. They have one vote for every 50,000 Redeemable Preference Shares held.
- > On a distribution of assets of the Company, on a winding-up or other return of capital (subject to certain exceptions), the holders of Redeemable Preference Shares have priority over the holders of Ordinary Shares to receive the capital paid up on those shares.

- > Subject to the provisions of the Companies Act 2006, the Company has the right to redeem the Redeemable Preference Shares at any time on giving not less than seven days' written notice.

There are no specific restrictions on the transfer of shares in the Company, which is governed by the Articles and prevailing legislation.

The Company is not aware of any agreements between holders of shares that may result in restrictions on the transfer of shares or that may result in restrictions on voting rights. The Company is also not aware of any arrangements under which financial rights are held by a person other than the holder of the shares.

Action necessary to change the rights of shareholders

In order to vary the rights attached to any class of shares, the consent in writing of the holders of three-quarters in nominal value of the issued shares of that class or the sanction of an extraordinary resolution passed at a general meeting of such holders is required.

General meetings

AGMs and other general meetings, as from time to time may be required, where a special resolution is to be passed or a Director is to be appointed, require 21 clear days' notice to shareholders. Subject to the Companies Act 2006, other general meetings require 14 clear days' notice.

For all general meetings, a quorum of two shareholders present in person or by proxy, and entitled to vote on the business transacted, is required unless each of the two persons present is a corporate representative of the same corporation; or each of the two persons present is a proxy of the same shareholder.

Shareholders and their duly appointed proxies and corporate representatives are entitled to be admitted to general meetings.

Limitations on the rights to own shares

There are no limitations on the rights to own shares.

Property

Substantially all of our properties are held freehold, free of material encumbrances and are fit for their purpose.

For more information please refer to Note 7 to the Group Financial Statements on page 156.

Trade Marks

AstraZeneca, the AstraZeneca logotype and the AstraZeneca symbol are all trade marks of the Group.

The following brand names which appear in *italics* in this Annual Report are trade marks of the Group:

Trade mark			
<i>Accolate</i>	<i>Farxiga</i>	<i>Nolvadex</i>	<i>Symlin</i>
<i>Arimidex</i>	<i>Faslodex</i>	<i>Onglyza</i>	<i>Synagis</i> ²
<i>Atacand</i>	<i>Fluenz</i>	<i>Oxis Turbuhaler</i>	<i>Tagrisso</i>
<i>Atacand HCT</i>	<i>FluMist</i>	<i>Plendil</i>	<i>Tenormin</i> ³
<i>Atacand Plus</i>	<i>Forxiga</i>	<i>Pressair</i>	<i>Toprol-XL</i>
<i>Axanum</i>	<i>Genuair</i>	<i>Prilosec</i>	<i>Turbuhaler</i>
<i>Bricanyl</i>	<i>Iressa</i>	<i>Pulmicort</i>	<i>Vimovo</i>
<i>Brilinta</i>	<i>Kombiglyze</i>	<i>Pulmicort Flexhaler</i>	<i>Xigduo</i>
<i>Brilique</i>	<i>Komboglyze</i>	<i>Pulmicort Respules</i>	<i>Xylocaine</i>
<i>Bydureon</i>	<i>Losec</i>	<i>Pulmicort Turbuhaler</i>	<i>Zestril</i> ³
<i>Byetta</i>	<i>Lynparza</i>	<i>Respules</i>	<i>Zoladex</i>
<i>Caprelsa</i>	<i>Meronem</i>	<i>Rhinocort</i>	<i>Zomig</i>
<i>Casodex</i>	<i>Merrem</i>	<i>Seloken</i>	<i>Zurampic</i>
<i>Cosudex</i>	<i>Movantik</i>	<i>Seroquel</i>	
<i>Crestor</i>	<i>Moventig</i>	<i>Seroquel XR</i>	
<i>Diprivan</i>	<i>Myalept</i> ¹	<i>Symbicort</i>	
<i>EMLA</i>	<i>Naropin</i>	<i>Symbicort SMART</i>	
<i>Entocort</i>	<i>Nexium</i>	<i>Symbicort Turbuhaler</i>	

¹ AstraZeneca assigned this trade mark to Aegerion effective 9 January 2015.

² AstraZeneca owns this trade mark in the US only. AbbVie owns it in the rest of the world.

³ AstraZeneca assigned these trade marks in the US to Alvogen effective 9 January 2015.

