IASLC World Conference on Lung Cancer 2018
Roche Analyst Call

*Tuesday, 25 September 2018*
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Agenda

Welcome
Karl Mahler, Head of Investor Relations

Roche lung cancer portfolio key data

- **IMpower133:** Primary PFS, OS, and Safety in a Ph1/3 Study of 1L Atezolizumab + Carboplatin + Etoposide in extensive-stage SCLC

- **IMpower132:** PFS, OS and Safety Results of 1L Atezolizumab + Carboplatin/Cisplatin + Pemetrexed in Stage IV Non-Squamous NSCLC.

- Efficacy and Safety of **Entrectinib** in Locally Advanced or Metastatic ROS1 Fusion-Positive NSCLC

Alan Sandler, Global Head of Lung/Head and Neck Franchise, Pharma Development

Roche Lung Cancer program overview

Sushil Patel, Franchise Head, Lung & Rare Cancers, Global Product Strategy

Q&A
Karl Mahler, Head of Investor Relations
Replace and extend the business

*Through continuously improving standard of care*

<table>
<thead>
<tr>
<th>Replace existing businesses</th>
<th>Entering new franchises</th>
</tr>
</thead>
<tbody>
<tr>
<td>MabThera/Rituxan</td>
<td>Gazyva, Venclexta, polatuzumab vedotin, mosunetuzumab (aCD20/CD3 TCB1)</td>
</tr>
<tr>
<td>Herceptin</td>
<td>Perjeta, Kadcyla, H+P SC</td>
</tr>
<tr>
<td>Avastin</td>
<td>Tecentriq, entrectinib, ipatasertib</td>
</tr>
<tr>
<td>Lucentis</td>
<td>faricimab (VA2) Port Delivery System</td>
</tr>
<tr>
<td>Tamiflu</td>
<td>baloxavir marboxil</td>
</tr>
</tbody>
</table>

### Major oncology news flow for the remainder of ‘18

#### World Lung
- **IMpower133**: Tecentriq in extensive-stage SCLC
- **IMpower132**: Tecentriq in Stage IV Non-Squamous NSCLC
- **STARTRK-2**: Entrectinib in ROS1 Fusion-Positive NSCLC

#### ESMO
- **IMpassion130**: Tecentriq + Abraxane in triple-negative BC
- **IMpower130**: Tecentriq + Abraxane in 1L non-sq NSCLC
- **BF1RST**: blood based TMB prospective study in 1L NSCLC
- **STARTRK2**: Entrectinib in NTRK+ solid tumors

#### ASH
- **Mosunetuzumab** (CD20/CD3): Ph I monotherapy data in NHL
- **RG6026**: CD20/CD3 TCB: Ph I monotherapy data in NHL
- **Venclexta, Gazyva** – various

*SMA*=spinal muscular atrophy; NMO=Neuromyelitis Optica; SC=subcutaneous; H+P=Herceptin+Perjeta; World Lung=IASLC World Conference on Lung Cancer; ESMO= European Society of Medical Oncology; ASH= American Society of Hematology
Broad portfolio in NSCLC today and looking ahead

*Ability to cover all key segments*

<table>
<thead>
<tr>
<th>NSCLC (NSq)</th>
<th>NSCLC (Sq)</th>
<th>SCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALK</strong></td>
<td><strong>EGFR</strong></td>
<td><strong>ROS</strong></td>
</tr>
<tr>
<td><strong>Neo-/ Adj</strong></td>
<td><strong>Non-Driver</strong></td>
<td><strong>PD-L1+</strong></td>
</tr>
</tbody>
</table>

- **IMpower010 (adj)**
  - Tecentriq

- **IMpower030 (neoadj)**
  - Tecentriq + platinum-based chemo

- **IMpower110**
  - Tecentriq

- **IMpower150**
  - Tecentriq + Avastin + CP

- **IMpower130**
  - Tecentriq + CnP

- **IMpower132**
  - Tecentriq + pemetrexed

- **Avastin**

- **IMpower131**
  - Tecentriq + CnP

- **IMpower133**
  - Tecentriq + carboplatin + etoposide

- **OAK, POPLAR, BIRCH**

- **Tecentriq**

- **Neo-**

- **Tarceva**

- **±**

- **Tarceva ± Avastin + entrectinib ± entrectinib**

- **IMpower150**
  - Tecentriq + Avastin + CP

- **IMpower130**
  - Tecentriq + CnP

- **IMpower132**
  - Tecentriq + pemetrexed

- **Avastin**

- **IMpower131**
  - Tecentriq + CnP

- **IMpower133**
  - Tecentriq + carboplatin + etoposide

- **Tecentriq**

- **Neo-**

- **Tecentriq ± Avastin + entrectinib ± entrectinib**

- **IMpower150**
  - Tecentriq + Avastin + CP

- **IMpower130**
  - Tecentriq + CnP

- **IMpower132**
  - Tecentriq + pemetrexed

- **Avastin**

- **IMpower131**
  - Tecentriq + CnP

- **IMpower133**
  - Tecentriq + carboplatin + etoposide

- **Tecentriq**

- **Neo-**

- **Tecentriq ± Avastin + entrectinib ± entrectinib**

- **IMpower150**
  - Tecentriq + Avastin + CP

- **IMpower130**
  - Tecentriq + CnP

- **IMpower132**
  - Tecentriq + pemetrexed

- **Avastin**

- **IMpower131**
  - Tecentriq + CnP

- **IMpower133**
  - Tecentriq + carboplatin + etoposide

- **Tecentriq**
Roche lung cancer portfolio key data

**IMpower133**: Primary PFS, OS, and Safety in a Ph1/3 Study of 1L Atezolizumab + Carboplatin + Etoposide in extensive-stage SCLC

