Forward-looking statements

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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 / webinar should be construed as a profit forecast.
Agenda

Welcome

Oncology strategy and commercial update

DNA damage response (DDR)

Immuno-oncology: Late- & early-stage development

Haematology

Summary and Q&A
Focused strategy

Three therapy areas

- Respiratory, Inflammation & Autoimmunity
- Cardiovascular & Metabolic Disease
- Oncology

Commitment to further focus the portfolio
Delivering the late-stage pipeline

2015-2016: Great progress for patients and science

- **Faslodex 500mg** approval CN (breast cancer 2L)
- **Brodalumab** submission US, EU (psoriasis)
- **Tagrisso** approval US, EU, JP (lung cancer)
- **Durvalumab** Breakthrough US (bladder cancer)
- **Benralizumab** Phase III positive (severe asthma)
- **Saxa/dapa** submission EU (type-2 diabetes)
- ** Cediranib** submission EU (ovarian cancer)
- **Iressa** approval US (lung cancer)
- **Brilinta/Brilique** Phase III miss (stroke)
- **CAZ AVI** positive opinion EU (serious infections)
- **Lynparza** Phase III miss (gastric cancer)
- **Faslodex** Phase III positive (breast cancer 1L)
- **Bydureon Pen** approval JP (type-2 diabetes)
- **Brilinta/Brilique** approval US, EU (post/prior MI)
- **Acalabrutinib** Orphan Drug EU (blood cancers)
- **MEDI-551** Orphan Drug US (neuromyelitis optica)
- **AZD3293** Phase III un-gating (Alzheimer’s disease)
- **ZS-9** submission EU (hyperkalaemia)

Illustrative timeline of 2015 and 2016 main late-stage pipeline newsflow

- Favourable
- Unfavourable
Key late-stage medicines & lifecycle
Phase III trials or under regulatory review*

Respiratory, Inflammation, Autoimmunity
- brodalumab* (psoriasis)
- benralizumab (severe asthma, COPD)
- tralokinumab (severe asthma)
- PT010 (COPD, asthma)
- anifrolumab (lupus)

Cardiovascular & Metabolic Disease
- ZS-9* (hyperkalaemia)
- roxadustat (anaemia)

Oncology
- cediranib* (ovarian cancer)
- selumetinib (lung cancer)
- durvalumab (multiple cancers)
- durva + treme (multiple cancers)
- acalabrutinib (blood cancers)
- moxetumomab (leukaemia)

Infection, Neuroscience (opportunistic)
- CAZ AVI* (serious infections)
- AZD3293 (Alzheimer’s disease)

Other medicines
- Brilinta/Brilique (heart disease)
- PT010 (COPD, asthma)
- Lynparza (multiple cancers)
- Tagrisso (lung cancer)

Status as of 29 April 2016 (Q1 2016 Results)
New medicine with larger potential
### Key late-stage medicines & lifecycle

**Phase III trials or under regulatory review**

#### Respiratory, Inflammation, Autoimmunity
- brodalumab* (psoriasis)
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#### Oncology
- cediranib* (ovarian cancer)
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#### Infection, Neuroscience (opportunistic)
- CAZ AVI* (serious infections)
- AZD3293 (Alzheimer’s disease)

* New medicine with larger potential

Status as of 29 April 2016 (Q1 2016 Results)
Oncology strategy and commercial update

Mondher Mahjoubi
Senior Vice President, Global Product Strategy Oncology
Oncology: Scientific leadership around four key platforms

Personalised healthcare as key driver

- Tumour drivers and resistance
- DNA damage response (DDR)
- Immuno-oncology (IO)
- Antibody conjugates
Oncology: Aiming for first or best in class
Deliver six new medicines to patients by 2020

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1st PARP inhibitor</td>
<td>Beyond BRCA and ovarian cancer</td>
<td>Leader in DDR</td>
</tr>
<tr>
<td>1st EGFR-T790M inhibitor</td>
<td>Earlier lines and combinations</td>
<td>Leader in EGFRm</td>
</tr>
<tr>
<td></td>
<td>Best-in-class BTK inhibitor</td>
<td>IO in haematology</td>
</tr>
<tr>
<td></td>
<td>Lead with IO/IO combination</td>
<td>Leader in IO</td>
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<td></td>
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<td>Next wave of innovation</td>
</tr>
</tbody>
</table>
Tagrisso: Fastest development time
Rationally-designed and targeted treatment

