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:

The preliminary announcement contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group. 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 the preliminary announcement 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 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; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions 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 to manage a crisis; 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 that new products do not perform as we expect; the risk of environmental liabilities; the risks associated with conducting business in emerging markets; the risk of reputational damage; the risk of illegal trade in our products; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; 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.

Forward-looking statements
Agenda

1. AstraZeneca Oncology
   Mondher Mahjoubi
   Head of Oncology, Global Product & Portfolio Strategy

2. The power of combinations in IO
   Mohammed M. Dar
   VP, Oncology Clinical Development, MedImmune

3. Clinical experience w/MEDI4736 + treme
   Scott Antonia
   Moffitt Cancer Center, Tampa, FL, USA

4. Small-molecule combinations
   Susan Galbraith
   Head of Oncology, Innovative Medicines Biotech Unit

5. Maximising value across tumour types
   Robert Iannone
   Head of Immuno-Oncology, Global Medicines Development

6. Closing and Q&A
   Pascal Soriot
   Chief Executive Officer
Mondher Mahjoubi
Head of Oncology, Global Product & Portfolio Strategy
Oncology: Achieving scientific leadership

- **Iressa**
  - Filing (US)
- **MEDI4736 (PD-L1)**
  - Fast Track (US)
- **AZD9291**
  - Breakthrough (US)
- **Lynparza**
  - Approval (US, EU)
- **AZD9291**
  - Filing (US)
- **Iressa**
  - Approval (US)
- **MEDI4736**
  - Filing ovarian cancer (EU)
- **cediranib (VEGFR)**
  - Filing NSCLC 3L
- **AZD9291**
  - Three Phase III starts in NSCLC: 2L, 1L and adjuvant
- **MEDI4736**
  - 16 Phase II-III registration studies
- **tremelimumab**
  - Orphan Drug (US)
- **tremelimumab**
  - Filing mesothelioma 2L
- **selumetinib (MEK)**
  - Filing uveal melanoma
- **savolitinib (MET)**
  - Filing pRCC (US)

**Illustrative**

- **Small molecule**
- **Large molecule**
### Genetic drivers of cancer and resistance

<table>
<thead>
<tr>
<th>Compound</th>
<th>Details</th>
</tr>
</thead>
</table>
| **AZD9291** (EGFR) | - Updated PFS of 13.5 months (AURA 2L study)  
- Encouraging data in EGFR-mutated 1L lung cancer  
- Combination with savolitinib to overcome resistance |
| **savolitinib** (MET) | - Responses in MET-amplified gastric cancer and papillary renal cancer |
| **AZD2014** (mTOR) | - Encouraging data in ovarian & lung cancers in combination with paclitaxel |
| **AZD5363** (AKT) | - Responses in AKT1-mutated tumours, combinations with Lynparza, paclitaxel and enzalutamide |

### DNA damage repair

<table>
<thead>
<tr>
<th>Compound</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lynparza</strong> (PARP)</td>
<td>- Promising clinical activity in prostate cancer</td>
</tr>
<tr>
<td><strong>AZD1775</strong> (WEE-1)</td>
<td>- Proof of concept in p53-mutated ovarian cancer</td>
</tr>
</tbody>
</table>
Immuno-Oncology (IO): Building leadership

1. Create a diverse portfolio
   - Optimising T-cell function and memory
   - Inhibition by micro-environment
   - Antigen presentation and innate immunity

2. Maximise value across tumour types
   - Solid tumours
   - Haematology
   - Early-stage disease

3. Unlock the power of combinations
   - IO-IO combinations
   - IO-SM combinations
MEDI4736: Potential against haematological cancers
Celgene joint development plan across wide range of uses

<table>
<thead>
<tr>
<th>Lymphoma</th>
<th>DLBCL(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FL(^2)</td>
</tr>
<tr>
<td></td>
<td>Relapsed / refractory settings</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>Front line</td>
</tr>
<tr>
<td></td>
<td>Relapsed / refractory</td>
</tr>
<tr>
<td>Myelodysplastic syndrome</td>
<td>Relapsed / refractory</td>
</tr>
</tbody>
</table>