**IMpower132**: PFS, OS and Safety Results of 1L Atezolizumab + Carboplatin/Cisplatin + Pemetrexed in Stage IV Non-Squamous NSCLC

Efficacy and Safety of Entrectinib in Locally Advanced or Metastatic ROS1 Fusion-Positive NSCLC

Alan Sandler, M.D.
*Global Head of Lung/Head and Neck Franchise, Pharma Development*
SCLC accounts for ~15% of all lung cancers

**Disease characteristics of SCLC**

**Treatment and prognosis**
SCLC is highly sensitive to initial chemotherapy, but most patients relapse and die from their disease within 2 years

**Aggressive**
Fast-growing tumour characterised by high mitotic rate and early metastasis, requiring rapid intervention

**Clinical presentation**
Patients typically present with short anamnesis and symptoms of dyspnoea and persistent cough

**Neuroendocrine tumour**
Originating from neuroendocrine cells

**Comorbidities**
Patients frequently exhibit COPD, ischaemic cardiomyopathy and hypertension

**Smoking**
SCLC occurs almost exclusively in smokers

SCLC treatment is determined by disease staging

**Limited-stage SCLC (~1/3 of patients)**
- Surgery (excluding patients with N1–3 disease)
- Chemotherapy + thoracic irradiation

**Extensive-stage (ES) SCLC (~2/3 of patients)**
- Platinum-based chemotherapy (4–6 cycles maximum)
- Standard treatment for ES-SCLC is usually cisplatin or carboplatin + etoposide for 4–6 cycles, followed by active surveillance
- Chemotherapy + thoracic irradiation

There has been no progress in the 1L treatment of ES-SCLC in over 30 years\(^1\)
- 1L standard-of-care treatment for ES-SCLC remains platinum (carboplatin or cisplatin) with etoposide\(^2\)–\(^4\)
- Outcomes remain poor with a median OS of \(~10\) months\(^4,5\)
- Immunotherapy has shown clinical activity in refractory or metastatic SCLC\(^6\)–\(^8\)
  - Preclinical data suggest that there may be synergy between anti–PD-L1 treatment and chemotherapy that could improve outcomes\(^9\)
  - Nivolumab has been approved in the 3L treatment of metastatic SCLC as a single agent\(^10\)

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**IMpower133: Global Phase 1/3, randomized, placebo-controlled trial evaluated atezolizumab + carboplatin + etoposide in 1L ES-SCLC**

- **Induction (4 x 21-day cycles)**
  - **Atezolizumab (1200 mg IV, Day 1)**
  - + carboplatin
  - + etoposide
  - **Placebo**
  - + carboplatin
  - + etoposide
  - Carboplatin: AUC 5 mg/mL/min IV, Day 1
  - Etoposide: 100 mg/m² IV, Days 1–3

- **Maintenance**
  - **Atezolizumab**
  - Treat until PD or loss of clinical benefit
  - **Placebo**
  - PCI per local standard of care

**Patients with (N = 403):**
- Measurable ES-SCLC (RECIST v1.1)
- ECOG PS 0 or 1
- No prior systemic treatment for ES-SCLC
- Patients with treated asymptomatic brain metastases were eligible

**Stratification:**
- Sex (male vs. female)
- ECOG PS (0 vs. 1)
- Brain metastases (yes vs. no)\(^a\)

**Co-primary end points:**
- Overall survival
- Investigator-assessed PFS

**Key secondary end points:**
- Objective response rate
- Duration of response
- Safety

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\(^a\) Only patients with treated brain metastases were eligible. ECOG PS = Eastern Cooperative Oncology Group Performance Status; IV = intravenous; PCI = prophylactic cranial irradiation; PD = progressive disease; PFS = progression-free survival; R = randomized; RECIST = Response Evaluation Criteria In Solid Tumors.
Overall survival

Overall Survival (%)

No. at risk

Atezolizumab Placebo

Atezolizumab Placebo

100 90 80 70 60 50 40 30 20 10 0

Overall survival

Atezolizumab + CP/ET (N=201) Placebo + CP/ET (N=202)

OS events, n (%) 104 (51.7) 134 (66.3)

Median OS, months (95% CI) 12.3 (10.8, 15.9) 10.3 (9.3, 11.3)

HR (95% CI) 0.70 (0.54, 0.91) P = 0.0069

Median follow-up, monthsa 13.9

No. at risk

Atezolizumab 201 191 187 182 180 174 159 142 130 121 108 92 74 58 46 33 21 11 5 3 2 1

Placebo 202 194 189 186 183 171 160 146 131 114 96 81 59 36 27 21 13 8 3 3 2 2

a Clinical data cutoff date: April 24, 2018, 11 months after the last patient was enrolled. RECIST, Response Evaluation Criteria In Solid Tumors.
Investigator-assessed progression-free survival

