Investor science event: Late-stage pipeline webcast

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

14 December 2017
Forward-looking statements

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Agenda & introduction

Presenter

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Executive Vice President, Global Medicines Development and Chief Medical Officer

Participants for Q&A

Rob Iannone
Head of Immuno-Oncology, Global Medicines Development

Klaus Edvardsen
Head of Oncology, Global Medicines Development

Elisabeth Björk
Head of Cardiovascular and Metabolic Diseases, Global Medicines Development

Colin Reisner
Head of Respiratory, Global Medicines Development and Chief Medical Officer, Pearl Therapeutics
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
# Late-stage pipeline news flow

Unprecedented activity level in ‘17

<table>
<thead>
<tr>
<th>Forxiga</th>
<th>type-2 diabetes</th>
<th>Approval (CN)</th>
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<tbody>
<tr>
<td>Siliq</td>
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### Regulatory actions

#### Significant patient benefits anticipated to support return to growth

1. The Committee for Medicinal Products for Human Use.
2. Chronic obstructive pulmonary disease.
3. Progression-free survival.
R&D productivity: Sustainable progress
A new AstraZeneca with science-based culture

### Scientific publications
- **High-impact publications**
- **Medium-impact publications**
- **Other publications**

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

### FDA BTDs granted in AZN’s main therapy areas 2016-2017

<table>
<thead>
<tr>
<th>Therapy Area</th>
<th>AZN</th>
<th>CP1</th>
<th>CP2</th>
<th>CP3</th>
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<td>Other</td>
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### Sustainable level of potential new medicines in Phase II trials

- **Oncology**
- **CVMD**
- **Respiratory**
- **Other**

Source: Internal analysis. Includes Breakthrough Therapy Designations (BTD) in the three main AstraZeneca therapy areas.
Significant opportunities exist in all three therapy areas.

### Oncology
- **Lynparza**<sup>1, 2</sup>
  - multiple cancers
- **Tagrisso**<sup>1, 2</sup>
  - lung cancer
- **Imfinzi**<sup>1, 2</sup>
  - multiple cancers
- **Calquence**<sup>1</sup>
  - blood cancers
- **Imfinzi + treme**
  - multiple cancers
- **moxetumomab**
  - leukaemia
- **selumetinib**
  - thyroid cancer
- **savolitinib**
  - kidney cancer

### Cardiovascular and Metabolic Diseases
- **ZS-9**<sup>2</sup>
  - hyperkalaemia
- **roxadustat**<sup>2</sup>
  - anaemia

### Respiratory
- **Fasenra**<sup>1</sup>
  - severe, uncontrolled asthma<sup>2</sup> / COPD
- **PT010**
  - COPD / asthma
- **tezepelumab**
  - severe, uncontrolled asthma

### Other
- **anifrolumab**
  - lupus
- **lanabecestat**
  - Alzheimer’s disease

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

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<tr>
<th>Multiple cancers</th>
<th>Lung cancers</th>
<th>Blood cancers</th>
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<tbody>
<tr>
<td>• Ovarian and breast cancers</td>
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<tr>
<td>• Lifecycle programme (2018+), incl. prostate cancer</td>
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<tr>
<td>• Merck collaboration</td>
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<tr>
<td>• 2nd line / T790Mm¹</td>
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<td></td>
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<tr>
<td>• 1st line / EGFRm²</td>
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<tr>
<td>• Adjuvant EGFRm (2022+)</td>
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<tr>
<td>• Locally-advanced/Stage III, unresectable NSCLC³</td>
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<tr>
<td>• Lifecycle programme (2018+)</td>
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<td>• First AstraZeneca medicine in blood cancer</td>
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<tr>
<td>• MCL⁴ initial indication</td>
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<tr>
<td>• Lifecycle programme (2019+)</td>
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</table>

**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.

¹ 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)

...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)

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

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

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

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

~25k
2nd line platinum-sensitive recurrent ovarian cancer patients

5-10%
breast cancer patients with BRCA mutation

Epidemiology: Internal estimates based on external market research, top eight countries.
Significant opportunity to further expand through Merck collaboration

~14 Potential launches

1) Establish leadership
2) Expand patient segments
3) Add VEGF(r) combinations
4) New combinations and tumour types

Extensive lifecycle programme underway

Ovarian cancer
- 1L SOLO-1 trial
  - Data 2018
- bevacizumab (VEGF) combo
  - PAOLA-1
  - Data 2019+
- cediranib (VEGF(r)) combo
  - Data 2019

Breast cancer
- 1L SOLO-1 trial
  - Data H1 2018
- Early breast cancer
  - OlympiAD trial
  - Data 2019+