Further indications and combinations to be determined

---

1 DLBCL = Diffuse Large B-Cell Lymphoma
2 FL = Follicular Lymphoma
IO: Backbone with various combination partners targeting specific tumour biology - lung cancer example

- Lung
- Head & Neck
- Bladder
- Breast
- Haematology
- Melanoma

PD-1/PD-L1: Promise of durable responses in multiple tumour types

Not all lung cancers are the same: Combo therapies will address tumour biology
The power of combinations in IO

Mohammed M. Dar
Vice President, Oncology Clinical Development, MedImmune
Optimising anti-tumour immunity
Portfolio addresses major escape mechanisms

Key: New since ASCO 2014

Optimising T-cell function and memory
- PD-L1
- CTLA-4
- OX40 FP
- OX40 hAb
- mOX40 combos with MEDI4736, treme, rituximab
- OX40 FP combo with MEDI4736
- CART* (Juno)

Antigen presentation
- Chemo
- Oncolytic Virus* (Omnis VSV-ifnb)
- NKG2A (Innate Pharm)
- ADC (NME-2015)
- TKI combos (AZD9291, Iressa, BRAF/MEK*)
- Ibrutinib*
- Vaccines (Advaxis*, others)

Inhibition by micro-environment
- IDO* (NME-2015)
- CCR4*
- CXCR2
- STAT3

*Clinical collaboration
MEDI4736: Trend towards overall survival in NSCLC

- Preliminary OS data from study 1108 are encouraging and suggest that patients with PD-L1 positive tumours may have improved OS compared to patients with PD-L1 negative tumours.

Unmet need remains in PD-L1 negative tumours.
The promise of combinations
Stimulating both innate and adaptive immunity

Like T-cells, NK cells are also capable of killing tumour cells
NKG2A is expressed both on NK and T-cells and acts as checkpoint (different from KIR)
The ligand, HLA-E, is expressed on multiple solid and liquid tumours (potential selection)
The promise of combinations
PD-L1 + OX40 and CTLA-4 + OX40

Pre-clinical\textsuperscript{1} data with PD-L1

- **PD-L1**: CR=0/10
- **OX40**: CR=1/10
- **PD-L1 + OX40**: CR=5/10

Pre-clinical\textsuperscript{1} data with CTLA-4

- **CTLA-4**: CR=2/14
- **OX40**: CR=3/14
- **CTLA-4 + OX40**: CR=10/14

\textsuperscript{1} Mouse model used in experiments
CR = complete response
McGlinchey et al. Poster AACR 2014
Translation of IO strategy into the clinic: OX40 programme

- **muOX40**
  - **MEDI6469**
  - muOX40 + treme or MEDI4736
  - muOX40 + rituximab
  - Advanced malignancies
  - DLBCL

- **huOX40FP**
  - **MEDI6383**
  - huOX40FP
  - huOX40FP + MEDI4736
  - Advanced malignancies

- **huOX40mAb**
  - **MEDI0562**
  - huOX40mAb + combinations
  - Advanced malignancies

Safety and biomarker learnings

Optimal OX40 construct to be selected based on clinical efficacy by year end
**MEDI4736 + treme target two different escape pathways**

**Scientific rationale**

1. **Dendritic cells (DC) process tumour neoantigen**
   - Tumour
   - Ag
   - DC
2. **Blocking of B7 binding to CTLA-4 allows T-cell activation**
   - CD8 T-cell priming
   - DC
   - Antigen recognition
   - B7
   - CTLA-4
3. **Activated T-cell attacks tumour and is sustained in the presence of PD-L1 blockade**
   - Tumour
   - CD8 T
   - MEDI4736
   - tremelimumab
   - PD-L1
   - IFN-γ
**Study 006: Dose selection for MEDI4736 + treme**

