AstraZeneca

What science can do

AstraZeneca Annual Report and Form 20-F Information 2017

Science

can

prevent disease in adolescents

Today, non-communicable diseases (NCDs) kill 40 million people each year, with Type 2 diabetes, cancer, heart and respiratory disease accounting for over 80% of these deaths. One way we are addressing this global health issue is to focus on prevention and, more specifically, on youth. With over 1.2 billion adolescents in the world today, improving adolescent health and wellbeing will not only have major benefits for adolescents, and for those around them, but will also improve the health benefits of future generations.

The AstraZeneca Young Health Programme (YHP) is a global disease prevention programme with a focus on adolescents. Launched in 2010, it tackles the NCD epidemic by focusing on risk behaviours. Our programming, advocacy and research looks at the primary risk factors that lead to disease later in life. By encouraging more young people to adopt healthy habits, it is more likely to lead to healthier outcomes.

"Through the YHP, I trained to become a Peer Educator and now use street theatre to educate young people about their health concerns. Due to YHP many young people have given up smoking and are seeking access to healthcare facilities. Since being part of the YHP, my confidence has grown and the increased responsibility has given me a clearer sense of purpose. The YHP has changed my life."

- 30 NGO partners
- 21 countries around the world on five continents
- 1.6 million youths reached with health information
- 12,800 health workers trained
- 14,600 peer educators trained
- Breakthrough research – Johns Hopkins, Imperial College
- New evidence – Population Reference Bureau policy briefs and data sheets on risk behaviours

AstraZeneca Young Health Programme
A global community investment initiative

with founding partners

Johns Hopkins Bloomberg School of Public Health

PLAN International

Photo: Marco Betti and AstraZeneca Young Health Programme.

Development Pipeline
as at 31 December 2017

AstraZeneca-sponsored or directed trials

Phase III/Pivotal Phase II/Registration

New Molecular Entities (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 Acceptance Date/Submission Status			
				US	EU	Japan	China
Oncology							
Calquence[#] (acalabrutinib)	BTK inhibitor	B-cell malignancy	Q1 2015	Launched			
savolitinib[#] SAVOIR	MET inhibitor	papillary renal cell carcinoma	Q3 2017	2020	2020		
selumetinib ASTRA	MEK inhibitor	differentiated thyroid cancer	Q3 2013	H2 2018 (Orphan Drug Designation)	H2 2018		
moxetumomab pasudotox[#] PLAIT	anti-CD22 recombinant immunotoxin	hairy cell leukaemia	Q2 2013	H1 2018 (Orphan Drug Designation)			
Imfinzi[#] + tremelimumab ARCTIC	PD-L1 mAb + CTLA-4 mAb	3rd line NSCLC	Q2 2015	H1 2018	H1 2018	H1 2018	
Imfinzi[#] + tremelimumab MYSTIC	PD-L1 mAb + CTLA-4 mAb	1st line NSCLC	Q3 2015	H2 2018	H2 2018	H2 2018	
Imfinzi[#] + tremelimumab NEPTUNE	PD-L1 mAb + CTLA-4 mAb	1st line NSCLC	Q4 2015	2019	2019	2019	2020
Imfinzi[#] + tremelimumab + chemotherapy POSEIDON	PD-L1 mAb + CTLA-4 mAb	1st line NSCLC	Q2 2017	2019	2019	2019	2020
Imfinzi[#] + tremelimumab + SoC CASPIAN	PD-L1 mAb + CTLA-4 mAb + SoC	1st line SCLC	Q1 2017	2019	2019	2019	
Imfinzi[#] + tremelimumab KESTREL	PD-L1 mAb + CTLA-4 mAb	1st line HNSCC	Q4 2015	H2 2018	H2 2018	H2 2018	
Imfinzi[#] + tremelimumab EAGLE	PD-L1 mAb + CTLA-4 mAb	2nd line HNSCC	Q4 2015	H2 2018	H2 2018	H2 2018	
Imfinzi[#] + tremelimumab DANUBE	PD-L1 mAb + CTLA-4 mAb	1st line bladder cancer	Q4 2015	2019	2019	2019	
Imfinzi[#] + tremelimumab HIMALAYA	PD-L1 mAb + CTLA-4 mAb	1st line hepatocellular carcinoma	Q4 2017	2021	2021	2021	2021
Lynparza[#¶] + cediranib CONCERTO	PARP inhibitor + VEGF inhibitor	recurrent platinum-resistant ovarian cancer	Q1 2017	2019			
CVMD							
Epanova	omega-3 carboxylic acids	severe hypertriglyceridaemia		Approved		2020	
ZS-9 (sodium zirconium cyclosilicate)	potassium binder	hyperkalaemia			Accepted[1]	2019	
roxadustat[#] OLYMPUS (US) ROCKIES (US)	hypoxia-inducible factor prolyl hydroxylase inhibitor	anaemia in CKD/end-stage renal disease	Q3 2014	H2 2018			Accepted[2]

Compound	Mechanism	Area Under Investigation	Date Commenced Phase	Estimated Regulatory Acceptance Date/Submission Status US	EU	Japan	China
Respiratory							
Bevespi (PT003)	LABA/LAMA	COPD		Launched	Accepted	H2 2018	H2 2018
Fasenra[#] (benralizumab[#]) CALIMA SIROCCO ZONDA BISEBORA GREGALE	IL-5R mAb	severe, uncontrolled asthma		Launched	Approved	Approved	2021
PT010	LABA/LAMA/ICS	COPD	Q3 2015	2019	2019	H2 2018	H2 2018
tezepelumab NAVIGATOR SOURCE	TSLP mAb	severe, uncontrolled asthma	Q1 2018	2021	2021	2021	
Other							
anifrolumab[#] TULIP	Type 1 IFN receptor mAb	systemic lupus erythematosus	Q3 2015	2019 (Fast Track)	2019	2019	
lanabecestat[#] AMARANTH + extension, DAYBREAK-ALZ	beta-secretase inhibitor	Alzheimer's disease	Q2 2016	2020 (Fast Track)	2020	2020	

[#] Collaboration.
[¶] Registrational Phase II trial.
[1] CHMP positive opinion received.
[2] FibroGen completed rolling regulatory submission in China.

Phases I and II
NMEs and significant additional indications

Compound	Mechanism	Area Under Investigation	Phase	Date Commenced Phase
Oncology				
Imfinzi[#]	PD-L1 mAb	solid tumours	II	Q3 2014
Imfinzi[#] + tremelimumab	PD-L1 mAb + CTLA-4 mAb	gastric cancer	II	Q2 2015
Imfinzi[#] + tremelimumab	PD-L1 mAb + CTLA-4 mAb	biliary tract, oesophageal	II	Q4 2013
Imfinzi[#] + tremelimumab + chemo	PD-L1 mAb + CTLA-4 mAb	1st line pancreatic ductal adenocarcinoma, oesophageal and SCLC	I	Q2 2016
Imfinzi[#] + AZD5069	PD-L1 mAb + CXCR2 antagonist	pancreatic ductal adenocarcinoma	II	Q2 2017
Imfinzi[#] + AZD5069 or *Imfinzi*[#] + AZD9150[#]	PD-L1 mAb + CXCR2 antagonist or PD-L1 mAb + STAT3 inhibitor	HNSCC	II	Q3 2015
Imfinzi[#] + dabrafenib + trametinib	PD-L1 mAb + BRAF inhibitor + MEK inhibitor	melanoma	I	Q1 2014
Imfinzi[#] + AZD1775[#]	PD-L1 mAb + Wee1 inhibitor	solid tumours	I	Q4 2015
Imfinzi[#] + MEDI0680	PD-L1 mAb + PD-1 mAb	solid tumours	II	Q3 2016
Imfinzi[#] or *Imfinzi*[#] + (tremelimumab or AZD9150[#])	PD-L1 mAb or PD-L1 mAb + (CTLA-4 mAb or STAT3 inhibitor)	diffuse large B-cell lymphoma	I	Q3 2016
Imfinzi[#] + *Iressa*	PD-L1 mAb + EGFR inhibitor	NSCLC	I	Q2 2014
Imfinzi[#] + MEDI0562[#]	PD-L1 mAb + humanised OX40 agonist	solid tumours	I	Q2 2016
Imfinzi[#] + MEDI9197[#]	PD-L1 mAb + TLR 7/8 agonist	solid tumours	I	Q2 2017
Imfinzi[#] + oleclumab (MEDI9447)	PD-L1 mAb + CD73 mAb	solid tumours	I	Q1 2016
Imfinzi[#] + monalizumab	PD-L1 mAb + NKG2a mAb	solid tumours	I	Q1 2016
Imfinzi[#] + selumetinib	PD-L1 mAb + MEK inhibitor	solid tumours	I	Q4 2015
Imfinzi[#] + tremelimumab	PD-L1 mAb + CTLA-4 mAb	solid tumours	I	Q4 2013
tremelimumab + MEDI0562[#]	CTLA-4 mAb + humanised OX40 agonist	solid tumours	I	Q2 2016
Imfinzi[#] + azacitidine	PD-L1 mAb + azacitidine	myelodysplastic syndrome	I	Q2 2016

Development Pipeline
continued

Compound	Mechanism	Area Under Investigation	Phase	Date Commenced Phase
Imfinzi# + MEDI0457#	PD-L1 mAb + DNA HPV vaccine	HNSCC	II	Q4 2017
Imfinzi# + RT (platform) CLOVER	PD-L1 mAb + RT	locally-advanced HNSCC, NSCLC, SCLC	I	Q1 2018
Lynparza# + AZD6738	PARP inhibitor + ATR inhibitor	gastric cancer	II	Q3 2016
Lynparza# + AZD1775#	PARP inhibitor + Wee1 inhibitor	solid tumours	I	Q3 2015
Lynparza# + *Imfinzi*# MEDIOLA	PARP inhibitor + PD-L1 mAb	solid tumours	II	Q2 2016
Tagrisso + (selumetinib# or savolitinib#) TATTON	EGFR inhibitor + (MEK inhibitor or MET inhibitor)	advanced EGFRm NSCLC	II	Q2 2016
Tagrisso BLOOM	EGFR inhibitor	CNS metastases in advanced EGFRm NSCLC	II	Q4 2015
AZD1775# + chemotherapy	Wee1 inhibitor + chemotherapy	ovarian cancer	II	Q1 2015
AZD1775#	Wee1 inhibitor	solid tumours	I	Q3 2015
vistusertib	mTOR inhibitor	solid tumours	II	Q1 2013
AZD5363#	AKT inhibitor	breast cancer	II	Q1 2014
AZD4547	FGFR inhibitor	solid tumours	II	Q4 2011
AZD0156	ATM inhibitor	solid tumours	I	Q4 2015
AZD1390	ATM inhibitor	healthy volunteer trial	I	Q4 2017
AZD2811#	Aurora B inhibitor	solid tumours	I	Q4 2015
AZD4573	CDK9 inhibitor	haematological malignancies	I	Q4 2017
AZD4635	A2aR inhibitor	solid tumours	I	Q2 2016
AZD4785	KRAS inhibitor	solid tumours	I	Q2 2017
AZD5153	BRD4 inhibitor	solid tumours	I	Q3 2017
AZD5991	MCL1 inhibitor	haematological malignancies	I	Q3 2017
Calquence + vistusertib	B-cell malignancy + mTor inhibitor	haematological malignancies	I	Q3 2017
AZD6738	ATR inhibitor	solid tumours	I	Q4 2013
AZD8186	PI3k inhibitor	solid tumours	I	Q2 2013
AZD9496	selective oestrogen receptor degrader	oestrogen receptor +ve breast cancer	I	Q4 2014
MEDI-565#	CEA BiTE mAb	solid tumours	I	Q1 2011
MEDI0562#	humanised OX40 agonist	solid tumours	I	Q1 2015
MEDI1873	GITR agonist fusion protein	solid tumours	I	Q4 2015
MEDI3726#	PSMA antibody drug conjugate	prostate cancer	I	Q1 2017
MEDI4276	HER2 bi-specific antibody drug conjugate	solid tumours	I	Q4 2015
MEDI5083	immune activator	solid tumours	I	Q1 2017
MEDI7247	antibody drug conjugate	haematological malignancies	I	Q2 2017
MEDI9197#	TLR 7/8 agonist	solid tumours	I	Q4 2015
oleclumab (MEDI9447)	CD73 mAb	solid tumours	I	Q3 2015
CVMD				
verinurad	URAT1 inhibitor	CKD	II	Q2 2017
MEDI0382	GLP-1/glucagon dual agonist	Type 2 diabetes/obesity	II	Q3 2016
MEDI6012	LCAT	CV disease	II	Q4 2015
AZD4831	myeloperoxidase	HF with a preserved ejection fraction	I	Q3 2016
AZD5718	FLAP	coronary artery disease	II	Q4 2017
AZD8601#	VEGF-A	CV disease	I	Q1 2017
MEDI5884#	cholesterol modulation	CV disease	II	Q4 2017
Respiratory				
abediterol#	LABA	asthma/COPD	II	Q4 2007
tezepelumab#	TSLP mAb	atopic dermatitis	II	Q2 2015
AZD1419#	inhaled TLR9 agonist	asthma	II	Q4 2016
AZD7594	inhaled SGRM	asthma/COPD	II	Q3 2015
AZD8871#	MABA	COPD	II	Q1 2017
PT010	LABA/LAMA/ICS	asthma	II	Q2 2014
AZD5634	inhaled ENaC	cystic fibrosis	I	Q1 2016
AZD7594 + abediterol#	inhaled SGRM + LABA	asthma/COPD	I	Q4 2016
AZD7986#	DPP1	COPD	II	Q4 2017
AZD9567	oral SGRM	rheumatoid arthritis/respiratory	II	Q4 2015
AZD1402#	inhaled IL-4Ra	asthma	I	Q4 2017
MEDI3506	IL-33 mAb	COPD	I	Q2 2017

Compound	Mechanism	Area Under Investigation	Phase	Date Commenced Phase
Other				
anifrolumab#	Type 1 IFN receptor mAb	lupus nephritis	II	Q4 2015
anifrolumab#	Type 1 IFN receptor mAb	systemic lupus erythematosus (subcutaneous)	II	Q1 2017
inebilizumab#	CD19 mAb	neuromyelitis optica	II (Orphan drug US, EU)	Q1 2015
mavrilimumab#	GM-CSFR mAb	rheumatoid arthritis	II	Q1 2010
MEDI3902	Psl/PcrV bispecific mAb	prevention of nosocomial pseudomonas aeruginosa pneumonia	II (Fast Track, US)	Q2 2016
suvratoxumab (MEDI4893)	mAb binding to *S. aureus* toxin	prevention of nosocomial *Staphylococcus aureus* pneumonia	II (Fast Track, US)	Q4 2014
prezalumab# (MEDI5872#)	B7RP1 mAb	primary Sjögren's syndrome	II	Q3 2015
MEDI8852	influenza A mAb	influenza A treatment	II (Fast Track, US)	Q4 2015
MEDI8897#	RSV mAb-YTE	passive RSV prophylaxis	II (Fast Track, US)	Q1 2015
AZD0284	RORg	psoriasis/respiratory	I	Q4 2016
MEDI0700#	BAFF/B7RP1 bispecific mAb	systemic lupus erythematosus	I	Q1 2016
MEDI1814#	amyloid beta mAb	Alzheimer's disease	I	Q2 2014
MEDI4920	anti-CD40L-Tn3 fusion protein	primary Sjögren's syndrome	I	Q2 2014
MEDI7352	NGF/TNF bi-specific mAb	osteoarthritis pain	I	Q1 2016
MEDI7734	ILT7 mAb	myositis	I	Q3 2016
MEDI9314	IL-4R mAb	atopic dermatitis	I	Q1 2016

Collaboration.