The following brand names which appear in *italics* in this Annual Report are trade marks licensed to the Group by the entities set out below:

Trade mark	Licensor or Owner
<i>Bretaris</i>	Almirall, S.A.
<i>Cubicin</i>	Cubist Pharmaceuticals, Inc.
<i>Daliresp/Daxas</i>	Takeda GmbH
<i>Duaklir</i>	Almirall, S.A.
<i>Eklira</i>	Almirall, S.A.
<i>Epanova</i>	Chrysalis Pharma AG
<i>Tudorza</i>	Almirall, S.A.
<i>Zinforo</i>	Forest Laboratories Holdings Limited
<i>Zytiga</i> ¹	Janssen Pharmaceutical K.K.

¹ AstraZeneca has been licensed this trade mark for use in Japan only.

The following brand names which appear in *italics* throughout this Annual Report are not owned by or licensed to the Group and are owned by the entities set out below:

Trade mark	Owner
<i>Plavix</i>	SANOFI S.A.
<i>Invokana</i>	Johnson & Johnson Corporation
<i>Lipitor</i>	Pfizer Ireland Pharmaceuticals
<i>messenger RNA Therapeutics</i>	Moderna Therapeutics, Inc.

Glossary

Market definitions

Region	Country				
US	US				
Europe	Albania*	Czech Republic	Hungary	Luxembourg*	Serbia and Montenegro*
	Austria	Denmark	Iceland*	Malta*	Slovakia
	Belgium	Estonia*	Ireland	Netherlands	Slovenia*
	Bosnia and Herzegovina*	Finland	Israel*	Norway	Spain
	Bulgaria	France	Italy	Poland	Sweden
	Croatia	Germany	Latvia*	Portugal*	Switzerland
	Cyprus*	Greece	Lithuania*	Romania	UK
Established ROW	Australia Japan				
	Canada New Zealand				
Emerging Markets	Algeria	Costa Rica	Iraq*	Other Africa*	Sudan*
	Argentina	Cuba*	Jamaica*	Pakistan*	Syria*
	Aruba*	Dominican Republic*	Jordan*	Palestine*	Taiwan
	Bahamas*	Ecuador	Kazakhstan	Panama	Thailand
	Bahrain*	Egypt	Kuwait*	Peru	Trinidad and Tobago*
	Barbados*	El Salvador	Lebanon*	Philippines	Tunisia*
	Belarus*	Georgia*	Libya*	Qatar*	Turkey
	Belize*	Guatemala	Malaysia	Russia	Ukraine*
	Bermuda*	Honduras	Mexico	Saudi Arabia	United Arab Emirates
	Brazil	Hong Kong	Morocco*	Singapore	Uruguay*
	Chile	India	Netherlands Antilles*	South Africa	Venezuela
	China	Indonesia	Nicaragua	South Korea	Vietnam*
	Colombia	Iran*	Oman*	Sri Lanka*	Yemen*

* IMS Health, IMS Midas Quantum Q3 2015 data is not available or AstraZeneca does not subscribe for IMS Health quarterly data for these countries.

The above table is not an exhaustive list of all the countries in which AstraZeneca operates, and excludes countries with revenue in 2015 of less than \$1 million.

Established Markets means US, Europe and Established ROW.

North America means US and Canada.

Other Established ROW means Australia and New Zealand.

Other Emerging Markets means all Emerging Markets except China.

Other Africa includes Angola, Botswana, Ethiopia, Ghana, Kenya, Mauritius, Mozambique, Namibia, Nigeria, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe.

Asia Area comprises India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand and Vietnam.

US equivalents

Terms used in this Annual Report	US equivalent or brief description
Accruals	Accrued expenses
Allotted	Issued
Called-up share capital	Issued share capital
Creditors	Liabilities/payables
Debtors	Receivables and prepaid expenses
Earnings	Net income
Employee share schemes	Employee stock benefit plans
Fixed asset investments	Non-current investments
Freehold	Ownership with absolute rights in perpetuity
Interest payable	Interest expense
Loans	Long-term debt
Prepayments	Prepaid expenses
Profit	Income
Profit and loss account	Income statement/consolidated statement of comprehensive income
Share premium account	Premiums paid in excess of par value of Ordinary Shares
Short-term investments	Redeemable securities and short-term deposits

Glossary continued

The following abbreviations and expressions have the following meanings when used in this Annual Report:

Abbott – Abbott Laboratories.

AbbVie – AbbVie Inc.