**Design:** Zone-based dose escalation and Phase Ib expansion phase

**Population:** Stage III-IV NSCLC patients who have failed systemic therapy (no restrictions on # of prior therapies)

<table>
<thead>
<tr>
<th>1st endpoint: Safety (28-day DLT period)</th>
<th>2nd endpoint: Efficacy (RECIST response Q8 wks)</th>
<th>Exploratory endpoints: Peripheral pharmacodynamics, tumour PD-L1 status</th>
</tr>
</thead>
</table>

MEDI4736 + treme show efficacy regardless of PD-L1 status
Treme doses beyond 1 mg/kg do not increase efficacy

<table>
<thead>
<tr>
<th></th>
<th>M10-20 Q4/2W T1 mg/kg</th>
<th>M10-20 Q4/2W T3 mg/kg</th>
<th>M15 Q4W T10 mg/kg</th>
<th>All cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>All evaluable subjects</td>
<td>27</td>
<td>24</td>
<td>9</td>
<td>63²</td>
</tr>
<tr>
<td>ORR[2] - n (%)</td>
<td>9 (33%)</td>
<td>6 (25%)</td>
<td>2 (22%)</td>
<td>17 (27%)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(17% - 54%)</td>
<td>(10% - 47%)</td>
<td>(3% - 60%)</td>
<td>(17% - 40%)</td>
</tr>
<tr>
<td>PD-L1 positive (n)</td>
<td>9</td>
<td>5</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>ORR[2] - n (%)</td>
<td>3 (33%)</td>
<td>2 (40%)</td>
<td>1 (25%)</td>
<td>6 (33%)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(7% - 70%)</td>
<td>(5% - 85%)</td>
<td>(1% - 81%)</td>
<td>(13% - 59%)</td>
</tr>
<tr>
<td>PD-L1 negative (n)</td>
<td>13</td>
<td>14</td>
<td>4</td>
<td>33²</td>
</tr>
<tr>
<td>ORR[2] - n (%)</td>
<td>5 (38%)</td>
<td>3 (21%)</td>
<td>1 (25%)</td>
<td>9 (27%)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(14% - 68%)</td>
<td>(5% - 51%)</td>
<td>(1% - 81%)</td>
<td>(13% - 46%)</td>
</tr>
<tr>
<td>PD-L1 unknown (n)</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>12²</td>
</tr>
<tr>
<td>ORR[2] - n (%)</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
<td>0 (0%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(1% - 72%)</td>
<td>(1% - 72%)</td>
<td>(0% - 98%)</td>
<td>(2% - 48%)</td>
</tr>
</tbody>
</table>

Dose selected for Phase III studies

1 Includes confirmed and unconfirmed complete response (CR) or partial response (PR). In patients with measurable disease at baseline, ≥1 follow-up scan + those that discontinued due to PD or death without any follow-up scan. All subjects were dosed ≥sixteen weeks prior to the cut-off date.
2 Includes three subjects (two PD-L1 negative and one PD-L1 unknown) treated at M3 Q4W + T1 mg/kg.
Responses with MEDI4736 + treme: Rapid and durable
Similar activity across PD-L1 positive and negative subsets

M = MEDI4736; PD-L1 = programmed death-ligand 1; Q#W = every # weeks; SD = stable disease; T = tremelimumab
MEDI4736 + treme increases ORR over monotherapy
Important improvement in PD-L1 negative patients

Response rates at doses selected for pivotal studies

- **All**
  - Mono Study 1108: 16% (32/200)
  - Combo Study 6: 33% (9/27)

- **PD-L1+**
  - Mono Study 1108: 27% (23/84)
  - Combo Study 6: 33% (3/9)

- **PD-L1-**
  - Mono Study 1108: 5% (5/92)
  - Combo Study 6: 38% (5/13)

Monotherapy = M10 mg/kg Q2W in NSCLC (all lines) in 1108 (data cut-off = 27 Feb 2015)
Combination therapy = M10-20/T1 in 006 (data cut-off = 15 Apr 2015)
ORR = overall response rate
**MEDI4736 + treme show promising activity**