Significant Life-cycle Management

Compound	Mechanism	Area Under Investigation	Date Commenced Phase	Estimated Regulatory Acceptance Date/Submission Status			
				US	EU	Japan	China
Oncology							
Calquence# (acalabrutinib)	BTK inhibitor	1st line chronic lymphocytic leukaemia	Q3 2015	2020 (Orphan Drug Designation)	2020 (Orphan designation)		
Calquence# (acalabrutinib)	BTK inhibitor	relapsed/refractory chronic lymphocytic leukaemia, high risk	Q4 2015	2019 (Orphan Drug Designation)	2019 (Orphan designation)		
Calquence# (acalabrutinib)	BTK inhibitor	1st line mantle cell lymphoma	Q1 2017	2023			
Faslodex FALCON	oestrogen receptor antagonist	1st line hormone receptor +ve advanced breast cancer		Approved	Approved	Approved	Approved
Imfinzi# PACIFIC	PD-L1 mAb	locally-advanced (Stage 3), NSCLC	Q2 2014	Accepted (Breakthrough Therapy Designation & Priority Review)	Accepted	Accepted	
Imfinzi# PEARL (China)	PD-L1 mAb	1st line NSCLC	Q1 2017				2020
Lynparza# OlympiAD	PARP inhibitor	gBRCA metastatic breast cancer	Q2 2014	Approved (Priority Review)	H1 2018	Accepted (Orphan drug designation, Priority Review)	H2 2018
Lynparza# SOLO-2	PARP inhibitor	2nd line or greater BRCAm PSR ovarian cancer, maintenance monotherapy	Q3 2013	Approved (Priority Review)	Accepted	Approved (Orphan drug designation)	Accepted
Lynparza# SOLO-1	PARP inhibitor	1st line BRCAm ovarian cancer	Q3 2013	H2 2018	H2 2018	H2 2018	2019
Lynparza# SOLO-3	PARP inhibitor	gBRCA PSR ovarian cancer	Q1 2015	H2 2018			
Lynparza# POLO	PARP inhibitor	pancreatic cancer	Q1 2015	2019	2019		
Lynparza# PROfound	PARP inhibitor	prostate cancer	Q1 2017	2020 (Breakthrough Therapy Designation)	2020	2020	2020
Lynparza# OlympiA	PARP inhibitor	gBRCA adjuvant breast cancer	Q2 2014	2020	2020	2020	
Tagrisso FLAURA	EGFR inhibitor	1st line advanced EGFRm NSCLC	Q1 2015	Accepted (Breakthrough Therapy Designation)	Accepted	Accepted	H2 2018
Tagrisso ADAURA	EGFR inhibitor	adjuvant EGFRm NSCLC	Q4 2015	2022	2022	2022	2022

Development Pipeline
continued

Compound	Mechanism	Area Under Investigation	Date Commenced Phase	Estimated Regulatory Acceptance Date/Submission Status			
				US	EU	Japan	China
CVMD							
Brilinta[1] THALES	P2Y12 receptor antagonist	acute ischaemic stroke or transient ischaemic attack	Q1 2018	2020	2020	2020	2020
Brilinta[1] THEMIS	P2Y12 receptor antagonist	CV outcomes trial in patients with Type 2 diabetes and coronary artery disease without a previous history of MI or stroke	Q1 2014	2019	2019	2019	2020
Brilinta[1] HESTIA	P2Y12 receptor antagonist	prevention of vaso-occlusive crises in paediatric patients with sickle cell disease	Q1 2014	2021	2021		
Farxiga[2] DECLARE-TIMI 58	SGLT2 inhibitor	CV outcomes trial in patients with Type 2 diabetes	Q2 2013	2019	2019		
Farxiga[2]	SGLT2 inhibitor	Type 1 diabetes	Q4 2014	H2 2018	H1 2018	H2 2018	
Farxiga[2]	SGLT2 inhibitor	worsening HF or CV death in patients with chronic HF	Q1 2017	2020	2020	2020	2020
Farxiga[2]	SGLT2 inhibitor	renal outcomes and CV mortality in patients with CKD	Q1 2017	2021	2021	n/a	2021
Xigduo XR/*Xigduo*[3]	SGLT2 inhibitor/ metformin FDC	Type 2 diabetes		Launched	Launched		2020
Qtern	DPP-4 inhibitor/ SGLT2 inhibitor FDC	Type 2 diabetes		Launched	Launched		
Bydureon BCise/Bydureon autoinjector[4]	GLP-1 receptor agonist	Type 2 diabetes	Q1 2013	Launched	Accepted		
Bydureon EXSCEL	GLP-1 receptor agonist	Type 2 diabetes outcomes trial	Q2 2010	H1 2018	H1 2018		H2 2018
saxagliptin/dapagliflozin/ metformin	DPP-4 inhibitor/ SGLT2 inhibitor	Type 2 diabetes	Q2 2017	H1 2018	H1 2018		
Epanova STRENGTH	omega-3 carboxylic acids	CV outcomes trial in statin-treated patients at high CV risk, with persistent hypertriglyceridaemia plus low HDL-cholesterol	Q4 2014	2020	2020	2020	2020
Respiratory							
Fasenra[#] (benralizumab[#]) TERRANOVA GALATHEA	IL-5R mAb	COPD	Q3 2014	H2 2018	H2 2018	2019	
Symbicort SYGMA	ICS/LABA	as-needed use in mild asthma	Q4 2014		2018		2019
Duaklir Genuair[#]	LAMA/LABA	COPD		H1 2018	Launched		2019
Other							
Nexium	proton-pump inhibitor	stress ulcer prophylaxis					Accepted
Nexium	proton-pump inhibitor	paediatrics		Launched	Launched	Approved	
linaclotide[#]	GC-C receptor peptide agonist	irritable bowel syndrome with constipation (IBS-C)					Accepted

[#] Collaboration.
[1] *Brilinta* in the US and Japan; *Brilique* in ROW.
[2] *Farxiga* in the US; *Forxiga* in ROW.
[3] *Xigduo* XR in the US; *Xigduo* in the EU.
[4] *Bydureon BCise* in the US; *Bydureon* autoinjector in the EU.

Terminations/Discontinued projects

NME/Line Extension	Compound	Reason for Discontinuation	Area Under Investigation
Symbicort – breath actuated inhaler	ICS/LABA	Strategic	asthma/COPD
AZD3241	myeloperoxidase inhibitor	Safety/efficacy	multiple system atrophy
AZD9412[#]	inhaled interferon beta	Strategic	asthma/COPD
AZD4076	anti-miR103/107 oligonucleotide	Safety/efficacy	non-alcoholic fatty liver disease/non-alcoholic steatohepatitis (NASH)
MEDI4166	PCSK9/GLP-1 mAb + peptide fusion	Safety/efficacy	diabetes/cardiovascular
verinurad	selective uric acid reabsorption inhibitor (URAT-1)	Strategic	chronic treatment of hyperuricemia in patients
NME	MEDI8111	Strategic	trauma/bleeding
NME	AZD9898[#]	Safety/efficacy	asthma
NME	MEDI-573	Safety/efficacy	metastatic breast cancer
NME	tralokinumab STRATOS 1,2 TROPOS MESOS	Safety/efficacy	severe, uncontrolled asthma

[#] Collaboration.

Completed Projects/Divestitures

Compound	Mechanism	Area Under Investigation	Completed/ Divested	Estimated Regulatory Submission Acceptance			
				US	EU	Japan	China
Tagrisso AURA, AURA2, (AURA17 Asia regional)	EGFR inhibitor	≥2nd line advanced EGFRm T790M NSCLC	Completed	Launched (Breakthrough Therapy, Priority Review, Orphan drug)	Launched (Accelerated assessment)	Launched	Launched
Tagrisso AURA3	EGFR inhibitor	≥2nd line advanced EGFRm T790M NSCLC	Completed	Launched	Launched		
Brilinta/Brilique	P2Y12 receptor antagonist	arterial thrombosis	Completed	Launched	Launched	Launched	Launched
Onglyza SAVOR-TIMI 53	DPP-4 inhibitor	Type 2 diabetes outcomes trial	Completed	Launched	Launched	Launched	*Onglyza* SAVOR-TIMI 53
Farxiga/Forxiga	SGLT2 inhibitor	Type 2 diabetes	Completed	Launched	Launched	Launched	Launched
Imfinzi (durvalumab[#])	PD-L1 mAb	≥2nd line advanced bladder cancer	Completed	Approved, Launched (Breakthrough Therapy & Priority Review)	n/a	n/a	n/a
AZD9150	STAT3 inhibitor	haematological malignancies	Completed				
MEDI0680	PD-1 mAb	solid tumours	Completed				
Kombiglyze XR/*Komboglyze*[1]	DPP-4 inhibitor/ metformin FDC	Type 2 diabetes		Launched	Launched		Launched

[#] Collaboration.
[1] *Kombiglyze* XR in the US; *Komboglyze* in the ROW.

Patent Expiries of Key Marketed Products

Patents covering our products are or may be challenged by third parties. 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 210. Many of our products are subject to challenges by third parties. Details of material challenges by third parties can be found in Note 28 to the Financial Statements from page 182. The expiry dates shown below include granted SPC/PTE and/or Paediatric Exclusivity periods (as appropriate). In Europe, the exact SPC situation may vary by country as different Patent Offices grant SPCs at different rates. Expiry dates in red relate to new molecular entity patents, the remaining dates relate to other patents. The expiry dates of relevant regulatory data exclusivity periods are not represented in the table below. 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 221.

Key marketed products	Description	US	China	EU[1]	Japan	US Product Sales ($m)			Aggregate Revenue for China, Japan and Europe[2] Product Sales ($m)		
						2017	2016	2015	**2017**	2016	2015
Atacand[3]	An angiotensin II antagonist for the 1st line treatment of hypertension and symptomatic heart failure	expired	[4]	expired	[4]	**19**	36	34	**86**	97	106
Bevespi Aerosphere	A combination of a long-acting muscarinic antagonist and a long-acting beta-2 adrenergic agonist used for the long-term maintenance treatment of airflow obstruction in COPD	2030-2031	2030	2030	2030	**16**	2	–	**–**	–	–
Brilinta/ Brilique	An oral P2Y12 platelet inhibitor for acute coronary syndromes (ACS) or extended therapy in high-risk patients with a history of myocardial infarction (MI)	2018-2024, 2021-2030	2018, 2019[5], 2021[6]	2018-2024, 2021[7]-2027	2023-2024, 2025-2030	**509**	348	240	**402**	347	268
Bydureon/ Bydureon BCise	A once-weekly injectable glucagon-like peptide-1 (GLP-1) receptor agonist available as a single-dose tray, a single-dose pen or autoinjector device indicated as monotherapy and as part of combination therapy adjunct to diet and exercise to improve glycaemic control in adults with Type 2 diabetes	2018-2028, 2030[8]	2020-2028, 2029[8]	2017-2028, 2029[8]	2018-2028, 2029[8]	**458**	463	482	**93**	109	90
Byetta	A twice-daily injectable GLP-1 receptor agonist indicated to improve glycaemic control in adults with Type 2 diabetes	2017-2020[9]	2020	2017-2021	2018-2020	**114**	164	209	**39**	62	86
Calquence	A selective inhibitor of Bruton tyrosine kinase indicated for the treatment of mantle cell lymphoma (MCL) and in development for the treatment of multiple B-cell malignancies and other cancers	2032, 2036	2032	2032	2032	**–**	–	–	**–**	–	–
Crestor	A statin for dyslipidaemia and hypercholesterolaemia	2018-2022[10]	2020-2021	2017, 2020	2017, 2023	**373**	1,223	2,844	**1,528**	1,698	1,642
Daliresp/ Daxas	An oral PDE4 (phosphodiesterase-4) inhibitor for adults with severe COPD to decrease their number of exacerbations (US only)	2020, 2023-2024	2023	2019[11], 2023		**167**	134	104	**26**	15	–
Duaklir	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	2020, 2025*, 2022-2027[12]	2020, 2022-2027	2025, 2022-2029	2025, 2021-2029	**–**	–	–	**77**	62	26
Fasenra	A monoclonal antibody for add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype, which directly targets and depletes eosinophils by recruiting natural killer cells and inducing apoptosis (programmed cell death)	2020, 2028-2034	2021, 2028	2020, 2028	2020	**–**	–	–	**–**	–	–
Faslodex	An injectable oestrogen receptor antagonist. It is used for the treatment of hormone receptor positive advanced breast cancer whose disease has progressed following treatment with prior endocrine therapy	2021[13]		2021[14]	2026	**492**	438	356	**352**	311	269
Farxiga/ Forxiga	A selective inhibitor of human sodium-glucose co-transporter 2 (SGLT2 inhibitor) indicated as monotherapy and as part of combination therapy adjunct to diet and exercise to improve glycaemic control in adult patients with Type 2 diabetes	2020, 2025*, 2020-2030	2020-2023, 2028	2020-2027	2024-2025, 2028	**355**	358	229	**245**	175	121
Fluenz tetra/ *FluMist* Quadravalent	A live-attenuated vaccine indicated for active immunisation for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine	2018-2026	2020-2025	2020-2026	2020-2025	**–**	33	206	**76**	65	83
Imfinzi	A human monoclonal antibody that blocks PD-L1 interaction with PD-1 and CD80 on T cells, countering the tumour's immune-evading tactics and inducing an immune response. It is currently indicated in the US for the treatment of locally advanced or metastatic urothelial carcinoma	2030	2030	2030	2030	**19**	–	–	**–**	–	–
Iressa	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)	2017[15]	2023	2019[16], 2023	2018, 2023	**39**	23	6	**367**	358	396
Kombiglyze XR[17]	Combines saxagliptin (*Onglyza*) and extended release metformin (metformin XR) in a once-daily tablet for Type 2 diabetes	2023, 2025	2021, 2025	2021-2026, 2025	[18]	**111**	145	154	**–**	–	–