ACA (Affordable Care Act) – the Patient Protection and Affordable Care Act which was signed into law on 23 March 2010 as amended by the Health Care and Education Reconciliation Act which was signed into law on 30 March 2010.

Acerta Pharma – Acerta Pharma B.V.

ACS – Acute Coronary Syndrome.

Actavis – Actavis plc.

ADC Therapeutics – ADC Therapeutics Sàrl.

ADR – an American Depositary Receipt evidencing title to an ADS.

ADS – an American Depositary Share representing one underlying Ordinary Share.

AGM – an Annual General Meeting of the Company.

Aegerion – Aegerion Pharmaceuticals, Inc.

Almirall – Almirall, S.A.

Amgen – Amgen, Inc.

Amplimmune – Amplimmune, Inc.

Amylin – Amylin Pharmaceuticals, LLC (formerly Amylin Pharmaceuticals, Inc.).

ANDA – an abbreviated new drug application, which is a marketing approval application for a generic drug submitted to the FDA.

Annual Report – this Annual Report and Form 20-F Information 2015.

API – active pharmaceutical ingredient.

Ardea – Ardea Biosciences, Inc.

Articles – the Articles of Association of the Company.

Astellas – Astellas Pharma Inc.

Astra – Astra AB, being the company with whom the Company merged in 1999.

AstraZeneca – the Company and its subsidiaries.

AZIP – AstraZeneca Investment Plan.

BACE – beta secretase cleaving enzyme.

biologic(s) – a class of drugs that are produced in living cells.

biosimilars – a copy of a biologic that is sufficiently similar to meet regulatory requirements.

BMS – Bristol-Myers Squibb Company.

Board – the Board of Directors of the Company.

Bureau Veritas – Bureau Veritas UK Limited.

Celgene – Celgene International Sàrl.

CEO – the Chief Executive Officer of the Company.

CER – constant exchange rates.

CFDA – China Food and Drug Administration.

CFO – the Chief Financial Officer of the Company.

CHMP – the Committee for Medicinal Products for Human Use.

CIS – Commonwealth of Independent States.

Code of Conduct – the Group's Code of Conduct.

Company or Parent Company – AstraZeneca PLC (formerly Zeneca Group PLC (Zeneca)).

COPD – chronic obstructive pulmonary disease.

Corporate Integrity Agreement (CIA) – the agreement described in the US Corporate Integrity Agreement reporting section on page 50.

CROs – contract research organisations.

CVMD – Cardiovascular and Metabolic diseases.

CV – cardiovascular.

Daiichi Sankyo – Daiichi Sankyo, Inc.

Definiens – Definiens AG.

Director – a director of the Company.

DOJ – the United States Department of Justice.

earnings per share (EPS) – profit for the year after tax and non-controlling interests, divided by the weighted average number of Ordinary Shares in issue during the year.

EC – European Commission.

EFPIA – European Federation of Pharmaceutical Industries and Associations.

EGFR – epidermal growth factor receptor.

EMA – European Medicines Agency.

EPO – European Patent Office.

EVP – Executive Vice-President.

EU – the European Union.

FDC – fixed-dose combination.

FDA – the US Food and Drug Administration, which is part of the US Department of Health and Human Services Agency, which is the regulatory authority for all pharmaceuticals (including biologics and vaccines) and medical devices in the US.

FibroGen – FibroGen, Inc.

Forest – Forest Laboratories Holdings Limited.

FRC – Financial Reporting Council.

GAAP – Generally Accepted Accounting Principles.

GMD – Global Medicines Development.

GPPS – Global Product and Portfolio Strategy.

gross margin – the margin, as a percentage, by which sales exceed the cost of sales, calculated by dividing the difference between the two by the sales figure.

Group – AstraZeneca PLC and its subsidiaries.

GSK – GlaxoSmithKline plc.

Gulf – Bahrain, Kuwait, Oman, Pakistan, Qatar and the United Arab Emirates.

Heptares – Heptares Ltd.

HHA – Healthy Heart Africa programme.

HR – human resources.

IA – the Group's Internal Audit Services function.

IAS – International Accounting Standards.

IAS 19 – IAS 19 'Employee Benefits'.

IAS 32 – IAS 32 'Financial Instruments: Presentation'.

IAS 39 – IAS 39 'Financial Instruments: Recognition and Measurement'.

IASB – International Accounting Standards Board.

IFRS – International Financial Reporting Standards or International Financial Reporting Standard, as the context requires.

IFRS 8 – IFRS 8 'Operating Segments'.