- 32 months from first in human to first approval; leapfrogged competition
- US, EU, Japan approved within six months
- Aggressive development plan, including China
Tagrisso: Reaching more patients through life cycle
Transforming outcomes for patients with EGFRm lung cancer

Establish in 2L+ T790M NSCLC

Expand in 1L EGFRm NSCLC

Transform survival with combinations and sequencing

Expand in adjuvant EGFRm NSCLC

2016 - 2017 2018 - 2020 2021+
**Tagrisso: Patient example**

**BLOOM trial effective in CNS**

**Diagnosis of advanced NSCLC June 2013 with most-recent disease progression March 2015**

- *Tagrisso* 160mg once daily started 20 May 2015
- Response ongoing from week 6. Week 12 images not presented as minimal changes were observed during weeks 6-12
- Stable extracranial disease since week 6; partial response since week 12
- Normal neurological function since baseline

Source: ASCO 2016, abstract 9002
**Tagrisso: Potential in 1L EGFRm NSCLC**
Early, but very promising data from Phase I

**Tony Mok**
Discussion of *Tagrisso* data at ELCC - Geneva, 13 April 2016

- Number of EGFRm +ve patients who received *Tagrisso* in 1L setting: 60
- Percentage of patients who attained partial response: 77%
- Median number of months of PFS in 1L setting: 19.3 months

Source: ELCC 2016, AstraZeneca data on file
## Tagrisso: Key data timeline

### Overview of clinical programme

<table>
<thead>
<tr>
<th>Study</th>
<th>Phase</th>
<th>Title</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>AURA 2L EGFRm T790M</td>
<td>Phase I</td>
<td>AURA</td>
<td>2015</td>
</tr>
<tr>
<td>AURA17 2L EGFRm T790M</td>
<td>Phase II</td>
<td>AURA17</td>
<td>2016</td>
</tr>
<tr>
<td>TATTON Phase Iib combinations with savolitinib and selumetinib</td>
<td>Phase III</td>
<td>TATTON</td>
<td>2017</td>
</tr>
<tr>
<td>AURA2 2L EGFRm T790M</td>
<td>Phase I</td>
<td>AURA2</td>
<td>2017</td>
</tr>
<tr>
<td>BLOOM EGFRm CNS disease</td>
<td>Phase III</td>
<td>BLOOM</td>
<td>2018+</td>
</tr>
<tr>
<td>FLAURA 1L EGFRm</td>
<td>Phase III</td>
<td>FLAURA</td>
<td>2018+</td>
</tr>
<tr>
<td>ADAURA Adjuvant EGFRm</td>
<td>Phase III</td>
<td>ADAURA</td>
<td>2018+</td>
</tr>
</tbody>
</table>
**Lynparza: Ovarian cancer**

Long-term survival benefit in BRCAm patients

- **First PARPi to show long-term OS data**
- Long-term responders indicate IO-like benefit with 15% of patients on treatment for five years
- sBRCA patients show similar benefit to gBRCA
- Future patient selection to be based on HRRm test, including BRCAwt/HRRm patients (~8% of all ovarian cancer patients)

Source: ASCO 2016, abstract 5501
**Lynparza: Expanding beyond BRCA**

Two dimensions driving life-cycle programme

- Combination with DDR
- Combination with IO
- Monotherapy
  - BRCAm
  - HRRm

Combination with VEGF
  - Biomarker negative

**Expanding patient population**
### Lynparza: Future newsflow

**Expected regulatory submissions**

<table>
<thead>
<tr>
<th>Study 8</th>
<th>(prostate cancer)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PAOLA</strong></td>
<td>bevacizumab combination (ovarian cancer)</td>
</tr>
<tr>
<td><strong>SOLO-1</strong></td>
<td>(1L BRCAm ovarian cancer)</td>
</tr>
<tr>
<td><strong>OlympiA</strong></td>
<td>(adjuvant BC)</td>
</tr>
<tr>
<td><strong>SOLO-2</strong></td>
<td>(2L BRCAm PSR ovarian cancer)</td>
</tr>
<tr>
<td><strong>POLO</strong></td>
<td>(pancreatic cancer)</td>
</tr>
<tr>
<td><strong>OlympiAD</strong></td>
<td>(advanced breast cancer)</td>
</tr>
<tr>
<td><strong>SOLO-3</strong></td>
<td>(3L+ gBRCAm PSR ovarian cancer)</td>
</tr>
</tbody>
</table>

| 2017 | 2018+ |

| **Phase II** | **Phase III** |
Beyond *Lynparza*: DDR

Developing chemo-free regimen, extending survival

<table>
<thead>
<tr>
<th>Scientific leadership in DDR</th>
</tr>
</thead>
</table>