Key marketed products	Description	US	China	EU[1]	Japan	US Product Sales ($m)			Aggregate Revenue for China, Japan and Europe[2] Product Sales ($m)		
						2017	2016	2015	**2017**	2016	2015
Lynparza	An oral poly ADP-ribose polymerase (PARP) inhibitor that may exploit tumour DNA damage response (DDR) pathway deficiencies to potentially kill cancer cells. It is indicated in the EU and US for the treatment of women with BRCAm ovarian cancer	2022-2024, 2028*, 2029[19], 2024-2031	2021-2024, 2024-2027, 2029[19]	2021-2029, 2024-2027	2021-2024, 2024-2027	**141**	127	70	**130**	81	23
Movantik/ Moventig	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	2022-2027, 2028*, 2032	2024	2022-2024, 2029*[20]	2022-2024	**120**	90	28	**2**	–	–
Nexium	A proton pump inhibitor used to treat acid-related diseases	2018-2020[21]	2018-2019	2018	2018, 2018-2019	**499**	526	870	**973**	975	985
Onglyza	An oral dipeptidyl peptidase 4 (DPP-4) inhibitor for Type 2 diabetes	2023, 2028	2021, 2025	2024, 2025	[18]	**209**	231	266	**114**	120	124
Pulmicort	An inhaled corticosteroid for maintenance treatment of asthma	2018-2019[22]	2018[23]	2018[23]	2018[23]	**156**	174	200	**847**	732	662
Qtern	A once-daily oral treatment combination of dapagliflozin (10mg) and saxagliptin (5mg) indicated as an adjunct to diet and exercise to improve glycaemic control in adults with Type 2 diabetes who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin	2020, 2025*, 2020-2029	2020-2023	2020-2027	2024-2025	**4**	–	–	**–**	–	–
Seloken/ Toprol-XL	A beta-blocker once-daily tablet for control of hypertension, heart failure and angina	expired	expired	expired	expired	**37**	95	89	**470**	462	436
Seroquel XR	Generally approved for the treatment of schizophrenia, bipolar disorder, major depressive disorder and, on a more limited basis, for generalised anxiety disorder	2017[24]	2017	2017	[25]	**175**	515	716	**82**	134	201
Symbicort	A combination of an inhaled corticosteroid and a fast onset LABA for maintenance treatment of asthma and COPD	2017-2029[26]	2017-2018[27]	2018-2019[27]	2017-2020[27]	**1,099**	1,242	1,520	**1,201**	1,276	1,375
Synagis	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	2023		2023	2023	**317**	325	285	**370**	352	377
Tagrisso	An EGFR-TKI indicated for patients with metastatic EGFR T790M mutation-positive NSCLC	2032	2032	2032	2034	**405**	254	15	**486**	158	4
Tudorza/ Eklira Genuair	A LAMA for the maintenance treatment of COPD	2020, 2025*, 2022-2027	2020, 2022-2027	2025, 2022-2029	2025, 2021-2029	**66**	77	103	**74**	84	77
Xigduo	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	2020, 2025*, 2020-2030	2020-2023	2020-2028	2024-2025, 2030	**134**	99	32	**58**	37	21
Zoladex	A luteinising hormone-releasing hormone (LHRH) agonist used to treat prostate cancer, breast cancer and certain benign gynaecological disorders	2022	2021	2021	2021	**15**	35	28	**483**	498	485

* Date represents expiry of a pending SPC/PTE and/or Paediatric Exclusivity period.
[1] Expiry in major EU markets.
[2] The Product Sales reflected are of Europe Region as defined in Market definitions on page 235.
[3] *Atacand HCT* in US.
[4] Takeda retained rights.
[5] The patent was invalidated during invalidation proceedings at the Chinese Patent Office (SIPO). The patentee has appealed that decision.
[6] The patent was invalidated during invalidation proceedings at the Chinese Patent Office (SIPO).
[7] The patent was revoked during opposition proceedings at the European Patent Office (EPO). The patentee has appealed that decision.
[8] Patent expiry date relates to *BCise*.
[9] Settled with two generic companies with a licensed entry date of 15 October 2017, or later, subject to regulatory approval.
[10] A settlement agreement in the US permitted Watson Laboratories, Inc. and Actavis, Inc. (together, Watson) to begin selling its generic version of *Crestor* and its rosuvastatin zinc product from 2 May 2016.
[11] There is eight years' data exclusivity and two years' market exclusivity for *Daxas* in the EU to 5 July 2020.
[12] Not filed for approval in US.
[13] Settled with various generic companies for licensed entry dates of 25 March 2019 or later.
[14] In Germany, the patent has been revoked, and AstraZeneca is appealing; generics have launched pending appeal.
[15] In the US, *Iressa* has seven years' orphan drug exclusivity to 13 July 2022.
[16] SPCs expire 2 March 2019. There is eight years' data exclusivity and two years' market exclusivity for *Iressa* in the EU to 24 June 2019.
[17] *Komboglyze/Kombiglyze* XR revenue is included in the *Onglyza* revenue figure.
[18] AstraZeneca does not have commercialisation rights.
[19] Patent expiry date relates to the tablet formulation.
[20] ProStrakan Group (a subsidiary of Kyowa Hakko Kirin Co. Ltd) is exclusively licensed in the EU, Iceland, Norway, Switzerland and Liechtenstein.
[21] Licence agreements have allowed generic companies to launch generic capsule versions in the US.
[22] A licence agreement with Teva permits its 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*.
[23] The 2018 expiry relates to the formulation in the *Turbuhaler* presentation and to a process useful for the *Respules* product.
[24] Licence agreements with various generics companies allowed launches of generic versions of *Seroquel XR* in the US as of 1 November 2016.
[25] Rights licensed to Astellas.
[26] Patent expiry dates relate to the *Symbicort* pMDI product, including any granted Paediatric Exclusivity term.
[27] Patent expiry dates relate to the *Symbicort Turbuhaler* product.

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 63, which are included below along with the other risks that we face. 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 78, 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. Therefore, other risks, unknown or not currently considered material, could have a material adverse effect on our financial condition or results of operations.

Product pipeline and IP risks	Impact
Failure or delay in delivery of pipeline or launch of new products	
Our continued success depends on the development and successful launch of innovative new drugs. The development of pharmaceutical product candidates is a complex, risky and lengthy process involving significant financial, R&D and other resources. A project may fail at any stage of the process due to various factors, including failure to obtain the required regulatory or marketing approvals for the product candidate or for its manufacturing facilities, unfavourable clinical efficacy data, safety concerns, failure to demonstrate adequate cost-effective benefits to regulatory authorities and/or payers and the emergence of competing products. More details of projects that have suffered setbacks or failures during 2017 can be found in the Therapy Area Review. 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. More complex and stringent regulations govern the manufacturing and supply of biologics products, thus impacting the production and release schedules of such products more significantly. In addition to developing products in-house, we also expand our product portfolio and geographical presence through licensing arrangements and strategic collaborations, which are key to growing and strengthening our business. The success of such arrangements is largely dependent on the technology and other IP rights we acquire or license, and the resources, efforts and skills of our partners. Disputes or difficulties in our relationship with our collaborators or partners may arise, for example, due to conflicting priorities or conflicts of interest between parties. In many cases we make milestone payments well in advance of the commercialisation of the products, with no assurance that we will recoup these payments. We experience strong competition from other pharmaceutical companies in respect of licensing arrangements, strategic collaborations, and acquisition targets.	Failure or delay in development of new product candidates 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 plans or meet targets and expectations on page 219. Since our business model and strategy rely on the success of relatively few compounds, the failure of any compound in our late-stage pipeline or in-line products may have a significant negative effect on our business or results of operations. Significant delays to anticipated launch dates of new products could have a material adverse effect on our financial position 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. Furthermore, in immuno-oncology in particular, speed to market is critical given the large number of clinical trials being conducted by other companies. 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. Failure to complete collaborative projects in a timely, cost-effective manner may limit our ability to access a greater portfolio of products, IP technology and shared expertise. Disputes and difficulties with our partners may erode or eliminate the benefits of our alliances and collaborations. In addition, failure to perform on the part of parties to externalisation transactions may diminish the future value of those transactions or, in some cases, allow a competitor to beat us to market with a similar or first-in-class product. Delay of launch can also erode the term of patent exclusivity. Competition from other pharmaceutical companies means that 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.

Product pipeline and IP risks	Impact

Difficulties in obtaining or maintaining regulatory drug approval for products

We are subject to strict controls on the commercialisation processes for our pharmaceutical products, including their development, manufacture, distribution and marketing. The criteria for establishing safety, efficacy and quality, which are essential for securing marketing approvals, may vary by country and by region. Regulators can refuse to grant approval or may require additional data before approval is granted, even though the medicine may already be launched in other countries.

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. While we seek to manage many of these risks, unanticipated and unpredictable policymaking by governments and regulators, limited regulatory authority resources or conflicting priorities often lead to severe delays in regulatory approvals.

We may be required to conduct additional clinical trials after a drug's approval because a regulatory authority may have a concern that impacts the benefit/risk profile of one of our marketed drugs or drugs currently in development. For our marketed drugs, new data and meta-analyses have the potential to drive changes in the approval status or labelling. In addition, 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. Such transparency, while important, could lead to inappropriate or incorrect data analyses which may damage the integrity of our products and our Company's reputation.

Delays in regulatory reviews and approvals could delay our ability to market our products and may adversely affect our revenue. In addition, post-approval requirements, including additional clinical trials, could result in increased costs, and may impact the labelling and approval status of currently marketed products.

Failure to obtain, defend and enforce effective IP protection and IP challenges by third parties

A pharmaceutical product may be protected from being copied for a limited period of time under certain patent rights and/or related IP rights, such as Regulatory Data Protection or Orphan Drug status. Typically, products protected by such rights generate significantly higher revenues than those not protected. Our ability to obtain, maintain, defend and enforce patents and other IP rights in relation to our products is an important element in protecting and recouping our investment in R&D and creating long-term value for the business. Some countries in which we operate do not offer robust IP protection. This may be because IP laws are still developing, the scope of those laws is limited or the political environment does not support such legislation.

We may also face challenges early in the patent application process and throughout a patent's life. The grounds for these challenges could be the validity of a patent and/or its effective scope and are based on ever-evolving legal precedents. We are experiencing increased challenges in the US and elsewhere in the world and there can be no guarantee of success for either party in patent proceedings and litigation.

We also bear the risk that our products may be found to infringe patents owned or licensed by third parties, including research-based and generic pharmaceutical companies and individuals. These third parties may seek remedies for patent infringement, including injunctions (for example, preventing the marketing of one of our products) and damages (for example, research-based competitors are alleging infringement of their patents and are seeking damages in relation to our marketing of *Imfinzi* and *Calquence*).

Details of material patent proceedings and litigation matters can be found in Note 28 to the Financial Statements from page 182.

Limitations on the availability of patent protection, the ability to obtain related IP rights or the use of compulsory licensing in certain countries in which we operate, as well as our ability to defend and enforce our patents, could allow for earlier entry of generic or biosimilar competitor products. This could have a material adverse effect on the pricing and sales of our products and, consequently, could materially adversely affect our revenues.

Third parties may be awarded remedies for alleged infringement of their IP, for example injunctions and damages for alleged patent infringement. In the US, courts may order enhanced (ie up to treble) damages for alleged wilful infringement of patents. From time to time we may acquire licences, discontinue activities and/or modify processes to avoid claims of patent infringement. These steps could entail significant costs and our revenue and margins could be materially adversely affected.

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 32, the Competitive pressures including expiry or loss of IP rights and generic competition risk on page 212 and Note 28 to the Financial Statements from page 182.

Commercialisation risks	Impact

Competitive pressures including expiry or loss of IP rights, and generic competition

A pharmaceutical product competes with other products marketed by research-based pharmaceutical companies and with generic or biosimilar drugs marketed by generic drug manufacturers.

Approval of competitive products for the same or similar indication as one of our products may result in immediate and significant decreases in our revenues.

Generic versions of products, including biosimilars, 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. Expiry or loss of IP rights can materially adversely affect our revenues and financial condition due to the launch of cheaper generic copies of the product in the country where the rights have expired or been lost (see the table in the Patent Expiries of Key Marketed Products section from page 208). For example in 2017, our US Product Sales of *Crestor* fell to $373 million (2016: $1,223 million), following the launch of generics.

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.

Generic manufacturers may also take advantage of the failure of certain countries to properly enforce Regulatory Data Protection or other related IP rights and may launch generics during this protected period. This is a particular risk in some Emerging Markets where appropriate patent protection or other related IP rights may be difficult to obtain or enforce.

The biosimilars market has experienced notable growth in 2017, with approval of several monoclonal antibody biosimilars in the US and Europe. This trend is expected to continue. Increased regulatory and legal activity related to the launch and approval of these therapeutics is anticipated. Regulatory authorities in other territories continue to implement or consider abbreviated approval processes for biosimilars, allowing quicker entry to market for such products and earlier than anticipated competition for patented biologics.

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, we are currently facing challenges from numerous generic drug manufacturers regarding our patents relating to key products, including *Brilinta*, *Faslodex*, *Byetta*, *Daliresp*, *Onglyza* and *Crestor*.

IP rights protecting our products may be challenged 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 bear the risk that courts may decide that our IP rights are invalid and/or that third parties do not infringe our asserted IP rights.

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.

Details of material patent litigation matters can be found in Note 28 to the Financial Statements from page 182.

If we are not successful in obtaining, maintaining, defending or enforcing our exclusive rights to market our products, particularly in the US where we achieve our highest Product Sales, our revenue and margins could be materially adversely affected. In addition, unsuccessful assertion of our IP rights may lead to damages or other liabilities to third parties that could materially adversely affect our financial performance.

Unfavourable resolution of current and potential future patent litigation may 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.

Commercialisation risks	Impact

Price controls and reductions

Most of our key markets have experienced the implementation of various cost control or reimbursement mechanisms for pharmaceutical products.

In the US, there is significant pricing pressure driven by payer consolidation, restrictive reimbursement policies, and cost control tools, such as exclusionary formularies and price protection clauses. Many formularies employ 'generic first' strategies and/or require physicians to obtain prior approval for the use of a branded medicine where a generic alternative exists. These mechanisms can be used by payers to limit the use of branded products and put pressure on manufacturers to reduce net prices. In addition, patients are seeing changes in the design of their health plan benefits and may experience variation in how their plans cover their medications, including increases in the out-of-pocket payments for their branded medications. Patient out-of-pocket spending is generally in the form of a co-payment or co-insurance, but there is a growing trend towards high deductible health plans that require that patients pay the full list price of their drugs and services until they meet certain out-of-pocket thresholds. Ongoing scrutiny of the US pharmaceutical industry, focused largely on pricing, is placing increased emphasis on the value of medications. This scrutiny will likely continue across many stakeholders, including policymakers and legislators.

The new US political leadership continues to consider a range of legislative and regulatory proposals to address the high costs of prescription drugs as well as reforms to the US healthcare system. These may include changes to the ACA, modifications to Medicare and other government programmes, and policies aimed at reducing drug prices such as importation schemes. For more information, please see Pricing of medicines in the Marketplace section from page 12. However, many of these proposals have not achieved broad support from policymakers and, in the near term, legislators have shifted focus away from healthcare reform. It is difficult to predict what specific proposals could be enacted and to determine the implications for the healthcare system and pharmaceutical industry. However, healthcare reform remains a key campaign promise of the current administration and proposals that would significantly modify existing laws and regulations, including the ACA, government programmes and policies relating to drug pricing, could affect private health insurance, coverage through Medicaid and the health insurance exchange marketplaces, Medicare coverage and savings provisions, and other facets of the US healthcare market, with potentially significant impacts on the pharmaceutical industry.

In Europe, the industry continues to be exposed 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 which may eventually lead to a change in the overall pricing and reimbursement landscape.

In Emerging Markets, governments are increasingly controlling pricing in the self-pay sector and favouring locally manufactured drugs. In addition, the emergence of price referencing has been seen in some markets combined with a call from authorities to provide greater global price transparency.

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.

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 from page 12 and on the next page in the following risk factor.

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, could materially adversely affect our business or results of operations.

We expect these pricing pressures will continue and may increase.