IMED – Innovative Medicines and Early Development.

Immunocore – Immunocore Limited.

Innate Pharma – Innate Pharma S.A.

IP – intellectual property.

IS – information services.

ISAs – International Standards on Auditing.

IT – information technology.

KPI – key performance indicator.

Krona or SEK – references to the currency of Sweden.

Kyowa Hakko Kirin – Kyowa Hakko Kirin Co., Ltd.

LCM projects – significant life-cycle management projects (as determined by potential revenue generation), or line extensions.

Lean – means enhancing value for customers with fewer resources.

Lilly – Eli Lilly and Company.

LTI – long-term incentive, in the context of share plan remuneration arrangements.

MAA – a marketing authorisation application, which is an application for authorisation to place medical products on the market. This is a specific term used in the EU and European Economic Area markets.

MAb – monoclonal antibody, a biologic that is specific, that is, it binds to and attacks one particular antigen.

major market – US, EU, Japan and China.

MAT – moving annual total.

MedImmune – MedImmune, LLC (formerly MedImmune, Inc.).

Merck – Merck Sharp & Dohme Corp. (formerly Merck & Co., Inc.).

MI – myocardial infarction.

Moderna Therapeutics – Moderna Therapeutics, Inc.

Myriad – Myriad Genetics, Inc.

NDA – a new drug application to the FDA for approval to market a new medicine in the US.

NME – new molecular entity.

Novartis – Novartis Pharma AG.

NSAID – a non-steroidal anti-inflammatory drug.

NSCLC – non-small cell lung cancer.

NSTE-ACS – non-ST-Elevation acute coronary syndromes.

NYSE – the New York Stock Exchange.

n/m – not meaningful.

Omthera – Omthera Pharmaceuticals, Inc.

operating profit – sales, less cost of sales, less operating costs, plus operating income.

Ordinary Share – an ordinary share of \$0.25 each in the share capital of the Company.

Orphan Drug – a drug which has been approved for use in a relatively low-incidence indication (an orphan indication) and has been rewarded with a period of market exclusivity; the period of exclusivity and the available orphan indications vary between markets.

OTC – over-the-counter.

Paediatric Exclusivity – in the US, a six-month period of exclusivity to market a drug which is awarded by the FDA in return for certain paediatric clinical studies using that drug. This six-month period runs from the date of relevant patent expiry. Analogous provisions are available in certain other territories (such as European Supplementary Protection Certificate (SPC) paediatric extensions).

PD-L1 – an anti-programmed death-ligand 1.

Pearl Therapeutics – Pearl Therapeutics, Inc.

Pfizer – Pfizer, Inc.

PhRMA – Pharmaceutical Research and Manufacturers of America.

Phase I – the phase of clinical research where a new drug or treatment is tested in small groups of people (20 to 80) to check that the drug can achieve appropriate concentrations in the body, determine a safe dosage range and identify side effects. This phase includes healthy volunteer studies.

Phase II – the phase of clinical research which includes the controlled clinical activities conducted to evaluate the effectiveness of the drug in patients with the disease under study and to begin to determine the safety profile of the drug. Phase II studies are typically conducted in small or medium sized groups of patients and can be divided into Phase IIa studies, which tend to be designed to assess dosing requirements, and Phase IIb studies, which tend to assess safety and efficacy.

Phase III – the phase of clinical research which is performed to gather additional information about effectiveness and safety of the drug, often in a comparative setting, to evaluate the overall benefit/risk profile of the drug. Phase III studies usually include between several hundred and several thousand patients.

PHC – personalised healthcare.

PMDA – Pharmaceuticals and Medical Devices Agency of Japan.

pMDI – pressurised metered-dose inhaler.

pound sterling, £, GBP or pence – references to the currency of the UK.

Pozen – POZEN, Inc.

primary care – general healthcare provided by physicians who ordinarily have first contact with patients and who may have continuing care for them.

Proof of Concept – data demonstrating that a candidate drug results in a clinical change on an acceptable endpoint or surrogate in patients with the disease.

PSP – AstraZeneca Performance Share Plan.

PTE – Patent Term Extension, an extension of up to five years in the term of a US patent relating to a drug which compensates for delays in marketing resulting from the need to obtain FDA approval. The analogous right in the EU is an SPC.

Qiagen – Qiagen Manchester Limited.

R&D – research and development.

Redeemable Preference Share – a redeemable preference share of £1 each in the share capital of the Company.