**Table: Clinical Data**

<table>
<thead>
<tr>
<th></th>
<th>Atezolizumab + CP/ET (N=201)</th>
<th>Placebo + CP/ET (N=202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS events, n (%)</td>
<td>171 (85.1)</td>
<td>189 (93.6)</td>
</tr>
<tr>
<td>Median PFS, months (95% CI)</td>
<td>5.2 (4.4, 5.6)</td>
<td>4.3 (4.2, 4.5)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.77 (0.62, 0.96)</td>
<td></td>
</tr>
<tr>
<td>Median follow-up, months(^a)</td>
<td>13.9</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Clinical data cutoff date: April 24, 2018, 11 months after the last patient was enrolled. CI, confidence interval; HR, hazard ratio.
## Overall survival in key subgroups

### Median Overall Survival (months)

<table>
<thead>
<tr>
<th>Population</th>
<th>Atezolizumab + CP/ET</th>
<th>Placebo + CP/ET</th>
<th>OS Hazard Ratio&lt;sup&gt;a&lt;/sup&gt; (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n = 261)</td>
<td>12.3</td>
<td>10.9</td>
<td>0.74 (0.54, 1.02)</td>
</tr>
<tr>
<td>Female (n = 142)</td>
<td>12.5</td>
<td>9.5</td>
<td>0.65 (0.42, 1.00)</td>
</tr>
<tr>
<td>&lt; 65 years (n = 217)</td>
<td>12.1</td>
<td>11.5</td>
<td>0.92 (0.64, 1.32)</td>
</tr>
<tr>
<td>≥ 65 years (n = 186)</td>
<td>12.5</td>
<td>9.6</td>
<td>0.53 (0.36, 0.77)</td>
</tr>
<tr>
<td>ECOG PS 0 (n = 140)</td>
<td>16.6</td>
<td>12.4</td>
<td>0.79 (0.49, 1.27)</td>
</tr>
<tr>
<td>ECOG PS 1 (n = 263)</td>
<td>11.4</td>
<td>9.3</td>
<td>0.68 (0.50, 0.93)</td>
</tr>
<tr>
<td>Brain metastases (n = 35)</td>
<td>8.5</td>
<td>9.7</td>
<td>1.07 (0.47, 2.43)</td>
</tr>
<tr>
<td>No brain metastases (n = 368)</td>
<td>12.6</td>
<td>10.4</td>
<td>0.68 (0.52, 0.89)</td>
</tr>
<tr>
<td>Liver metastases (n = 149)</td>
<td>9.3</td>
<td>7.8</td>
<td>0.81 (0.55, 1.20)</td>
</tr>
<tr>
<td>No liver metastases (n = 254)</td>
<td>16.8</td>
<td>11.2</td>
<td>0.64 (0.45, 0.90)</td>
</tr>
<tr>
<td>bTMB &lt; 10 (n = 139)</td>
<td>11.8</td>
<td>9.2</td>
<td>0.70 (0.45, 1.07)</td>
</tr>
<tr>
<td>bTMB ≥ 10 (n = 212)</td>
<td>14.6</td>
<td>11.2</td>
<td>0.68 (0.47, 0.97)</td>
</tr>
<tr>
<td>bTMB &lt; 16 (n = 271)</td>
<td>12.5</td>
<td>9.9</td>
<td>0.71 (0.52, 0.98)</td>
</tr>
<tr>
<td>bTMB ≥ 16 (n = 80)</td>
<td>17.8</td>
<td>11.9</td>
<td>0.63 (0.35, 1.15)</td>
</tr>
<tr>
<td>ITT (N = 403)</td>
<td>12.3</td>
<td>10.3</td>
<td>0.70 (0.54, 0.91)</td>
</tr>
</tbody>
</table>

Clinical data cutoff date: April 24, 2018. bTMB (blood tumor mutational burden) assessed as reported in Gandara DR, et al. Nat Med, 2018. a Hazard ratios are unstratified for patient subgroups and stratified for the ITT.
### Most frequently observed AEs

#### Treatment-related AEs — no. (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Atezolizumab + CP/ET (N = 198)</th>
<th>Placebo + CP/ET (N = 196)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>26 (13.1)</td>
<td>45 (22.7)</td>
</tr>
<tr>
<td>Anemia</td>
<td>49 (24.7)</td>
<td>28 (14.1)</td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>7 (3.5)</td>
<td>28 (14.1)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>12 (6.1)</td>
<td>20 (10.1)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>15 (7.6)</td>
<td>10 (5.1)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>0</td>
<td>6 (3.0)</td>
</tr>
</tbody>
</table>

#### Immune-related AEs — no. (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Atezolizumab + CP/ET (N = 198)</th>
<th>Placebo + CP/ET (N = 196)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>33 (16.7)</td>
<td>4 (2.0)</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>11 (5.6)</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Infusion-related reaction</td>
<td>7 (3.5)</td>
<td>4 (2.0)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>3 (1.5)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Colitis</td>
<td>1 (0.5)</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0</td>
<td>1 (0.5)</td>
</tr>
</tbody>
</table>
Summary

- IMpower133 is the first study in over 20 years to show a clinically meaningful improvement in OS over the current standard-of-care in 1L ES-SCLC

- The addition of atezolizumab to carboplatin and etoposide provided a significant improvement in OS and PFS, compared with carboplatin and etoposide alone in 1L ES-SCLC
  - mOS: 12.3 vs. 10.3 months; HR: 0.70 (p = 0.0069); 12-month OS: 51.7% vs. 38.2%
  - mPFS: 5.2 vs. 4.3 months; HR: 0.77 (p = 0.017); 12-month PFS: 12.6% vs. 5.4%

