Late-stage pipeline conference call
Introduction

Thomas Kudsk Larsen
Head of Investor Relations
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:

This document 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. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and AstraZeneca 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: the loss or expiration of, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; effects of patent litigation in respect of IP rights; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions, including licensing and collaborations, will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure of outsourcing; the risks associated with manufacturing biologics; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the risk that new products do not perform as we expect; failure to achieve strategic priorities or to meet targets or expectations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the risk of misuse of social medial platforms and new technology; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the risks from pressures resulting from generic competition; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; economic, regulatory and political pressures to limit or reduce the cost of our products; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; and the risk of failure of information technology and cybercrime. Nothing in this presentation/webcast should be construed as a profit forecast.
Meet the experts

2015 review
Sean Bohen

Respiratory, Inflammation & Autoimmunity
Bing Yao & David Chang

Cardiovascular & Metabolic Disease
Elisabeth Björk

Oncology
Mohammed Dar & Antoine Yver

Closing
Sean Bohen

- Introduction
2015 review

Sean Bohen
Executive Vice President, Global Medicines Development & Chief Medical Officer
2015: Delivering the late-stage pipeline

A great year for patients and science

- **Brilinta/Brilique**
  - Phase III PEGASUS

- **Iressa**
  - approval (US)

- **lesinurad**
  - submission (EU)

- **saxa/dapa**
  - submission (EU)

- **CAZ AVI**
  - submission (EU)

- **cediranib**
  - submission (EU)

- **saxa/dapa**
  - Complete Response Letter (US)

- **Tagrisso**
  - approval (US)

- **Faslodex**
  - approval 500mg (CN)

- **PT003**
  - submission (US)

- **Tagrisso**
  - submission (US, EU)

- **selumitinib**
  - Phase III endpoint not met (uveal melanoma)

- **PT003**
  - submission (US)

- **Brilinta**
  - post-MI approval (US)

- **Tagrisso**
  - submission (JP)

- **Brilinta**
  - ACS, post-MI submission (JP)
2015-2016: Delivering promises from Investor Day 2014
Building pipeline for long-term sustainability

- Focus on distinctive science in three therapy areas
- Shift toward more targeted specialty-care programmes, often with companion diagnostics
- High-quality early and mid-stage programmes to ensure sustainability of pipeline

* Based on first major market submission acceptance/approval
Goals updated as of latest announcements
## Key late-stage new medicines and lifecycle programmes

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<th>Oncology</th>
<th>Other</th>
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<td>selumetinib</td>
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<td>anifrolumab</td>
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<td>IFNAR</td>
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<td>Hyperkalaemia</td>
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<td>URAT-1</td>
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<td>benralizumab</td>
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<td>Severe asthma, COPD</td>
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<td>IL-13</td>
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<td>Severe asthma</td>
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<td><strong>Additional uses</strong></td>
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<td>Lynparza</td>
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<td>P2Y12</td>
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<td>PARP</td>
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<td>Stroke</td>
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<td>Various indications</td>
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<td>Tagrisso</td>
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<tr>
<td>P2Y12</td>
<td></td>
<td>EGFR T790M</td>
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<tr>
<td>Peripheral Arterial Disease</td>
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<td>Various indications</td>
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</table>

1. Pending completion of ZS Pharma acquisition
### Highlights of today

#### Respiratory, Inflammation & Autoimmunity

- **Phase III**
  - PT010 LAMA/LABA/ICS COPD
  - anifrolumab IFNAR Lupus (SLE)
  - benralizumab IL-5R Severe asthma, COPD
  - brodalumab IL-17R Psoriasis
  - tralokinumab IL-13 Severe asthma

- **Under review**
  - PT003 LAMA/LABA COPD
  - lesinurad URAT-1 Gout

#### Cardiovascular & Metabolic Disease

- **Phase III**
  - roxadustat HIF-PH Anaemia CKD/ESRD
  - ZS-9 Potassium binder Hyperkalaemia

- **Under review**
  - Additional uses
    - **Brilinta**
      - P2Y12 Stroke
    - **Brilique**
      - P2Y12 Peripheral Arterial Disease

#### Oncology

- **Phase III**
  - selumetinib MEK 2L KRASm NSCLC
  - durvalumab PD-L1 3L PD-L1 pos. NSCLC
  - cediranib VEGF PSR ovarian cancer
  - Tagrisso (EU, JP) EGFR T790M 2L T790Mm NSCLC
  - tremelimimumab CTLA-4 Mesiiothelioma