**Establish *Lynparza* leadership as monotherapy**

**Launch AZD1775 (Wee1) monotherapy and combination**

**Expand *Lynparza* beyond BRCA**

**Launch *Lynparza* combinations**

**Deliver next-generation DDR medicines (AZD0156, AZD2811, AZD6738 and others)**
DDR abrogation is frequent across multiple cancer types

Cancer patients with targetable DDR defects

~40-50%

DDR abrogations include:
Cell cycle, oncogenic driver and homologous recombination repair

Source: AstraZeneca data on file
DDR

Susan Galbraith
Senior Vice President, Head of Oncology, IMED Biotech Unit
Targeting DNA damage response (DDR)
An Achilles heel where dependencies can be targeted selectively

DDR deficiency is an early (truncal) event leading to:

- **Deep responses**: Homogeneity across tumours with all cancer cells targeted
- **High response rates**: Reduced opportunity for innate resistance
- **Wide therapeutic index**: Selective sensitivity to DDR drugs (unlike chemotherapies)

**DDR engages the immune response**

- Synergistic opportunities with IO agents
Emerging evidence: DDR provides potential for cure

**Lynparza in BRCAm ovarian cancer**
- Patients still alive after eight years+
- ~25% patients are long-term responders (≥ two years)

**AZD1775 + carboplatin in platinum-resistant ovarian cancer**
- 42% ORR in combination with platinum chemotherapy
- 3/22 patients showed responses lasting one to three years

**Lynparza + AZD1775 in pre-clinical SCLC PDX model**
- Five/seven cures after only 21 days of treatment with mice alive after more than one year

Source: ASCO 2016, abstract 5501; AstraZeneca data on file
Patient selection

Critical component of delivering medical benefit

Reason to believe HRD LOH is NOT the right patient selection

- BRCAwt/HRD +ve patients in Study 19: No statistically-significant benefit
- HRD score cut-off base currently being refined

Reason to believe **HRRm test is better** in identifying BRCAwt patients likely to benefit from Lynparza

**Study 19**

Source: ECC 2015, Hodgson et al.
### Patient selection

**Example in prostate cancer**

<table>
<thead>
<tr>
<th>AstraZeneca HRR 15 gene panel</th>
<th>Genomic aberrations in DNA repair in patients with mCRPC*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA1</td>
<td>FANCL</td>
</tr>
<tr>
<td>BRCA2</td>
<td>FANCN(PALB2)</td>
</tr>
<tr>
<td>ATM</td>
<td>BARD1</td>
</tr>
<tr>
<td>RAD51B</td>
<td>CHEK1</td>
</tr>
<tr>
<td>RAD51C</td>
<td>CHEK2</td>
</tr>
<tr>
<td>RAD54L</td>
<td>CDK12</td>
</tr>
<tr>
<td>RAD51D</td>
<td>PPP2R2A</td>
</tr>
<tr>
<td>FANCJ/BRIP1</td>
<td></td>
</tr>
</tbody>
</table>

**Source:** J. Mateo et al. The New England Journal of Medicine, 2015; 373:1697-1708
Next-generation sequencing
Platform transforming accessibility to patients

<table>
<thead>
<tr>
<th>Hot-spot activating mutation for a single gene</th>
<th>Multiple deficiencies for two genes</th>
<th>Multiple deficiencies for multiple genes</th>
<th>Multiple deficiencies for multiple genes and multiple DDR mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g. EGFR</td>
<td>e.g. BRCA1/2 (PARPi sensitive)</td>
<td>Homologous Recombination Repair (HRR) (broader PARPi sensitivity)</td>
<td>Broad DDR test</td>
</tr>
<tr>
<td>Approved</td>
<td>Approved</td>
<td>In validation</td>
<td>In translation</td>
</tr>
</tbody>
</table>