Pancreatic cancer
- POLO trial
  - Data 2019
- DDR combos
  - WEE1
  - ATM
  - ATR
  - Aurora B

Prostate cancer
- PROFOUND trial
  - Data 2019+

Imfinzi, Keytuda combos
- MEDIOLA, new trials

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

1. Vascular endothelial growth factor (receptor).
Lynparza
Next-generation combinations underway

**Lynparza**

**Lynparza + Imfinzi**
MEDIOLA Phase II trial

- **Ovarian cancer n=30**
  (3rd-line and later platinum-sensitive, gBRCAm)

- **Breast cancer n=38**
  (1st to 3rd-line HER2-negative, non-platinum refractory, gBRCAm)

- **Small-cell lung cancer n=34**
  (Relapsed 3-6 months post 1st-line platinum chemo)

- **Gastric cancer n=37**
  (2nd-line)

- **Potential additional indication (future)**

**Lynparza + novel DDR**
VIOLETTE Phase II trial

- **Triple-negative breast cancer**
  - HRR’m (BRCA)
  - HRRm (non-BRCA)
  - Non-HRRm

- **Lynparza + ATR (AZD6738)**
  (n=150)

- **Lynparza + WEE1 (AZD1775)**
  (n=150)

- **Lynparza**
  (n=150)

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1. Homologous recombination repair.
**Lung cancer: Tagrisso and Imfinzi**

### Early-stage disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Total Patients</th>
<th>Treated Patients</th>
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<tbody>
<tr>
<td>I-III</td>
<td>155k</td>
<td>Tagrisso’s ADAURA trial, Imfinzi’s ADJUVANT trial</td>
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</table>

### Late-stage disease

<table>
<thead>
<tr>
<th>Stage IV</th>
<th>Total Patients</th>
<th>1st line</th>
<th>2nd line</th>
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<tbody>
<tr>
<td>1st line</td>
<td>370k</td>
<td>70k</td>
<td>25k</td>
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<tr>
<td>2nd line</td>
<td>250k</td>
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- Tagrisso’s FLAURA trial
- Imfinzi’s MYSTIC, PEARL trials
- Tagrisso’s AURA 3 trial
- E.g. Imfinzi’s PACIFIC trial

### Treatment Strategies

- **Stage I-III**
  - Total 155k patients
  - Tagrisso’s ADAURA trial
  - Imfinzi’s ADJUVANT trial

- **Stage III**
  - Total 105k patients
  - Imfinzi’s PACIFIC trial

- **Stage IV 1st line**
  - Total 370k patients
  - Tagrisso’s FLAURA trial
  - E.g. Imfinzi’s MYSTIC, PEARL trials

- **Stage IV 2nd line**
  - Total 250k patients
  - Tagrisso’s AURA 3 trial
  - E.g. Imfinzi’s PACIFIC trial

### Treated Patients

- **Early-stage disease**
  - 80k adjuvant patients
  - 76k unresectable patients

- **Late-stage disease**
  - 70k 1L EGFRm patients
  - 25k 2L T790M EGFRm 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=0.001)

‘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


Lung cancer: Imfinzi
Durable advantage in Stage III, unresectable NSCLC

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

PACIFIC regulatory status

Eight
Regulatory decisions anticipated in 2018
• H1: US (Priority review)
• H2: EU, JP, others


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

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

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

Median PFS (95% CI) months
12-month PFS rate (95% CI)
15-month PFS rate (95% CI)
Durvalumab (N=416) 16.8 (15.0–18.1) 55.9% (51.0–60.4) 44.2% (37.7–50.5)
Placebo (N=337) 5.6 (4.6–7.8) 35.3% (29.0–41.7) 27.0% (19.5–34.5)
Patients with no EGFR-mutated or ALK-translocated tumours
~75-80% of patients

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

Stage / progression of disease

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<th>Stage III</th>
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<tr>
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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

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head &amp; neck cancer</td>
<td>KESTREL 1st line (H1 2018)</td>
</tr>
<tr>
<td></td>
<td>EAGLE 2nd line (H1 2018)</td>
</tr>
<tr>
<td>Liver cancer (HCC)</td>
<td>HIMALAYA 1st line (2019)</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>ALPS 2nd line (Phase II) (Data in-house; ASCO GI 2018)</td>
</tr>
<tr>
<td></td>
<td>PA.7 1st line (Phase II CTx combo)</td>
</tr>
</tbody>
</table>