- **Under review**
  - Additional uses
    - Lynparza PARP Various indications
    - Tagrisso EGFR T790M Various indications

#### Other

- **Under review**
  - CAZ AVI Cephalosporin/BLI Serious infections

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1. Pending completion of ZS Pharma acquisition
Bing Yao, Senior Vice President, Head of Respiratory, Inflammation & Autoimmunity iMED, MedImmune

David Chang, Vice President and Head, Inflammation, Autoimmunity & Neuroscience, Global Medicines Development
PT003: A novel co-suspension MDI

Fixed-dose combination of LAMA/LABA

• For long-term maintenance treatment of airflow obstruction in patients with moderate to severe COPD¹

• Only LAMA/LABA² combination developed in a pressurised Metered Dose Inhaler (pMDI)

• First product using the Pearl co-suspension formulation technology
PT003: Phase III demonstrated superiority to monotherapy
Patients with moderate-to-severe COPD

- Statistically-significant improvements in lung function
- Symptomatic benefit observed based upon self-administered computerised TDI\textsuperscript{1}
- Secondary endpoints generally supportive
- Well-tolerated, with similar safety profile to mono-components and placebo

\textsuperscript{1} TDI = Transition Dyspnea Index
\textsuperscript{2} FEV = Forced Expiratory Volume
PT003: Key milestones

**Regulatory submission**
- (US)
- Q3 2015

**Regulatory approval**
- (US)
- PDUFA Q2 2016

**Launch**
- (US)

**Regulatory submission**
- (EU)
- H2 2016

**Regulatory submission**
- (JP, CN)
- 2017

Novel fixed-dose combination of LAMA/LABA in unique pMDI device

* Regulatory submission confirmed upon acceptance
COPD: Addresses all disease severities

**Near term**

- LAMA/LABA: Duaklir & PT003
- Symbicort + Eklira

**Medium term**

- LAMA/LABA: Duaklir & PT003
- Symbicort + Eklira
- FDC triple (PT010)

**Biologics**

- e.g. benralizumab (IL-5R)
  - Near term
  - Medium term
  - 2018

**Disease severity**

- Mild
- Moderate-severe
  - ≤1 exacerbation
- Very severe
  - >2 exacerbations

*Represents relative prevalence of COPD diagnosed population per disease state*
Unique mechanism for eosinophilic inflammation

Benralizumab depletes eosinophils in a different way to anti-IL-5 ligand approaches

- Binds to IL-5 receptor (IL-5Rα) on eosinophils and basophils
- Leads to Antibody-Dependent Cell-mediated Cytotoxicity (ADCC) and death of eosinophils and basophils via apoptosis
- Efficiently depletes inflammatory cells in the bone marrow, blood, lung and sputum
- In Phase III for severe asthma and COPD
Benralizumab: Targeting best-in-class efficacy

**Differentiated profile**

- Differentiated mode of action resulting in potent reduction of eosinophils
- Rapid onset of action
- Improvement in lung function and asthma control
- Reduction in asthma exacerbation
- Convenient pre-filled syringe; every four week dosing or potentially every eight week dosing

**Phase IIb: Exacerbation rate reduction**

![Graph showing annual exacerbation rate reduction relative to placebo.](image)

Baseline blood eosinophil count cut-off (cells per μL)

**Severe asthma: Phase III data H1 2016**

Source: M. Castro et al., Lancet Respiratory Medicine, 2014
Benralizumab: Comprehensive programme in severe asthma