- **Cell-cycle deregulation**
- **Oncogenic driver**
- **HRR**

- Approved
- In validation
- In translation
DDR engages the immune response

**Mechanisms**

- Generate immune-cell diversity through V(D)J recombination
- Generate neo-antigens through mutational control (MMR)
- Inflammatory response
- CDK1 regulation required for immune-mediated cell killing
- ‘Anti-viral’ early warning system / immune priming

**Biomarker evidence**

- CD4 and CD8 iTILs in Breast Tumour Samples

**Clinical evidence**

- MSI-H is caused by MMR deficiency, but also impacts DNA double-strand break-repair capability due to microsatellite deletions in ATM gene

Source: AstraZeneca data on file; NEJM
Emergence of a new cancer-treatment paradigm

40-50% with DDR defects

- Loss of one or more DNA repair pathways
- Increased levels of endogenous DNA damage
- DNA replication stress
- Genomic instability

Source: AstraZeneca data on file
AZD1775
Potential for monotherapy post PARPi

Monotherapy
Best percentage change tumour size*

<table>
<thead>
<tr>
<th>Best response</th>
<th>(N=12), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial response (PR)</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Stable disease (SD)</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Progressive disease (PD)</td>
<td>4 (33)</td>
</tr>
</tbody>
</table>

* Two additional patients with stable disease had evaluable, but not measurable, disease; †Patient had clinical progression; ‡Patient had new lesion

9/12 ovarian patient-derived tumour models resistant to Lynparza respond to AZD1775 single agent

Source: AACR 2016
Lynparza + AZD1775 combination

Phase I clinical data

Response to treatment (N=11)

- Cohort 1: AZD1775 125 mg
- Lynparza 100 mg
- Cohort 2: AZD1775 150 mg
- Lynparza 100 mg
- Cohort 3 arm 1: AZD1775 175 mg
- Lynparza 100 mg
- Cohort 3 arm 2: AZD1775 150 mg
- Lynparza 200 mg

Best response of target lesion (%)
- CR/PR: 13/23 (56%)
- SD: 3/23 (13%)
- CB: 16/23 (70%)

Preclinical data

Lynparza + AZD1775 in TNBC patient-derived tumour models show improved activity vs Lynparza monotherapy

Phase II 2016

- Ovarian (30 patients) (15 gBRCA, PARPi failures)
- SCLC (30 patients) (15 MYC amplified)
- TNBC (30 patients) (15 CCNE1 amplified)

Source: AstraZeneca data on file; AACR 2016, O’Connor; ASCO 2016, abstract 5562
AZD0156 (ATM) and AZD6738 (ATR)

Combinations with Lynparza in Phase I

Maximising DNA damage in S-phase

- **ATM** coordinates the repair of double-strand breaks (DSBs)
- **ATR** is required to repair stalled DNA replication forks
- **PARP** detects and triggers the repair of single-strand breaks (SSBs). Inhibition of PARP causes stalled replication forks and a build up of SSBs which convert to DSBs

Lynparza + AZD0156 and Lynparza + AZD6738 in two breast-cancer models

Source: AstraZeneca data on file
Summary

1. DDR deficiencies are common in multiple cancers (40-50%)

2. Targeting DDR deficiencies is clinically validated and a subset of patients experience long-term benefit

3. Patient selection is critical. NGS test development is underway for HRR panel for Lynparza and AZD1775

4. There is a significant scientific rationale and clinical evidence that DDR and immune responses are linked and potentially synergistic

5. AstraZeneca portfolio of DDR-targeting agents is the broadest with multiple agents in proof-of-concept studies
IO: Late-stage development

Rob Iannone, MD, MSCE
Senior Vice President, IO, Global Medicines Development
CTLA-4 and PD-L1

IO strategy built on fundamental checkpoints in anti-cancer immunity

CTLA-4: ‘Hard-wired’ negative regulator of T-cell activation

PD-L1: Adaptive resistance; induces T-cell exhaustion
CTLA-4 and PD-L1
IO strategy built on fundamental checkpoints in anti-cancer immunity
**Durvalumab monotherapy: 2L urothelial bladder cancer**

**Breakthrough Therapy Designation granted**

- **PD-L1 +ve (≥25% staining on TCs or ICs)**: 76% (19/25) had a reduction in tumour size (RECIST 1.1 ORR = 46%)
- **PD-L1 -ve (<25% staining on TCs or ICs)**: 36% (4/11) had a reduction in tumour size (RECIST 1.1 ORR = 0%)