The continued disparities in EU and US pricing systems could lead to marked price differentials between regions, 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. Strengthened collaboration by governments may accelerate the development of further cost-containment policies (such as joint procurement). Increased and simplified access to national and regional prices in markets and the publication of these prices in centralised databases have facilitated the uptake and efficiency of price referencing across the world.

Commercialisation risks	Impact

Economic, regulatory and political pressures

Operating in over 100 countries, we are subject to political, socio-economic and financial factors both globally and in individual countries.

A sustained global economic downturn may further exacerbate pressure from governments and other healthcare payers on medicine prices and volumes of sales in response to pressures on budgets, and may cause a slowdown or a decline in growth in some markets. Those 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. Other customers may cease to trade, which may result in losses from writing off debts, or a reduction in demand for products.

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.

The majority of our cash investments are managed centrally and are invested in collateralised bank deposits, fixed income securities in government, financial and non-financial securities and 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, financial institution and non-financial institution default risk.

On 23 June 2016, the UK held a referendum on the UK's continuing membership of the EU, the outcome of which was a decision for the UK to leave the EU (Brexit). On 29 March 2017, the UK Government formally notified the EU under Article 50 of the UK's intention to leave the EU. This notification began the process of negotiation that will likely determine the future terms of the UK's relationship with the EU. Absent a negotiated agreement, the UK will leave the EU on 29 March 2019 and relevant EU law and agreements will cease to apply. Until the Brexit negotiation process is completed, it is difficult to anticipate the potential impact on AstraZeneca's market share, sales, profitability and results of operations. The Group operates from a global footprint and retains flexibility to adapt to changing circumstances. The uncertainty during and after the period of negotiation is also expected to increase volatility and may have an economic impact on the countries in which we operate, particularly in the UK and Eurozone. The Board reviews the potential impact of Brexit as an integral part of its Principal Risks (as outlined from page 63) rather than as a stand-alone risk. As the process of Brexit evolves, the Board will continue to assess its impact on the Company.

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.

While we have adopted cash management and treasury policies to manage the risk of not being able to access a sustainable flow of liquid funds (see the Financial risk management policies section of the Financial Review from page 79), 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 and non-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 Company 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 from page 79.

It is still early to judge the impact of Brexit as it is unclear as to the trading relationships the UK will be able to negotiate with the EU and other significant trading partners. Any deterioration in market access or trading terms including customs duties, VAT or other tariffs that constitute real cost, delay or restrictions to the movement of goods and increased administration may materially adversely impact our financial performance.

Commercialisation risks	Impact

Failures or delays in the quality and execution of our commercial strategies

Commercial success of our Growth Platforms is a critical factor in sustaining or increasing global Product Sales and replacing lost Product Sales due to patent expiry. The successful launch of a new pharmaceutical product involves substantial investment in sales and marketing activities, launch stocks and other items. We may ultimately be unable to achieve commercial success for various reasons, including 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.

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.

We face particular challenges in Emerging Markets, 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).
- The need to impose developed market compliance standards.
- The need to meet a more diverse range of national regulatory, clinical, manufacturing and distribution requirements.
- Potential inadvertent breaches of local and international law.
- Not being able to recruit appropriately skilled and experienced personnel.
- Difficulty in identifying the most effective sales and marketing channels and routes to market.
- Intervention by national governments or regulators restricting market access and/or introducing adverse price controls.
- Difficulty in managing local partnerships such as co-promotion and co-marketing; both driving performance and adhering to AstraZeneca's compliance standards which are often higher than the market norm.
- Difficulties in cash repatriation due to strict foreign currency controls and lack of hard currency reserves in some Emerging Markets.
- Complexity inherent within a direct exports business from UK and Sweden operations to countries where we do not have a legal entity.

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. Disputes or difficulties in our relationship with our collaborators or partners may also arise, often due to conflicting priorities or conflicts of interest between parties.

Failure to execute our commercial strategies could materially adversely impact our business or results of operations.

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*.

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.

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.

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.

Supply chain and business execution risks	Impact

Failure to maintain supply of compliant, quality products

We may experience difficulties, delays and interruptions in the manufacturing and supply of our products for various reasons, including:

- Demand significantly in excess of forecast demand, which may lead to supply shortages (this is particularly challenging before launch).
- 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 in construction of new facilities or the expansion of existing facilities, including those intended to support future demand for our products (the complexities associated with biologics facilities, especially for drug substance, increase the probability of delay).
- The 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.

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 and drug substances and/or finished drug products for some of our biologics medicines), equipment, formulated drugs and packaging, critical product components 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. We expect that external capacity for biologics drug substance production will remain constrained for the next few years and, accordingly, may not be readily available for supplementary production in the event that we experience an unforeseen need for such capacity.

Difficulties with manufacturing and supply, forecasting, distribution or third-party suppliers may result in product shortages, which may lead to lost Product Sales and materially adversely affect our reputation and revenues. Even slight variations in components or any part of the manufacturing process may lead to a product that is non-compliant and does not meet quality standards. This could lead to recalls, spoilage, product shortage, regulatory action and/or reputational harm.

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 our supply chains, 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, for example, counterfeit and/or illegally diverted products replace sales of genuine products in a market or genuine products are recalled following discovery of counterfeit products.

Reliance on third-party goods and services

AstraZeneca spends approximately $10 billion each year with trade suppliers. The spend supports the length of our value chain from discovery to manufacture and commercialisation of our medicines.

Many of our business-critical operations, including certain R&D processes, IT systems, HR, finance, tax and accounting services have been outsourced to third party providers. We are therefore heavily reliant on these third parties not just to deliver timely and high quality services, but also to comply with applicable laws and regulations and adhere to our ethical business expectations of third party providers.

The failure of outsource providers to deliver timely services, and to the required level of quality, or the failure of outsource providers to co-operate with each other, could materially adversely affect our financial condition or results of operations. Moreover, the failure of these third parties to operate in an ethical manner could adversely impact our reputation both internally and externally or even result in non-compliance with applicable laws and regulations.

Our business and financial results could also be materially adversely affected by disruptions caused by our failure to successfully manage either the integration of outsourced services or the transition process of insourcing services from third parties.

Supply chain and business execution risks	Impact

Failure of information security, data protection and cybercrime

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. In addition, we must ensure that the personal data which we, or third-party vendors operating on our behalf, hold and process is protected in a manner that complies with the EU GDPR which was approved by the EU on 28 May 2016, and will enter into force in May 2018.

Examples of sensitive information that we protect include clinical trial records (patient names and treatments), personal information (employee bank details, home address), IP related to manufacturing process and compliance, key research science techniques, AstraZeneca property (theft) and privileged access (rights to perform IT tasks).

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 this 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.

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.

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 unauthorised data loss from within AstraZeneca. It may also lead to 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 sensitive information.

Any significant disruption to these IT systems, including breaches of data security or cyber security, failure to integrate new and existing IT systems or failure to prepare for emerging EU GDPR and other applicable laws, could harm our reputation and materially adversely affect our financial condition or results of operations.

While we invest 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 or other sensitive information, damage to our reputation, regulatory penalties, financial losses and/or other costs.

The inability to effectively back up and restore data could lead to permanent loss of data that could result in non-compliance with applicable laws and regulations, and otherwise harm our business.

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. We may be unable to ward off such attacks which could have an adverse affect on our business.

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, such as 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 and/or additional legal obligations. Similarly, the involuntary public disclosure of commercially sensitive information or an information loss could adversely affect our business or results of operations. In addition, negative posts or comments about us (or, for example, the safety of our products) on social media websites or other digital channels could harm our reputation.

Failure of critical processes

Unexpected events and/or events beyond our control could result in the failure of critical processes within the Company or at third parties on whom we are reliant.

The business faces threats to business continuity from many directions. Examples of material threats include:

> Disruption to our business if there is instability in a particular geographic region, including as a result of war, terrorism, riots, unstable governments, civil insurrection or social unrest.
> Natural disasters in areas of the world prone to extreme weather events and earthquakes.
> Cyber threats similar to those detailed in the Failure of information security, data protection and cybercrime section above.

Failure of critical processes may result in an inability to research, manufacture or supply products to patients. AstraZeneca has developed a Business Resilience framework which is designed to mitigate such risks. However, there is no guarantee that these measures will be sufficient to prevent business interruption.

This may expose the Company to litigation and/or regulatory action which may result in fines, loss of revenue and adversely affect the Company's financial results.

Any expected gains from productivity initiatives are uncertain

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 or may not be achieved at all. 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.

Our failure to successfully implement these planned cost-reduction measures, either through the successful implementation 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.

Failure to attract and retain key personnel, and engage successfully with our employees

We rely heavily on recruiting and retaining talented employees with a diverse range of skills and capabilities to meet our strategic objectives.

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 and in the UK the added uncertainty created by Brexit could impact the hiring and retention of staff in some business-critical areas.

The successful delivery of our business objectives is dependent on high levels of engagement, commitment and motivation of the workforce.

The inability to attract and retain highly skilled personnel 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.

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 materially adversely affect our business or results of operations.

Legal, regulatory and compliance risks	Impact

Failure to adhere to applicable laws, rules and regulations

Our many business operations are subject to a wide range of laws, rules and regulations from governmental and non-governmental bodies around the world.

Any failure to comply with these applicable laws, rules and regulations may result in us being investigated by relevant agencies and authorities and/or in legal proceedings being filed against us. Such investigations or proceedings could result in us becoming subject to civil or criminal sanctions and/or being forced to pay fines or damages. Relevant 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.

Material examples of statutes, rules and regulations impacting business operations include:

- Compliance with Good Manufacturing Practice.
- Local, national and international environment or occupational health and safety laws and regulations.
- Trade control laws governing our imports and exports including nationally and internationally recognised trade agreements, embargoes, trade and economic sanctions and anti-boycott requirements.
- Competition laws and regulations, including challenges from competition authorities and private damages actions.
- Rules and regulations established to promote ethical supply chain management.
- Financial regulations including, but not limited to, external financial reporting, taxation and money laundering.
- Employment practices.
- Disclosure of payments to healthcare professionals under the Sunshine Act and EFPIA legislation.
- Appropriate disclosure of community support, patient group support and product donations.

We have environmental and/or occupational health and safety-related liabilities at some current, formerly owned, leased and third-party sites. For more information on the most significant of these and for details on other significant litigation matters, please refer to Note 28 to the Financial Statements from page 182.

Failure to comply with applicable laws, rules and regulations; manage our liabilities; or to adequately anticipate or proactively manage emerging policy and legal developments could materially adversely affect our licence to operate, or results of operations; adversely affect our reputation; cause harm to people or the environment; and/or lead to fines or other penalties. 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. If regulatory issues concerning compliance with environmental, 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.

Safety and efficacy of marketed products is questioned

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.

Any unforeseen safety concerns or adverse events relating to our products or failure to comply with laws, rules and regulations relating to provision of appropriate warnings concerning the dangers and risks of our products that result in injuries 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 28 to the Financial Statements from page 182.

Serious safety concerns or adverse events relating to our products could lead to product recalls, seizures, loss of product approvals and interruption of supply and could materially adversely impact patient access, our reputation and financial revenues.

Significant product liability claims could also arise which 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 219.

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 28 to the Financial Statements from page 182 describes the material legal proceedings in which we are currently involved.

Governmental investigations, for example under the US Foreign Corrupt Practices Act or federal or state False Claims Acts or other types of 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.

Legal, regulatory and compliance risks	Impact

Failure to adhere to increasingly stringent anti-bribery and anti-corruption legislation

There is an increasing global focus on the implementation and enforcement of anti-bribery and anti-corruption legislation.

Two relevant pieces of legislation include the UK Bribery Act and the US Foreign Corrupt Practices Act, and many other countries where we operate are also enforcing their own laws more aggressively and/or adopting tougher new measures. There has also been an increase in co-operation and co-ordination between regulators across countries with respect to investigation and enforcement.

We have been the subject of anti-corruption investigations and there can be no assurance that we will not, from time to time, be subject to informal enquiries 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, reimburser or prescriber, among others. To the extent we are the subject of any such pending and material matters, details are included in Note 28 to the Financial Statements from page 182.

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.

Economic and financial risks	Impact

Failure to achieve strategic plans or meet targets and expectations

From time to time, we 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 78). 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 those that we are unaware of and/or that are beyond our control.

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.

Any failure to successfully implement our business strategy, whether determined by internal or external risk factors, 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.

Unexpected deterioration in the Company's financial position

A wide range of financial risks could result in a material deterioration in the Company's financial position.

As a global business, currency fluctuations can significantly affect our results of operations, which are reported in US dollars. Approximately 31% of our global 2017 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 and Australian dollar.

Our consolidated balance sheet contains significant investments in intangible assets, including goodwill. The nature of the biopharmaceutical business is high risk and requires that we invest in a large number of projects in an effort to develop a successful portfolio of approved products. Our ability to realise value on these significant investments is often contingent upon, among other things, regulatory approvals, market acceptance, competition and legal developments. As such, in the course of our many acquisitions and R&D activities, we expect that some of our intangible assets will become impaired and be written off at some time in the future.

Inherent variability of biologics manufacturing increases the risk of write-offs of these product batches. Due to the value of the materials used, the carrying amount of biologic products is much higher than that of small molecule products. As we continue to grow our biologics business, we also increase the risk of potential impairment charges.

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, as of February 2006, we adjusted our product liability coverage profile, accepting uninsured exposure above $100 million. 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 *Farxiga* and *Nexium* in the US are not covered by third-party product liability insurance. See Note 28 to the Financial Statements from page 182 for details.

Movements in the exchange rates used to translate foreign currencies into US dollars may materially adversely affect our financial condition or results of operations. 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 and settlement dates. In addition, there are foreign exchange differences arising on the translation of investments in subsidiaries.

We have significant investments in goodwill and intangible assets as a result of our acquisitions of various businesses and our purchases of certain assets, such as product development and marketing rights. Impairment losses may materially adversely affect our financial condition or results of operations. Details of the carrying values of goodwill and intangible assets, and the estimates and assumptions we make in our impairment testing, are included in Notes 8 and 9 to the Financial Statements from page 154.

Financial liabilities arising 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, could require us to make significant provisions relating to legal proceedings and could materially adversely affect our financial condition or results of operations.

For more information, please see the Adverse outcome of litigation and/or governmental investigations risk on page 218.

The resolution of tax disputes regarding the profits to be taxed in individual territories 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, EPS and post-tax earnings. Claims, regardless of their merits or their outcome, are costly, divert management attention and may adversely affect our reputation.

Economic and financial risks	Impact

Unexpected deterioration in the Company's financial position *continued*

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.

The Company'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 which are now being progressively implemented by tax authorities around the world.

Our defined benefit pension obligations are largely backed by assets invested across the broad investment market. Our most significant obligations relate to defined benefit pension funds in the UK, Sweden and the US. The largest obligation is in the UK.

If any double tax treaties should be withdrawn or amended, especially in a territory where a member of the AstraZeneca 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 financial condition or results of operations, as could a negative outcome of a tax dispute or a failure by tax authorities to agree through competent authority proceedings. Changes to the application of double tax treaties, as a result of the parent company of the Group no longer being an EU entity following Brexit, could also result in adverse consequences such as those described above. See the Financial risk management policies section of the Financial Review on page 79 for tax risk management policies and Note 28 to the Financial Statements from page 182 for details of current tax disputes.