<table>
<thead>
<tr>
<th>Patient population</th>
<th>CALIMA</th>
<th>SIROCCO</th>
<th>ZONDA</th>
<th>BISE</th>
<th>GREGALE</th>
<th>BORA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults/adolescents with severe asthma, inadequately controlled on high-dose ICS/LABA</td>
<td>Adults with severe asthma, inadequately controlled on high-dose ICS/LABA and chronic OCS therapy</td>
<td>Adults with mild-moderate asthma</td>
<td>Adults with severe asthma, inadequately controlled on medium-dose &amp; high-dose ICS/LABA± chronic OCS</td>
<td>Adults with severe asthma, inadequately controlled on medium-dose &amp; high-dose ICS/LABA± chronic OCS</td>
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<tr>
<td>Estimated enrolment</td>
<td>N = 1,096 high dose + 216 medium dose</td>
<td>N = 1,134</td>
<td>N = 200</td>
<td>N = 200</td>
<td>N = 120</td>
<td>N = 2,550</td>
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<tr>
<td>Endpoints</td>
<td>Safety and efficacy</td>
<td></td>
<td>Functionality, reliability, and performance of at-home administration with pre-filled syringe</td>
<td></td>
<td>Safety and tolerability</td>
<td></td>
</tr>
<tr>
<td>Top-line results</td>
<td>H1 2016</td>
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<td>2017</td>
</tr>
</tbody>
</table>

Regulatory submissions expected H2 2016
Anifrolumab: Targeting type-I interferon system in SLE

• Central pathogenic mediator in SLE\(^1,2\)
• Mixed trial results for sifalimumab\(^3\) and rontalizumab\(^4\)
• All type-I IFN signalling is mediated by type-I IFN-\(\alpha\) receptor (IFNAR)\(^5\)
• Inhibiting IFNAR has potential to block the biological effects of all type-I IFNs\(^6\)
• Anifrolumab is unique, fully human, IgG1 K monoclonal antibody that binds to IFNAR\(^7\) and prevents binding of type-I IFNs

IFN: interferon; IFNAR: type-I IFN-\(\alpha\) receptor; SLE: Systemic Lupus Erythematosus

2. Crow MK. *J Immunol* 2014;192:5459-68
5. Ivashkiv LB et al. *Nat Rev Immunol* 2014;14:36-49
Anifrolumab: Phase II trial conclusions

- Substantial benefit achieved across multiple global and organ-specific disease activity measures
- Greater efficacy in patients with high IFN gene signatures supports the pathobiology of this treatment strategy
- Safety and tolerability acceptable
- Phase III trial underway with 300mg as maximum dosage

Targeting IFNAR is a promising therapeutic approach for patients with SLE who do not respond to currently-available therapies

Source: Furie, R. Anifrolumab, an Anti-Interferon-A receptor Monoclonal Antibody, in Moderate to Severe Systemic Lupus Erythematosus (SLE), ACR 2015
Anifrolumab: Potential differentiators in SLE

**First-in-class mechanism of action**
- Most-advanced molecule targeting IFNAR
- Blocks all type-I interferons (not just IFN-α)

**Potential best-in-disease efficacy**
- Statistical significance achieved:
  - 26.0% treatment difference vs. placebo on SRI(4)\(^1\) response at day 365 with a sustained reduction of OCS\(^2\)
  - 29.8% treatment difference vs. placebo on reduction of OCS dosage at day 365 to \(\leq 7.5\text{mg/day}\)\(^3\)

**Personalised healthcare approach**
- Complementary IFN test

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1. Systemic Lupus Erythematosus Responder Index
2. Oral Corticosteroids
3. In patients receiving \(\geq 10\text{mg/day}\) of oral corticosteroids at baseline
Anifrolumab: Development status

**Phase III SLE programme initiated**
- Final data available 2018
- Regulatory submission 2019

**Lifecycle management programme**
- Phase II lupus nephritis trial expected to start in due course
- Phase I subcutaneous administration trial also expected to start in due course
Cardiovascular & Metabolic Disease

Elisabeth Björk
Vice President, Cardiovascular & Metabolic Disease Head, Global Medicines Development
Cardiovascular & Metabolic Disease strategy
Aim to reduce morbidity, mortality and organ damage by addressing multiple CV risk factors
**Brilinta/Brilique: PARTHENON programme potential to deliver four launches in four years**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients enrolled</th>
<th>Comparator</th>
<th>OAP(^1) access (cumulative)</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLATO</strong> Acute Coronary Syndrome</td>
<td>18,624</td>
<td>clopidogrel</td>
<td>10%</td>
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<tr>
<td><strong>PEGASUS</strong> Prior Myocardial Infarction</td>
<td>21,412</td>
<td>placebo</td>
<td>20%</td>
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<tr>
<td><strong>SOCRATES</strong> Stroke/Transient Ischaemic Attack (TIA)</td>
<td>13,200</td>
<td>aspirin</td>
<td>31%</td>
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<tr>
<td><strong>EUCLID</strong> Peripheral Arterial Disease (PAD)</td>
<td>13,887</td>
<td>clopidogrel</td>
<td>69%</td>
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<tr>
<td><strong>THEMIS</strong> Diabetes</td>
<td>19,000</td>
<td>placebo</td>
<td>84%</td>
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**1.5 million**

