

Investor science event: Late-stage pipeline webcast

Sean Bohen, EVP, Global Medicines Development, Chief Medical Officer

14 December 2017



Forward-looking statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement:

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Agenda & introduction



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Global Medicines Development
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Participants for Q&A



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Medicines Development and
Chief Medical Officer, Pearl
Therapeutics



Agenda



Oncology



Cardiovascular and Metabolic Diseases



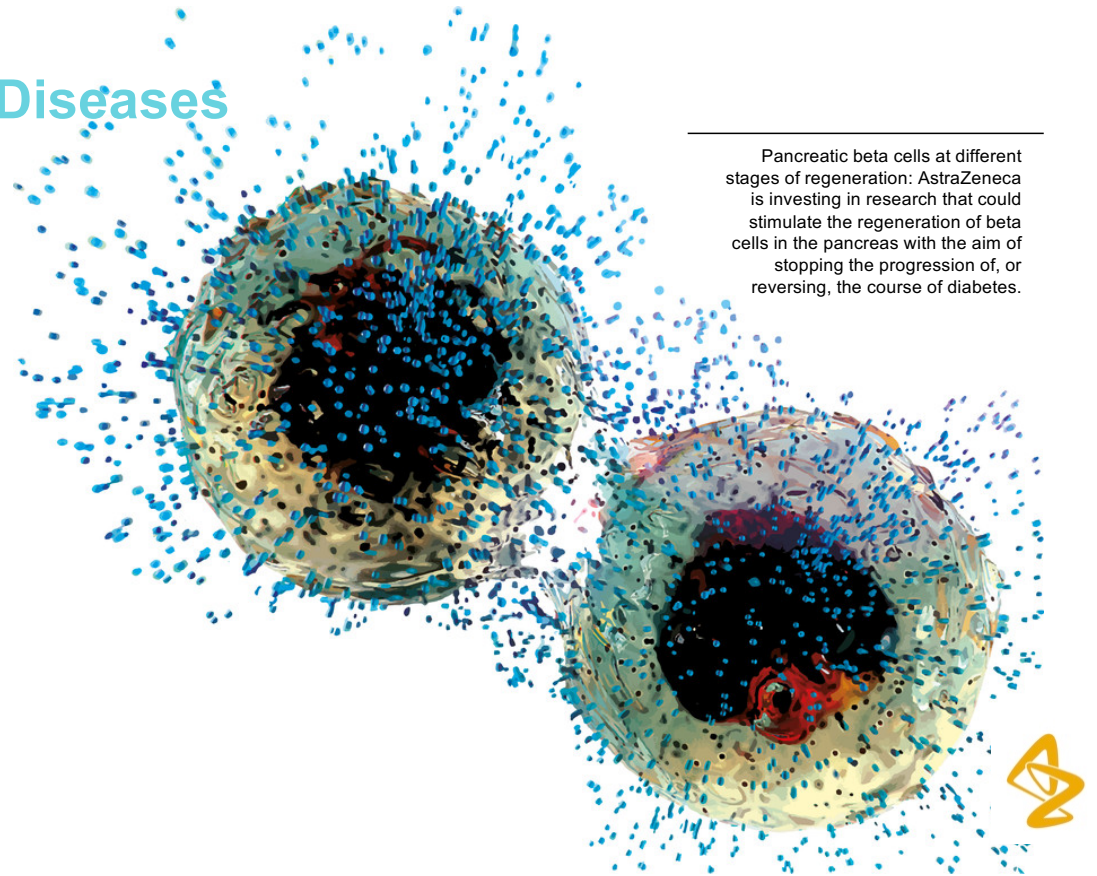
Respiratory



Other & news flow 2018-2019



Q&A



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

Updated epidemiology data

- First release of comprehensive company-compiled epidemiology data since 2014
- Contains current, best AstraZeneca estimates of patient numbers in major indications and countries relevant for key approved medicines and new potential medicines in development
- Spreadsheet format for easy use
- Available from astrazeneca.com/investors



Epidemiology: Internal estimates based on external market research, top eight countries (China, France, Germany, Italy, Japan, Spain, UK, US), 2017.



Late-stage pipeline news flow

Unprecedented activity level in '17

Forxiga type-2 diabetes Approval (CN)	Siliq psoriasis Approval (US, by partner)	benralizumab severe, uncontrolled asthma Regulatory submission (JP)	Imfinzi bladder cancer Approval (US)	Kyntheum psoriasis Approval (EU, by partner)	Lynparza ovarian cancer 2L, 4L/tablets Approval (US)	Symbicort COPD exacerbations Approval (US)	Imfinzi lung cancer (PACIFIC) Reg. submission (US, EU, JP)	Tagrisso lung cancer (FLAURA) Reg. submission (EU, JP)
Tagrisso lung cancer (AURA3) Full approval (US, EU)	Qtern type-2 diabetes Approval (US)	ZS-9 hyperkalaemia CHMP ¹ opinion (EU)	Faslodex breast cancer 1L Approval (EU, JP)	Bevespi COPD ² Reg. submission (EU)	Farxiga + Bydureon type-2 diabetes Approval (US, EU)	Calquence mantle cell lymphoma Approval (US)	roxadustat anaemia Completed reg. submission (CN, by partner)	Fasenra severe, uncontrolled asthma Approval (US)
Tagrisso lung cancer Approval (CN)	ZS-9 hyperkalaemia Complete Response (US)	Lynparza ovarian cancer 2L Reg. submission (EU, JP)	Lynparza breast cancer Reg. submission (US, JP)	Faslodex breast cancer Approval (US)	Bydureon BCise type-2 diabetes autoinjector Reg. submission (EU)	Brilique prior myocardial infarction Approval (CN)	Bydureon BCise type-2 diabetes autoinjector Approval (US)	Fasenra severe, uncontrolled asthma CHMP opinion (EU)

Regulatory actions

Significant patient benefits anticipated to support return to growth

Data & designations

Lynparza breast cancer Phase III positive	Farxiga type-2 diabetes CVD-REAL study	Imfinzi lung cancer (PACIFIC) Phase III positive (PFS ¹)	Tagrisso lung cancer (FLAURA) Phase III positive	tralokinumab severe, uncontrolled asthma Phase III negative	Farxiga type-1 diabetes Phase III positive	Duaklir COPD Phase III positive	Tagrisso lung cancer (FLAURA) Breakthrough Therapy Designation (US)
inebilizumab neuromyelitis optica spectrum disorder Orphan Drug (EU)	Lynparza ovarian cancer Orphan Drug designation (JP)	Bydureon type-2 diabetes (CVOT) Phase III met primary safety objective; did not meet primary efficacy objective	Imfinzi lung cancer (MYSTIC) Phase III negative (PFS)	Calquence mantle cell lymphoma Breakthrough Therapy Designation (US)	moxetumomab hairy cell leukaemia Phase III positive	tezepelumab severe, uncontrolled asthma Phase IIb positive	Imfinzi lung cancer (PACIFIC) Breakthrough Therapy Designation (US)

1. The Committee for Medicinal Products for Human Use.

2. Chronic obstructive pulmonary disease.

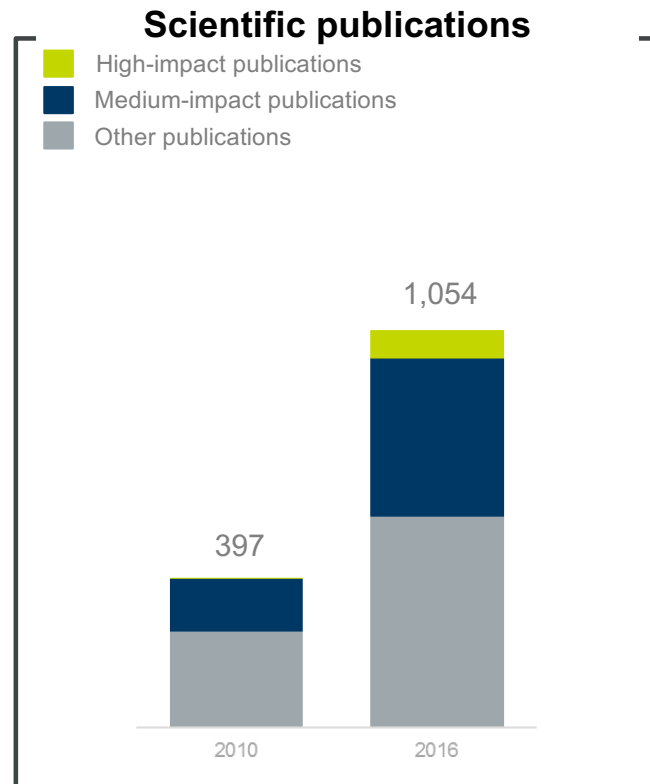
1. Progression-free survival.

Status as of 14 December 2017. **Favourable** / **unfavourable** news.