* Unconfirmed response (all other patients with best tumour shrinkage ≥30% had confirmed responses); ▲ Unconventional response

Response evaluable population (n = 42); patients who initiated trial therapy ≥12 weeks prior to DCO and had ≥1 follow-up scans

Source: ASCO 2016, abstract 4502
Durvalumab monotherapy: 1L NSCLC
1L cohort from Study 1108 (Phase I/II)

**PD-L1 +ve: Durvalumab monotherapy**
29% ORR (95% CI: 17 - 43) in PD-L1 +ve tumours

**PD-L1 -ve: Durvalumab monotherapy**
11% ORR (95% CI: 0 - 48) in PD-L1 -ve tumours

* Response-evaluable population = patients with ≥24 weeks follow up
** PD-L1 +ve defined as ≥25% tumour cells stained for PD-L1 at any intensity
*** PD-L1 -ve defined as <25% tumour cells stained for PD-L1 at any intensity

Source: ASCO 2016, abstract 9029
Durva + treme: Clinical activity in PD-L1 low/-ve NSCLC

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

Durva + treme combinations address large unmet need:
PD-L1 low/-ve tumours in lung cancer

The RECIST1.1 ORR for PD-L1 negative 2L+ patients was 23% (6/26) and responses appear durable

# Durva and durva + treme clinical programmes

**Leading in early and first-line settings in key cancers**

<table>
<thead>
<tr>
<th></th>
<th>ADJUVANT</th>
<th>PACIFIC</th>
<th>MYSTIC</th>
<th>NEPTUNE</th>
<th>Chemotherapy combination</th>
<th>KESTREL</th>
<th>DANUBE</th>
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<tbody>
<tr>
<td><strong>Trial design</strong></td>
<td>Phase III (randomised)</td>
<td>Phase III (randomised)</td>
<td>Phase III (randomised)</td>
<td>Phase III (randomised)</td>
<td>Phase III (randomised)</td>
<td>Phase III (randomised)</td>
<td>Phase III (randomised)</td>
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<tr>
<td></td>
<td>EGFR/ALK wt Non-sq/sq</td>
<td>EGFR/ALK wt Non-sq/sq</td>
<td>EGFR/ALK wt Non-sq</td>
<td>EGFR/ALK wt Non-sq</td>
<td>EGFR/ALK wt Non-sq</td>
<td>EGFR/ALK wt Non-sq</td>
<td>Cis-eligible</td>
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<tr>
<td></td>
<td>Arms: durvalumab durva + treme SoC</td>
<td>Arms: durva + treme SoC</td>
<td>Arms: durva + treme SoC</td>
<td>Arms: durva + chemo durva + treme SoC</td>
<td>Arms: durvalumab durva + treme SoC</td>
<td>Arms: durvalumab durva + treme SoC</td>
<td>Cis-ineligible</td>
</tr>
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<td><strong>Primary endpoints</strong></td>
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<td>PFS OS</td>
<td>OS</td>
<td>TBD</td>
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<td><strong>Data readout</strong></td>
<td>2020</td>
<td>H1 2017</td>
<td>H1 2017 (PFS) 2018 (OS)</td>
<td>2018</td>
<td>TBD</td>
<td>2018</td>
<td>2018</td>
</tr>
</tbody>
</table>

- **Non-small cell lung cancer**
- **Head & neck cancer**
- **Bladder cancer**

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*First line*
**Lynparza + durvalumab (MEDIOLA trial)**
Leading with novel anti-PDL1 plus targeted-therapy combinations

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**Key features:**
- Phase II proof-of-concept basket trial
- Dose finding established in National Cancer Institute (NCI) D081KC00001
- Rigorous translational science

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**PARPi / IO-naïve**

- gBRCAm ovarian 3L and later platinum sensitive
  - N=30
- gBRCAm HER2-negative breast 1L, 2L, 3L not platinum refractory
  - N=38
- SCLC relapsed 3-6 months post 1L platinum
  - N=34
- Gastric 2L
  - N=37
- Additional indication (future)

---

**Baseline tumour biopsy and blood**

**Repeat tumour biopsy and blood**

**Repeat tumour biopsy and blood: C2D1**

**Lynparza monotherapy**
- (4w run-in)

**Combination Lynparza + durvalumab**
- (to progression)

Source: ASCO 2016, abstract 3015
IO: Early-stage development

David Berman
Senior Vice President, R&D Oncology, MedImmune
Building on anti-PD1/L1 cornerstone with new MOAs