Large unmet medical need in PD-L1 negative NSCLC patients

<table>
<thead>
<tr>
<th>PD-1/PD-L1 class monotherapy</th>
<th>Durable clinical benefit for a <strong>subset</strong> of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-1/PD-L1 + CTLA-4 MoA combination</td>
<td>Strongest <strong>clinically-validated</strong> IO-IO combination to date</td>
</tr>
<tr>
<td>MEDI4736 + treme</td>
<td>Promising clinical activity in NSCLC especially in PD-L1 neg. subset with <strong>manageable safety profile</strong></td>
</tr>
<tr>
<td>IO-IO combination strategy</td>
<td>Develop novel IO combinations targeting patients who are less likely to respond to PD-1/PD-L1 monotherapy</td>
</tr>
</tbody>
</table>

**MoA** = mode of action
Clinical experience with MEDI4736 + treme

Scott Antonia
Department Chair and Program Leader, Thoracic Oncology and Program Leader of the Immunology Program at Moffitt Cancer Center, Tampa, FL, USA
## Study overview

### Study design

<table>
<thead>
<tr>
<th>Key elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph Ib zone-based dose escalation design with ability to expand selected cohorts for safety/PD/efficacy</td>
</tr>
<tr>
<td>Previously-treated patients with NSCLC</td>
</tr>
</tbody>
</table>

### Key eligibility criteria

<table>
<thead>
<tr>
<th>Key inclusion criteria</th>
<th>Key exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECOG PS 0–1</td>
<td>Active or prior auto-immune disease</td>
</tr>
<tr>
<td>Adequate organ function</td>
<td>Prior severe or persistent adverse events (AE)</td>
</tr>
<tr>
<td>Immunotherapy-naïve: No prior immunotherapy*</td>
<td>Current/prior immunosuppressive medication ≤14 days before first MEDI4736 and tremelimumab dose</td>
</tr>
<tr>
<td>Any number of prior therapies</td>
<td></td>
</tr>
</tbody>
</table>

*PD-L1 immunohistochemical staining on automated BenchMark ULTRA® platform using the PD-L1 SP263 assay (see ASCO 2015 Poster 8033)

### Study endpoints

<table>
<thead>
<tr>
<th>Primary</th>
<th>Secondary</th>
<th>Exploratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td>PK</td>
<td>PD-L1 status*</td>
</tr>
<tr>
<td>Tolerability</td>
<td>Immunogenicity</td>
<td>Serum PD-L1</td>
</tr>
<tr>
<td></td>
<td>Anti-tumor activity</td>
<td></td>
</tr>
</tbody>
</table>
MEDI4736 + tremelimumab: PK/PD summary

- PK exposure consistent with respective monotherapy studies; suggesting no PK interaction
- Dose as low as 1 mg/kg of tremelimumab in combination demonstrated log fold greater peripheral pharmacodynamic activity (T-cell proliferation/activation) compared to MEDI4736 monotherapy
Treme 1 mg/kg Q4W well tolerated in combo with MEDI4736

- Related grade 3/4 AEs and discontinuations due to related AEs were lowest in the 1 mg/kg Q4W tremelimumab cohorts
- AEs did not appear related to dose or schedule of MEDI4736

<table>
<thead>
<tr>
<th></th>
<th>M10-20 Q4/2W T1 mg/kg n=56</th>
<th>M10-20 Q4/2W T3 mg/kg n=34</th>
<th>M15 Q4W T10 mg/kg n=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related AE</td>
<td>35 (63%)</td>
<td>30 (88%)</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>Related G3/4 AE</td>
<td>16 (29%)</td>
<td>18 (53%)</td>
<td>7 (78%)</td>
</tr>
<tr>
<td>Related death</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Related serious AE</td>
<td>10 (18%)</td>
<td>17 (50%)</td>
<td>7 (78%)</td>
</tr>
<tr>
<td>Related AE leading to discontinuation</td>
<td>4 (7%)</td>
<td>12 (35%)</td>
<td>4 (44%)</td>
</tr>
</tbody>
</table>
### Related grade 3/4 events of special interest