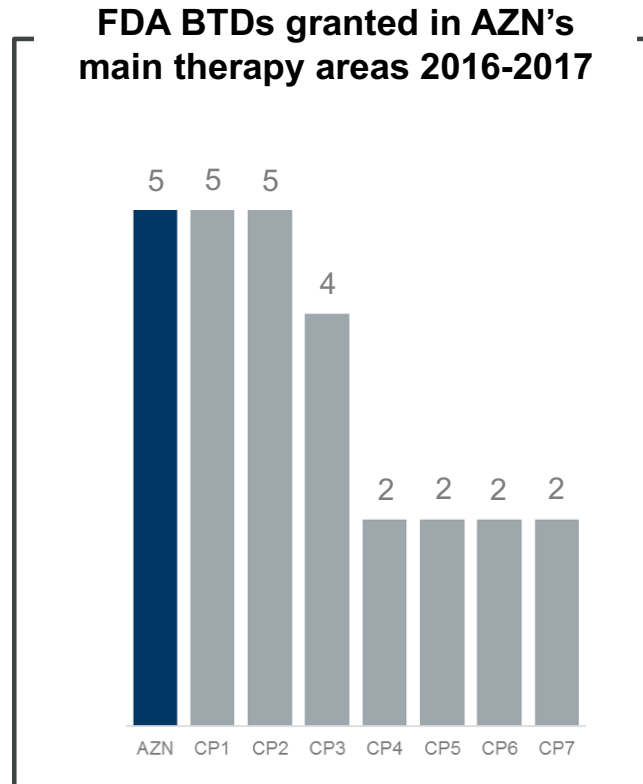


R&D productivity: Sustainable progress

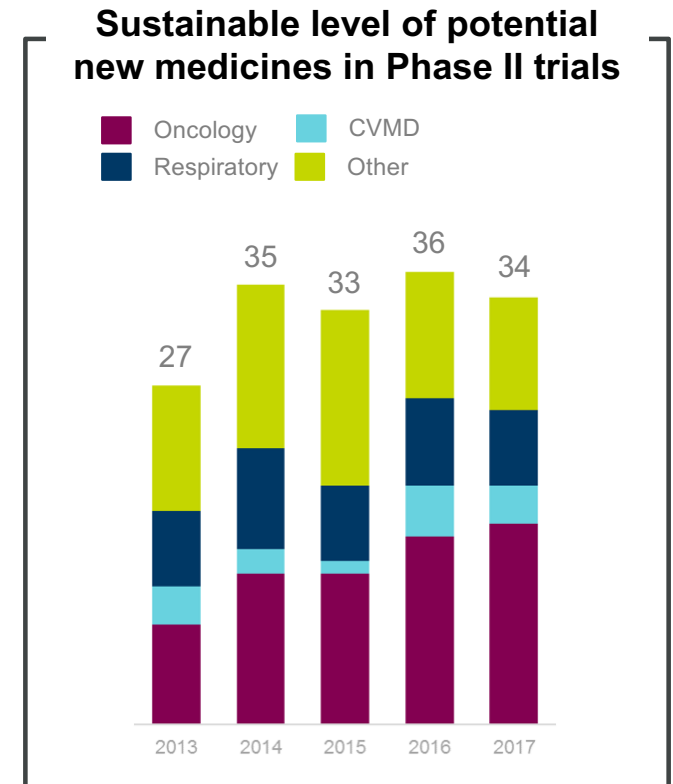
A new AstraZeneca with science-based culture



Source: Internal analysis. High-impact (rating > 15); medium-impact (rating > 5); other (rating < 5).



AstraZeneca (AZN) and industry peers/competitors (CP) 1-7.
Source: Internal analysis based on focr.org. Includes Breakthrough Therapy Designations (BTD) in the three main AstraZeneca therapy areas.



Late-stage pipeline and key lifecycle medicines

Significant opportunities exist in all three therapy areas

Oncology
Lynparza ^{1, 2} multiple cancers
Tagrisso ^{1, 2} lung cancer
Imfinzi ^{1, 2} multiple cancers
Calquence ¹ blood cancers
Imfinzi + treme multiple cancers
moxetumomab leukaemia
selumetinib thyroid cancer
savolitinib kidney cancer

Cardiovascular and Metabolic Diseases
ZS-9 ² hyperkalaemia
roxadustat ² anaemia

Other
anifrolumab lupus
lanabecestat Alzheimer's disease

Respiratory
Fasenra ¹ severe, uncontrolled asthma ² / COPD
PT010 COPD / asthma
tezepelumab severe, uncontrolled asthma

1. Lifecycle development programme.
2. Under regulatory review in major jurisdiction.
Status as of 14 December 2017.



Agenda



Oncology



Cardiovascular and Metabolic Diseases



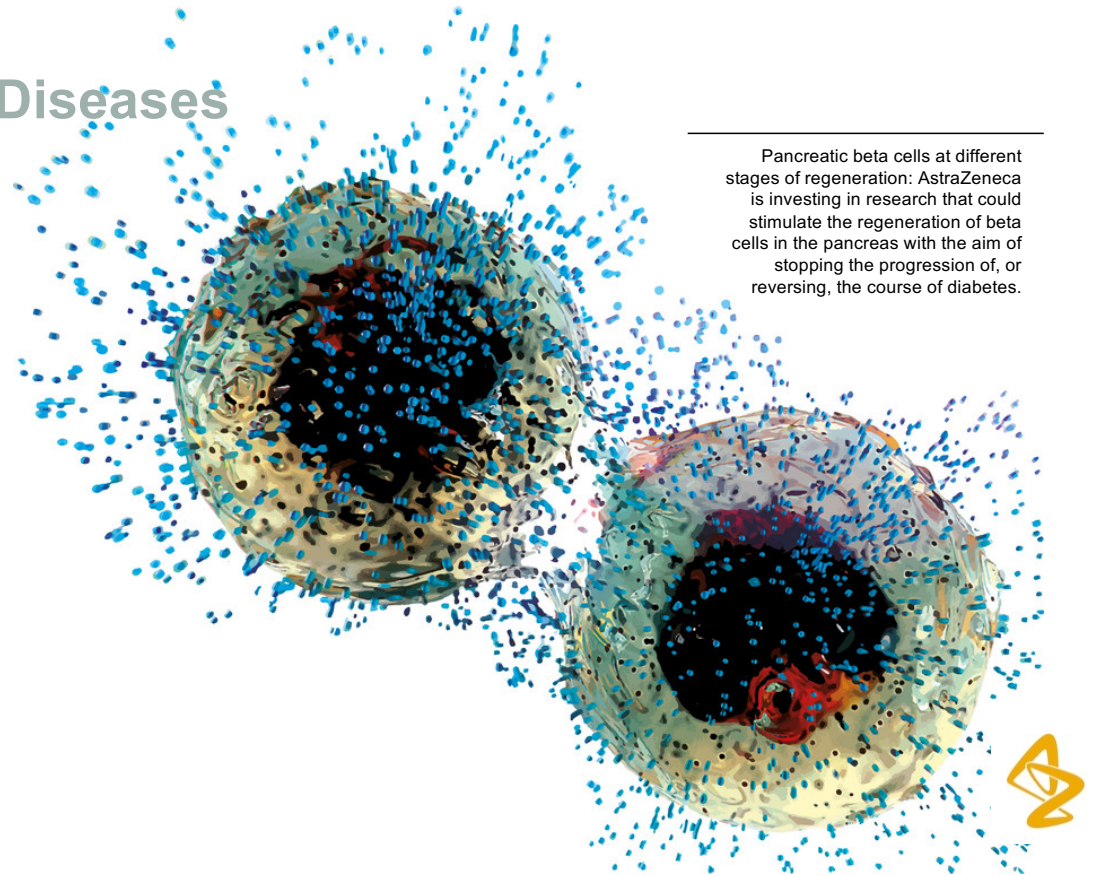
Respiratory



Other & news flow 2018-2019



Q&A







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

Oncology

Strategic priorities support the return to growth



Multiple cancers	Lung cancers		Blood cancers
			
<ul style="list-style-type: none"> • Ovarian and breast cancers • Lifecycle programme (2018+), incl. prostate cancer • Merck collaboration 	<ul style="list-style-type: none"> • 2nd line / T790Mm¹ • 1st line / EGFRm² • Adjuvant EGFRm (2022+) 	<ul style="list-style-type: none"> • Locally-advanced/Stage III, unresectable NSCLC³ • Lifecycle programme (2018+) 	<ul style="list-style-type: none"> • First AstraZeneca medicine in blood cancer • MCL⁴ initial indication • Lifecycle programme (2019+)

Rich and early pipeline, including combinations

1. Substitution of threonine (T) with methionine (M) at position 790 of exon 20 mutation.
2. Epidermal growth factor receptor mutation.
3. Non-small cell lung cancer.
4. Mantle cell lymphoma.
- () First / next data anticipated.



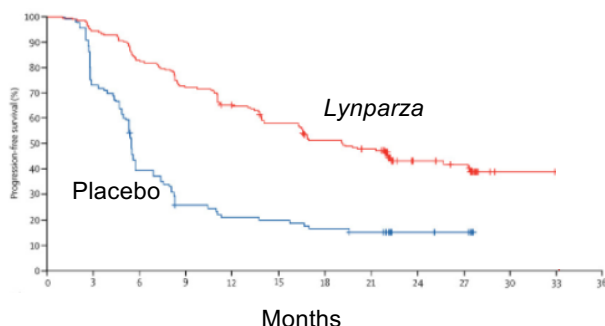
Lynparza

The PARP inhibitor with Phase III data in ovarian and breast cancer



Impressive patient benefit in ovarian cancer...

SOLO-2 trial in 2nd-line BRCAm¹ ovarian cancer
Investigator-assessed PFS
(HR 0.30; 95% confidence interval (CI) 0.22-0.41, p=0.0001)

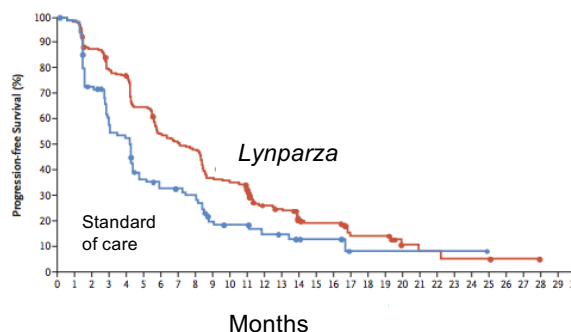


~25k

2nd line platinum-sensitive recurrent ovarian cancer patients

...and impressive patient benefit in breast cancer

OlympiAD trial in 1st to 3rd-line breast cancer
BICR²-assessed PFS
(HR 0.58; CI 0.43-0.80, p=0.0009)



5-10%

breast cancer patients with BRCA mutation

Regulatory status

Ovarian cancer

- US: Approved 2nd line (broad label), 4th line/tablets
- Europe: Approved; SOLO-2 trial/tablets under review
- JP: SOLO-2, other data under review for first approval
- CN: SOLO-2 under review for first approval

Breast cancer (gBRCA)

- US: Under review
- EU: Regulatory submission in H1 2018
- JP: Under review

AstraZeneca

MERCK
INVENTING FOR LIFE

Source: Pujade-Lauraine, et al., The Lancet Oncology, 2017.
Epidemiology: Internal estimates based on external market research, top eight countries.