Changes in tax regimes, such as the recently announced changes to the US federal tax regime effective 1 January 2018, could result in a material impact on the Company'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 the OECD, governments and tax authorities through public consultations to ensure international institutions and governments understand the business implications of proposed law changes. Specific OECD BEPS recommendations that we expect to impact the Company include changes to patent box regimes, restrictions of interest deductibility and revised transfer pricing guidelines.

Sustained falls in asset values could reduce pension fund solvency levels, which may result in requirements for additional cash, restricting the cash available for our business. Changes to funding regulations for defined benefit pensions may also result in a requirement for additional cash contributions by the Company. If the present value of the liabilities increases 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 and the price of new debt issuances. See Note 20 to the Financial Statements from page 164 for further details of the Group's pension obligations.

Failure in financial control or the occurrence of fraud

Effective internal controls are necessary for us to provide reliable financial reports and are designed to prevent and detect fraud. Lapses in controls and procedures could undermine the ability to prevent fraud or provide accurate disclosure of financial information on a timely basis. Testing of our internal controls can provide only reasonable assurance with respect to the preparation and fair presentation of financial statements and may not prevent or detect misstatements or fraud.

Significant resources may be required to remediate any lapse or deficiency in internal controls.

Any such deficiency may also trigger investigations by a number of organisations, for example, the SEC, the DOJ or the UK Serious Fraud Office and may result in fines being levied against the Company or individual directors or officers.

Serious fraud may lead to potential prosecution or even imprisonment of senior management.

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 relate to Product Sales.

	World			Emerging Markets			US		Europe			Established ROW		
2017	Sales $m	Actual %	CER %	Sales $m	Actual %	CER %	Sales $m	Actual %	Sales $m	Actual %	CER %	Sales $m	Actual %	CER %
Oncology:														
Tagrisso	955	126	126	135	n/m	n/m	405	59	187	146	142	228	175	183
Faslodex	941	13	13	115	20	18	492	12	256	12	11	78	15	18
Zoladex	735	(10)	(10)	353	(1)	(1)	15	(57)	141	(10)	(8)	226	(16)	(15)
Iressa	528	3	3	251	8	8	39	70	112	(7)	(8)	126	(8)	(6)
Lynparza	297	36	35	18	n/m	n/m	141	11	130	60	58	8	n/m	n/m
Arimidex	217	(6)	(4)	118	7	10	7	(50)	34	(8)	(8)	58	(18)	(15)
Casodex	215	(13)	(11)	108	1	4	(1)	n/m	22	(19)	(19)	86	(23)	(21)
Imfinzi	19	n/m	n/m	–	–	–	19	n/m	–	–	–	–	–	–
Calquence	3	n/m	n/m	–	–	–	3	n/m	–	–	–	–	–	–
Others	114	10	13	28	12	16	–	–	3	(63)	(63)	83	17	20
Total Oncology	4,024	19	19	1,126	19	20	1,120	25	885	21	20	893	10	12
Cardiovascular & Metabolic Diseases:														
Crestor	2,365	(30)	(30)	784	9	11	373	(70)	666	(23)	(23)	542	(8)	(6)
Brilinta	1,079	29	29	224	19	21	509	46	295	14	13	51	16	11
Farxiga	1,074	29	28	232	74	73	489	7	242	29	28	111	91	90
Seloken/Toprol-XL	695	(6)	(4)	593	11	12	37	(61)	52	(42)	(41)	13	(19)	(19)
Onglyza	611	(15)	(16)	130	(8)	(10)	320	(15)	104	(21)	(21)	57	(19)	(20)
Bydureon	574	(1)	(1)	9	125	75	458	(1)	88	(12)	(11)	19	73	73
Atacand	300	(5)	(3)	178	10	12	19	(47)	86	(11)	(11)	17	(15)	(15)
Byetta	176	(31)	(30)	12	(50)	(50)	114	(30)	34	(24)	(22)	16	(24)	(24)
Symlin	48	20	20	–	–	–	48	20	–	–	–	–	–	–
Others	344	(13)	(12)	205	(10)	(7)	4	n/m	92	(23)	(24)	43	(14)	(12)
Total Cardiovascular & Metabolic Diseases	7,266	(10)	(10)	2,367	11	12	2,371	(26)	1,659	(12)	(13)	869	(1)	–
Respiratory:														
Symbicort	2,803	(6)	(6)	439	9	10	1,099	(12)	819	(10)	(10)	446	2	2
Pulmicort	1,176	11	12	840	20	23	156	(10)	92	(7)	(8)	88	(2)	(1)
Daliresp/Daxas	198	29	28	4	–	–	167	25	26	73	73	1	–	–
Tudorza/Eklira	150	(12)	(12)	2	n/m	n/m	66	(14)	73	(12)	(11)	9	–	–
Duaklir	79	25	25	–	n/m	n/m	–	–	77	24	24	2	–	–
Bevespi	16	n/m	n/m	–	–	–	16	n/m	–	–	–	–	–	–
Fasenra	1	n/m	n/m	–	–	–	1	n/m	–	–	–	–	–	–
Others	283	(10)	(9)	103	(25)	(24)	4	(44)	129	10	10	47	(6)	(6)
Total Respiratory	4,706	(1)	(1)	1,388	12	13	1,509	(8)	1,216	(5)	(5)	593	1	1
Other:														
Nexium	1,952	(4)	(3)	684	(1)	2	499	(10)	248	(1)	(3)	521	(3)	(1)
Synagis	687	1	1	–	–	–	317	(2)	370	5	5	–	–	–
Seroquel XR	332	(55)	(55)	62	(10)	(12)	175	(66)	78	(42)	(42)	17	–	–
Losec/Prilosec	271	(2)	(1)	140	9	10	11	10	77	(7)	(7)	43	(22)	(20)
Movantik/Moventig	122	34	34	–	n/m	n/m	120	33	2	n/m	n/m	–	–	–
FluMist/Fluenz	78	(25)	(28)	(1)	n/m	n/m	–	(100)	76	17	12	3	(50)	(50)
Others	714	(38)	(38)	383	(34)	(32)	47	(55)	142	(47)	(49)	142	(28)	(28)
Total Other	4,156	(18)	(17)	1,268	(14)	(12)	1,169	(28)	993	(14)	(15)	726	(11)	(9)
Total Product Sales	20,152	(5)	(5)	6,149	6	8	6,169	(16)	4,753	(6)	(7)	3,081	–	1

Geographical Review
continued

	World			Emerging Markets			US		Europe			Established ROW		
2016	Sales $m	Actual %	CER %	Sales $m	Actual %	CER %	Sales $m	Actual %	Sales $m	Actual %	CER %	Sales $m	Actual %	CER %
Oncology:														
Tagrisso	423	n/m	n/m	10	100	100	254	n/m	76	n/m	n/m	83	100	100
Faslodex	830	18	19	96	10	25	438	23	228	10	11	68	26	15
Zoladex	816	–	–	355	3	6	35	25	156	(8)	(4)	270	(1)	(7)
Iressa	513	(6)	(5)	233	(14)	(10)	23	n/m	120	(7)	(5)	137	–	(8)
Lynparza	218	n/m	n/m	7	n/m	n/m	127	81	81	n/m	n/m	3	n/m	n/m
Arimidex	232	(7)	(6)	110	7	15	14	(26)	37	(24)	(24)	71	(10)	(18)
Casodex	247	(7)	(9)	107	1	8	2	100	27	(7)	(7)	111	(15)	(23)
Others	104	(21)	(26)	25	(17)	(13)	–	n/m	8	(65)	(65)	71	18	7
Total Oncology	3,383	20	20	943	–	6	893	74	733	16	18	814	11	2
Cardiovascular & Metabolic Diseases:														
Crestor	3,401	(32)	(32)	721	5	12	1,223	(57)	866	(5)	(4)	591	4	(5)
Brilinta	839	36	39	189	69	80	348	45	258	12	15	44	19	22
Farxiga	835	70	72	133	82	96	457	75	187	48	52	58	81	72
Seloken/Toprol-XL	737	4	9	536	4	12	95	7	90	(6)	(5)	16	33	25
Onglyza	720	(8)	(6)	142	(11)	(4)	376	(10)	132	(6)	(5)	70	6	11
Bydureon	578	–	–	4	(50)	(25)	463	(4)	100	22	23	11	38	25
Atacand	315	(13)	(8)	162	(17)	(9)	36	6	97	(8)	(8)	20	(20)	(20)
Byetta	254	(20)	(19)	24	–	13	164	(22)	45	(26)	(25)	21	(5)	(9)
Symlin	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Others	437	(28)	(26)	228	(35)	(30)	40	(27)	119	(17)	(17)	50	(14)	(21)
Total Cardiovascular & Metabolic Diseases	8,116	(14)	(13)	2,139	1	8	3,202	(31)	1,894	–	1	881	6	(1)
Respiratory:														
Symbicort	2,989	(12)	(10)	402	2	10	1,242	(18)	909	(15)	(12)	436	8	5
Pulmicort	1,061	5	8	698	15	21	174	(13)	99	(15)	(14)	90	2	(3)
Daliresp/Daxas	154	48	48	4	n/m	n/m	134	29	15	100	100	1	n/m	n/m
Tudorza/Eklira	170	(11)	(9)	1	–	n/m	77	(25)	83	8	9	9	–	–
Duaklir	63	n/m	n/m	1	–	n/m	–	–	60	n/m	n/m	2	n/m	n/m
Bevespi	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Fasenra	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Others	316	22	27	137	8	13	11	(39)	118	34	38	50	108	108
Total Respiratory	4,753	(5)	(3)	1,243	10	17	1,638	(16)	1,284	(7)	(4)	588	12	8
Other:														
Nexium	2,032	(19)	(18)	690	(9)	(3)	554	(39)	251	(12)	(11)	537	(2)	(10)
Synagis	677	2	2	–	–	–	325	14	352	(7)	(7)	–	–	–
Seroquel XR	735	(28)	(27)	69	(17)	(7)	515	(28)	134	(33)	(32)	17	(32)	(32)
Losec/Prilosec	276	(19)	(17)	128	(15)	(9)	10	(44)	83	(14)	(13)	55	(26)	(31)
Movantik/Moventig	91	n/m	n/m	1	–	–	90	n/m	–	–	–	–	–	–
FluMist/Fluenz	104	(64)	(59)	1	n/m	n/m	33	(84)	64	(16)	3	6	(14)	(14)
Others	1,152	(23)	(20)	580	(9)	(4)	105	(54)	269	(27)	(21)	198	(29)	(27)
Total Other	5,067	(20)	(19)	1,469	(9)	(4)	1,632	(31)	1,153	(18)	(15)	813	(13)	(17)
Total Product Sales	21,319	(10)	(8)	5,794	–	6	7,365	(22)	5,064	(5)	(3)	3,096	2	(4)

All commentary in this section relates to Product Sales. The market definitions used in the geographical areas review below are defined in the Glossary on page 235.

2017 in brief

Sales decreased 5% in the year to $20,152 million (2016: $21,319 million; 2015: $23,641 million).

In 2017, sales in Emerging Markets increased 6% (CER: increased 8%) to $6,149 million (2016: $5,794 million; 2015: $5,822 million). China sales grew by 12% (CER: increased 15%) to $2,955 million (2016: $2,636 million; 2015: $2,530 million), representing 48% of total Emerging Markets sales. *Onglyza* and *Iressa* were included on the National Reimbursement Drug List (NRDL) in China in the year, as were *Brilinta*, *Faslodex* and *Seroquel XR*; the benefits of this inclusion are anticipated to favourably impact Product Sales after 2017. *Crestor* also had its 2nd line usage restriction removed and *Zoladex* was reclassified from the hormone and endocrine classification to oncology, which is expected to continue to support growth. *Tagrisso* was launched in China in April 2017.

In Emerging Markets, excluding China, Latin America sales were impacted by ongoing economic conditions, with sales in Latin America (ex-Brazil) declining by 12% (CER: declining by 10%) to $453 million (2016: $516 million; 2015: $643 million). Brazil sales increased by 4% (CER: decreased 5%) to $361 million (2016: $348 million; 2015: $381 million). Russia sales decreased by 1% (CER: decreased 14%) to $231 million (2016: $233 million; 2015: $231 million).

Sales in the US decreased 16% to $6,169 million (2016: $7,365 million; 2015: $9,474 million). The decline reflected generic medicine launches that impacted sales of *Crestor* and *Seroquel XR*. Unfavourable managed-care pricing and continued competitive intensity impacted sales of *Symbicort,* which declined by 12% to $1,099 million (2016: $1,242 million; 2015: $1,520 million). The New Oncology Growth Platform in the US, however, grew by 50% to $607m, primarily reflecting encouraging *Tagrisso* sales growth of 59% to $405 million (2016: $254 million; 2015: $15 million) in the year. The New CVMD Growth Platform increased sales by 5% in the US to $1,942 million (2016: $1,848 million; 2015: $1,662 million), reflecting strong performances from *Farxiga* and *Brilinta*. *Brilinta* grew by 46% in the US to $509 million (2016: $348 million; 2015: $240 million).

Sales in Europe decreased 6% (CER: decreased 7%) to $4,753 million in the year (2016: $5,064 million; 2015: $5,323 million). The New Oncology Growth Platform in Europe grew by 102% (CER: increased 99%) to $317 million (2016: $157 million; 2015: $27 million), partly driven by *Tagrisso* sales of $187 million (2016: $76 million; 2015: $4 million). *Lynparza* sales of $130 million (2016: $81m; 2015: $23m) represented growth of 60% (CER: growth at 58%). *Forxiga* sales growth of 29% (28% at CER) to $242 million (2016: $187 million; 2015: $126 million) was accompanied by *Brilique* growth of 14% (CER: growth of 13%) to $295 million (2016: $258 million; 2015: $230 million). These performances were more than offset by declines in other areas, including a 10% decline in *Symbicort* sales to $819 million (2016: $909 million; 2015: $1,076 million). *Symbicort* maintained its position, however, as the number one ICS/LABA medicine, despite competition from branded and analogue medicines. *Crestor* sales declined by 23% to $666 million (2016: $866 million; 2015: $916 million), reflecting the entry of generic medicines in certain markets in the year.

Sales in the Established Rest of World (ROW) in 2017 remained stable (CER: increased 1%) at $3,081 million (2016: $3,096 million; 2015: $3,022 million). Japan sales increased by 1% (CER: increased 4%) to $2,208 million (2016: $2,184 million; 2015: $2,020 million), partly reflecting the launch of *Tagrisso* and a new label for *Faslodex*. EGFR T790M-mutation testing rates in Japan continued to exceed 90% through the year, with full-year *Tagrisso* sales of $219 million (2016: $82 million; 2015: $nil) reflecting a high penetration rate in the currently-approved 2nd line setting. *Faslodex* sales in Japan were favourably impacted by a new label in the year; *Faslodex* sales in Japan increased by 14% (CER: increased 17%) to $72 million (2016: $63 million; 2015: $51 million).

The first *Crestor* competitor medicine was launched in Japan in the third quarter of 2017 and further generic competition entered the market in the fourth quarter of 2017. Full-year *Crestor* sales in Japan declined by 6% (CER: declined by 4%) to $489 million (2016: $521 million; 2015: $468 million). *Nexium* sales in Japan increased by 1% (CER: increased 4%) in the year to $439 million (2016: $436 million; 2015: $405 million) and sales of *Forxiga* increased by 89% (CER: increased 93%) in the year to $53 million (2016: $28 million; 2015: $16 million).