Estimate of patients treated with Brilinta/Brilique

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**20,000**

Estimated number of deaths prevented with Brilinta/Brilique
SOCRATES: Top-line data anticipated H1 2016
First large-scale prospective international trial in acute stroke and TIA

It’s exciting to have an antiplatelet that can be used acutely. Anytime we have another option in our armamentarium, that’s always a good day." Stroke key thought leader

Acute ischemic stroke or high-risk TIA (≤24 hours from symptom onset)

Brilinta/Brilique 90mg 2x/day

aspirin 100mg

90 days

2015 2016 2017

● Last patient in ● Top-line data ● Launches
Initiating treatment with Brilinta/Brilique within 24 hours of a stroke may reduce the risk of recurrent events.

Approximately 3–15% of patients who have an acute stroke will have a subsequent stroke within 90 days.

Post-event risk of recurrent stroke relative to background risk:

- **Very high risk**: TIA incidence per 1,000, Cancelli et al., Stroke 2011
- **High risk**: AIS incidence per 1,000, Bamford 1990
- **Recurrence risk**: 13% for first year, and 4% annually thereafter, Burn 1994
  - 7d: 10%, 30d: 13%, 90d: 18% risk, Cull

**SOCRATES**: Early treatment to address recurrent risk

- **SOCRATES**
- **Early treatment to address recurrent risk**
- **1,000x greater risk**
- **100x greater risk**
- **10x greater risk**
- **0 3 6 9 12 15 18 Months**
- **Post-event risk of recurrent stroke relative to background risk**
- **90 days very high risk**
- **12 months high risk**
- **Permanently raised risk**
EUCLID: PAD large and growing area of patient need
Clear precedent exists for superiority to clopidogrel

PAD is almost half as prevalent as type-2 diabetes (T2D)\(^1\)

**T2D**
(72m patients)

**PAD**
(27m patients)

PLATO trial; PAD patients: 15% RRR (CVD/MI/stroke)\(^2\)
PLATO trial; PAD patients: 26% RRR (all-cause mortality)\(^2\)

1. DRG major market prevalence estimates, 2014 Pharmacor reports
**EUCLID: Trial design**

13,887 patients enrolled

- **Patients (≥50 years) with established PAD**
  - **Brilinta/Brilique** 90mg 2x/day
  - **Clopidogrel** 75mg 1x/day

- Follow-up visits at 2, 6, 12 months; every 6 months after 1st year
  - Telephone visits at 3-month intervals between regular visits

- **Duration**: Approximately 18-month recruitment and 18-month follow-up

**Primary endpoint**
Cardiovascular death, myocardial infarction or ischaemic stroke (RRR=15%; 0.7% ARR per year)

PAD established as either:
A. Prior lower-extremity (LE) revascularisation (=57% trial)
B. No prior LE revascularisation, but symptomatic PAD (IC\(^1\) or CLI\(^2\)) with ABI\(^3\) ≤0.80 at enrolment (=43% trial)

**Key exclusion criteria:**
- Ongoing or planned need for DAPT\(^4\) at enrolment e.g. recent (<30 days) or imminent (<90 days) coronary or LE revascularisation
- Recent or planned (90 days) major LE amputation
- Poor metaboliser for CYP2C19 (-/-)

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1. Intermittent Claudication 2. Critical Limb Ischemia 3. Ankle-Brachial Index 4. Dual Antiplatelet Therapy
Roxadustat: A potential first-in-class oral treatment that mimics the body’s natural response at high altitude

- Higher doses of rEPO\(^1\) predict mortality regardless of haematocrit

- Mechanism for increased CV risk with rEPO is uncertain, but may involve:
  - supra-physiologic EPO levels
  - rapid rate of Hb rise
  - high Hb targets
  - effects on blood pressure

- Phase III programme designed to avoid these concerns through the novel mechanism of action and intermittent dosing
Roxadustat: Comprehensive development programme

roxadustat Phase III trials (Fibrogen, Astellas, AstraZeneca)