Source: Robson, et al., The New England Journal of Medicine, 2017.
Epidemiology: Internal estimates based on external market research, top eight countries.

1. Breast cancer susceptibility gene 1/2 mutation.
2. Blinded independent central review.

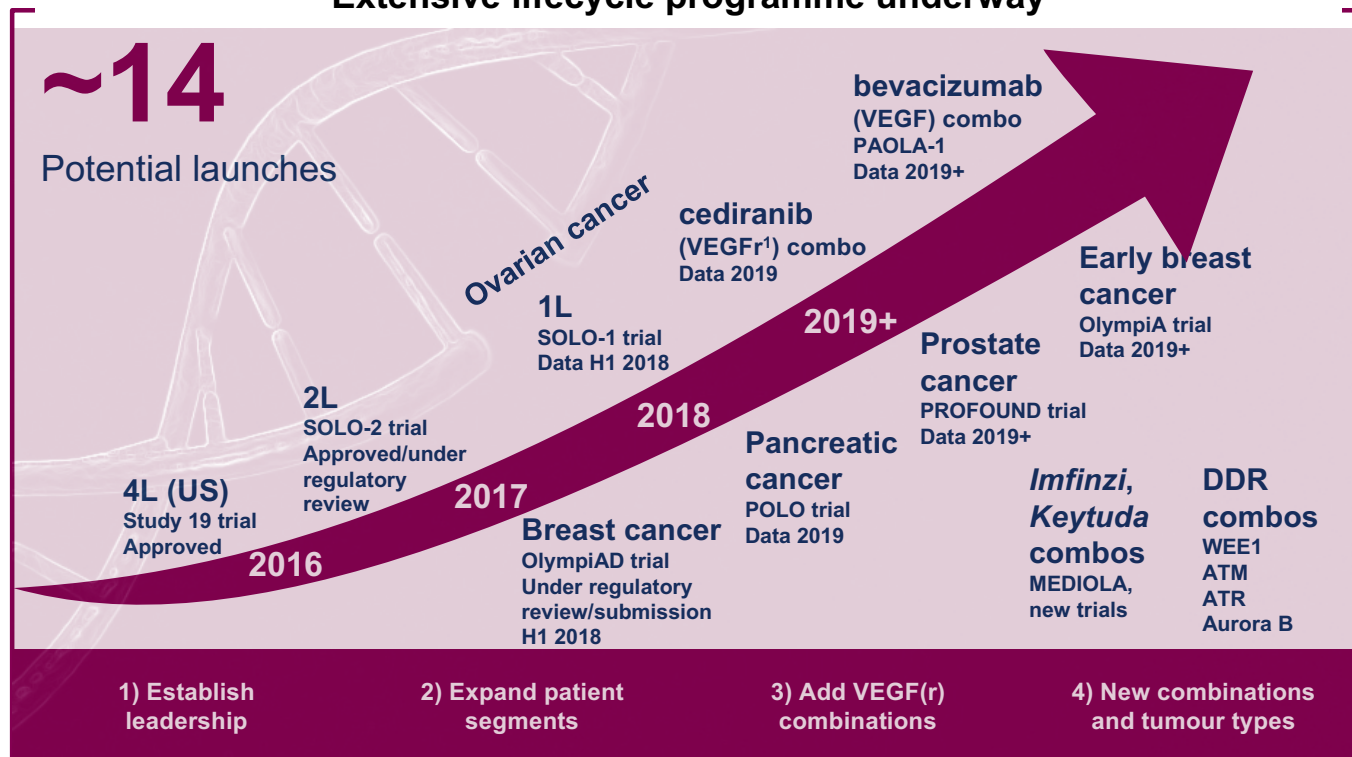


Lynparza

Significant opportunity to further expand through Merck collaboration



Extensive lifecycle programme underway



Status of Merck collaboration

- Collaboration infrastructure set up and agreed
- Joint steering committee and subteams created
- Agreed development plans
- More new trials expected to be announced in H1 2018

AstraZeneca



1. Vascular endothelial growth factor (receptor).

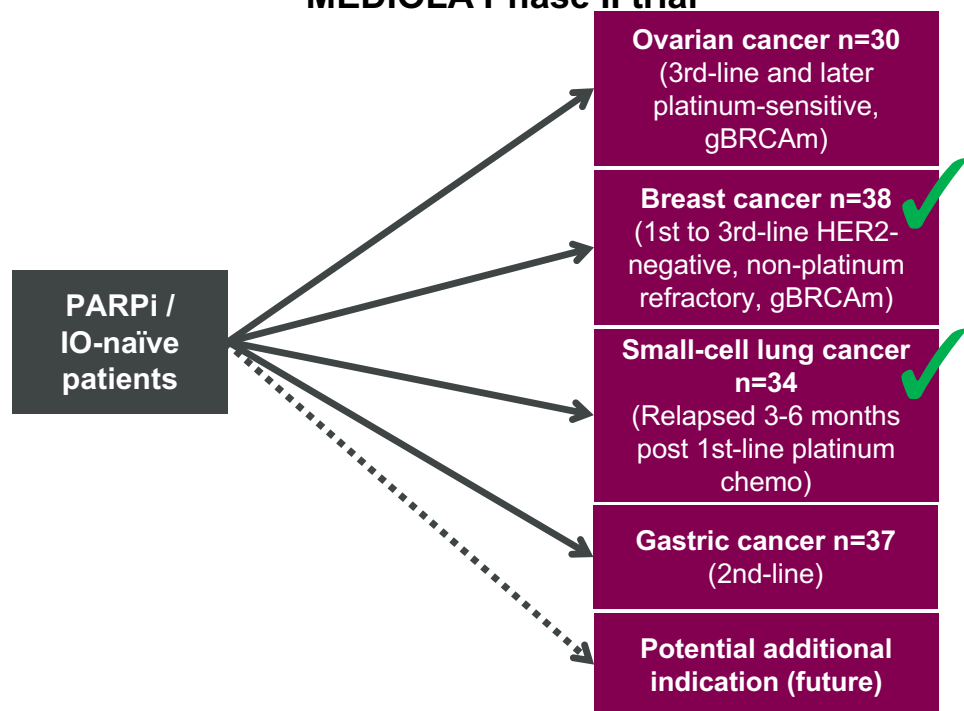


Lynparza

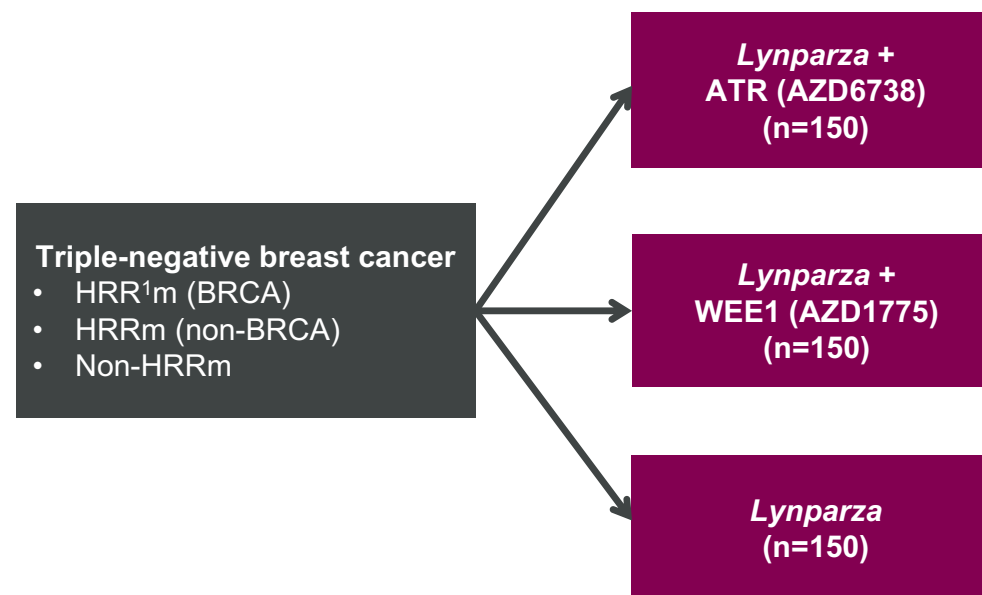
Next-generation combinations underway



Lynparza + Imfinzi MEDIOLA Phase II trial



Lynparza + novel DDR VIOLETTE Phase II trial



1. Homologous recombination repair.

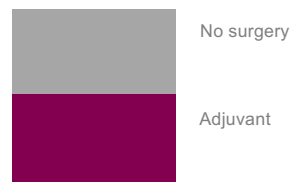


Lung cancer: *Tagrisso* and *Imfinzi*

Early-stage disease

Stage I-III
Total 155k patients

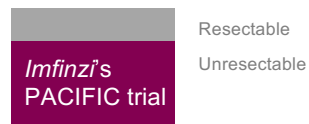
Tagrisso's
ADAURA trial
Imfinzi's
ADJUVANT trial



80k

adjuvant
patients

Stage III
Total 105k patients

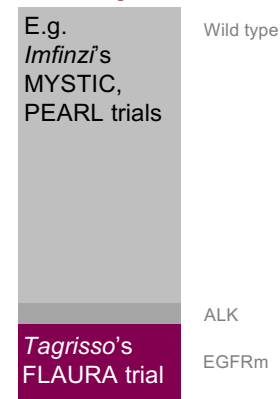


76k

unresectable
patients

Late-stage disease

Stage IV 1st line
Total 370k patients



70k

1L EGFRm
patients

Stage IV 2nd line
Total 250k patients



25k

2L T790M EGFRm
patients

Treated patients. Epidemiology: Internal estimates based on external market research, top eight countries, China generally includes a market-access adjustment.