- The safety profile of atezolizumab plus carboplatin and etoposide was as expected with no new findings
  - Rates of hematologic side effects were similar between treatment groups
  - Administration of atezolizumab did not compromise the ability to deliver standard carboplatin plus etoposide
  - The incidence and types of immune-related AEs were similar to those seen with atezolizumab monotherapy

- These data suggest that atezolizumab plus carboplatin and etoposide is a new standard of care for the first-line treatment of ES-SCLC

- Full data published today in the NEJM
Roche lung cancer portfolio key data

**IMpower133**: Primary PFS, OS, and Safety in a Ph1/3 Study of 1L Atezolizumab + Carboplatin + Etoposide in extensive-stage SCLC

**IMpower132**: PFS, OS and Safety Results of 1L Atezolizumab + Carboplatin/Cisplatin + Pemetrexed in Stage IV Non-Squamous NSCLC

Efficacy and Safety of **Entrectinib** in Locally Advanced or Metastatic ROS1 Fusion-Positive NSCLC

**Alan Sandler, M.D.**

*Global Head of Lung/Head and Neck Franchise, Pharma Development*
**IMpower132 Study Design**

**Chemotherapy-naive patients with Stage IV non-squamous NSCLC without EGFR or ALK genetic alteration**

Stratification factors:
- Sex
- Smoking status
- ECOG PS
- Chemotherapy regimen

N = 578

**Co-primary endpoints:** INV-assessed PFS and OS

**Secondary endpoints:** INV-assessed ORR and DOR, PRO and safety measures

**Exploratory analyses:** clinical and biomarker subgroup analyses
- Biomarker-evaluable tissue not mandatory for enrolment (was available from 60% of patients)

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**Induction therapy**

- **Arm APP**
  - Atezolizumab
  - Carbo or cisplatin + pemetrexed
  - 4 or 6 cycles

- **Arm PP**
  - Carbo or cisplatin + pemetrexed
  - 4 or 6 cycles

**Maintenance therapy**

- **Atezolizumab**
  - + pemetrexed

- **Pemetrexed**

**Maintenance Treatment until PD by RECIST v1.1 or loss of clinical benefit**

**Chemotherapy-naive patients** with Stage IV non-squamous NSCLC without EGFR or ALK genetic alteration

**Survival follow-up**

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DOR, duration of response; INV, investigator; R, randomization; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcomes. Atezolizumab: 1200 mg IV q3w; Carboplatin: AUC 6 mg/mL/min IV q3w; Cisplatin: 75 mg/m² IV q3w; Pemetrexed: 500 mg/m² IV q3w. NCT02657434. Data cutoff: May 22, 2018
Final Investigator-Assessed PFS, ORR and DOR

HR 0.60 (95% CI: 0.49, 0.72)

\[ P < 0.0001 \]

Minimum follow-up, 11.7 mo
Median follow-up, 14.8 mo

APP, atezolizumab + carboplatin/cisplatin + pemetrexed; CR, complete response; DOR, duration of response; HR, hazard ratio; IRF, independent review facility; ORR, objective response rate; PP, carboplatin/cisplatin + pemetrexed; PR, partial response. IRF-assessed median PFS was 7.2 mo with APP and 6.6 mo with PP (stratified HR: 0.758 [95% CI: 0.623, 0.923] \( P = 0.055 \)). Data cutoff: May 22, 2018.
# PFS in Key Patient Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)</th>
<th>HR (95% CI)(^a)</th>
<th>Median PFS, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>APP</td>
<td>PP</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>194 (34)</td>
<td>0.51 (0.36–0.71)</td>
<td>8.3</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>384 (66)</td>
<td>0.64 (0.51–0.79)</td>
<td>7.5</td>
</tr>
<tr>
<td>&lt; 65 y</td>
<td>320 (55)</td>
<td>0.63 (0.49–0.80)</td>
<td>6.9</td>
</tr>
<tr>
<td>≥ 65 y</td>
<td>258 (45)</td>
<td>0.55 (0.42–0.73)</td>
<td>8.4</td>
</tr>
<tr>
<td>White(^b)</td>
<td>396 (69)</td>
<td>0.67 (0.54–0.84)</td>
<td>6.9</td>
</tr>
<tr>
<td>Asian</td>
<td>136 (24)</td>
<td>0.42 (0.28–0.63)</td>
<td>10.2</td>
</tr>
<tr>
<td>ECOG PS 0(^b)</td>
<td>240 (42)</td>
<td>0.56 (0.42–0.76)</td>
<td>8.6</td>
</tr>
<tr>
<td>ECOG PS 1</td>
<td>336 (58)</td>
<td>0.63 (0.49–0.79)</td>
<td>6.8</td>
</tr>
<tr>
<td>Received carboplatin</td>
<td>352 (61)</td>
<td>0.54 (0.43–0.69)</td>
<td>8.1</td>
</tr>
<tr>
<td>Received cisplatin</td>
<td>226 (39)</td>
<td>0.65 (0.48–0.88)</td>
<td>7.1</td>
</tr>
<tr>
<td>Intended 4 cycles</td>
<td>387 (67)</td>
<td>0.54 (0.43–0.67)</td>
<td>7.8</td>
</tr>
<tr>
<td>Intended 6 cycles</td>
<td>191 (33)</td>
<td>0.71 (0.51–0.98)</td>
<td>7.6</td>
</tr>
<tr>
<td>Current or former smoker</td>
<td>511 (88)</td>
<td>0.61 (0.50–0.74)</td>
<td>7.5</td>
</tr>
<tr>
<td>Never smoker</td>
<td>67 (12)</td>
<td>0.49 (0.28–0.87)</td>
<td>8.6</td>
</tr>
<tr>
<td>Liver metastases</td>
<td>73 (13)</td>
<td>0.77 (0.47–1.25)</td>
<td>4.4</td>
</tr>
<tr>
<td>No liver metastases</td>
<td>505 (87)</td>
<td>0.56 (0.46–0.69)</td>
<td>8.4</td>
</tr>
<tr>
<td><strong>ITT population</strong></td>
<td>578 (100)</td>
<td>0.60 (0.49–0.72)</td>
<td>7.6</td>
</tr>
</tbody>
</table>