Dialysis vs. epoetin alfa

- **Efficacy** (powered for non-inferiority on Hb)
  - SIERRAS (N = 600)
  - PYRENEES (N = 750)
  - HIMALAYAS (N = 750)

- **CV safety** (meta-analysis powered for superiority on MACE)
  - Above trials plus ROCKIES (N = 1,425)

Non-dialysis vs. placebo

- **Efficacy** (powered for superiority on Hb)
  - ANDES (N = 600)
  - ALPS (N = 600)

- **CV safety** (meta-analysis powered for non-inferiority)
  - Above trials plus OLYMPUS (N = 2,600)

**MACE**: All-cause mortality, MI, stroke

**MACE+**: Add unstable angina leading to hospitalisation or heart failure requiring hospitalisation

**Composite safety endpoint**: Add deep-vein thrombosis, pulmonary embolism, vascular access thrombosis or hypertensive emergency
# ZS-9: ~1,700 patients in clinical trial programme

<table>
<thead>
<tr>
<th>Trial</th>
<th>Published</th>
<th>Trial type</th>
<th># Patients</th>
<th>Duration</th>
<th>Endpoint</th>
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<tbody>
<tr>
<td>ZS002</td>
<td><a href="#">Kidney</a></td>
<td>Phase II</td>
<td>N = 90</td>
<td>48 hours</td>
<td>∆ serum K+ level (3 doses) ✔</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Double-blind RCT</td>
<td>Serum K 5.0–6.0 mEq/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZS003</td>
<td><a href="#">NEJM</a></td>
<td>Phase III</td>
<td>N = 753</td>
<td>14 days</td>
<td>∆ serum K+ level (4 doses) ✔</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Double-blind RCT</td>
<td>Serum K 5.0–6.5 mEq/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZS004e</td>
<td><a href="#">JAMA</a></td>
<td>Phase III</td>
<td>N = 258</td>
<td>1 month + 11 months extension</td>
<td>Maintenance of serum K+ (28 days) ✔</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Double-blind RCT</td>
<td>Serum K &gt;5.0 mEq/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZS005</td>
<td></td>
<td>Open-label safety trial</td>
<td>N = 750</td>
<td>12 months</td>
<td>Safety &amp; tolerability of long-term dose (initiated Q2 2014)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Serum K &gt;5.0 mEq/L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ZS-9: Efficacy and safety

• 99% of patients achieved normokalaemia within 24-72hrs

• Mean potassium levels were maintained throughout the 12-month period

• Rates of edema and hypertension were consistent with the patient population over this time frame

Mohammed Dar, Vice President, Oncology Clinical Development, MedImmune
Antoine Yver, Head of Oncology, Global Medicines Development
## Immuno-Oncology (IO) strategy

Focus on combination & first-mover indications

### Speed

- Durvalumab in PD-L1 positive 3L+ NSCLC & 2L SCCHN
- Durva + treme in PD-L1 negative 2L SCCHN

### Differentiation

- Early-stage disease: Adjuvant and stage III, unresectable NSCLC
- Durva + treme combo (chemo-free regimen)
  - Including 1st line
  - Irrespective of PD-L1 status

### Leadership

- Novel combinations e.g. durvalumab + *Tagrisso*
- New tumour types and haematological malignancies (Celgene strategic collaboration)
IO: Clinical activity in lung cancer

Greatest unmet medical need is in PD-L1 negative tumours

60-70% of patients below 10% PD-L1 expression level

IO combinations address major unmet medical need:
PD-L1 negative tumours in lung cancer

Source: Internal estimates based on market research.

*PD-L1 positive: Patients with moderate/high level of PD-L1 expression; represent ~30%. **PD-L1 negative: Patients with low level of PD-L1 expression or no PD-L1 expression; represent ~70%. Note: Patient number estimates in 2020. EGFRm: 14%, ALKm: 5%

Durvalumab: Promising activity in PD-L1 positive NSCLC

- Durvalumab monotherapy shows promising overall response rate (ORR) in PD-L1 positive NSCLC patients
- Data emerging in additional indications (Study 1108)
Durvalumab works in tandem with tremelimumab to further break down the tumour defence and extends the benefit of immunotherapy to more patients (PD-L1 negative).
IO: NSCLC top priority
First in early stage and differentiated with durva + treme