Lung cancer: *Tagrisso*

Potential to transform EGFR-mutated lung cancer

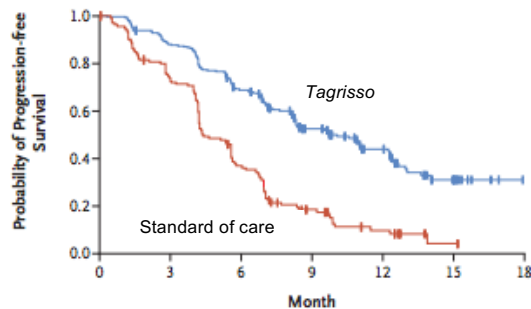


Establish in 2nd line

~10 months

Progression-free survival

AURA3 trial in 2nd-line T790M NSCLC
(HR 0.30; CI 0.23-0.41, p=0.001)



'New standard of care for EGFR T790M-positive NSCLC patients'

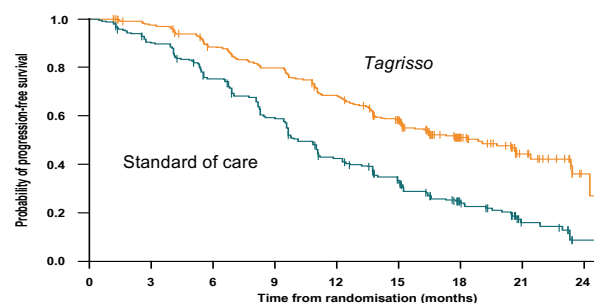
Approved US, EU, JP, CN, others

Expand to 1st line

~19 months

Progression-free survival

FLAURA trial in 1st-line EGFRm NSCLC
(HR 0.46; 0.37-0.57, p=0.0001)



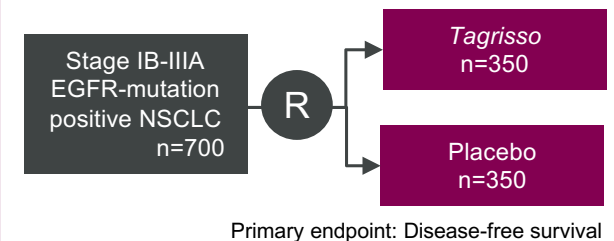
'Potential new standard of care for EGFR-mutated NSCLC patients'

Regulatory submissions EU, JP

Extend to adjuvant

Up to 3 years

Treatment duration



'Potential backbone for all EGFR-mutated patients (ADAURA trial)'

Phase III data anticipated in 2022

Source: Mok, et al., The New England Journal of Medicine, 2017.

Source: Soria, et al., The New England Journal of Medicine, 2017.

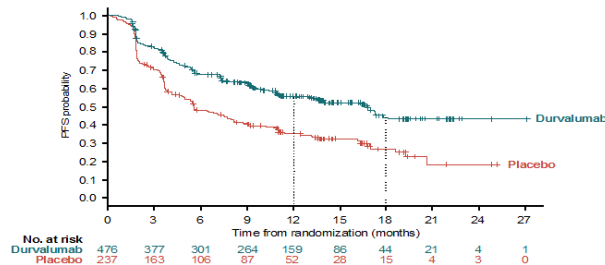


Lung cancer: *Imfinzi*

Durable advantage in Stage III, unresectable NSCLC



PACIFIC PFS by BICR (Intention-to-treat population)



Stratified hazard ratio, 0.52 (95% CI, 0.42–0.65)
Two-sided $P < 0.0001$

	Durvalumab (N=476)	Placebo (N=237)
Median PFS (95% CI), months	16.8 (13.0–18.1)	5.6 (4.6–7.8)
12-month PFS rate (95% CI)	55.9% (51.0–60.4)	35.3% (29.0–41.7)
18-month PFS rate (95% CI)	44.2% (37.7–50.5)	27.0% (19.9–34.5)

PACIFIC regulatory status

Eight

Regulatory submissions¹

Regulatory decisions anticipated in 2018

- H1: US (Priority review)
- H2: EU, JP, others



Imfinzi is not approved for lung cancer use yet.

Lifecycle programme already well underway

- PACIFIC
 - Final OS data in 2019
- IDO combination
 - *Imfinzi* with epacadostat (IDO1 inhibitor)
- Other lifecycle opportunities being evaluated

Significant potential to expand further on Stage III opportunity

Source: Antonia, et al., The New England Journal of Medicine, 2017.

1. Australia, Brazil, Canada, EU, Japan, South Korea, Switzerland, US.



Lung cancer: Trials in non-small cell lung cancer

Overview of medicines in current and ongoing Phase IIIs



Patients with no EGFR-mutated or ALK-translocated tumours
~75-80% of patients

 *Imfinzi* + treme
 *Imfinzi*

ADJUVANT
(2020)

PACIFIC¹ ✓
(2019 final OS)

PEARL
(2020)
POSEIDON CTx
(2019)
NEPTUNE
(H2 2018)
MYSTIC
(H1 2018 final OS)

ARCTIC
(H1 2018)

Patients with EGFR-mutated tumours
~15-20% of patients, but double in Asia

Tagrisso
ADAURA (2022)

Iressa ✓
IPASS / IFUM, etc. ✓
Tagrisso ✓
FLAURA

Tagrisso ✓
AURA 3 [T790Mm]

Stage / progression of disease

Stage I-IIIa
Stage III
Stage I-III [early / non-metastatic]

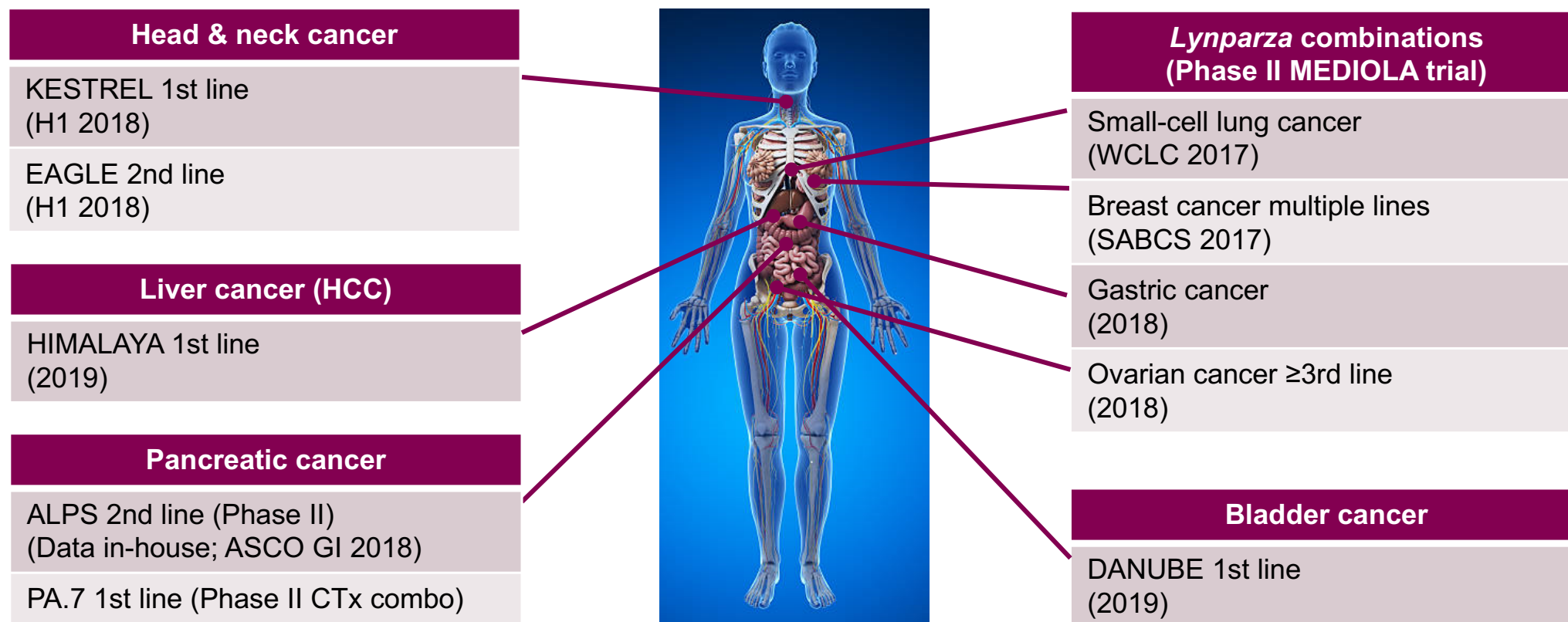
1st line
2nd/3rd line
Stage IV [metastatic]

1. PACIFIC trial also included patients with EGFR and T790M-mutated and anaplastic lymphoma kinase (ALK)-translocated tumours.
() First / next data anticipated.



Imfinzi beyond NSCLC

Prioritising opportunities in select cancers with unmet need



() First / next data anticipated.

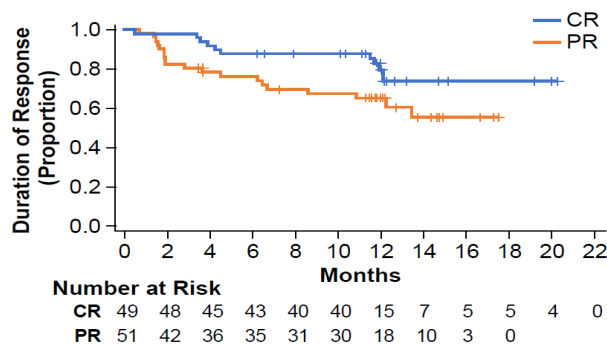


Calquence

AstraZeneca's entry into blood-cancer treatment



Best-in-class BTK inhibitor in MCL



Median duration of response (DoR) was not reached; the 12-month DoR rate was 72% (95% CI: 62%, 80%)

~3k

annual US diagnoses of MCL

Calquence (acalabrutinib) US-approved in MCL

- For adults with previously-treated mantle cell lymphoma



40%

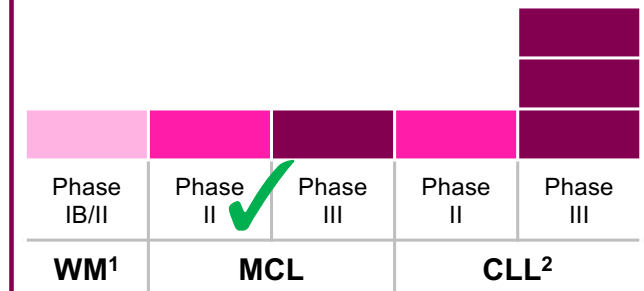
complete response rate

80%

objective response rate

Upcoming news flow in haematology

CLL randomised Phase III data in 2019



21

clinical trials

>2,500

patients in clinical trials

Source: ASH 2017, abstract 155.