Comparison to MEDI4736 monotherapy

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Event</th>
<th>Mono (study 1108) n=228</th>
<th>M10-20 Q4/2W T1 mg/kg n=56</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any event</td>
<td></td>
<td>3%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td>&lt;1%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Colitis</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pneumonitis</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td><strong>Skin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rash (maculopapular)</td>
<td>&lt;1%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td><strong>Endocrine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyperthyroidism</td>
<td>&lt;1%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Hypothyroidism</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Thyroiditis</td>
<td>&lt;1%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td><strong>Investigations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ALT increased</td>
<td>&lt;1%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>AST increased</td>
<td>1%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Amylase increased</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Lipase increased</td>
<td>0%</td>
<td>7%</td>
</tr>
</tbody>
</table>
Time to response and duration of response

- Time to and on-treatment response
- Off-treatment response
- Time to response
- D/C treatment
- Response ongoing

Patient continued to be treated after initial PD

Weeks since treatment initiation
MEDI4736 + treme combination:
High level of activity and manageable safety

- MEDI4736 20 mg Q4W and tremelimumab 1 mg/kg Q4W (M20T1 Q4W) has been selected for Phase III development
  - Maximizes PD-L1 inhibition
  - Demonstrates manageable safety
  - Incorporates biologically-active dose of tremelimumab associated with clinical activity

- Across all dose cohorts:
  - AEs were manageable and generally reversible using standard treatment guidelines
    - 31% of patients received corticosteroids for management of AEs

High level of clinical activity was seen in pre-treated NSCLC patients, especially in patients with PD-L1 negative tumors
Small-molecule combinations

Susan Galbraith
Head of Oncology, Innovative Medicines Biotech Unit
Combination of targeted therapy and immune checkpoints

**Targeted therapies: High response rate**

*Example of AZD9291*

**IO: High duration of response**

Potential synergistic effect

High RR and median PFS of targeted therapies with extended duration of response of IO
Potential for well-tolerated, durable benefit in BRAFm melanoma

**BRAFi + MEKi + MEDI4736**
Unprecedented ORR (69%) and DCR (100%)

Tumour size change from baseline: Cohort A

<table>
<thead>
<tr>
<th>Clinical activity, n (%)</th>
<th>Cohort A (n=26)</th>
<th>Cohort B (n=19)</th>
<th>Cohort C (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR</strong></td>
<td>18 (69)</td>
<td>4 (21)</td>
<td>2 (13)</td>
</tr>
<tr>
<td><strong>DCR</strong></td>
<td>26 (100)</td>
<td>15 (79)</td>
<td>12 (80)</td>
</tr>
<tr>
<td><strong>DoR, wks (range)</strong></td>
<td>(7.7+, 50.6+)</td>
<td>(7.9+, 24.7+)</td>
<td>(7.0+, 8.0+)</td>
</tr>
</tbody>
</table>

Data cut-off: 30 April 2015
**Lynparza + MEDI4736**  
DNA damage prone to immune response

### Rationale
- BRCA-mutant breast and ovarian cancers associated with a CXCR3+ T-cell lymphocytic infiltrate: Immune response associated with DNA damage\(^1,2\)
- High CXCL10, IDO, IFN gene expression

### T-cell infiltrates in BC

<table>
<thead>
<tr>
<th>Sporadic</th>
<th>BRCA-pathway deficient</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Sporadic T-cell infiltrate" /></td>
<td><img src="image2.png" alt="BRCA-pathway deficient T-cell infiltrate" /></td>
</tr>
</tbody>
</table>

### Combination trials to start by Q3 2015
- DDR deficient ovarian cancer (BRCA, ATM etc.)
- DDR deficient SCLC, TNBC, bladder, gastric, NSCLC, H\&N, cervical and pancreatic cancer
- Add tremelimumab if doublet combination well tolerated

---

\(^1\) Lakhani et al Breast Cancer Res. 1999;1(1):31-5;  
EGFRm+ NSCLC: SM-IO combination strategy

**1L EGFRm+**
- Targeted therapy: AZD9291, Iressa

**2L EGFRm+**
- T790M+
  - Targeted therapy + IO: Iressa, MEDI4736
- T790M-
  - Targeted therapy + IO: AZD9291 + MEDI4736