\(^a\) Hazard ratio, stratified HR for ITT; unstratified for all other subgroups.

\(^b\) Patients with other/unknown race (n = 46) and unknown baseline ECOG PS (n = 2) not included. Data cutoff: May 22, 2018.

APP, atezolizumab + carboplatin/cisplatin + pemetrexed; PP, carboplatin/cisplatin + pemetrexed.
**IMpower150: Addition of Avastin to Tecentriq and chemo prolongs survival of patients with liver metastases**

Adding Avastin to Tecentriq and chemo led to clinical benefit in patients with liver metastases supporting previous reports of Avastin efficacy in these patients.

**Arm B vs Arm C**

- **Overall Survival (%)**
- **Time (months)**
- **HR\(^a\), 0.54**
- **(95% CI: 0.33, 0.88)**

**Arm A vs Arm C**

- **Overall Survival (%)**
- **Time (months)**
- **HR\(^a\), 0.85**
- **(95% CI: 0.53, 1.36)**

Data cutoff: January 22, 2018.\(^a\) Unstratified HR.\(^b\) Patients with a sensitizing \textit{EGFR} mutation or \textit{ALK} translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.\(^1\) Sandler A et al. N Engl J Med 2006;355:2542-2550
Interim OS Analysis

HR: 0.81 (95% CI: 0.64, 1.03)  
\( P = 0.0797 \)

Minimum follow-up: 11.7 mo  
Median follow-up: 14.8 mo

<table>
<thead>
<tr>
<th></th>
<th>APP</th>
<th>PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-mo OS</td>
<td>59.6%</td>
<td>55.4%</td>
</tr>
</tbody>
</table>

APP, atezolizumab + carboplatin/cisplatin + pemetrexed; PP, carboplatin/cisplatin + pemetrexed.

Data cutoff: May 22, 2018. Frequency of OS events: 44% and 49% in arms APP and PP respectively.
Safety Summary

<table>
<thead>
<tr>
<th></th>
<th>APP (n = 291)</th>
<th>PP (n = 274)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All-cause AEs, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3-4</td>
<td>286 (98%)</td>
<td>266 (97%)</td>
</tr>
<tr>
<td>Grade 5</td>
<td>21 (7%)</td>
<td>14 (5%)</td>
</tr>
<tr>
<td><strong>TRAEs, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3-4</td>
<td>267 (92%)</td>
<td>239 (87%)</td>
</tr>
<tr>
<td>Grade 5</td>
<td>156 (54%)</td>
<td>107 (39%)</td>
</tr>
<tr>
<td><strong>SAEs, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Grade</td>
<td>134 (46%)</td>
<td>84 (31%)</td>
</tr>
<tr>
<td>Tx-related SAEs</td>
<td>96 (33%)</td>
<td>43 (16%)</td>
</tr>
<tr>
<td><strong>AEs leading to withdrawal, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Of any treatment</td>
<td>69 (24%)</td>
<td>48 (18%)</td>
</tr>
<tr>
<td>Of atezolizumab</td>
<td>44 (15%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>AESI, n (%)</strong></td>
<td>141 (49%)</td>
<td>104 (38%)</td>
</tr>
</tbody>
</table>

### AEs of Special Interest, n (%)

<table>
<thead>
<tr>
<th></th>
<th>All Grade</th>
<th>Grade 3-4</th>
<th>All Grade</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>71 (24%)</td>
<td>9 (3%)</td>
<td>58 (21%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>23 (8%)</td>
<td>1 (&lt;1%)</td>
<td>6 (2%)</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>16 (6%)</td>
<td>6 (2%)</td>
<td>6 (2%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Hepatitis (Diagnosis)</td>
<td>13 (5%)</td>
<td>7 (2%)</td>
<td>2 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>Infusion-Related Reactions</td>
<td>8 (3%)</td>
<td>1 (&lt;1%)</td>
<td>2 (1%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>6 (2%)</td>
<td>1 (&lt;1%)</td>
<td>3 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>Severe Cutaneous Adverse Reaction</td>
<td>4 (1%)</td>
<td>2 (1%)</td>
<td>2 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>4 (1%)</td>
<td>1 (&lt;1%)</td>
<td>2 (1%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Colitis</td>
<td>5 (2%)</td>
<td>2 (1%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- PRO data also support the positive benefit-risk profile demonstrated by these clinical data

APP: atezolizumab + carboplatin/cisplatin + pemetrexed; AE, adverse event; AESI, adverse event of special interest; PP, carboplatin/cisplatin + pemetrexed; SAE, serious adverse event; TRAE, treatment-related adverse event.a Grade 5 event observed. Data cutoff: May 22, 2018.
Conclusions