Source: US prescribing information.

1. Waldenström macroglobulinemia; a type of non-Hodgkin lymphoma.
2. Chronic lymphocytic leukaemia.



Agenda



Oncology



Cardiovascular and Metabolic Diseases



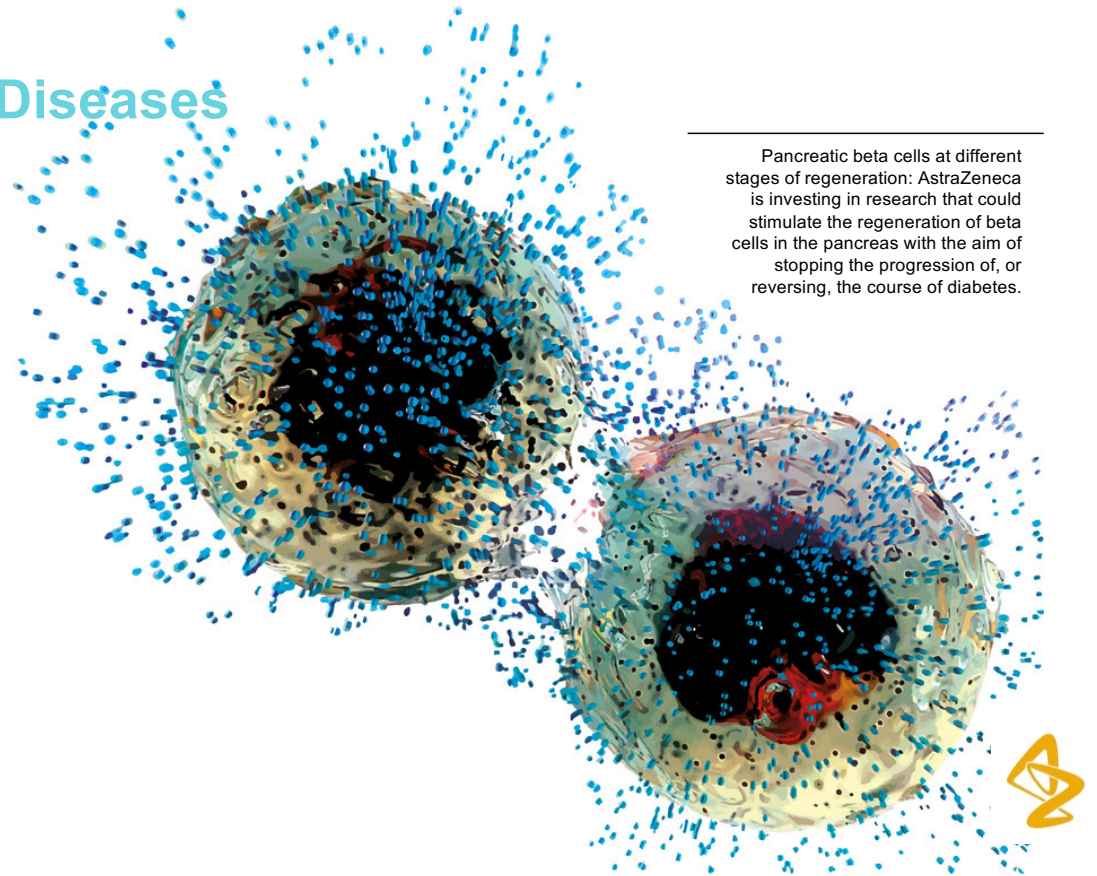
Respiratory



Other & news flow 2018-2019

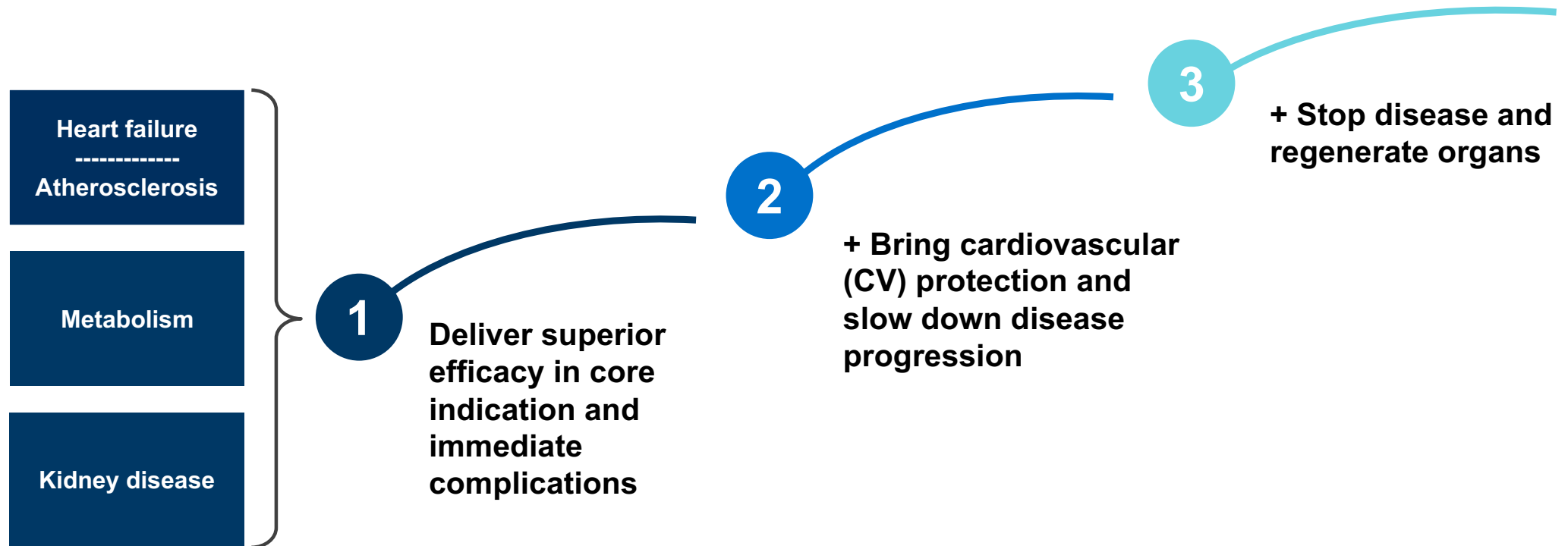


Q&A



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

CVMD: Changing clinical practice today, and pushing the boundaries of science tomorrow



Opportunities outside acute coronary syndrome



THEMIS

T2DM¹ with established CAD²

Patients >50 years + drug treated for T2DM + high risk for CV events

Brilinta
60mg BID

Primary endpoint:
Prevention of major CV events

Placebo

Safety endpoint:
Time to first TIMI major bleeding event

Status

THEMIS

- 19,200 patients with type-2 diabetes
- Enrolment completed in 2016
- Data readout in 2019



THALES

Stroke



Brilinta 90mg +
ASA³

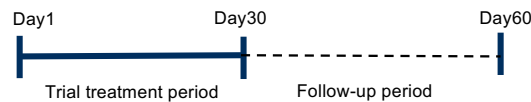
Standard of care

Primary endpoint:
Stroke + death

Placebo + ASA

Standard of care

Secondary endpoint:
IS³, disability (mRS⁴)



THALES

- 2nd trial in stroke, initiating
- 13,000 patients
- Data readout anticipated in 2020

1. Type-2 diabetes mellitus.

2. Coronary artery disease.

3. Ischemic stroke.

4. Modified Rankin scale measuring disability of neurological patients.





Focus on establishing CV benefit in type-2 diabetes

CVD-REAL

Real-world observational study

SGLT2 inhibitors vs other glucose-lowering medicines

51%

reduction in all-cause mortality

39%

reduction in risk of hospitalisation for heart failure

46%

risk of composite endpoint of hospitalisation for heart failure and death from any cause

Database	N	# of events	HR (95% CI)
US	143,264	424	0.44 (0.36, 0.54)
Norway	25,050	622	0.58 (0.50, 0.69)
Denmark	18,468	477	0.57 (0.48, 0.67)
Sweden	18,378	364	0.50 (0.41, 0.63)
UK	10,462	96	0.66 (0.44, 1.00)
Total	215,622	1983	0.54 (0.48, 0.60)

Hazard Ratio: 0.25 0.50 1.00 2.00

Favor SGLT2i ← → Favor oGLD

DECLARE Phase III trial

- Primary efficacy endpoints
 - Superiority for MACE (CV death, non-fatal myocardial infarction or non-fatal stroke)
 - Superiority for the composite endpoint of CV death or hospitalisation for heart failure
- Primary safety endpoint
 - Non-inferiority for MACE
- Data anticipated in H2 2018

~17,000 patients

including patients with multiple CV risk factors (~10,000) or established CVD (~7,000)