**Improving response rates and prolonging duration of response**

- Other combinations

**TATTON study**
AZD9291 + MEDI4736: TATTON study
Potential for new SoC in EGFRm+ NSCLC

Basket study in EGFRm+ NSCLC after progression on prior EGFRi

AZD9291 + MEDI4736 arm
- Both drugs tolerated at full dose
- One grade 3 AE at this dose (WBC decrease)
- One complete response
- 9/14 (64%) PRs (four confirmed PRs)
  - 6/7 (85%) in T790M+
  - 3/7 (43%) in T790M-

EGFR remains one of the major tumour drivers despite progression on EGFRi
Combination with MEDI4736 might increase RR and DoR in 2L EGFR+ NSCLC

Best percentage change from baseline in target lesion size

-100% -80% -60% -40% -20% 0% 20% 40% 60% 80%

Unknown
T790M positive
T790M negative
**Iressa + MEDI4736 in EGFRm TKI-naïve NSCLC**

Providing evidence of good combinability for MEDI4736

**Initial clinical data**

- Both drugs tolerated at full dose
- Two expansion cohorts at full doses:
  - Arm 1 concomitant (n=6 evaluable)
  - Arm 2 four weeks monotherapy *Iressa* then combination (n=8 evaluable)
- 9/14 (64%) partial responses
- AEs of interest: Grade 3 AST/ALT

**Tumour assessment: Expansion phase**

*Iressa + MEDI4736 combination in 1L EGFR+ NSCLC to be tested in Phase III study*
Significant opportunities across multiple tumour types

### Additional small molecule + MEDI4736 combinations

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Indication</th>
<th>Study start</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDO</td>
<td>Solid tumours</td>
<td>Dec 2014</td>
</tr>
<tr>
<td>BTK/ITK</td>
<td>DLBCL, FL, solid tumours</td>
<td>Mar 2015</td>
</tr>
<tr>
<td>STAT3</td>
<td>Solid tumours</td>
<td>Q3 2015</td>
</tr>
<tr>
<td>CXCR2</td>
<td>Solid tumours</td>
<td>Q3 2015</td>
</tr>
<tr>
<td>FGFR</td>
<td>Bladder cancer</td>
<td>Q3 2015</td>
</tr>
<tr>
<td>PI3Kβ/δ</td>
<td>Bladder cancer</td>
<td>Q3 2015</td>
</tr>
<tr>
<td>PI3Kδ</td>
<td>Haematological tumours</td>
<td>2015</td>
</tr>
</tbody>
</table>
## Small-molecule combinations

SM + MEDI4736 potential tested in >2,700 patients

<table>
<thead>
<tr>
<th>Tolerability</th>
<th>MEDI4736 is tolerated in combination at full dose with multiple SMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>Encouraging preliminary efficacy data. Update with larger patient numbers and duration of follow-up later this year</td>
</tr>
<tr>
<td>IO-targeted therapy combination strategy</td>
<td>Well-tolerated combination therapy delivering both high response rate and high durability of response leading to improved survival</td>
</tr>
</tbody>
</table>
IO: Maximising value across tumour types

Robert Iannone
Head of Immuno-Oncology, Global Medicines Development
Focus on combination & first-mover indications

**Speed**
- Mono MEDI4736 in PD-L1 positive NSCLC 3L+ / Head & Neck (SCCHN) 2L
- MEDI4736 + treme in PD-L1 negative SCCHN 2L

**Differentiation**
- Early-stage disease e.g. Adjuvant and stage III unresectable NSCLC
- Chemo-free regimen e.g. MEDI4736 + treme

**Leadership**
- Novel combinations e.g. MEDI4736 + AZD9291
- New tumour types e.g. haematological malignancies
## NSCLC: IO development programmes