• IMpower132 met its co-primary endpoint of investigator-assessed PFS in the ITT population

• The addition of atezolizumab to carboplatin/cisplatin + pemetrexed improved median PFS in the ITT population (7.6 mo vs 5.2 mo, HR 0.60) and across key clinical subgroups

• Atezolizumab + pemetrexed + carboplatin or cisplatin has a manageable safety profile consistent with known safety risks of the individual therapies; no new safety signals were identified

• OS data showed a numerical improvement of 4.5 months at this interim analysis; final analysis is anticipated in 1H 2019
Roche lung cancer portfolio key data

**IMpower133**: Primary PFS, OS, and Safety in a Ph1/3 Study of 1L Atezolizumab + Carboplatin + Etoposide in extensive-stage SCLC

**IMpower132**: PFS, OS and Safety Results of 1L Atezolizumab + Carboplatin/Cisplatin + Pemetrexed in Stage IV Non-Squamous NSCLC

Efficacy and Safety of **Entrectinib** in Locally Advanced or Metastatic ROS1 Fusion-Positive NSCLC

**Alan Sandler, M.D.**
*Global Head of Lung/Head and Neck Franchise, Pharma Development*
Entrectinib is an oral, potent and selective ROS1/NTRK/ALK tyrosine kinase inhibitor that is CNS active.

- **More potent than crizotinib** against ROS1 in preclinical studies\(^1\)

- **Potent pan-TRK inhibitor** in clinical development; demonstrated clinical activity in multiple tumor histologies

- **Designed to cross the blood–brain barrier** and remain within CNS, with demonstrated clinical activity in primary brain tumors and secondary CNS metastases\(^{1,2}\)

---

Limitations of current treatment options for **ROS1+ NSCLC**

**ROS1+ NSCLC Patients**
- ~2% of NSCLC patients
- ~64% are female
- ~68% are never-smokers
- ~50 years median age (Lung cancer overall 72 years)

- Crizotinib is the only approved agent for ROS1+ NSCLC\(^1\)
- Ceritinib was recently added as an option in the NCCN guidelines\(^2\)
- Patients with ROS1+ NSCLC typically relapse within 1 year of starting first-line crizotinib\(^3\)
- The CNS is the first and only site of progression in nearly half of patients\(^3\)

Integrated analysis of three studies: entrectinib in ROS1+ NSCLC

**Integrated analysis**

**Efficacy population**
- 53 ROS1+, ROS1-inhibitor-naïve NSCLC patients

**Safety population**
- 355 patients have received entrentinib (all tumor types and gene rearrangements)

**Primary endpoints**
- ORR and DOR

**Secondary endpoints**
- PFS and OS
- Intracranial ORR and DOR†
- Safety and tolerability

**STARTRK-2**
- Phase II, multicenter, global basket study 600 mg QD, 28-day cycle
- N=37 ROS1+ patients

**STARTRK-1**
- Phase I dose escalation
- N=7 ROS1+ patients

**ALKA-372-001**
- Phase I dose escalation
- N=9 ROS1+ patients

Data cut-off 31 May 2018


*BICR, measured by RECIST v1.1; †Patients with measurable CNS lesions at baseline and patients with measurable and non-measurable CNS lesions at baseline
BICR, blinded independent central review; CBR, clinical benefit rate; RECIST, Response Evaluation Criteria In Solid Tumors; RP2D, recommended Phase II dose
Objective response rate (BICR assessment)

**Change in tumor size: ROS1+ NSCLC population**

**Best percent change from baseline in tumor size**
- **CNS disease at baseline**
- **No CNS disease at baseline**

### ORR (95% CI)
- **Total (N=53):** 41 (77.4) (63.8, 87.7)
- **CNS disease at baseline (n=23):** 17 (73.9) (51.6, 89.8)
- **No CNS disease at baseline (n=30):** 24 (80.0) (61.4, 92.3)

### Other response rates
- **CR:**
  - Total (N=53): 3 (5.7)
  - CNS disease at baseline (n=23): 0
  - No CNS disease at baseline (n=30): 3 (10.0)
- **PR:**
  - Total (N=53): 38 (71.7)
  - CNS disease at baseline (n=23): 17 (73.9)
  - No CNS disease at baseline (n=30): 21 (70.0)
- **SD:**
  - Total (N=53): 1 (1.9)
  - CNS disease at baseline (n=23): 0
  - No CNS disease at baseline (n=30): 1 (3.3)
- **PD:**
  - Total (N=53): 4 (7.5)
  - CNS disease at baseline (n=23): 4 (17.4)
  - No CNS disease at baseline (n=30): 0
- **Non-CR/PD:**
  - Total (N=53): 3 (5.7)
  - CNS disease at baseline (n=23): 0
  - No CNS disease at baseline (n=30): 3 (10.0)
- **Missing or unevaluable:**
  - Total (N=53): 4 (7.5)
  - CNS disease at baseline (n=23): 2 (8.7)
  - No CNS disease at baseline (n=30): 2 (6.7)

### Clinical benefit rate* (95% CI)
- 41 (77.4) (63.8, 87.7)

*Includes SD for at least 6 months. Data cut-off date: 31 May 2018 (median follow-up: 15.5 months). ROS1-inhibitor-naive patients with ROS1+ NSCLC (integrated analysis population); CI, confidence interval; CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SLD, sum of longest diameters.
Duration of response (BICR assessment)