Regulatory Data Protection (RDP) – see the Intellectual Property section on page 60.

Regulatory Exclusivity – any of the IP rights arising from generation of clinical data and includes Regulatory Data Protection, Paediatric Exclusivity and Orphan Drug status.

Roche – F. Hoffmann-La Roche AG.

RSV – respiratory syncytial virus.

Sanofi – SANOFI S.A.

Sarbanes-Oxley Act – the US Sarbanes-Oxley Act of 2002.

SEC – the US Securities and Exchange Commission, the governmental agency that regulates the US securities industry and stock markets.

Seroquel – Seroquel IR and Seroquel XR.

SET – Senior Executive Team.

SG&A costs – selling, general and administrative costs.

SGLT2 – sodium-glucose co-transporter 2.

Shionogi – Shionogi & Co. Ltd.

SLE – systemic lupus erythematosus.

SPC – supplementary protection certificate.

specialty care – specific healthcare provided by medical specialists who do not generally have first contact with patients.

Spirogen – Spirogen Sàrl.

Takeda – Takeda Pharmaceutical Company Limited.

Teva – Teva Pharmaceuticals USA, Inc.

Total Revenue – the sum of Product Sales and Externalisation Revenue.

TSR – total shareholder return, being the total return on a share over a period of time, including dividends reinvested.

UK – United Kingdom of Great Britain and Northern Ireland.

UK Corporate Governance Code – the UK Corporate Governance Code published by the FRC in September 2014 that sets out standards of good practice in corporate governance for the UK.

US – United States of America.

US dollar, US\$, USD or \$ – references to the currency of the US.

Valeant – Valeant Holdings Ireland/Valeant Pharmaceutical International Inc.

Ventana – Ventana Medical Systems, Inc.

WHO – World Health Organization, the United Nations' specialised agency for health.

YHP – Young Health Programme.

ZS Pharma – ZS Pharma, Inc.

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Important information for readers of this Annual Report

Cautionary statement regarding forward-looking statements

The purpose of this Annual Report is to provide information to the members of the Company. The Company and its Directors, employees, agents and advisers do not accept or assume responsibility to any other person to whom this Annual Report is shown or into whose hands it may come and any such responsibility or liability is expressly disclaimed. In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act of 1995 and the UK Companies Act 2006, we are providing the following cautionary statement: This Annual Report contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Forward-looking statements are statements relating to the future which are based on information available at the time such statements are made, including information relating to risks and uncertainties. Although we believe that the forward-looking statements in this Annual Report are based on reasonable assumptions, the matters discussed in the forward-looking statements may be influenced by factors that could cause actual outcomes and results to be materially different from those expressed or implied by these statements. The forward-looking statements reflect knowledge and information available at the date of the preparation of this Annual Report and the Company undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things, those factors identified in the Risk section from page 212 of this Annual Report. Nothing in this Annual Report should be construed as a profit forecast.

Inclusion of Reported performance, Core financial measures and constant exchange rate growth rates

AstraZeneca's determination of non-GAAP measures together with our presentation of them within our financial information may differ from similarly titled non-GAAP measures of other companies.

Statements of competitive position, growth rates and sales

In this Annual Report, except as otherwise stated, market information regarding the position of our business or products relative to its or their competition is based upon published statistical sales data for the 12 months ended 30 September 2015 obtained from IMS Health, a leading supplier of statistical data to the pharmaceutical industry. Unless otherwise noted, for the US, dispensed new or total prescription data and audited sales data are taken, respectively, from IMS Health National Prescription Audit and IMS National Sales Perspectives for the 12 months ended 31 December 2015; such data is not adjusted for Medicaid and similar rebates. Except as otherwise stated, these market share and industry data from IMS Health have been derived by comparing our sales revenue with competitors' and total market sales revenues for that period. Except as otherwise stated, growth rates are given at CER. For the purposes of this Annual Report, unless otherwise stated, references to the world pharmaceutical market or similar phrases are to the 54 countries contained in the IMS Health database, which amounted to approximately 97% (in value) of the countries audited by IMS Health.

AstraZeneca websites

Information on or accessible through our websites, including www.astrazeneca.com, www.astrazenecaclinicaltrials.com and www.medimmune.com, does not form part of and is not incorporated into this Annual Report.

External/third party websites

Information on or accessible through any third party or external website does not form part of and is not incorporated into this Annual Report.

Figures

Figures in parentheses in tables and in the Financial Statements are used to represent negative numbers.

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