1) PD-1/L1 blockade is highly active, but not every patient responds
2) Some tumours are insensitive to PD-1/L1 blockade

Our strategy

- Identify mechanisms by which tumors evade immune system
- Develop IO combinations to address multiple mechanisms
- Identify patients most likely to benefit
Enhancement of anti-tumour immunity

**Broad clinical-stage IO pipeline**

1. No effective anti-tumour immunity
2. Sub-optimal or exhausted anti-tumour immunity
3. Anti-tumour immunity suppressed by TME

**Goal:** Highly active anti-tumour immunity

---

**Immune status**

- "Cold" tumour
- Example: PD-L1+ tumour
- Example: CD73+ tumour

**Therapeutic aim**

- Prime new response
- Potentiate existing response
- Reverse tumour immuno-suppression

**Clinical pipeline**

- TLR 7/8
- PD-L1
- hOX40
- CD73
- NME
- CTLA-4
- GITR
- CXCR2
- DNA vaccine
- PD-1
- NKG2A
- STAT3

**Eliminate tumour**
Unlocking the power of IO combinations

Multiple ongoing IO combinations based on complementary MOAs

<table>
<thead>
<tr>
<th>Durvalumab combination (sponsored)</th>
<th>Durvalumab combination (clinical collaboration)</th>
<th>Tremelimunab combination</th>
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<tbody>
<tr>
<td>CTLA-4</td>
<td>IDO</td>
<td>hOX40</td>
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<td>hOX40</td>
<td>HDAC</td>
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<td>CD73</td>
<td>IMCgp100</td>
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<tr>
<td>NKG2A</td>
<td>CSF-1R</td>
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<td>PD-1</td>
<td>TGFβR-1</td>
<td></td>
</tr>
<tr>
<td>STAT3</td>
<td>CD19-CART</td>
<td></td>
</tr>
<tr>
<td>CXCR2</td>
<td>CCR4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HPVE7</td>
<td></td>
</tr>
</tbody>
</table>
Develop the science
Guiding the IO portfolio and identification of new targets

MOA-based prioritisation

Develop the science
Identify which tumours to study
Identify markers of adaptive resistance
Understand immune landscape of tumours

Source: ASCO 2016, abstract 3036
TLR 7/8 (MEDI9197) primes new immune response
Activates ‘sensor’ and ‘presenter’ dendritic cells (DC)

Lipid tail increases tumour retention

Developing predictive signature

Imiquimod validates TLR7

Source: ASCO 2016, abstract TPS3095

IO synergy with antibody conjugates

**Highly potent warhead**
(pyrrolobenzodiazepine, PBD)

- Cross-links DNA & induces apoptosis in dividing and resting cells
- Kills cancer stem cells
- Synthetic lethality with BRCA & other DNA-repair defects
- Clinically validated

**Synergy with anti-PDL1**

- Un-treated
- NME-PBD
- α-PD-L1
- NME-PBD + α-PD-L1

**Novel antibody engineering**

- Bi-paratopic technology, induces higher order lattice clustering to drive internalisation
- Proprietary site-specific conjugation
- Alternative scaffold technology
- Half-life extension technology
- Non-natural amino acid technology

Source: AstraZeneca data on file
### Early-stage IO

**Expected key data**

<table>
<thead>
<tr>
<th>hOX40</th>
<th>durvalumab + CD73</th>
<th>durvalumab + hOX40</th>
</tr>
</thead>
<tbody>
<tr>
<td>GITR</td>
<td>durvalumab + NKG2A</td>
<td>durvalumab + PD-1</td>
</tr>
<tr>
<td>TLR 7/8</td>
<td>hOX40 + tremelimumab</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>2016</th>
<th>2017 / 2018+</th>
</tr>
</thead>
</table>

Phase I
Haematology

Sean Bohen
Executive Vice President, Global Medicines Development & Chief Medical Officer
Establish leadership in haematology

**Complementary strategies**

**Elevating the standard of care in B-cell cancers**

- Acalabrutinib has opportunity to become SoC in CLL and NHL
- Acerta as Haematology Centre of Excellence

**Driving towards a cure in multiple haematological-disease states**

- Immediate access to a portfolio of effective small-molecule medicines
- Aspiration to cure patients with durvalumab combinations in areas of high unmet medical need