**Duration of response (BICR assessment)**

- **Median DOR 24.6 months**
  (95% CI: 11.4–34.8)

- **Median follow-up from first response:** 16.6 months

### Data cut-off date: 31 May 2018, ROS1-inhibitor-naïve patients with ROS1+ NSCLC (integrated analysis population) NE, not estimable
Progression-free survival (BICR assessment)

Median PFS 19.0 months
(95% CI: 12.2–36.6)

Median follow-up: 15.5 months

Data cut-off date: 31 May 2018, ROS1-inhibitor-naïve patients with ROS1+ NSCLC (integrated analysis population)
## Intracranial ORR and DOR: CNS disease at baseline (BICR)

### Intracranial response – patients with CNS metastases at baseline by BICR (n=20*)

<table>
<thead>
<tr>
<th>Intracranial ORR, n (%) (95% CI)</th>
<th>11 (55) (31.53–76.94)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>4 (20.0)</td>
</tr>
<tr>
<td>PR</td>
<td>7 (35.0)</td>
</tr>
<tr>
<td>SD</td>
<td>0</td>
</tr>
<tr>
<td>PD</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Non-CR/PD–NE</td>
<td>6 (30.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intracranial median DOR, months (95% CI)</th>
<th>12.9 (5.6–NE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with event, n (%)</td>
<td>5 (45.5)</td>
</tr>
<tr>
<td>Disease progression, n</td>
<td>3</td>
</tr>
<tr>
<td>Death, n</td>
<td>2</td>
</tr>
<tr>
<td>6 months</td>
<td></td>
</tr>
<tr>
<td>Patients remaining at risk, n</td>
<td>7</td>
</tr>
<tr>
<td>Event-free probability</td>
<td>0.71</td>
</tr>
</tbody>
</table>

*Patients with assessible CNS metastases at baseline as per BICR. ROS1-inhibitor-naïve patients with ROS1+ NSCLC (integrated analysis population)
Entrectinib safety summary

- 355 patients have been treated with entrectinib across three clinical studies
- Most AEs were grade 1–2 and reversible
- Treatment-related AEs
  - Leading to discontinuation from study treatment: 3.9%
  - Leading to dose reduction: 27.3%
  - Leading to dose interruption: 25.4%
  - Serious AEs: 8.5%
  - No grade 5 events

<table>
<thead>
<tr>
<th>Most common (≥10%) treatment-related AEs, n (%)</th>
<th>Safety evaluable population (N=355)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grades</td>
</tr>
<tr>
<td>Dyseusia</td>
<td>147 (41.4)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>92 (25.9)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>90 (25.4)</td>
</tr>
<tr>
<td>Constipation</td>
<td>80 (22.5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>71 (20.0)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>70 (19.7)</td>
</tr>
<tr>
<td>Weight increased</td>
<td>69 (19.4)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>63 (17.7)</td>
</tr>
<tr>
<td>Blood creatinine increased</td>
<td>52 (14.6)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>52 (14.6)</td>
</tr>
<tr>
<td>Peripheral oedema</td>
<td>49 (13.8)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>44 (12.4)</td>
</tr>
<tr>
<td>Anaemia</td>
<td>40 (11.3)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>40 (11.3)</td>
</tr>
<tr>
<td>Aspartate aminotransferase (AST) increased</td>
<td>39 (11.0)</td>
</tr>
</tbody>
</table>

*Grade 4 AST increase reported in one patient

*One Grade 4 event (increased aspartate aminotransferase) and no Grade 5 events were evaluated by investigators to be related to study treatment Data cut-off date: May 31 2018 (median duration of entrectinib treatment: 9.17 months (Q1, Q3: 4.60, 14.65), integrated analysis population
Overall conclusions

• In ROS1+ NSCLC patients treated with entrectinib, a clinically meaningful, deep and durable systemic response was observed in patients with and without CNS metastases
  – response rate 77.4%; median DOR 24.6 months
  – median PFS 26.3 months (without CNS metastases) and 13.6 months (with CNS metastases)

• Clinically meaningful and durable intracranial activity was also demonstrated in patients with baseline CNS disease
  – intracranial ORR 55%
  – intracranial mDOR 12.9 months

• Entrectinib was tolerable with a manageable safety profile
  – most of the AEs were managed with dose interruption/reduction and the discontinuation rate was low
Key Takeaways

**IMpower133**
- IMpower133 is the first study in over 30 years to show a clinically meaningful improvement in OS over the current standard-of-care in 1L ES-SCLC
- The addition of atezolizumab to carboplatin and etoposide provided a significant improvement in OS and PFS, compared with carboplatin and etoposide alone in 1L ES-SCLC
  - mOS: 12.3 vs. 10.3 months; HR: 0.70 (P = 0.0069)

**IMpower132**
- The addition of atezolizumab to carboplatin/cisplatin + pemetrexed improved median PFS in the ITT population (7.6 mo vs 5.2 mo, HR 0.60) and across key clinical subgroups.
- Interim OS data showed numerical improvement; next OS analysis is anticipated in 1H 2019

**Entrectinib**
- In ROS1 fusion-positive locally advanced or metastatic NSCLC there was a clinically meaningful, deep and durable systemic response in both patients with and without CNS metastases
  - response rate 77.4%; median DOR 24.6 months
  - median PFS 26.3 months (without CNS mets) and 13.6 months (CNS mets)
Roche lung cancer program overview