<table>
<thead>
<tr>
<th>Adjuvant</th>
<th>Unresectable stage III</th>
<th>1st line</th>
<th>2nd line</th>
<th>3rd line</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADJUVANT</td>
<td>PACIFIC</td>
<td>MYSTIC (PFS)</td>
<td>ATLANTIC</td>
<td></td>
</tr>
<tr>
<td>durvalumab vs. placebo</td>
<td>durvalumab vs. placebo</td>
<td>durva + treme vs. durvalumab vs. SoC&lt;sup&gt;1&lt;/sup&gt;</td>
<td>durvalumab single-arm Phase II</td>
<td></td>
</tr>
</tbody>
</table>

- **NEPTUNE (OS)**
  - durva + treme vs. SoC<sup>1</sup>
  - durva + treme + chemo vs. SoC<sup>1</sup>

- **ARCTIC**
  - PD-L1 pos.: durvalumab vs. SoC<sup>1</sup>
  - PD-L1 neg.: durva + treme vs. CoC<sup>2</sup> vs. SoC<sup>1</sup>

- **durvalumab + Iressa vs. Iressa (EGFRm)**
- **durvalumab + Tagrisso vs. Tagrisso (T790Mm)**

First in early stages of the disease | Leadership in IO/IO and IO/SM combinations | Highest unmet medical need

- Durvalumab monotherapy
- Durva + treme
- Durvalumab + SM combo

IO: Additional tumour types
Leading with durva + treme and in early lines of treatment

<table>
<thead>
<tr>
<th>SCCHN 1st line</th>
<th>SCCHN 2nd line</th>
<th>Bladder 1st line</th>
<th>Gastric 2nd/3rd line</th>
<th>Liver 2nd line</th>
<th>Pancreatic 2nd line</th>
</tr>
</thead>
<tbody>
<tr>
<td>KESTREL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>durva + treme vs. durvalumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-L1 pos.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAWK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>durvalumab single-arm Phase II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-L1 neg.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONDOR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>durva + treme vs. durvalumab vs. tremelimumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EAGLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>durva + treme vs. durvalumab vs. tremelimumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Durvalumab monotherapy
Durva + treme

Change paradigm with chemo-free regimen

1. Standard of Care
1st/2nd/3rd line = First-line/second-line/third-line metastatic treatment
IO: Way to market
Data availability from key ongoing trials

Other tumour types

**Head & neck cancer**
- HAWK
  - PII 2L PD-L1 positive (single arm)
- CONDOR
  - PIII 2L PD-L1 negative

**Lung cancer**
- MYSTIC
  - PIII 1L (PFS endpoint)
- ARCTIC B
  - PIII 3L PD-L1 negative
- PACIFIC
  - PIII Stage III unresectable
- ARCTIC A
  - PIII 3L PD-L1 positive

**Detected**
- PII 2L mesothelioma (randomised)

- Durva + treme
- Durvalumab monotherapy
- Tremelimumab monotherapy

- **Atlanttic**
  - PII 3L PD-L1 positive (single-arm)

- **Hawk**
  - PII 2L PD-L1 positive (single arm)

- **Determine**
  - PII 2L mesothelioma (randomised)

**Timeline**
- 2015
- 2016
- 2017

**Atlanttic, Hawk** are potential upsides to base-case submission timeline
**Lynparza: Strategy built on three pillars**

<table>
<thead>
<tr>
<th>BRCAm</th>
<th>Other HRD</th>
<th>Combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target disease with BRCA mutations - germline and somatic</td>
<td>Expand to target other Homologous Recombination Repair Deficiency (HRD) tumours</td>
<td>Combine to induce HRD, target complimentary DNA Damage Repair (DDR) pathways or potential synergistic effects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian (current approval)</td>
</tr>
<tr>
<td>Breast (triple-negative)</td>
</tr>
<tr>
<td>Gastric</td>
</tr>
<tr>
<td>Pancreatic</td>
</tr>
<tr>
<td>Prostate</td>
</tr>
</tbody>
</table>
**Lynparza: Backbone in ovarian cancer**

**Step one**
- Establish Lynparza as standard of care in HRD

**Step two**
- Expand beyond HRD with VEGFi combos
- Displace chemo in 2L

**Step three**
- Enhance efficacy across segments through double combos
- **Lynparza + durvalumab + WEE1**

**Step four**
- Displace chemo in 1L with triple combos
- **Lynparza + VEGFi combos**
- **Lynparza + WEE1 combos**
- **Lynparza backbone**
**Lynparza: 3rd line+ prostate cancer**