Total now includes more than 5,600 patients

<table>
<thead>
<tr>
<th>Stage</th>
<th>Adjuvant</th>
<th>Unresectable stage III</th>
<th>1\textsuperscript{st} line</th>
<th>2\textsuperscript{nd} line</th>
<th>≥3\textsuperscript{rd} line</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ADJUVANT</td>
<td>PACIFIC</td>
<td>MYSTIC</td>
<td>MEDI4736 + treme vs. SoC</td>
<td>ATLANTIC</td>
</tr>
<tr>
<td></td>
<td>MEDI4736 vs. placebo</td>
<td>MEDI4736 vs. placebo</td>
<td>MEDI4736 + treme vs. MEDI4736 vs. SoC</td>
<td>MEDI4736 + treme vs. SoC</td>
<td>MEDI4736 PD-L1+ single arm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MEDI4736 + chemo vs. SoC</td>
<td>MEDI4736 + treme vs. SoC</td>
<td>ARCTIC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MEDI4736 + Iressa vs. Iressa (EGFRm+)</td>
<td>MEDI4736 + AZD9291 vs. AZD9291 (T790M+)</td>
<td>PD-L1+: MEDI4736 vs. SoC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PD-L1-: MEDI4736 + treme vs. CoC vs. SoC</td>
</tr>
</tbody>
</table>

**Leadership in early stages of the disease**

**Leadership in IO/IO and IO/SM combinations**

**Highest unmet medical need**

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1 CoC = contribution of components
Additional tumour types: Exploring the benefit of MEDI4736 + treme combination

- **SCCHN 2L**
  - PD-L1+
    - HAWK
      - MEDI4736 single-arm
  - PD-L1-
    - CONDOR
      - MEDI4736 + treme vs. MEDI4736 vs. treme

- **Gastric 2/3L**
  - Randomised Phase II MEDI4736 + treme vs. MEDI4736 vs. treme
  - **NEW**

- **Pancreas 2L**
  - Phase II MEDI4736 + treme
  - **NEW**

- **Bladder 1L**
  - Randomised Phase III MEDI4736 + treme vs. MEDI4736 vs. SoC
  - **NEW**

- **All**
  - EAGLE
    - MEDI4736 + treme vs. MEDI4736 vs. SoC

**MEDI4736 monotherapy**  **MEDI4736 + treme combination therapy**

Change paradigm with chemo-free regimen
**IO development summary**

Pivotal Phase II & Phase III studies in >8,300 patients

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th># of Phase II studies</th>
<th># of Phase III studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>SCCHN</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Gastric</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Bladder</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6</strong></td>
<td><strong>10</strong></td>
</tr>
</tbody>
</table>
IO: Maximising value across tumour types
Pioneer in IO combinations; registration studies well underway

• Well-tolerated MEDI4736 + tremelimumab combination dose has been selected for Phase III and studies have been initiated

• Comprehensive registration programme with MEDI4736 is underway across multiple tumour types, stages of disease, lines of therapy, and in combination with tremelimumab, small molecules and chemotherapy

• Clinical development of MEDI4736 has been accelerated in haematological malignancies in combination with effective therapies through the alliance with Celgene
Closing and Q&A

Pascal Soriot
Chief Executive Officer
AstraZeneca Immuno-Oncology
Pioneer in *next-generation* medicine

**Future**
IO Combo therapy
- PD-L1 + CTLA-4
- PD-L1 + OX40
- PD-L1 + NKG2A
- PD-L1 + small molecules / chemo

**Now**
IO Mono therapy
- PD-1 / PD-L1

**2011**
ipilimumab

**1990s**
- IL-2, IFN

**Leadership**
- Targeted small molecules, e.g. *Iressa*, *Lynparza*, AZD9291, MEK, mTOR, MET, WEE-1, SERD

**Legacy**
- Hormone-receptor positive breast and prostate cancers
Q&A
Please press *1 on your phone if you wish to ask a question

• Pascal Soriot, moderator
• Scott Antonia, Moffitt Cancer Center
• Mondher Mahjoubi
• Mohammed M. Dar
• Susan Galbraith
• Robert Iannone

Q&A expected to end at 10pm
Thank you for joining today’s ASCO investor science event

Please join for drinks in Continental Room C
ASCO 2015 investor science event

Chicago, IL, USA
01 June 2015