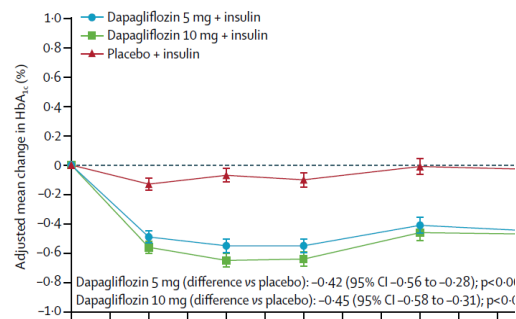




DEPICT-1

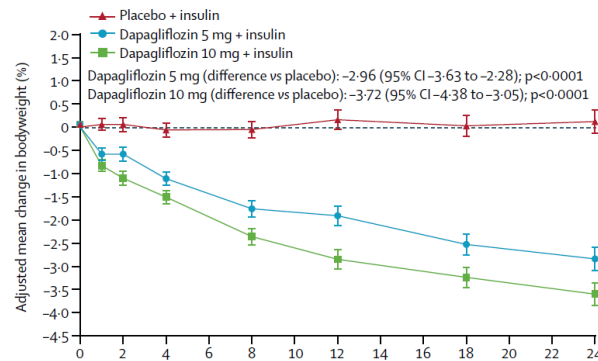
Change in HbA1c and bodyweight over 24 weeks

HbA1c reduction



Patients per timepoint	0	4	8	12	18	24
Dapagliflozin 5 mg + insulin	254	252	246	238	233	
Dapagliflozin 10 mg + insulin	254	249	251	247	241	
Placebo + insulin	257	256	248	237	233	

Bodyweight reduction



Patients per timepoint	0	4	8	12	18	24
Dapagliflozin 5 mg + insulin	259	259	255	250	249	243
Dapagliflozin 10 mg + insulin	258	257	246	254	251	249
Placebo + insulin	260	260	251	256	251	240

DEPICT Phase III programme

DEPICT-1

- HbA1c reduction at 24 weeks of 0.42-0.45% across two doses¹
- Daily insulin dose reduction 8.8-13.2%
- Weight loss of 2.96-3.72%

DEPICT-2

- Data being analysed; presentation anticipated in 2018

Potential for regulatory submission in 2018

Source: Source: Dandona P, Mathieu C, Phillip M, et al., Lancet Diabetes and Endocrinology, 2017.

1. DEPICT-1 tested *Farxiga* at 5mg and 10mg doses.



Farxiga



Extending the science into heart failure and chronic kidney disease

38 million

patients worldwide live with heart failure (HF)

200 million

patients worldwide live with chronic kidney disease (CKD)

422 million

patients worldwide live with diabetes (the majority with type-2 diabetes)¹⁻³

A large proportion of patients with type-2 diabetes have CKD and many have HF, or both.⁴ The prevalence of CKD, HF and type-2 diabetes continues to rise as populations age and associated risk factors, such as obesity, increase^{1-3,5}



- Evaluates *Farxiga* on the incidence of worsening **heart failure** or CV death in patients with chronic heart failure and reduced ejection fraction

- Anticipated data readout in 2019

~4,500
patients



- Evaluates *Farxiga* on **renal outcomes** and CV mortality in patients with CKD

- Anticipated data readout in 2020

~4,000
patients

1. Ojo A, et al., Transactions of the American Clinical and Climatological Association, 2014.
2. Braunwald E., The Lancet, 2015. 3. WHO, Global report on diabetes.
4. Suckling R, et al., Journal of Renal Care, 2012. 5. Bertoni AG, et al., Diabetes Care, 2004.



Bydureon

BCise and DURATION-7/8



Bydureon BCise autoinjector

- New, easy-to-use, once weekly medicine for type-2 diabetes
- Up to 1.4% HbA1c reduction; up to 3.1lbs weight loss
- Regulatory status
 - US: Approved
 - EU: Under review

Once-weekly
BYDUREON® BCise™
exenatide extended-release
injectable suspension



DURATION-7/8 Phase III trials

DURATION-7 (insulin + *Bydureon*)

- 25.1% of patients achieved target HbA1C levels. Lower fasting glucose levels and reduced body weight (1.5kg) benefits were also observed
- EU approved

DURATION-8 (*Farxiga* + *Bydureon*)

- *Farxiga* and *Bydureon* combo (on a background of metformin) in high-baseline HbA1c patients with inadequate glycemic control
- Reduction of HbA1c (2.0%), lower systemic blood pressure (4.3mm Hg) and weight loss (3.55kg) at 28 weeks
- US and EU approved

Source: US prescribing information.

Source: DURATION-8: Lancet Diabetes & Endocrinology. DURATION-7 not published yet.



ZS-9 (sodium zirconium cyclosilicate)

Potential best-in-class treatment for hyperkalaemia



Disease burden and unmet medical need

40-50%

patients with CKD have hyperkalaemia¹

~30%

mortality rate for hospitalised patients with severe hyperkalaemia if not treated rapidly²



Differentiated medicine and regulatory status

Properties

- 5-10g once daily; odourless/tasteless
- Non-systemically absorbed
- One-hour onset of action
- Long-term stability at room temperature
- No significant drug-drug interaction

Regulatory status

- EU CHMP positive opinion
- Significant progress made in addressing all manufacturing deficiencies identified by US FDA
- Anticipate further news in due course

1. National Kidney Foundation, Clinical Update on Hyperkalaemia, 2014.

2. An JN, Lee JP, Jeon HJ, et al., Severe hyperkalemia requiring hospitalization: Predictors of mortality. Critical Care, 2012.








Roxadustat

Potential first-in-class oral HIF-PHD inhibitor for anaemia of CKD



Phase III programme

Patient population	Company	Phase III trial
Anaemia in CKD patients not receiving dialysis	FIBROGEN	ANDES
	AstraZeneca 	OLYMPUS
	 astellas	ALPS
	 astellas	DOLOMITES
Anaemia in CKD in patients receiving dialysis	FIBROGEN	SIERRAS
	AstraZeneca 	ROCKIES
	 astellas	PYRENEES
Anaemia in newly-initiated dialysis patients	FIBROGEN	HIMALYAS

Targeting a competitive medicine profile

Non-dialysis patients (against placebo)

- Superior haemoglobin increase
- Non-inferior on major adverse CV events (MACE) based on pooled analysis¹

Dialysis patients (against erythropoietin)

- Non-inferior haemoglobin increase
- Non-inferior, potentially superior MACE; pooled analysis¹

Regulatory status

- China rolling regulatory submission completed
- US regulatory submission anticipated in H2 2018

Lifecycle programme started

- Phase III in anaemia of myelodysplastic syndrome

1. The MACE endpoint is event-driven.
In partnership with Fibrogen and their collaborator Astellas.



Agenda



Oncology



Cardiovascular and Metabolic Diseases



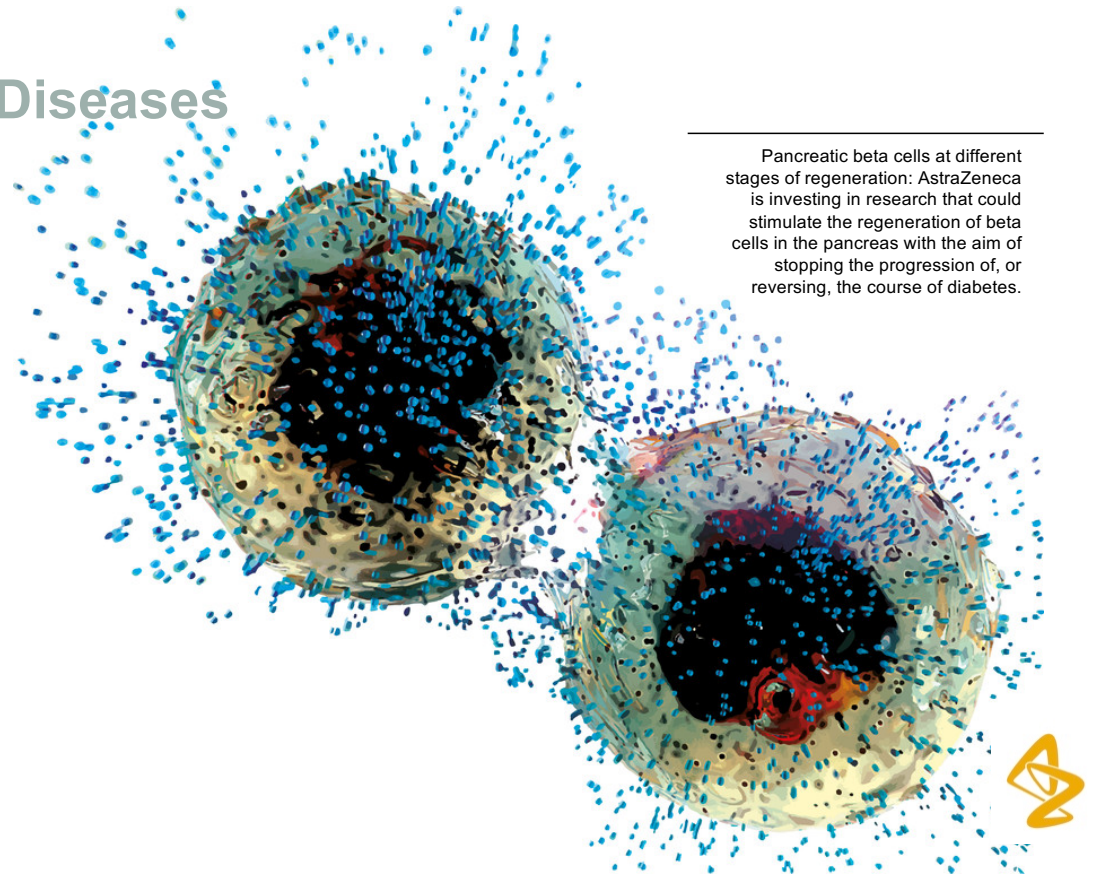
Respiratory



Other & news flow 2018-2019



Q&A



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

COPD



A common, preventable and treatable disease characterised by persistent respiratory symptoms and airflow limitation

~330 million

patients worldwide affected by COPD

3 million

deaths from COPD annually

3rd

predicted to be the third-leading cause of death by 2020

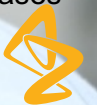
\$32 billion

in the US, COPD accounts for \$32bn of direct cost and \$20bn in indirect costs

56%

in the EU, COPD accounts for 56% of the €39 billion cost of respiratory diseases

Source: AstraZeneca data and Global Initiative for Chronic Obstructive Lung Disease.