Trial published in NEJM informs lifecycle

<table>
<thead>
<tr>
<th>DNA-repair defects</th>
<th>Responder</th>
<th>RR%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>All-comer</td>
<td>33</td>
<td>16</td>
</tr>
<tr>
<td>Biomarker negative</td>
<td>31</td>
<td>2</td>
</tr>
<tr>
<td>Biomarker positive</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>P-value</td>
<td>P&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

88% RR\(^1\) and 9.8m PFS in biomarker-positive patients (N = 16)

- Ongoing consultations with health authorities regarding later lines of treatment as well as 1st line settings
- Developing companion diagnostic to identify HRRm population\(^2\)

---

DNA-repair defects and olaparib in metastatic prostate cancer

1. Composite RR = RECIST + CTC conversion + PSA decline
2. HRRm = Patients with mutation in a panel of HRR genes including BRCA1, BRCA2, ATM
### Lynparza: Ongoing trials and expected newsflow

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic cancer</td>
<td><strong>POLO</strong> Phase III gBRCA</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td><strong>GOLD</strong> Phase III 2L</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>Phase II Metastatic castration-resistant</td>
</tr>
<tr>
<td>Breast cancer</td>
<td><strong>OlympiAD</strong> Phase III metastatic BRCAm</td>
</tr>
<tr>
<td></td>
<td><strong>OlympiA</strong> Phase III adjuvant</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td><strong>SOLO-1</strong> Phase III 1L BRCAm maintenance</td>
</tr>
<tr>
<td></td>
<td><strong>SOLO-2</strong> Phase III 2L BRCAm</td>
</tr>
<tr>
<td></td>
<td><strong>SOLO-3</strong> Phase III 3L+ PSR gBRCAm</td>
</tr>
</tbody>
</table>

**Timeline:**
- **2016**
- **2017**
- **2018**
- **2019+**
Tagrisso (osimertinib, formerly AZD9291)

- 2 yrs 8 mths Clinical development time
- 59% ORR 12.4 mths Duration of response
- <6 hrs Time to first product shipment after approval
- ~1.6m Global lung cancer deaths
- >80% Lung cancer is NSCLC
- 10% Typical 5-year survival rate
Tagrisso
Innovative therapy with large potential

- **Adjuvant**
  - United States: 3k
  - EU5: 3k
  - Japan: 8k
  - Patients treated: 14k

- **1st line**
  - United States: 12k
  - EU5: 9k
  - Japan: 18k
  - Patients treated: 39k

- **2nd line (T790M)**
  - United States: 4k
  - EU5: 3k
  - Japan: 8k
  - Patients treated: 15k

- Record development speed, breakthrough designation
- Crucial step to building leadership position in lung cancer market
- Opportunity for earlier treatment and combination therapy
**Tagrisso: Ongoing NSCLC trials and expected newsflow**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Phase</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AURA3</td>
<td>Phase III</td>
<td>2L EGFRm, T790Mm</td>
</tr>
<tr>
<td>AURA17</td>
<td>Phase II</td>
<td>2L EGFRm T790Mm</td>
</tr>
<tr>
<td>BLOOM</td>
<td>Phase I</td>
<td>EGFRm CNS disease</td>
</tr>
<tr>
<td>TATTON</td>
<td>Phase Ib</td>
<td>2L EGFRm</td>
</tr>
<tr>
<td>ADAURA</td>
<td>Phase III</td>
<td>Adjuvant EGFRm</td>
</tr>
</tbody>
</table>

**Philanthropic Contributions**

- **AURA**
  - Phase I/II
  - 2L EGFRm T790Mm

- **AURA2**
  - Phase II
  - 2L EGFRm T790Mm

- **FLAURA**
  - Phase III
  - 1L EGFRm

- **CAURAL**
  - Phase III (combo with durvalumab)
  - 2L EGFRm T790Mm

**Timeline**

- **2015**
- **2016**
- **2017**
- **2018+**
Tagrisso: CNS disease pre-clinical evidence