Sushil Patel
Franchise Head, Lung & Rare Cancers, Global Product Strategy
Lung cancer
Broad coverage with differentiated growth opportunities

**Lung cancer market**

<table>
<thead>
<tr>
<th>Incidence rates&lt;sup&gt;1&lt;/sup&gt;</th>
<th>EGFR 8%</th>
<th>ALK+ 3%</th>
<th>ROS1/NTRK+ 1%</th>
<th>NSq NSCLC: PDL1-high (9%)</th>
<th>PDL1-low (13%)</th>
<th>PDL1-neg (21%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sq NSCLC</td>
<td>30%</td>
<td></td>
<td></td>
<td>Early NSCLC</td>
<td>1L &amp; CIT-experienced</td>
<td></td>
</tr>
<tr>
<td>SCLC</td>
<td>15%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Driver mutations**

**NSCLC**

- EGFR, ALK, ROS1/NTRK

- Alecensa rapidly established as market leader in 1L ALK+
- Entrectinib setting a new SOC in ROS1+/NTRK+
- Tecentriq: Only CIT agent with positive data in 2L EGFR+/ALK+

**SCLC**

- Tecentriq to be first CIT in combination with chemo in 1L SCLC

**1L NSq NSCLC**

- Tecentriq: 3 positive Ph III trials, including multiple chemos
- Uniquely differentiated with abraxane and Avastin combinations
- Strong efficacy in patients with liver metastases (~20% pts)

**Early NSCLC**

- Pivotal studies in neoadjuvant and adjuvant started

**Novel combinations, biomarkers**

- 40% of NSCLC patients don’t respond to 1L CIT + chemo and no SOC established for CIT experienced patients

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**Total lung cancer market growing from USD ~14bn in 2017 to ~33bn in 2024<sup>2</sup>**

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CIT=Cancer Immunotherapy; SCLC=small cell lung cancer; NSCLC=non-small cell lung cancer, Sq=squamous, NSq=non-squamous, SOC=standard of care; 1 Datamonitor: incidence rates includes the 7 major markets (US, Japan, France, Germany, Italy, Spain, UK); 2 Evaluate Pharma
Strong focus on driver mutation based treatment in NSCLC
Comprehensive tumour profiling key to drive personalized treatment

- **PFS for Alecensa** in ALK positive patients was **34.8 months** vs 10.9 months for crizotinib (HR 0.43)
- **PFS** in patients with **CNS metastases** was **27.7 months** vs 7.4 months (HR 0.35)
- Alecensa established as standard of care in 1L ALK+ NSCLC

- **PFS for entrectinib** In ROS1 fusion-positive patients was **26.4 months**
- **PFS** in patients with **CNS metastases** was **13.6 months**

Camidge D. R. et al, ASCO 2018; *Investigator assessment; PFS=progression free survival; ITT=intent to treat; DOR=duration of response; HR=hazard ratio; CNS=central nervous system; ORR=overall response rate; Alecensa (alectinib) in collaboration with Chugai
**Broad portfolio in NSCLC today and looking ahead**

*Ability to cover all key segments*

<table>
<thead>
<tr>
<th>NSCLC (NSq)</th>
<th>NSCLC (Sq)</th>
<th>SCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALK</strong></td>
<td><strong>EGFR</strong></td>
<td><strong>ROS</strong></td>
</tr>
<tr>
<td>Neo-/ Adj</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Neo-/ Adj**
  - **ALK**: OAK, POPLAR, BIRCH
  - **Tarceva**
  - **Entrectinib**

- **1L**
  - **IMpower110**
    - Tecentriq
  - **IMpower150**
    - Tecentriq + Avastin + CP
  - **IMpower130**
    - Tecentriq + CnP
  - **IMpower132**
    - Tecentriq + pemetrexed
  - **IMpower10 (adj)**
    - Tecentriq
  - **IMpower030 (neoadj)**
    - Tecentriq + platinum-based chemo

- **2L**
  - **IMpower150**
    - Tecentriq + Avastin + CP
  - **IMpower110**
    - Tecentriq
  - **IMpower131**
    - Tecentriq + CnP
  - **IMpower133**
    - Tecentriq + carboplatin + etoposide

- **Avastin**

- **OAK, POPLAR, BIRCH**
  - **Tecentriq**

- **Tarceva**

- **IMpower110**
  - **Tecentriq**
Going beyond our molecules in lung cancer

**Diagnostics**
Improve diagnosis: leverage FMI partnership, develop blood-based diagnostics and explore novel CIT biomarkers

**Drugs**
Fully leverage our brands and communicate on Roche expertise and key partnerships

**Access**
Integrated pricing and access solutions (drugs, diagnostics, RWD e.g. Flatiron)

**Data/PHC 2.0**
Develop compelling solutions beyond therapeutics for key stakeholders e.g. Flatiron and Navify
Looking forward to ESMO

ESMO 2017 Congress
Roche virtual science event
Monday, 22nd October 2018

Key data at ESMO
- IMpassion130: Tecentriq + Abraxane in 1L triple-negative breast cancer
- Entrectinib NTRK data
- IMpower130: Tecentriq + Abraxane in 1L non-sq NSCLC
- BF1RST- blood based TMB prospective study in 1L NSCLC
- IMmotion151 Biomarker data
- ALESIA Alecensa in Chinese NSCLC patients

Abstracts submitted, presentations to be confirmed
Doing now what patients need next