Leverage breadth of portfolio and clinical-trial opportunities to become the partner of choice in haematology and transform care
AstraZeneca: Potential haematology leadership
Driven by access to rich portfolio across two growth platforms

**Acalabrutinib**

- Non-Hodgkins Lymphoma
- Mantle Cell Lymphoma
- Waldenström’s Macroglobulaemia
- Chronic Lymphocytic Leukaemia

**Durvalumab**

- Non-Hodgkins Lymphoma
- Hodgkins Lymphoma
- Multiple Myeloma
- Chronic Lymphocytic Leukaemia
- Acute Myeloid Leukaemia / Myelodysplastic Syndrome

Further indications and combinations to be determined
BTK inhibitor class
Cornerstone of treatment for B-cell malignancies

- **Long treatment duration** drives market growth ($19bn G7 market by 2024\(^1\))
- **Continuous BTK inhibition is critical** to improving treatment outcomes\(^2\)
- **Tolerability is key** to maintaining dose intensity and ability to combine with other treatments for improved efficacy
- Ibrutinib is the **only approved medicine** in the BTK-inhibitor class
- **Off-target activity** can lead to rash, diarrhoea, arthralgia/myalgia, severe bleeding and atrial fibrillation\(^3\)

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Acalabrutinib has the potential to become a best-in-class BTKi

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1 Decision Resources, NHL report Nov 2015
2 Dose adherence and baseline exposure analysis of the ibrutinib 420mg dose administered to patients with previously treated CLL; ASCO 2015 abstract 7012
M. Farooqui 2015. Atrial Fibrillation in CLL/SLL Patients on Ibrutinib; ASH abstract 2933
Acalabrutinib
Designed to deliver differentiated clinical profile, best-in-class potential

Highly-potent and selective BTK inhibition

<table>
<thead>
<tr>
<th>Kinase inhibition IC_{50} (nM)</th>
<th>acalabrutinib</th>
<th>ibrutinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTK</td>
<td>5.1</td>
<td>1.5</td>
</tr>
<tr>
<td>TEC</td>
<td>93</td>
<td>7.0</td>
</tr>
<tr>
<td>BMX</td>
<td>46</td>
<td>0.8</td>
</tr>
<tr>
<td>TXK</td>
<td>368</td>
<td>2.0</td>
</tr>
<tr>
<td>ERBB2</td>
<td>~1000</td>
<td>6.4</td>
</tr>
<tr>
<td>EGFR</td>
<td>&gt;1000</td>
<td>5.3</td>
</tr>
<tr>
<td>ITK</td>
<td>&gt;1000</td>
<td>4.9</td>
</tr>
<tr>
<td>JAK3</td>
<td>&gt;1000</td>
<td>32</td>
</tr>
<tr>
<td>BLK</td>
<td>&gt;1000</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Minimal effects on TEC, EGFR, or ITK signaling

Continued BTK inhibition

Short half-life prevents plasma accumulation and enables complete 24-hr BTK coverage (≥97%)\(^1\)

Improved safety and tolerability potential

Optimal disease-control potential

Source: Byrd et al. 2016

Covey AACR 2015, abstract 2596

Low inter-patient variability  Time of assessment
# Acalabrutinib

## ASCO 2016: Compelling efficacy in front-line CLL

### R/R CLL*: ASH 2015

<table>
<thead>
<tr>
<th>n (%)</th>
<th>All cohorts (N=60)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>0 (0)</td>
</tr>
<tr>
<td>PR</td>
<td>51 (85)</td>
</tr>
<tr>
<td>PR+L</td>
<td>6 (10)</td>
</tr>
<tr>
<td>SD</td>
<td>3 (5)</td>
</tr>
<tr>
<td>PD</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ORR (CR + PR)</td>
<td>51 (85%)</td>
</tr>
<tr>
<td>ORR (CR + PR + PRL)</td>
<td>57 (95%)</td>
</tr>
</tbody>
</table>

### FL CLL*: ASCO 2016

<table>
<thead>
<tr>
<th>n (%)</th>
<th>All cohorts (N=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>0 (0)</td>
</tr>
<tr>
<td>PR</td>
<td>63 (88)</td>
</tr>
<tr>
<td>PR+L</td>
<td>7 (10)</td>
</tr>
<tr>
<td>SD</td>
<td>2 (3)</td>
</tr>
<tr>
<td>PD</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ORR (CR + PR)</td>
<td>63 (88%)</td>
</tr>
<tr>
<td>ORR (CR + PR + PRL)</td>
<td>70 (97%)</td>
</tr>
</tbody>
</table>