COPD

Bevespi and PT010 next-generation inhaled medicines



Next-generation technology

AEROSPHERE™
DELIVERY TECHNOLOGY



Co-suspension formulation technology



Delivers consistently to the whole lung



>2x lung deposition, 75% increase in airway volume, 71% reduction in airway resistance

Bevespi Aerosphere Dual bronchodilator

- First medicine using Aerosphere and delivered in a pressurised metered-dose inhaler (pMDI)

Regulatory status

- EU: Under review; regulatory decision anticipated in H2 2018
- JP, CN: Regulatory submission in H1 2018



PT010

Dual bronchodilator plus ICS¹

Phase III programme underway

- First data readout anticipated in H1 2018

Regulatory plans

- First regulatory submission anticipated in H2 2018



1. Inhaled corticosteroids.



Asthma

Expanding to encompass more treatment guideline steps



~315 million

patients suffer from asthma worldwide

1 in 10 patients

with asthma have severe asthma, requiring high-dose ICS-based therapy plus other asthma medicines

					Step 5
	Step 1	Step 2	Step 3	Step 4	
Preferred controller choice		Low-dose ICS	Low-dose ICS/LABA**	Med/high ICS/LABA	Refer for add-on treatment e.g. novel biologics
Other options	Consider low-dose ICS	Leukotriene receptor antagonist (LTRA) Low-dose theophylline	Med/high ICS Low-dose ICS + LTRA (or +theoph)	Add tiotropium High-dose ICS + LTRA (or +theoph)	Add low-dose OCS
Reliever	As-needed short-acting beta ₂ -agonist (SABA)			As-needed SABA or low-dose ICS/formoterol	

Source: Global Initiative For Asthma (GINA), Global strategy for asthma management and prevention, <http://ginasthma.org>.



Asthma: *Fasenra*

Targeted, anti-eosinophil medicine; recently launched in the US



***Fasenra* (benralizumab) received US FDA approval for severe eosinophilic asthma¹**

51%²

reduction in the annual asthma exacerbation rate versus placebo

159mL³

Significant improvement in lung function as measured by forced expiratory volume in one second (FEV₁) versus placebo

75%⁵

median reduction in daily OCS⁴ use and discontinuation of OCS use in 52% of eligible patients



Under regulatory review in the EU, Japan and several other countries with decisions anticipated in H1 2018

Lifecycle programme

Asthma

- Autoinjector; GRECO Phase III trial readout anticipated in H2 2018

COPD

- Phase III VOYAGER programme is evaluating the efficacy and safety of *Fasenra* in patients with severe COPD
- Data readout anticipated in H2 2018

¹ Based on the results from the Phase III trials SIROCCO, CALIMA and ZONDA. ² SIROCCO: 51% reduction in AER vs. placebo at week 48 (.74 vs 1.52). CALIMA: 28% reduction vs. placebo at week 56 (.73 vs 1.01). ³ SIROCCO: At 48 weeks, an improvement in FEV₁ of 398mL (mean change from baseline) vs. 239mL for placebo, total of 159mL increase in FEV₁. CALIMA: At 56 weeks, an improvement in FEV₁ of 330mL (mean change from baseline) vs. 215mL for placebo, for total of 116mL increase in FEV₁. ⁴ Oral corticoid steroid. ⁵ Median reduction in OCS dose of 75% from baseline vs. 25% for placebo.
Source: US prescribing information.



Asthma: Tezepelumab

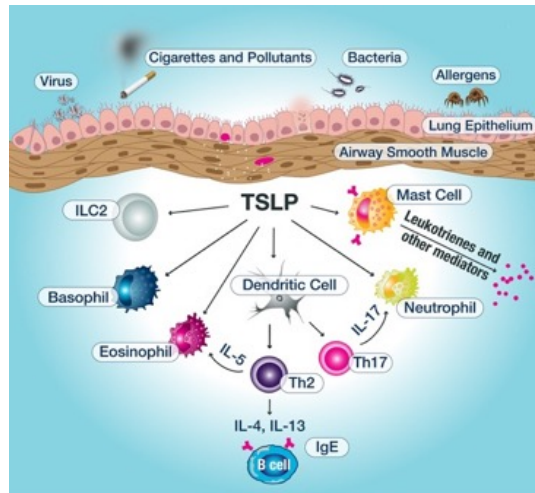
Significantly reduced asthma exacerbations for a broad population



Functions of thymic stromal lymphopoietin (TSLP)

- Epithelial-derived cytokine central to the regulation of type 2 immunity¹⁻⁴
- Expression is increased in the airways of patients with asthma, and correlates with Th2 cytokine and chemokine expression, and disease severity⁵⁻⁷
- Tezepelumab (AMG 157/MEDI9929) is a human IgG2 monoclonal antibody and potential new medicine that binds to TSLP, inhibiting its interaction with the TSLP receptor complex⁸

First-in-class treatment that blocks TSLP - an upstream driver of inflammation in asthma



Late-stage development

Phase IIb PATHWAY trial positive

- Presented at European Respiratory Society 2017 and results published in the New England Journal of Medicine
- Potential to help a broad group of patients; including those without presence of a Th2 biomarker

Phase III PATHFINDER programme

- First Phase III trial NAVIGATOR has initiated with a patient enrolled

1. Ziegler and Artis, Nature Immunology, 2010. 2. Soumelis, et al., Nature Immunology, 2002. 3. Allakhverdi, et al., Journal of Experimental Medicine, 2007. 4. Ziegler, et al., Advances in Pharmacology, 2013. 5. Shikotra, et al., Journal of Allergy and Clinical Immunology, 2012. 6. Ying, et al., The Journal of Immunology, 2005. 7. Ying, O'Connor B, et al., The Journal of Immunology, 2008. 8. Gauvreau GM, et al., The New England Journal of Medicine, 2014. Full references available upon request.



Agenda



Oncology



Cardiovascular and Metabolic Diseases



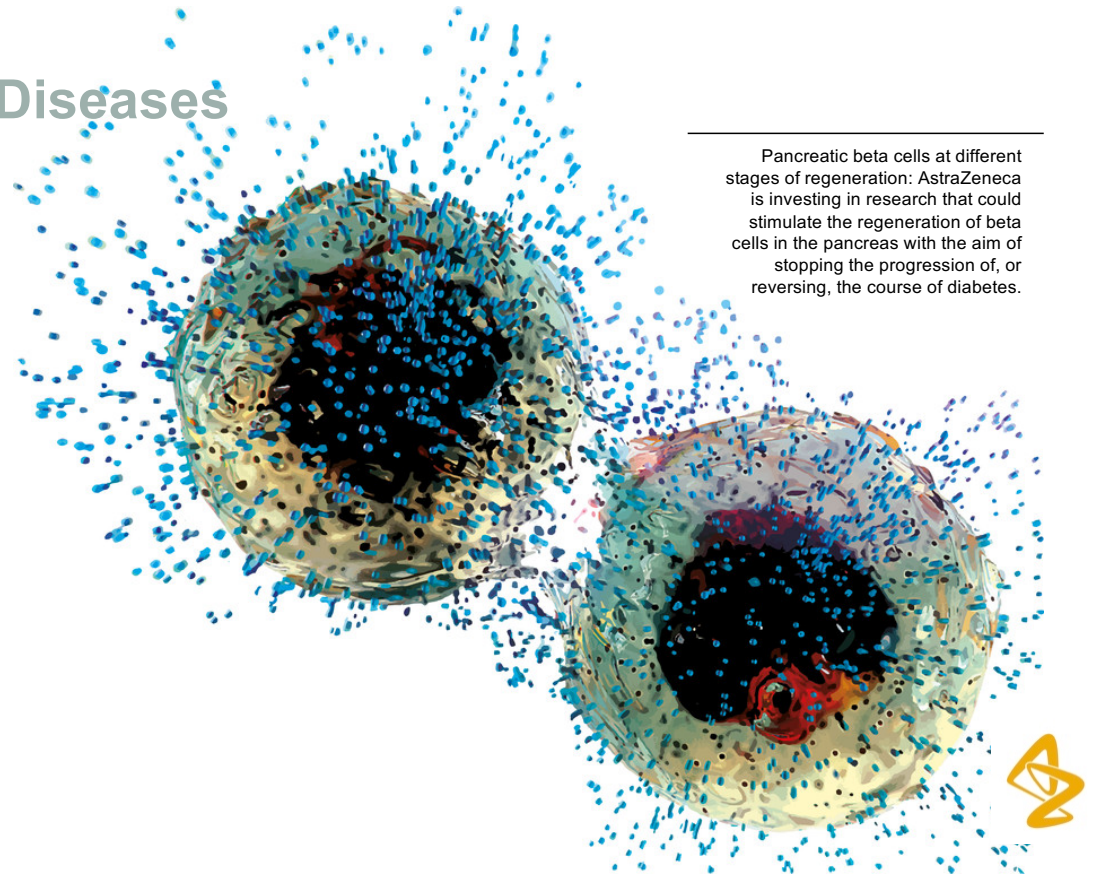
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Other & news flow 2018-2019



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Anifrolumab

Lupus Phase III on track for H2 2018



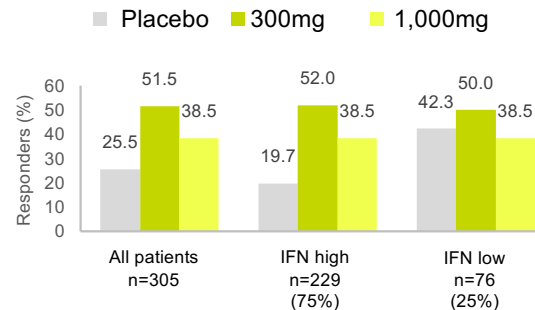
Large unmet patient need

Prevalence
SLE
(~615k)

Prevalence
SLE
extra-renal
(~480k)

Treated
moderate-
severe
(~265k)

Systemic Lupus Erythematosus (SLE) Responder Index 4 including OCS taper at day 365



	300mg	1,000mg	300mg	1,000mg	300mg	1,000mg
Delta	26.0%	13.0%	32.3%	18.8%	7.7%	-3.8%
OR ¹	3.08	1.84	4.3	2.52	1.47	0.89
90% CI	(1.86; 5.09)	(1.11; 3.04)	(2.34; 7.91)	(1.37; 4.64)	(0.55; 3.93)	(0.3; 2.35)
P	<0.001	0.048	<0.001	0.013	0.514	0.849

Phase III SLE programme now fully recruited

- Phase III trials TULIP 1 and TULIP 2 both fully recruited
- Primary endpoints at 48 weeks driving data-readout timelines

Lifecycle programme

- Phase II subcutaneous administration trial fully recruited
- Phase II lupus nephritis trial ongoing

Phase III data in H2 2018
Regulatory submission in 2019

Epidemiology: Internal estimates based on external market research, top eight countries.