2016 in brief

Sales decreased 10% (CER: decreased 8%) in the year to $21,319 million (2015: $23,641 million; 2014: $26,095 million).

Sales growth for the year in Emerging Markets remained stable (CER: increased 6%) at $5,794 million (2015: $5,822 million; 2014: $5,827 million). Sales growth was impacted by challenging macro-economic conditions in Latin America, such as the current economic situation in Venezuela, where ex-Brazil sales decreased 20% (CER: decreased 7%) to $516 million (2015: $643 million; 2014: $730 million). The effects of significant reductions in Saudi Arabian governmental healthcare spending, as well as the reduction of AstraZeneca's activities in Venezuela, also adversely impacted sales. China sales increased 4% (CER: increased 10%) to $2,636 million (2015: $2,530 million; 2014: $2,242 million), and represent 45% of the Group's Emerging Markets sales. Sales in Brazil decreased 9% (CER: increased 2%) to $348 million (2015: $381 million; 2014: $451 million). The increase after eliminating exchange rate impacts reflects the strong performance of *Forxiga*, which increased 40% (CER: increased 50%) to $28 million (2015: $20 million; 2014: $5 million). Oncology medicines, which decreased 8% (CER: increased 1%) to $82 million (2015: $89 million; 2014: $99 million), and *Seloken*, which decreased 6% (CER: increased 6%) to $63 million (2015: $67 million; 2014: $84 million). Russia sales increased 1% (CER: increased 13%) to $233 million (2015: $231 million; 2014: $312 million), led by strong performances in Cardiovascular & Metabolic Diseases medicine sales, which increased 23% (CER: increased 38%) to $80 million (2015: $65 million; 2014: $89 million).

In 2016, sales in the US decreased 22% to $7,365 million (2015: $9,474 million; 2014: $10,120 million). The decline in US sales reflected the competition from generic *Crestor* medicines that entered the US market from July 2016. Unfavourable managed-care pricing and continued competitive intensity also impacted the sales of *Symbicort*.

Sales in Europe decreased 5% (CER: decreased 3%) to $5,064 million in the year (2015: $5,323 million; 2014: $6,638 million). Strong growth in sales of *Forxiga*, up 48% (CER: up 52%) to $187 million (2015: $126 million; 2014: $66 million), and *Brilique*, up 12% (CER: up 15%) to $258 million (2015: $230 million; 2014: $231 million), was more than offset by a 15% decrease in *Symbicort* sales (CER: 12% decrease) to $909 million (2015: $1,076 million; 2014: $1,462 million). However, *Symbicort* maintained its position as the number one ICS/LABA medicine by volume, despite competition from analogue medicines. *Lynparza* and *Tagrisso* sales increased to $81 million (2015: $23 million; 2014: $nil) and $76 million (2015: $4 million; 2014: $nil) respectively.

Sales in the Established ROW in 2016 increased 2% (CER: decreased 4%) to $3,096 million (2015: $3,022 million; 2014: $3,510 million). Sales of *Forxiga* in Established ROW increased 81% (CER: increased 72%), to $58 million (2015: $32 million; 2014: $17 million). *Nexium* sales decreased 2% (CER: decreased 10%) to $537 million (2015: $549 million; 2014: $606 million). Japan sales increased 8% (CER: decreased 3%) to $2,184 million (2015: $2,020 million;

Geographical Review *continued*

2014: $2,227 million), reflecting the biennial price reduction effective from April 2016 of around 6% after eliminating the exchange rate impact. The CER percentage decline in Japan was partly mitigated by stable sales of *Crestor* of $521 million (2015: $468 million; 2014: $502 million) in the year. Since the launch of *Tagrisso* in Japan in March 2016, sales amounted to $82 million (2015 & 2014: $nil).

Sales by Region

Emerging Markets

Sales in Emerging Markets increased 6% (CER: increased 8%) to $6,149 million (2016: $5,794 million; 2015: $5,822 million).

Oncology

Oncology sales in the Emerging Markets increased 19% (CER: increased 20%) to $1,126 million (2016: $943 million; 2015: $943 million).

Sales of *Tagrisso* were $135 million in the year (2016: $10 million; 2015: $nil).

Sales of *Iressa* increased by 8% to $251 million (2016: $233 million; 2015: $272 million). China sales increased by 24% (CER: increased 28%) to $144 million (2016: $116 million; 2015: $146 million), reflecting an improvement in patient access following the conclusion of the national negotiation process in 2016; *Iressa* was subsequently included on the NRDL. Other Emerging Markets sales were adversely impacted by competition from branded and generic medicines, most notably in the Republic of Korea.

Sales of *Faslodex* grew by 20% (CER: increased 18%) to $115 million (2016: $96 million; 2015: $87 million). In 2017, AstraZeneca received a label extension for *Faslodex* in Russia in the 1st line monotherapy setting, based on data from the FALCON trial. Russia sales grew by 29% in the year (CER: increased 14%) to $18 million (2016: $14 million; 2015: $9 million).

Sales of *Zoladex* declined by 1% to $353 million in the year (2016: $355 million; 2015: $345 million).

Cardiovascular & Metabolic Diseases

Cardiovascular & Metabolic Diseases sales in Emerging Markets increased 11% (CER: increased 12%) to $2,367 million (2016: $2,139 million; 2015: $2,120 million).

Sales of *Brilinta* for the year grew by 19% (CER: increased 21%) to $224 million (2016: $189 million; 2015: $112 million). Growth in Emerging Markets was reflected in a continued outperformance of the growth of the oral anti-platelet market. Encouraging sales performances were delivered in many markets.

Farxiga sales increased by 74% (CER: increased 73%) to $232 million (2016: $133 million; 2015: $73 million), reflecting ongoing launches and improved levels of patient access. In March 2017, *Forxiga* became the first SGLT2-inhibitor medicine to be approved in China.

Onglyza sales in Emerging Markets declined by 8% (CER: decreased 10%) to $130 million (2016: $142 million; 2015: $159 million). *Onglyza*, however, entered the NRDL in China in the year, underpinning fourth quarter 2017 Emerging Markets sales growth.

Respiratory

Respiratory sales in Emerging Markets increased 12% (CER: increased 13%) to $1,388 million (2016: $1,243 million; 2015: $1,132 million).

Sales of *Symbicort* grew by 9% (CER: increased 10%) to $439 million (2016: $402 million; 2015: $394 million), partly reflecting growth in China of 13% (CER: increased 17%) to $177 million (2016: $156 million; 2015: $124 million) and in Latin America (ex-Brazil), where sales grew by 24% (CER: increased 30%) to $46 million (2016: $37 million; 2015: $42 million).

Pulmicort sales increased by 20% (CER: increased 23%) to $840 million (2016: $698 million; 2015: $609 million), reflecting strong underlying volume growth, with sales in China, Middle East and North Africa proving particularly encouraging. Usage in China continued to progress, with an increasing prevalence of acute COPD and paediatric asthma accompanied by continued investment by AstraZeneca in new hospital nebulisation centres by around 2,000 to 15,000.

Other

Other sales in Emerging Markets decreased 14% (CER: decreased 12%) to $1,268 million (2016: $1,469 million; 2015: $1,627 million).

Nexium sales declined by 1% (CER: increased 2%) to $684 million (2016: $690 million; 2015: $761 million).

US

Sales in the US decreased 16% to $6,169 million (2016: $7,365 million; 2015: $9,474 million).

Oncology

Oncology sales in the US increased 25% to $1,120 million (2016: $893 million; 2015: $514 million).

Tagrisso sales in the US were $405 million (2016: $254 million; 2015: $15 million) and grew by 59%, with a steady increase in epidermal growth factor receptor (EGFR) T790M-mutation testing rates. In September 2017, the US National Comprehensive Cancer Network clinical-practice guidelines were updated to include the use of *Tagrisso* in the 1st line treatment of patients with metastatic EGFR-mutated non-small cell lung cancer (NSCLC). The use of *Tagrisso* in this indication is not yet approved by the FDA.

Iressa sales in the US increased by 70% to $39 million (2016: $23 million; 2015: $6 million).

Sales of *Lynparza* grew by 11% in the year to $141 million (2016: $127 million; 2015: $70 million). First-half sales were adversely impacted by the introduction of competing poly ADP ribose polymerase (PARP) inhibitor medicines. A much-improved performance in the second half, however, reflected the launch of tablets for patients regardless of BRCA-mutation status, for the treatment of 2nd line ovarian cancer. By the end of November 2017, *Lynparza* was the leading PARP inhibitor in the US, measured by total prescription volumes.

Faslodex sales increased by 12% to $492 million (2016: $438 million; 2015: $356 million), mainly reflecting a continued strong uptake of the combination with palbociclib, a medicine approved for the treatment of hormone-receptor-positive (HR+) breast cancer.

The sales of *Imfinzi* were $19 million (2016: $nil; 2015: $nil). *Imfinzi* launched in the US in May 2017. *Imfinzi* was approved under the FDA's Accelerated Approval pathway and launched on the same day as a fast-to-market, limited commercial opportunity, indicated for the 2nd line treatment of patients with locally-advanced or metastatic urothelial carcinoma (bladder cancer). AstraZeneca is actively preparing for the potential launch of *Imfinzi* in locally-advanced, unresectable NSCLC in the first half of 2018, reflecting the FDA regulatory submission acceptance and the award of Priority Review status in the fourth quarter of 2017.

The sales of *Calquence* were $3 million (2016 & 2015: $nil). *Calquence* delivered a promising performance in the number of new patient starts in previously-treated mantle cell lymphoma (MCL). The medicine was included within National Comprehensive Cancer Network guidelines from 15 November 2017.

Zoladex decreased 57% to $15 million (2016: $35 million; 2015: $28 million). On 31 March 2017, AstraZeneca completed an agreement with TerSera for the commercial rights to *Zoladex* in the US and Canada.

Cardiovascular & Metabolic Diseases

Cardiovascular & Metabolic Diseases sales in the US decreased 26% to $2,371 million (2016: $3,202 million; 2015: $4,634 million).

Sales of *Brilinta*, at $509 million (2016: $348 million; 2015: $240 million), represented an increase of 46% for the year. The performance was driven primarily by an increase in the average duration of therapy and strong growth in the number of patients sent home from hospital with *Brilinta*. Furthermore, *Brilinta* achieved a record total-prescription market share of 7.2% at the end of the year: days-of-therapy volume market-share data was particularly encouraging. The performance reflected the growth in demand, driven by updated preferred guidelines from the American College of Cardiology and the American Heart Association in 2016, as well as the narrowing of a competitor's label. *Brilinta* is the standard of care in the treatment of ST-segment elevation myocardial infarction and remained the branded oral anti-platelet market leader in the US in the period.

Farxiga sales in the year increased by 7% to $489 million (2016: $457 million; 2015: $261 million). The SGLT2-class growth was supported by growing evidence around cardiovascular (CV) benefits, including data from the CVD-REAL study that was published in March 2017.

Bydureon sales in the US declined by 1% to $458 million (2016: $463 million; 2015: $482 million), reflecting the prevailing level of competition and resulting price pressures. In the third quarter of the year, AstraZeneca launched the newly-approved injectable suspension autoinjector, known as *Bydureon BCise* in the US. The new autoinjector is a new formulation of *Bydureon* injectable suspension in an improved once-weekly, single-dose autoinjector device. It is designed for patient ease and convenience in a pre-filled device with a pre-attached hidden needle.

Crestor sales declined by 70% to $373 million (2016: $1,223 million; 2015: $2,844 million), reflecting the market entry in July 2016 of multiple *Crestor* generic medicines.

Respiratory

Respiratory sales in the US decreased 8% to $1,509 million (2016: $1,638 million; 2015: $1,945 million).

Sales of *Symbicort* in the US declined by 12% to $1,099 million (2016: $1,242 million; 2015: $1,520 million), in line with expectations of continued challenging conditions which were a result of the impact of managed-care access programmes on pricing within the class. Competition also remained intense from other classes, such as LAMA/LABA combination medicines.

Pulmicort sales in the US declined by 10% to $156 million (2016: $174 million; 2015: $200 million).

Daliresp/Daxas sales, representing 84% of global sales, increased by 25% to $167 million (2016: $134 million; 2015: $104 million), driven by increased adoption of the medicine which is the only oral, selective, long-acting inhibitor of the enzyme phosphodiesterase-4, an inflammatory agent in COPD.

Tudorza/Eklira sales in the US declined by 14% to $66 million (2016: $77 million; 2015: $103 million), reflecting lower levels of use of inhaled monotherapy medicines for COPD and the Group's commercial focus on the launch of *Bevespi*. On 17 March 2017, AstraZeneca announced that it had entered a strategic collaboration with Circassia for the development and commercialisation of *Tudorza* in the US. Circassia began its promotion of *Tudorza* in the US in May 2017. AstraZeneca will continue to book Product Sales of *Tudorza* in the US.

Bevespi was launched commercially in the US during early 2017. Prescriptions in the fourth quarter of 2017 tracked in line with other LAMA/LABA launches. The overall class in the US, however, continued to grow more slowly than anticipated. *Bevespi* was the first medicine launched using the Group's *Aerosphere* Delivery Technology delivered in a pressurised metered-dose inhaler.

Other

Other sales in the US decreased 28% to $1,169 million (2016: $1,632 million; 2015: $2,381 million).

Nexium sales in the US declined by 10% to $499 million (2016: $554 million; 2015: $902 million) in the year, reflecting a true-up adjustment.

Synagis sales decreased by 2% to $317 million (2016: $325 million; 2015: $285 million), constrained by the guidelines from the American Academy of Pediatrics Committee on Infectious Diseases, which restricted the number of patients eligible for preventative therapy with *Synagis*.

Sales of *Seroquel XR* in the US, where several competitors launched generic *Seroquel XR* medicines from November 2016, declined by 66% to $175 million (2016: $515 million; 2015: $716 million).

Europe

Sales in Europe decreased 6% (CER: decreased 7%) to $4,753 million (2016: $5,064 million; 2015: $5,323 million).

Oncology

Oncology sales in Europe increased 21% to $885 million (2016: $733 million; 2015: $635 million).

Tagrisso sales of $187 million (2016: $76 million; 2015: $4 million) represented growth of 146% (CER: increased 142%) were driven by a continued uptake, positive reimbursement decisions and a continued growth in testing rates. *Tagrisso* was reimbursed in 15 European countries at the end of the year and was under reimbursement review in additional European countries, with positive decisions anticipated in 2018.

Iressa sales declined in Europe by 7% (CER: decreased 8%) to $112 million (2016: $120 million; 2015: $128 million).

Lynparza sales in Europe increased by 60% (CER: increased 58%) to $130 million (2016: $81 million; 2015: $23 million), reflecting high BRCA-testing rates and a number of successful launches, most recently in Finland and the Republic of Ireland.

Sales of *Faslodex* increased by 12% (CER: increased 11%) to $256 million (2016: $228 million; 2015: $207 million).

Zoladex sales declined by 10% (CER: decreased 8%) to $141 million (2016: $156 million; 2015: $171 million), reflecting generic competition mainly in Central and Eastern Europe.

Cardiovascular & Metabolic Diseases

Cardiovascular & Metabolic Disease sales in Europe decreased 12% (CER: decreased 13%) to $1,659 million (2016: $1,894 million; 2015: $1,901 million).