---

PR+L = Partial Response with Lymphocytosis

ORR in del17p: 100%  
†30 Sept 2015; ASH 2015 data; best overall response assessment; median time to last response assessment = 11 months

‡Includes two SD patients (100 mg BID) with all nodes <1.5 cm at baseline CT

*Based on modified IWCLL 2008., †investigator assessed

---

PRL, PR with lymphocytosis

*Efficacy-evaluable patients had at least one response assessment after first dose of trial drug

*investigator assessed

Source: ASH 2015, ASCO 2016, abstract 7521
**Acalabrutinib**

**Favourable safety profile**

### R/R CLL: ASH 2015

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>All Grades, n (%)</th>
<th>Grades 3/4, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>26 (43)</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>24 (39)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Weight increased</td>
<td>16 (26)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>14 (23)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>14 (23)</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>13 (21)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Oedema peripheral</td>
<td>13 (21)</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12 (20)</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>12 (20)</td>
<td>0</td>
</tr>
<tr>
<td>Contusion</td>
<td>11 (18)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Arthralgia</strong></td>
<td>10 (16)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Petechiae</td>
<td>10 (16)</td>
<td>0</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>10 (16)</td>
<td>0</td>
</tr>
</tbody>
</table>

Multiple occurrences of the same event for a given subject were counted once for each system organ class and each preferred term.

### FL CLL: ASCO 2016

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>All Grades, n (%)</th>
<th>Grades 3/4, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>30 (41)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26 (35)</td>
<td>0</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>16 (22)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>13 (18)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Increased weight</td>
<td>13 (18)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Contusion</td>
<td>13 (18)</td>
<td>0</td>
</tr>
<tr>
<td>Rash</td>
<td>12 (16)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

There were no cases of atrial fibrillation or acalabrutinib-associated major bleeding.

---

Source: ASH 2015; ASCO 2016, abstract 7521
Acalabrutinib clinical development
Haematological malignancies represent first registration opportunity

<table>
<thead>
<tr>
<th>Indication</th>
<th>Trial design and line of therapy</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLL</td>
<td>acalabrutinib vs. ibrutinib</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>CLL relapsed/refractory</td>
<td></td>
</tr>
<tr>
<td></td>
<td>acalabrutinib + obinutuzumab vs. obinutuzumab + chlorambucil vs. acalabrutinib</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>CLL front/first line</td>
<td></td>
</tr>
<tr>
<td></td>
<td>acalabrutinib</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>CLL relapsed/refractory, ibrutinib-intolerant</td>
<td></td>
</tr>
<tr>
<td>MCL</td>
<td>acalabrutinib</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>MCL relapsed/refractory</td>
<td></td>
</tr>
<tr>
<td>WM</td>
<td>acalabrutinib</td>
<td>Ia/II</td>
</tr>
<tr>
<td></td>
<td>WM relapsed/refractory</td>
<td></td>
</tr>
</tbody>
</table>

- Early monotherapy and combination trials ongoing in Richter’s transformation, DLBCL, FL, MM
- Monotherapy and combination trials ongoing in multiple solid tumours (pancreatic, bladder, ovarian cancers and NSCLC, HNSCC and GBM)
Closing

Sean Bohen
Executive Vice President of Global Medicines Development and Chief Medical Officer
# Key takeaways

1. **Lynparza and Tagrisso** - encouraging launches and strong bases for further approvals

2. DDR - significant potential across multiple tumour types. AstraZeneca portfolio of DDR-targeting medicines is the broadest and leading the field

3. IO: Late-stage development - opportunities across a wide range of combination therapies with key data points in H1 2017

4. IO: Early-stage development - building on the anti-PD1/L1 cornerstone with OX40 next

5. Haematology - potential leadership driven by access to rich portfolio of assets across two growth platforms
Please press *1 on your phone if you wish to ask a question

- Pascal Soriot, moderator
- Sean Bohen
- Mondher Mahjoubi
- Susan Galbraith
- David Berman
- Rob Iannone
- Other members of the AstraZeneca Oncology team

Investor science event expected to end at 8:30 PM CDT
ASCO 2016 Investor Science Event

Chicago, IL, USA
6 June 2016