Brain to blood ratio AUC<sub>0–90 min</sub> (corrected for radioactivity in cerebral blood)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>[&lt;sup&gt;11&lt;/sup&gt;C]Tagrisso (N = 3)</td>
<td>2.6 ± 1.4</td>
</tr>
<tr>
<td>[&lt;sup&gt;11&lt;/sup&gt;C]CO-1686 (N = 2)</td>
<td>0.025</td>
</tr>
<tr>
<td>[&lt;sup&gt;11&lt;/sup&gt;C]gefitinib (N = 2)</td>
<td>0.28</td>
</tr>
</tbody>
</table>


Tagrisso: CNS disease leptomeningeal metastasis

Brain MRI at baseline

Brain MRI at four months 160mg 1x/day

AACR NCI EORTC meeting
Nov. 2015

- Oncology
Tagrisso: Reaching more patients through lifecycle

Establish
New standard of care in ≥2L EGFRm NSCLC with T790M resistance

Expand
Replace existing therapies in early EGFRm disease

Transform
Survival outcomes in all EGFRm NSCLC patients as backbone of combinations

2015 2018 2020

Combos
Adjuvant
1st line
2nd line (T790M)
Closing

Sean Bohen
Executive Vice President, Global Medicines Development & Chief Medical Officer
Key newsflow through 2016

<table>
<thead>
<tr>
<th>Regulatory approvals</th>
<th>Key regulatory submissions</th>
<th>Key Phase III readouts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>lesinurad</strong> - gout (US)</td>
<td><strong>brodalumab</strong> - psoriasis (US, EU)</td>
<td><strong>durvalumab</strong> - lung cancer (PII)</td>
</tr>
<tr>
<td><strong>H1 2016</strong></td>
<td><strong>ZS-9</strong>&lt;sup&gt;1&lt;/sup&gt; - hyperkalaemia (EU)</td>
<td><strong>H1 2016</strong></td>
</tr>
<tr>
<td><strong>PT003</strong> - COPD (US)</td>
<td><strong>Brilinta/Briliq</strong> - stroke</td>
<td><strong>benralizumab</strong> - severe asthma</td>
</tr>
<tr>
<td><strong>ZS-9</strong>&lt;sup&gt;1&lt;/sup&gt; - hyperkalaemia (US)</td>
<td><strong>durvalumab</strong> - lung cancer (US)</td>
<td><strong>Brilinta/Briliq</strong> - stroke</td>
</tr>
<tr>
<td><strong>Tagrisso</strong> - lung cancer (EU, JP)</td>
<td><strong>tremelimumab</strong> - mesothelioma</td>
<td><strong>Lynparza</strong> - breast cancer</td>
</tr>
<tr>
<td><strong>H2 2016</strong></td>
<td><strong>H2 2016</strong></td>
<td><strong>tremelimumab</strong> - mesothelioma (PII)</td>
</tr>
<tr>
<td><strong>saxa/dapa</strong> - type-2 diabetes (EU)</td>
<td><strong>benralizumab</strong> - severe asthma</td>
<td><strong>H2 2016</strong></td>
</tr>
<tr>
<td><strong>cediranib</strong> - ovarian cancer (EU)</td>
<td><strong>durvalumab</strong> - lung cancer (US)</td>
<td><strong>Brilinta/Briliq</strong> - PAD</td>
</tr>
<tr>
<td><strong>CAZ AVI</strong> - serious infections (EU)</td>
<td><strong>tremelimumab</strong> - mesothelioma (US, EU)</td>
<td><strong>Lynparza</strong> - ovarian cancer</td>
</tr>
<tr>
<td><strong>H2 2016</strong></td>
<td><strong>roxadustat</strong> - anaemia (CN)</td>
<td><strong>durvalumab</strong> - H&amp;N cancer (PII)</td>
</tr>
<tr>
<td><strong>benralizumab</strong> - severe asthma</td>
<td><strong>selumitinib</strong> - lung cancer</td>
<td><strong>selumitinib</strong> - lung cancer</td>
</tr>
</tbody>
</table>

1. Pending completion of ZS Pharma acquisition
Disciplined execution of science-driven pipeline

113 projects in clinical pipeline

3 approvals so far this year

16 new medicines\(^1\) in pivotal trials or under regulatory review

---

1. Pending completion of ZS Pharma acquisition
Q&A

Please press *1 on your phone to indicate that you wish to ask a question
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