Sales of *Brilique* in Europe increased by 14% (CER: increased 13%) to $295 million (2016: $258 million; 2015: $230 million), reflecting indication leadership across a number of markets and bolstered by the inclusion in the high-risk, post-myocardial infarction (HR PMI) guidelines from the European Society of Cardiology in 2017. Volume share reached 6.5% at the end of the year, with improvements delivered across the major markets: *Brilique* continued to outperform the oral anti-platelet market in the year. *Brilique* gained further reimbursement in key markets in its HR PMI indication in the 60mg dose.

Geographical Review *continued*

Forxiga sales in Europe increased by 29% (CER: increased 28%) to $242 million (2016: $187 million; 2015: $126 million) as the medicine continued to gain market share in the innovative oral class.

Onglyza sales in the year declined by 21% to $104 million (2016: $132 million; 2015: $141 million), reflecting the broader dynamic of shift away from the dipeptidyl peptidase-4 (DPP-4 class).

Bydureon sales in Europe declined by 12% (CER: decreased 11%) in the year to $88 million (2016: $100 million; 2015: $81 million), reflecting the impact of increased levels of competition.

Crestor sales declined by 23% to $666 million (2016: $866 million; 2015: $916 million), reflecting the launch of generic medicines in certain markets such as France and Spain.

Respiratory

Respiratory sales in Europe decreased 5% to $1,216 million (2016: $1,284 million; 2015: $1,383 million).

Symbicort sales declined by 10% to $819 million (2016: $909 million; 2015: $1,076 million), reflecting the level of competition from other branded and *Symbicort*-analogue medicines. However, *Symbicort* continued to retain its class-leadership position and stabilise volume share in the LABA/ICS class.

Other

Other sales in Europe decreased 14% (CER: decreased 15%) to $993 million (2016: $1,153 million; 2015: $1,404 million).

Sales of *Nexium* declined by 1% (CER: decreased 3%) to $248 million (2016: $251 million; 2015: $284 million) and *Seroquel XR* sales declined by 42% to $78 million (2016: $134 million; 2015: $202 million), reflecting the impact of generic competition.

FluMist/*Fluenz* sales in Europe increased by 17% (CER: increased 12%) to $76 million (2016: $64 million; 2015: $76 million), primarily driven by higher usage rates in the UK, which reflects the favourable impact of the UK National Immunisation Programme.

Established ROW

Sales in Established ROW remained stable (CER: increased 1%) to $3,081 million (2016: $3,096 million; 2015: $3,022 million).

Oncology

Oncology sales in Established ROW increased 10% (CER: increased 12%) to $893 million (2016: $814 million; 2015: $733 million).

Tagrisso's testing rates in Japan continued to exceed 90% through the year, with full-year sales of $219 million (2016: $82 million; 2015: $nil) reflecting a high penetration rate in the currently approved 2nd line EGFR T790M-mutation setting.

In June 2017, a label extension based upon the FALCON trial in the 1st line setting was approved in Japan, where *Faslodex* sales grew by 14% (CER: increased 17%) in the year to $72 million (2016: $63 million; 2015: $51 million). *Zoladex* sales fell by 16% (CER: decreased 15%) to $226 million (2016: $270 million; 2015: $272 million), driven by increased competition.

Cardiovascular & Metabolic Diseases

Cardiovascular & Metabolic Diseases sales in Established ROW decreased 1% (CER: stable) to $869 million (2016: $881 million; 2015: $834 million).

Sales of *Forxiga* in Established ROW increased 91% (CER: increased 90%) to $111 million (2016: $58 million; 2015: $32 million). In Japan sales of *Forxiga* grew at 89% (CER: increased 93%) to $53 million (2016: $28 million; 2015: $16 million).

In Japan, where Shionogi is a partner, *Crestor* maintained its position as the leading statin. Sales declined by 6% (CER: decreased 4%) to $489 million (2016: $521 million; 2015: $468 million), however, reflecting the recent entry of multiple *Crestor* competitors in the market in the second half of the year.

Respiratory

Respiratory sales in Established ROW increased 1% to $593 million (2016: $588 million; 2015: $527 million).

Symbicort sales increased 2% to $446 million (2016: $436 million; 2015: $404 million). In Japan, where Astellas assists as a promotional partner, sales declined by 3% (stable at CER) to $205 million (2016: $211 million; 2015: $176 million).

Other

Other sales in Established ROW decreased 11% (CER: decreased 9%) to $726 million (2016: $813 million; 2015: $928 million).

Sales of *Nexium* in Japan increased by 1% (CER: increased 4%) to $439 million (2016: $436 million; 2015: $405 million), which represented 84% of *Nexium* sales in Established ROW.

Sustainability: supplementary information

External assurance

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

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 them 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

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 (IEA), USEPA eGRID, US Green-e and the Association of Issuing Bodies (AIB) 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 2017 GHG emissions data. The assurance statement, including scope, methodology, overall opinion, and limitations and exclusions, is available on our website, www.astrazeneca.com.

Global greenhouse gas emissions data for the period 1 January 2017 to 31 December 2017

	Tonnes CO_2e		
	2017	2016	2015[1]
Emissions from: Scope 1: Combustion of fuel and operation of facilities[2]	**291,652**	309,661	318,633
Scope 2 (Market-based): Electricity (net of market instruments), heat, steam and cooling purchased for own use[3]	**182,847**	218,770	348,664
Scope 2 (Location-based): Electricity, heat, steam and cooling purchased for own use[3]	**278,870**	288,210	285,052
Company's chosen intensity measurement: Scope 1 + Scope 2 (Market-based) emissions reported above normalised to million US dollar revenue	**21.1**	23.0	27.0
Scope 3 Total: Emissions from all 15 Greenhouse Gas Protocol Scope 3 Categories[4] (one year in arrears)	**5,942,808**	7,497,338	6,310,359
Scope 3 in our Operational Footprint: Supply chain emissions: Upstream emissions from personal air travel, goods transport, waste incineration, and first tier active pharmaceutical ingredients and formulation & packaging suppliers (>90% of category spend, energy only, one year in arrears); Downstream emissions from HFA propellants released during patient use of our inhaled medicines	**1,184,050**	1,130,640	1,109,893
2016-2025 Strategy 'Operational Footprint' KPI: Scope 1 + Scope 2 (Market-based) + our Operational Footprint Scope 3 sources. Baseline year is 2015	**1,658,548**	1,659,071	1,777,190
2016-2025 Strategy Scope 3 intensity measurement KPI: Scope 3 emissions from all 15 Greenhouse Gas Protocol Scope 3 Categories normalised to million US dollar revenue. Includes Operational Scope 3 emissions. Baseline year is 2015 (one year in arrears)	**317**	375	300

[1] Regular review of the data is carried out to ensure accuracy and consistency. This has led to changes in the data from previous years. The data quoted in this Annual Report are generated from the revised data.
[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 imported electricity are calculated using the GHG Protocol Scope 2 Guidance (January 2015) requiring the dual reporting using two emissions factors for each site – market-based and location-based. Location-based factors are the grid average emissions factor for the country (or subregion in the US) that a site is in. Market-based factors are more specific to the site and local energy market, taking account of the residual energy mix a site is sourcing power from and any certified renewable power purchased by a site.
[4] GHG Protocol Scope 3 Categories: Purchased goods and services; Capital goods; Fuel- and energy-related activities; Upstream transportation and distribution; Waste generated in operations; Business travel; Employee commuting; Upstream leased assets; Downstream transportation and distribution; Processing of sold products; Use of sold products; End-of-life treatment of sold products; Downstream leased assets; Franchises; Investments.

Shareholder Information

The principal markets for trading in AstraZeneca shares are the London Stock Exchange, the Stockholm Stock Exchange and the New York Stock Exchange. Ordinary Shares of $0.25 each in AstraZeneca PLC are listed on the London Stock Exchange and the shareholder register is maintained by Equiniti Limited, the Ordinary Share registrar. Shares listed on the Stockholm Stock Exchange are issued under the Euroclear Services Agreement by Euroclear Sweden AB, the Swedish Central Securities Depositary. Shares listed on the New York Stock Exchange are in the form of American Depositary Shares (ADSs), evidenced by American Depositary Receipts (ADRs) issued by the Company's ADR depositary, Citibank, N.A. Two ADSs are equivalent to one Ordinary Share. Before 27 July 2015 the ratio was one ADS per one Ordinary Share.

Ordinary Share registrar

Equiniti Limited
Aspect House
Spencer Road
Lancing
West Sussex
BN99 6DA
UK
Tel (Freephone in UK): +44 (0)800 389 1580
Tel (outside UK): +44 (0)121 415 7033

Swedish Central Securities Depositary

Euroclear Sweden AB
PO Box 191
SE-101 23 Stockholm
Sweden
Tel: +46 (0)8 402 9000

ADR depositary

Citibank Shareholder Services
PO Box 43077
Providence
RI 02940-3077
USA
Tel (toll free in the US): +1 (888) 697 8018
Tel (outside the US): +1 (781) 575 4555
citibank@shareholders-online.com

Annual general meeting (AGM)

The 2018 AGM will be held on 18 May 2018. The meeting place will be in London, UK. Shareholders holding Ordinary Shares directly are entitled to attend and vote at the meeting or may submit a proxy voting instruction in advance, by following the instructions in the notice of AGM.

If you hold shares listed in Stockholm or hold ADRs, information relating to voting and attendance will be included in the relevant notice of AGM.

If you hold your shares through a nominee, your nominee provider will be able to advise you of their arrangements in relation to voting and attendance.

Dividends

Dividend dates for 2018 are shown in the financial calendar on page 229. A first interim dividend is normally announced in July/August and paid in September and a second interim dividend is normally announced in January/February and paid in March. Dividends are paid in GBP, SEK and US$, depending on where the eligible shares are listed. Further information on dividends declared can be found in the Shareholder Information section of AstraZeneca's website at www.astrazeneca.com.

Shareholders holding Ordinary Shares directly may opt for dividends to be paid straight to their bank or building society account, rather than being paid by cheque. To elect for this swift and secure method of payment, contact the Ordinary Share registrar, visit www.shareview.com or fill in the mandate form that will be sent to you with your next dividend cheque. If you hold shares listed in Stockholm, you should contact your personal broker or, if you hold a VP account, contact the bank that services your VP account. If you hold ADRs directly you should contact Shareholder Services on the number provided. If you hold your shares through a nominee, you should direct any queries relating to your shareholding and dividend payments to the nominee provider.

Shareholder communications

Copies of shareholder communications and annual reports are available on AstraZeneca's website at www.astrazeneca.com. If you hold Ordinary Shares directly, currently receive hard copies of shareholder communications and/or the annual report and would rather receive these documents electronically, you can manage your communication preferences at www.shareview.com or by contacting the Ordinary Share registrar. If your record on the Ordinary Share register has been duplicated you may receive multiple copies of shareholder communications; if this is the case please contact the Ordinary Share registrar so that this can be rectified.

Holders of shares listed in Stockholm should contact Computershare AB, PO Box 610, SE-182 16 Danderyd, (telephone +46 (0)8 588 04 200) and holders of ADRs should contact the ADR depositary or their personal broker with queries relating to shareholder communications.

Shareview

Holders of Ordinary Shares may create a portfolio at www.shareview.co.uk to view and manage their AstraZeneca shareholding. Shareview is a free and secure online service provided by the Ordinary Share registrar that allows users to, among other things, update personal details, manage communication preferences, view dividend information and manage direct dividend payments.

ShareGift

Shareholders that hold only a small number of shares, the value of which makes it uneconomical to sell them, may wish to consider donating them to charity through ShareGift, an independent charity share donation scheme (registered charity number 1052686). Further information about ShareGift can be found on its website at www.sharegift.org or by calling +44 (0)20 7930 3737.

The Unclaimed Assets Register

AstraZeneca provides information to the Unclaimed Assets Register (UAR) relating to unclaimed dividends paid on Ordinary Shares. The UAR database provides a facility to search for financial assets that may have been forgotten and can be contacted on +44 (0)333 000 0182 or uarenquiries@uk.experian.com.

Shareholder fraud warning

Shareholders of AstraZeneca and many other companies have reported receiving unsolicited calls and correspondence relating to their shareholdings and investment matters. Shareholders are advised to be very cautious of any unsolicited approaches and to note that reputable firms authorised by the Financial Conduct Authority (FCA) are very unlikely to make such approaches. Such approaches are likely to be part of a 'boiler room scam' attempting to defraud shareholders.

Shareholders are advised to familiarise themselves with the information on scams available on the FCA website, www.fca.org.uk/consumers and within the FAQs in the Investors section of AstraZeneca's website, www.astrazeneca.com.

Any suspected scams or fraudulent approaches should be reported to the FCA via its website and to AstraZeneca's Ordinary Share registrar, using the contact details on this page.

Investor Relations

AstraZeneca PLC
1 Francis Crick Avenue
Cambridge Biomedical Campus
Cambridge CB2 0AA
UK

www.astrazeneca.com/investors
irteam@astrazeneca.com
Tel (UK): +44 (0)20 3749 5717
Tel (US toll free): +1 866 381 7277

Financial calendar

Event	Provisional date
Second interim dividend for 2017	
Ex-dividend date	15 February 2018
Record date	16 February 2018
Payment date	19 March 2018
Announcement of first quarter results for 2018	18 May 2018
Annual general meeting (AGM)	18 May 2018
Announcement of second quarter results for 2018	26 July 2018
First interim dividend for 2018	
Ex-dividend date	9 August 2018
Record date	10 August 2018
Payment date	10 September 2018
Announcement of third quarter results for 2018	8 November 2018
Financial year end	31 December 2018

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 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA, UK (telephone +44 (0)20 3749 5000). 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.

In 1999, in connection with the merger between Astra and Zeneca, 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.

Issued share capital, shareholdings and share prices

At 31 December 2017, the Company had 87,934 registered holders of 1,266,221,605 Ordinary Shares. There were 107,486 holders of Ordinary Shares held under the Euroclear Services Agreement, representing 10.4% of the issued share capital of the Company and 1,849 registered holders of ADSs, representing 17.7% of the issued share capital of the Company.

Ordinary Shares in issue

	2013	2014	2015	2016	**2017**
Ordinary Shares in issue – millions					
At year end	1,257	1,263	1,264	1,265	**1,266**
Weighted average for year	1,252	1,262	1,264	1,265	**1,266**
Stock market price per Ordinary Share (London Stock Exchange)					
Highest (pence)	3612.0	4823.5	4863.0	5220.0	**5508.0**
Lowest (pence)	2909.5	3549.5	3903.5	3774.0	**4194.0**
At year end (pence)	3574.5	4555.5	4616.5	4437.5	**5121.0**

Analysis of shareholdings as a percentage of issued share capital at 31 December

Number of Ordinary Shares[1]	2013 %	2014 %	2015 %	2016 %	**2017 %**
1 – 250	0.5	0.5	0.5	0.5	**0.5**
251 – 500	0.6	0.6	0.6	0.5	**0.5**
501 – 1,000	0.8	0.7	0.7	0.6	**0.6**
1,001 – 5,000	1.1	1.0	0.9	0.8	**0.8**
5,001 – 10,000	0.2	0.2	0.2	0.2	**0.2**
10,001 – 50,000	1.0	1.0	0.9	0.9	**1.0**
50,001 – 1,000,000	12.3	13.3	13.0	12.3	**11.9**
Over 1,000,000	83.5	82.7	83.2	84.2	**84.5**

[1] Includes Euroclear and ADR holdings.