- **Lynparza combinations** (Phase II MEDIOLA trial)
  - Small-cell lung cancer (WCLC 2017)
  - Breast cancer multiple lines (SABCS 2017)
  - Gastric cancer (2018)
  - Ovarian cancer ≥3rd line (2018)

- **Bladder cancer**
  - DANUBE 1st line (2019)

(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%客观 response rate**

**Upcoming news flow in haematology**

- **CLL randomised Phase III data in 2019**

<table>
<thead>
<tr>
<th>Phase</th>
<th>WM</th>
<th>MCL</th>
<th>CLL</th>
</tr>
</thead>
<tbody>
<tr>
<td>IB/II</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

- **WM**: Waldenström macroglobulinemia; a type of non-Hodgkin lymphoma.
- **CLL**: Chronic lymphocytic leukaemia.

- **>2,500 patients in clinical trials**

Source: US prescribing information.
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

1. Deliver superior efficacy in core indication and immediate complications

2. + Bring cardiovascular (CV) protection and slow down disease progression

3. + Stop disease and regenerate organs
Brilinta
Opportunities outside acute coronary syndrome

**THEMIS**
- **T2DM**\(^1\) with established CAD\(^2\)
- Patients >50 years + drug treated for T2DM + high risk for CV events
- **Brilinta** 60mg BID
- **Placebo**
- **Primary endpoint:** Prevention of major CV events
- **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 + ASA\(^3\)**
- **Placebo + ASA**
- **Standard of care**
- **Primary endpoint:** Stroke + death
- **Secondary endpoint:** IS\(^4\), disability (mRS\(^4\))

**Status**
- **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.
Farxiga

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

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

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)

**Farxiga**
Extending the science into type-1 diabetes

**DEPICT-1**

**Change in HbA1c and bodyweight over 24 weeks**

**HbA1c reduction**

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

**Bodyweight reduction**

**DEPICT Phase III programme**

**DEPICT-1**
- HbA1c reduction at 24 weeks of 0.42-0.45% across two doses\(^1\)
- Daily insulin dose reduction 8.8-13.2%
- Weight loss of 2.96-3.72%

**DEPICT-2**
- Data being analysed; presentation anticipated in 2018


1. DEPICT-1 tested Farxiga at 5mg and 10mg doses.
Farxiga
Extending the science into heart failure and chronic kidney disease

<table>
<thead>
<tr>
<th>38 million</th>
<th>200 million</th>
<th>422 million</th>
</tr>
</thead>
<tbody>
<tr>
<td>patients worldwide live with heart failure (HF)</td>
<td>patients worldwide live with chronic kidney disease (CKD)</td>
<td>patients worldwide live with diabetes (the majority with type-2 diabetes)</td>
</tr>
</tbody>
</table>

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

• 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

**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

*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

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

### Phase III programme

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Company</th>
<th>Phase III trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia in CKD patients not receiving dialysis</td>
<td>FIBROGEN</td>
<td>ANDES</td>
</tr>
<tr>
<td></td>
<td>AstraZeneca</td>
<td>OLYMPUS</td>
</tr>
<tr>
<td></td>
<td>astellas</td>
<td>ALPS</td>
</tr>
<tr>
<td></td>
<td>astellas</td>
<td>DOLOMITES</td>
</tr>
<tr>
<td>Anaemia in CKD patients receiving dialysis</td>
<td>FIBROGEN</td>
<td>SIERRAS</td>
</tr>
<tr>
<td></td>
<td>AstraZeneca</td>
<td>ROCKIES</td>
</tr>
<tr>
<td></td>
<td>astellas</td>
<td>PYRENEES</td>
</tr>
<tr>
<td>Anaemia in newly-initiated dialysis patients</td>
<td>FIBROGEN</td>
<td>HIMALYAS</td>
</tr>
</tbody>
</table>

### Targeting a competitive medicine profile

**Non-dialysis patients** (against placebo)
- Superior haemoglobin increase
- Non-inferior on major adverse CV events (MACE) based on pooled analysis

**Dialysis patients** (against erythropoietin)
- Non-inferior haemoglobin increase
- Non-inferior, potentially superior MACE; pooled analysis