1. Odds Ratio.
Source: Furie R, et al., Arthritis & Rheumatology, 2016.

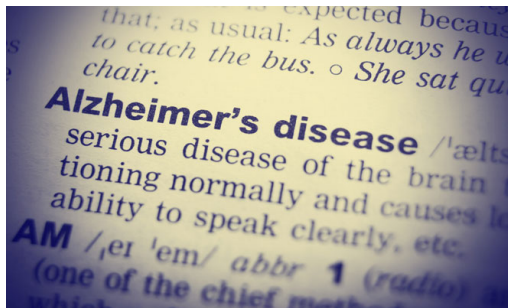


Lanabecestat



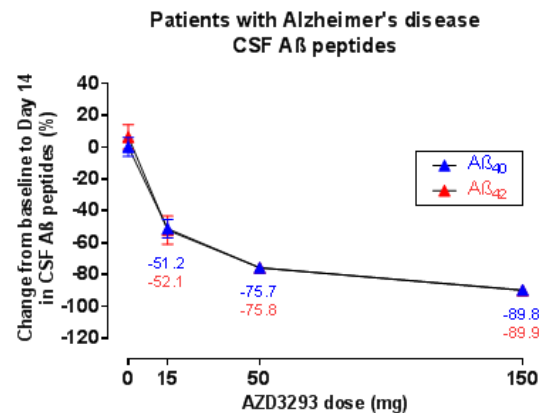
Alzheimer's disease programme and valuable partnership on track

Unmet need not addressed by any effective medicines



- 60%-80% of dementia cases
- 46 million patients living with dementia worldwide; anticipated to be >74 million in 2030 and 131 million in 2050
- Total estimated worldwide cost of dementia in 2015 was >\$800 billion

Lanabecestat depletes amyloid beta in cerebral spinal fluid



Late-stage development

- First Phase II/III trial AMARANTH (early Alzheimer's) completed recruitment
- Interim analysis for AMARANTH passed triggering milestone payment to AstraZeneca
- Second Phase III trial DAYBREAK-ALZ (mild Alzheimer's) recruiting
- FDA Fast Track Designation

**First Phase III data in 2019
Regulatory submission in 2020**

Source: Alzheimer's Association.

Source: AstraZeneca data on file.

In partnership with Eli Lilly and Company.



Late-stage pipeline news flow in 2018 and 2019

Unlocking and realising the potential of new medicines



	H1 2018	H2 2018	2019
Regulatory decision	Lynparza - ovarian cancer 2L (EU, JP) - breast cancer (US) Tagrisso - lung cancer (US) Imfinzi - lung cancer (PACIFIC) (US) Fasenra - severe, uncontrolled asthma(EU,JP)	Lynparza - breast cancer (JP) Tagrisso - lung cancer (EU, JP) Imfinzi - lung cancer (PACIFIC) (EU, JP) Bydureon BCise - type-2 diabetes (EU) Bevespi - COPD (EU)	-
Regulatory submission	Lynparza - breast cancer (EU) Imfinzi +/- treme - lung cancer 3L (ARCTIC) moxetumomab pasudotox - hairy cell leukaemia 3L Bevespi - COPD (JP) Duaklir - COPD (US)	Lynparza - ovarian cancer 1L Imfinzi + treme - lung cancer 1L (NEPTUNE) Imfinzi +/- treme - lung cancer 1L (MYSTIC) - head & neck cancer 1L, 2L (KESTREL, EAGLE) selumetinib - thyroid cancer roxadustat - anaemia (US) PT010 - COPD	Lynparza - pancreatic cancer 1L - ovarian cancer 3L Imfinzi +/- treme - lung cancer 1L (POSEIDON) - bladder cancer 1L (DANUBE) Brilinta - CAD ² /type-2 diabetes CVOT Farxiga - type-2 diabetes CVOT (DECLARE) Fasenra - COPD anifrolumab - lupus
Key Phase III data readouts	Lynparza - ovarian cancer 1L Imfinzi +/- treme - lung cancer 3L (ARCTIC) - lung cancer 1L (MYSTIC) (final OS) - head & neck cancer 1L, 2L (KESTREL, EAGLE) selumetinib - thyroid cancer PT010 - COPD	Lynparza - pancreatic cancer 1L Imfinzi + treme - lung cancer 1L (NEPTUNE) Farxiga - type-2 diabetes CVOT ¹ (DECLARE) Fasenra - COPD anifrolumab - lupus	Lynparza - ovarian cancer 3L Imfinzi - lung cancer (PACIFIC) (final OS) Imfinzi +/- treme - lung cancer 1L (POSEIDON) - bladder cancer 1L (DANUBE) - liver cancer 1L (HIMALAYA) Brilinta - CAD/type-2 diabetes CVOT Farxiga - HF lanabecestat - Alzheimer's disease

1. Cardiovascular outcomes trial.
 2. Coronary artery disease.
 Status as of 14 December 2017.



Summary



2017 a great year overall; 2018 news flow on track

2017 key opportunities being delivered, including:

- **Tagrisso** FLAURA trial under regulatory reviews
- **Imfinzi** PACIFIC trial under regulatory reviews
- **Fasenra** Launched US and under review EU, JP

2018 key opportunities on track

- **Oncology** lifecycle programmes for *Lynparza, Tagrisso, Imfinzi, Calquence*
- **Farxiga** DECLARE CV outcomes trials
- **Roxadustat** Phase III data
- **PT010** Phase III data
- **Anifrolumab** Phase III data

Unprecedented late-stage pipeline news flow in 2017 with an exciting 2018 ahead



Agenda



Oncology



Cardiovascular and Metabolic Diseases



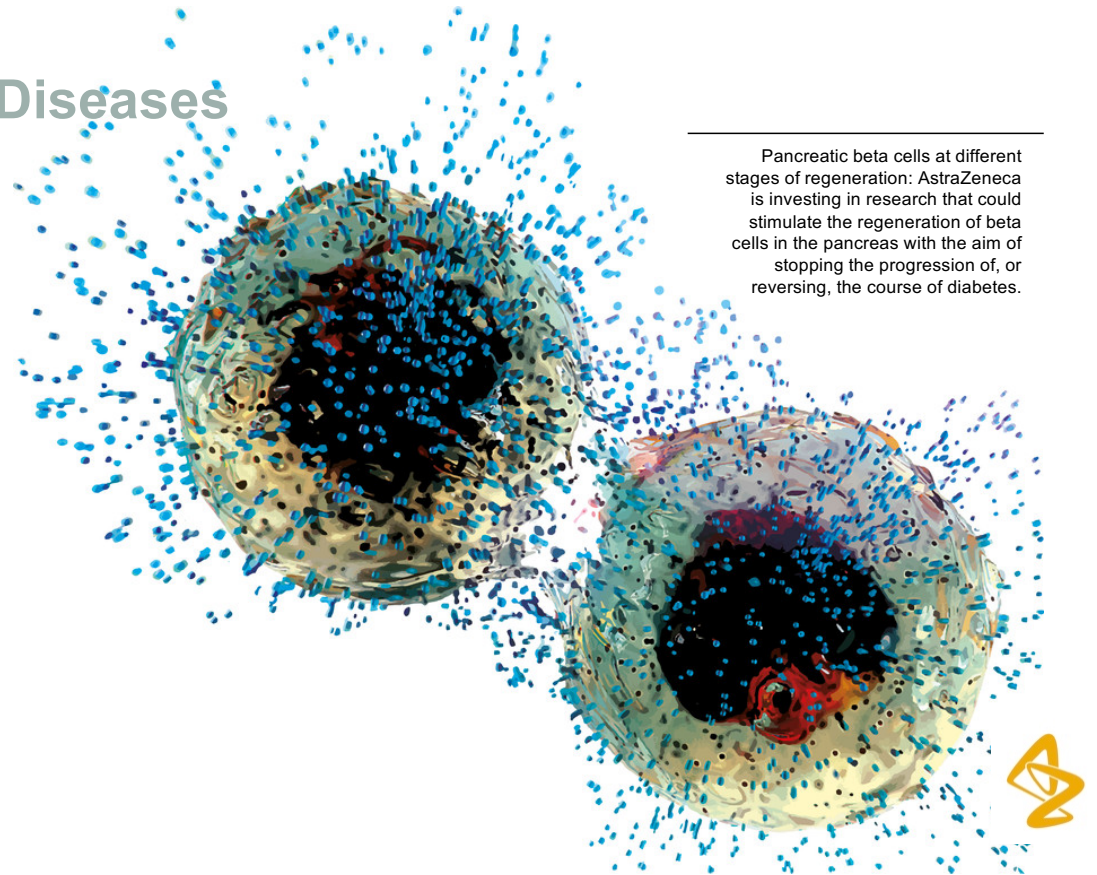
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Other & news flow 2018-2019



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Investor science event: Late-stage pipeline webcast

14 December 2017