Shareholder Information
continued

Reported high and low share prices during the year

		Ordinary Shares London Stock Exchange[1]		Ordinary Shares Stockholm Stock Exchange[2]		ADRs New York Stock Exchange[3]	
		High (pence)	Low (pence)	High (SEK)	Low (SEK)	High (US$)	Low (US$)
2016	– Quarter 1	4562.0	3890.0	584.0	452.8	33.90	27.95
	– Quarter 2	4467.0	3774.0	592.0	458.2	30.25	27.26
	– Quarter 3	5220.0	4469.5	556.0	456.6	34.50	29.97
	– Quarter 4	5096.0	4007.0	581.5	448.5	33.00	25.81
2017	– Quarter 1	4974.5	4194.0	558.0	470.6	31.80	26.72
	– Quarter 2	5508.0	4566.0	619.0	534.0	35.36	29.76
	– Quarter 3	5192.0	4325.0	578.0	466.2	34.16	28.88
	– Quarter 4	5180.0	4705.0	581.0	541.0	34.78	32.09
	– July	5192.0	4325.0	578.0	471.8	34.16	28.88
	– August	4564.0	4384.0	491.9	466.2	30.34	28.96
	– September	4955.0	4573.5	547.5	479.6	34.00	30.07
	– October	5176.0	5022.0	568.0	552.5	34.78	33.49
	– November	5180.0	4777.0	581.0	546.5	34.56	32.87
	– December	5121.0	4705.0	568.5	541.0	34.70	32.09

[1] For shares listed on the London Stock Exchange, the reported high and low middle market closing quotations are derived from the Daily Official List.
[2] For shares listed on the Stockholm Stock Exchange, the high and low closing sales prices are as stated in the Official List.
[3] For ADRs listed on the New York Stock Exchange, the reported high and low sales prices are as reported by Dow Jones (ADR quotations).

US holdings

At 31 January 2018, the proportion of Ordinary Shares represented by ADSs was 17.7% of the issued share capital of the Company. At 31 January 2018 there were 87,700 registered holders of Ordinary Shares, of which 703 were based in the US and there were 1,850 record holders of ADRs, of which 1,828 were based in the US.

Major shareholdings

At 31 December 2017, the following persons 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 Guidance and Transparency Rules:

Shareholder	Number of Ordinary Shares	Date of disclosure to Company[1]	**Number of Ordinary Shares disclosed as a percentage of issued share capital at 31 December 2017**
BlackRock, Inc.	100,885,181	8 December 2009	**7.97**
Investor AB	51,587,810	2 February 2012	**4.07**
The Capital Group Companies, Inc.	63,029,311	14 August 2017	**4.98**

[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 arises unless the holding passes a notifiable threshold in accordance with rules 5.1.2 or 5.1.5 of the UK Listing Authority's Disclosure Guidance and Transparency Rules.

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 2017 and 31 January 2018.

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

Shareholder	**31 January 2018**	31 January 2017	31 January 2016	31 January 2015
BlackRock, Inc.	**7.97**	7.97	7.98	7.99
Investor AB	**4.07**	4.08	4.08	4.08
The Capital Group Companies, Inc.	**4.98**	3.00	3.00	< 3.00

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.

Directors' and officers' shareholdings

At 31 January 2018, 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	**657,098**	**0.05**

Options to purchase securities from registrant or subsidiaries

(a) At 31 January 2018, options outstanding to subscribe for Ordinary Shares were:

Number of shares	Subscription price (pence)	Normal expiry date
2,116,201	**1882-3929**	**2017-2023**

The weighted average subscription price of options outstanding at 31 January 2018 was 3118 pence. All options were granted under Company employee share schemes.

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

Number of shares	Subscription price (pence)	Normal expiry date
2,495	**3307-3597**	**2018-2021**

(c) Included in paragraph (b) are options granted to individually named Directors. Details of these option holdings at 31 December 2017 are shown in the Remuneration Report on page 124.

During the period 1 January 2018 to 31 January 2018, no Director exercised any options.

Related party transactions

During the period 1 January 2018 to 31 January 2018, 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 30 to the Financial Statements on page 189).

Articles of Association

AstraZeneca PLC's current Articles were adopted by shareholders at the Company's AGM held on 24 April 2015. Any amendment to the Articles requires the approval of shareholders by a special resolution at a general meeting of the Company.

Objects

The Company's objects are unrestricted.

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 2017, the Company had 1,266,221,605 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 2017 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 a special resolution passed at a general meeting of such holders is required.

General meetings

AGMs 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.

Shareholder Information *continued*

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 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA, UK.

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 27 of the Financial Statements and Directors' Remuneration Report
Shareholder waiver of dividends	Page 98 in the Corporate Governance Report

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 153.

Tax information for shareholders

Taxation for US persons

The following summary of material UK and US federal income tax consequences of ownership of Ordinary Shares or ADR 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 2017. 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 (or certain specified 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.

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 up 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 the Company or its wholly-owned subsidiary, Zeneca Wilmington Inc.

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)		
2015	8.3950	1.5357
2016	8.5286	1.3673
2017	**8.5835**	**1.2835**
End of year spot rates (statement of financial position)		
2015	8.4114	1.4816
2016	9.1162	1.2272
2017	**8.2467**	**1.3468**

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			
Accolate[1]	*Diprivan*[3]	*Movantik*	*Seroquel XR*
Arimidex	*Duzallo*	*Moventig*	*Symbicort*
Atacand	*EMLA*[3]	*Myalept*[7]	*Symbicort SMART*
Atacand HCT	*Entocort*[4]	*Naropin*[3]	*Symbicort Turbuhaler*
Atacand Plus	*Farxiga*	*Nexium*	*Symlin*
BCise	*Fasenra*	*Nolvadex*	*Synagis*[9]
Bevespi Aerosphere	*Faslodex*	*Onglyza*	*Tagrisso*
Bricanyl	*Fluenz*	*Oxis Turbuhaler*	*Tenormin*[10]
Brilinta	*FluMist*	*Plendil*	*Toprol-XL*
Brilique	*Forxiga*	*Pressair*	*Turbuhaler*
Bydureon	*Genuair*	*Prilosec*	*Vimovo*
Byetta	*Imdur*[5]	*Pulmicort*	*Xigduo*
Calquence	*Imfinzi*	*Pulmicort Flexhaler*	*Xylocaine*[3]
Caprelsa[2]	*Iressa*	*Pulmicort Respules*	*Xylocard*[3]
Carbocaine[3]	*Kombiglyze*	*Pulmicort Turbuhaler*	*Xyloproct*[3]
Casodex	*Komboglyze*	*Qtern*	*Zavicefta*[11]
Citanest[3]	*Losec*	*Respules*	*Zestril*[10]
Cosudex	*Lynparza*	*Rhinocort*[8]	*Zoladex*
Crestor	*Marcaine*[3]	*Rhinocort Aqua*[8]	*Zomig*
Daliresp	*Meronem*[6]	*Seloken*	*Zurampic*
Daxas	*Merrem*[6]	*Seroquel*	

[1] AstraZeneca assigned this trade mark in the US to Par Pharmaceuticals Inc. effective 5 January 2015.
[2] AstraZeneca assigned this trade mark to Genzyme Corporation effective 30 September 2015.
[3] AstraZeneca divested these trade marks to Aspen group effective 1 November 2017.
[4] AstraZeneca assigned this trade mark in the US to Elan Pharma International Limited effective 15 December 2015, and in the rest of the world to Tillots Pharma AG effective 16 July 2015.
[5] AstraZeneca assigned this trade mark to Everest Future Limited effective 1 May 2016.
[6] AstraZeneca assigned *Meronem* and *Merrem* to Pfizer Inc. in most markets outside the US effective 23 December 2016.
[7] AstraZeneca assigned this trade mark to Aegerion effective 9 January 2015.
[8] AstraZeneca assigned *Rhinocort* and *Rhinocort Aqua* to Cilag GmbH International outside the US effective 5 December 2016.
[9] AstraZeneca owns this trade mark in the US only. AbbVie owns it in the rest of the world.
[10] AstraZeneca assigned these trade marks in the US to Alvogen Pharma US Inc. effective 9 January 2015.
[11] AstraZeneca assigned this trade mark to Pfizer Inc. effective 23 December 2016.

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
Duaklir	Almirall, S.A.
Eklira	Almirall, S.A.
Epanova	Chrysalis Pharma AG
Tudorza	Almirall, S.A.

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
Avastin	Genentech, Inc.
Darzalex	Johnson & Johnson
Keytruda	MSD
Lipitor	Pfizer Ireland Pharmaceuticals
messenger RNA Therapeutics	Moderna Therapeutics, Inc.
Vidaza	Celgene Corporation

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	Canada	Japan	New Zealand	
Emerging Markets	Algeria	Costa Rica	Iraq*	Pakistan*	Syria*
	Argentina	Cuba*	Jamaica*	Palestine*	Taiwan
	Aruba*	Dominican Republic*	Jordan*	Panama	Thailand
	Bahamas*	Ecuador*	Kazakhstan	Peru	Trinidad and Tobago*
	Bahrain*	Egypt	Kuwait*	Philippines	Tunisia*
	Barbados*	El Salvador	Lebanon*	Qatar*	Turkey
	Belarus*	Georgia*	Libya*	Russia	Ukraine*
	Belize*	Guatemala	Malaysia	Saudi Arabia	United Arab Emirates
	Bermuda*	Honduras	Mexico	Singapore	Uruguay*
	Brazil	Hong Kong	Morocco*	South Africa	Venezuela*
	Chile	India	Nicaragua	South Korea	Vietnam
	China	Indonesia	Oman*	Sri Lanka*	Yemen*
	Colombia	Iran*	Other Africa*	Sudan*	

* IQVIA, IQVIA Midas Quantum Q3 2017 data is not available or AstraZeneca does not subscribe for IQVIA 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 2017 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
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
Loans	Long-term debt
Prepayments	Prepaid expenses
Profit	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 US 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 syndromes.

Actavis – Actavis plc.

ADC Therapeutics – ADC Therapeutics Sàrl.

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

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

Aegerion – Aegerion Pharmaceuticals, Inc.

AGM – an Annual General Meeting of the Company.

Allergan – Allergan plc.

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 2017.

API – active pharmaceutical ingredient.

Aralez – Aralez Pharmaceuticals Trading DAC.

Ardea – Ardea Biosciences, Inc.

Articles – the Articles of Association of the Company.

Aspen – Aspen Global Incorporated.

Astellas – Astellas Pharma Inc.

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

AstraZeneca – the Company and its subsidiaries.

ATM – Ataxia telangiectasia mutated.

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.

CDP – a not-for-profit that runs the global disclosure system for investors, companies, cities, states and regions to manage their environmental impacts.

Celgene – Celgene International Sàrl/Celgene Corporation.

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.

Cilag – Cilag GmbH International.

Circassia – Circassia Pharmaceuticals plc.

CIS – Commonwealth of Independent States.

CMS – China Medical System Holdings Ltd.

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

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

COPD – chronic obstructive pulmonary diseases.

CREST – UK-based securities settlement system.

CRISPR – clustered regularly interspaced short palindromic repeats.

CRL – Complete Response Letter.

CROs – contract research organisations.

CRUK – Cancer Research UK.

CV – cardiovascular.

CVMD – Cardiovascular & Metabolic Diseases.

Daiichi Sankyo – Daiichi Sankyo, Inc.

Definiens – Definiens AG.

Director – a director of the Company.

DJSI – Dow Jones Sustainability Index.

DOJ – the United States Department of Justice.

DTR – UK Disclosure Guidance and Transparency Rules.

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.

Entasis – Entasis Therapeutics Ltd and Entasis Therapeutics Inc.

EPO – European Patent Office.

ESMO – European Society for Medical Oncology.

ESPC – Early Stage Product Committee.

ESRD – end-stage renal disease.

EVP – Executive Vice-President.

EU – the European Union.

EU 5 – European Union Five (France, Germany, Italy, Spain and the UK).

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.

FDC – fixed-dose combination.

FibroGen – FibroGen, Inc.

FRC – Financial Reporting Council.

GAAP – Generally Accepted Accounting Principles.

GDPR – General Data Protection Regulation.

Gilead – Gilead Sciences, Inc.

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.

Grünenthal – Grünenthal Group.

GSK – GlaxoSmithKline plc.

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.

ICS – inhaled corticosteroid.

IFPMA – International Federation of Pharmaceutical Manufacturers and Associations.

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.

Incyte – Incyte Corporation.

Innate Pharma – Innate Pharma S.A.

Insmed – Insmed, Inc.

IO – immuno-oncology.

IP – intellectual property.

Ironwood – Ironwood Pharmaceuticals, Inc.

IS – information services.

ISAs – International Standards on Auditing.

IT – information technology.

Johnson & Johnson – Johnson & Johnson.

KPI – key performance indicator.

krona or SEK – references to the currency of Sweden.

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

LABA – long-acting beta2-agonist.

LAMA – long-acting muscarinic antagonist.

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.

LEO Pharma – LEO Pharma A/S.

Lilly – Eli Lilly and Company.

LSPC – Late Stage Product Committee.

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 (JP) and China (CN).

MAT – moving annual total.

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

MEK – part of the mitogen-activated protein kinase (MAPK) pathway.

MI – myocardial infarction.

Moderna – Moderna Therapeutics, Inc.

MSD – Merck & Co., Inc., which is known as Merck in the US and Canada and MSD in other territories.

NCD – non-communicable disease.

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.

Novo Nordisk – Novo Nordisk A/S.

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.

OECD – the Organisation for Economic Co-operation and Development.

OIC – opioid-induced constipation.

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).

PARP – an oral poly ADP-ribose polymerase.

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.

Glossary *continued*

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 NV.

R&D – research and development.

Recordati – Recordati S.p.A.

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

Regulatory Data Protection (RDP) – see Intellectual Property on page 32.

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

RNA – ribonucleic acid.

Roche – F. Hoffmann-La Roche AG.

ROW – rest of world.

RSV – respiratory syncytial virus.

Sanofi – SANOFI S.A./Sanofi Pasteur, Inc.

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

SDRT – UK stamp duty reserve tax.

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.

SHE – Safety, Health and Environment.

Shionogi – Shionogi & Co. Ltd.

Shire – Shire plc.

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.

SSE – the Stockholm Stock Exchange.

Takeda – Takeda Pharmaceutical Company Limited.

TerSera – TerSera Therapeutics LLC.

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.

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 210 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 2017 obtained from IQVIA, 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 IQVIA National Prescription Audit and IQVIA National Sales Perspectives for the 12 months ended 31 December 2017; such data is not adjusted for Medicaid and similar rebates. Except as otherwise stated, these market share and industry data from IQVIA have been derived by comparing our sales revenue with competitors' and total market sales revenues for that period, and 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 IQVIA database, which amounted to approximately 96% (in value) of the countries audited by IQVIA.

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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MIX
Paper from responsible sources
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Registered office and corporate headquarters
AstraZeneca PLC
1 Francis Crick Avenue
Cambridge Biomedical Campus
Cambridge CB2 0AA
UK
Tel: +44 (0)20 3749 5000

This Annual Report is also available on our website, www.astrazeneca.com/annualreport2017