**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.
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 ICS

**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

<table>
<thead>
<tr>
<th>Preferred controller choice</th>
<th>Other options</th>
<th>Reliever</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td><strong>Step 2</strong></td>
<td><strong>Step 3</strong></td>
</tr>
<tr>
<td>Low-dose ICS</td>
<td>Leukotriene receptor antagonist (LTRA)</td>
<td>Med/high ICS/LABA**</td>
</tr>
<tr>
<td>Consider low-dose ICS</td>
<td>Low-dose ICS/LABA**</td>
<td>Add med/high ICS/LABA</td>
</tr>
<tr>
<td>Low-dose theophylline</td>
<td>Low-dose ICS/LABA**</td>
<td>Add tiotropium high-dose ICS/LTRA (or +theoph)</td>
</tr>
<tr>
<td><strong>Step 4</strong></td>
<td><strong>Step 5</strong></td>
<td></td>
</tr>
<tr>
<td>As-needed short-acting beta_2-agonist (SABA)</td>
<td>Add low-dose OCS</td>
<td></td>
</tr>
<tr>
<td>As-needed SABA or low-dose ICS/formoterol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*~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*

Asthma: *Fasenra*

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

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

- **51%** reduction in the annual asthma exacerbation rate versus placebo
- **159mL** significant improvement in lung function as measured by forced expiratory volume in one second (FEV₁) versus placebo
- **75%** median reduction in daily OCS use and discontinuation of OCS use in 52% of eligible patients

**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

**Under regulatory review in the EU, Japan and several other countries with decisions anticipated in H1 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 (1.24 vs 1.52); CALIMA: 28% reduction vs. placebo at week 56 (1.35 vs 1.81).
3. SIROCCO: At 48 weeks, an improvement in FEV₁ of 389mL (mean change from baseline) vs. 215mL for placebo, total of 174mL increase in FEV₁. CALIMA: At 56 weeks, an improvement in FEV₁ of 330mL (mean change from baseline) vs. 215mL for placebo, for total of 115mL increase in FEV₁.
5. Median reduction in OCS dose of 75% from baseline vs. 35% 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 immunity\(^1\)\(^-\)\(^4\)

- Expression is increased in the airways of patients with asthma, and correlates with Th2 cytokine and chemokine expression, and disease severity\(^5\)\(^-\)\(^7\)

- 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 complex\(^8\)

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

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.
**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**

- Placebo
- 300mg
- 1,000mg

**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.**
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.
Unlocking and realising the potential of new medicines

Late-stage pipeline news flow in 2018 and 2019

<table>
<thead>
<tr>
<th></th>
<th>H1 2018</th>
<th>H2 2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regulatory decision</strong></td>
<td>Lynparza - ovarian cancer 2L (EU, JP)</td>
<td>Lynparza - breast cancer (JP)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- breast cancer (US)</td>
<td>Tagrisso - lung cancer (EU, JP)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tagrisso - lung cancer (US)</td>
<td>Imfinzi - lung cancer (PACIFIC) (EU, JP)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Imfinzi - lung cancer (PACIFIC) (US)</td>
<td>Bydureon BCise - type-2 diabetes (EU)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasenra - severe, uncontrolled asthma(EU,JP)</td>
<td>Bevespi - COPD (EU)</td>
<td></td>
</tr>
<tr>
<td><strong>Regulatory submission</strong></td>
<td>Lynparza - breast cancer (EU)</td>
<td>Lynparza - ovarian cancer 1L</td>
<td>Lynparza</td>
</tr>
<tr>
<td></td>
<td>Imfinzi +/- treme - lung cancer 3L (ARCTIC)</td>
<td>Imfinzi +/- treme - lung cancer 1L (NEPTUNE)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>moxetumomab pasudotox - hairy cell leukaemia 3L</td>
<td>Imfinzi +/- treme - lung cancer 1L (MYSTIC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bevespi - COPD (JP)</td>
<td>- head &amp; neck cancer 1L, 2L (KESTRRL, EAGLE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duaklir - COPD (US)</td>
<td>selumetinib - thyroid cancer</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>roxadustat - anaemia (US)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PT010 - COPD</td>
<td></td>
</tr>
<tr>
<td><strong>Key Phase III data readouts</strong></td>
<td>Lynparza - ovarian cancer 1L</td>
<td>Lynparza - pancreatic cancer 1L</td>
<td>Lynparza</td>
</tr>
<tr>
<td></td>
<td>- lung cancer 3L (ARCTIC)</td>
<td>Imfinzi + treme - lung cancer 1L (NEPTUNE)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>- lung cancer 1L (MYSTIC) (final OS)</td>
<td>Farxiga - type-2 diabetes CVOT* (DECLARE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- head &amp; neck cancer 1L, 2L (KESTREL, EAGLE)</td>
<td>Fasenra - COPD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>selumetinib - thyroid cancer</td>
<td>anifrolumab - lupus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PT010 - COPD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**
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.
Use of AstraZeneca webcast, conference call and presentation slides

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Investor science event:
Late-stage pipeline webcast

14 December 2017