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Today’s Presenters

TERESA BITETTI
President of Global Oncology Business Unit

CHRIS ARENDT
Head of Oncology R&D
<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Topic</th>
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<tr>
<td>5:00 – 5:10</td>
<td>Teresa Bitetti, President of Global Oncology Business Unit</td>
<td>Introduction</td>
</tr>
<tr>
<td>5:10 – 5:30</td>
<td>Chris Arendt, Head of Oncology R&amp;D</td>
<td>EGFR Exon20 Insertion+ mNSCLC Overview</td>
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<td></td>
<td></td>
<td>Mobocertinib Phase 1/2 Data Summary</td>
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<tr>
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<td>Program Overview</td>
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<tr>
<td>5:30 – 5:35</td>
<td>Teresa Bitetti, President of Global Oncology Business Unit</td>
<td>Closing</td>
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<tr>
<td>5:35 – 6:00</td>
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<td>Question &amp; Answer Session</td>
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We Are Committed to Leveraging Scientific Innovation to Address the Unique and Urgent Needs of People Living with Cancer

**OUR FOUNDATION**
Demonstrated leadership in the treatment of hematologic cancers and solid tumors

**OUR FOCUS**
Harnessing the power of innate immunity to enhance and broaden the impact of immunotherapy

**OUR PARTNERS**
Differentiated immuno-oncology platforms and symbiotic partnerships
Mobocertinib – One of Several Upcoming Opportunities in the Oncology Pipeline

**Differentiated I/O Platforms and Partnerships**

- Innate immunomodulation
- Novel-scaffold immune checkpoint platforms and oncolytic virus
- Next-gen cell therapy & immune engager platforms

**Late-Stage**

<table>
<thead>
<tr>
<th>TARGET APPROVAL¹</th>
<th>FY21</th>
<th>FY22</th>
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<tbody>
<tr>
<td>mobocertinib</td>
<td></td>
<td></td>
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<td>pevonedistat</td>
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**Next-Gen Innate & Checkpoint Modulators**

<table>
<thead>
<tr>
<th>Pipeline</th>
<th>Cell Therapy</th>
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<tbody>
<tr>
<td>TAK-981</td>
<td>TAK-007</td>
</tr>
<tr>
<td>Multiple cancers</td>
<td>Hematologic malignancies</td>
</tr>
<tr>
<td>TAK-605</td>
<td>TAK-940</td>
</tr>
<tr>
<td>Multiple cancers</td>
<td>R/R B-Cell malignancies</td>
</tr>
<tr>
<td>TAK-676</td>
<td>TAK-102</td>
</tr>
<tr>
<td>Solid tumors</td>
<td>Solid tumors</td>
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</tbody>
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1. All timelines are current as of January 29, 2021 and are subject to change due to COVID-19. Projected approval dates depend on data read-outs; some target approval dates assume accelerated approval.
2. Projected approval date assumes filing on Phase 1/2 data.
There Remains a Critical Need for Patients with EGFR Exon20 Insertion+ mNSCLC, Who Have No Approved Targeted Options

EGFR Exon20 insertion mutations are present in up to **5-12% of EGFR-mutated NSCLC** tumors and **1-2% of all NSCLC** tumors.\(^1\-^2\)

EGFR Exon20 insertions are more prevalent in mNSCLC patients with adenocarcinoma, **never smokers/light smokers** and Asian populations.\(^3\-^4\)

Currently **no approved targeted treatment** options for these patients.

There is an **urgent need** to globally implement comprehensive genomic testing to identify all patients with EGFR Exon20 insertion mutations.

In previously treated patients with EGFR Exon20 insertions, current treatment options provide **limited clinical benefit**.

**Chemotherapy**, the current standard of care, demonstrates an **ORR of less than 15%** and a median **PFS around three to five months***.\(^5\-^7\)

EGFR TKIs and immunotherapy have also shown **minimal benefit**.

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*Average outcomes for second-line EGFR Exon20 insertion+ mNSCLC patients; ORR, objective response rate; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

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Mobocertinib Update
Design and Patient Cohorts in Phases 1/2 and EXCLAIM

Phase 1 Dose Escalation: 3+3 Design (Advanced non–small cell lung cancer; ECOG PS <2)

Phase 2 Expansion: Mobocertinib 160 mg QD
Phase 2: Primary endpoint: ORR by RECIST v1.1
Secondary endpoints: PFS, OS

COHORT 1
Refractory EGFR Exon20 insertion; no active, measurable CNS metastases

COHORT 2
Refractory HER2 Exon20 insertion or point mutation; no active, measurable CNS metastases

COHORT 3
Refractory EGFR or HER2 Exon20 insertions or point mutations with measurable, active CNS metastases

COHORT 4
Treatment naive or refractory Other EGFR mutations: +/- T790M, uncommon EGFR

COHORT 5
Refractory EGFR Exon20 insertion with prior response to EGFR TKI

COHORT 6
Treatment naive EGFR Exon20 insertions

COHORT 7
Refractory other tumor types (non-NSCLC) with EGFR/HER2 mutations

EXCLAIM Extension Cohort (N=96)
Previously treated patients EGFR Exon20 insertions

Total Prior Platinum Patient Population: N=114

Locations: United States only for Phases 1 and 2; United States, European Union, and Asia for Phase 2 extension cohort.

Prior Platinum: n=6
Prior Platinum: n=22
Prior Platinum: n=86

*Active or measurable (but not both) CNS metastases permitted

Active CNS metastases: Untreated or treated and progressing; measurable CNS metastases: ≥10 mm in longest diameter by contrast-enhanced MRI

CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor gene; HER2, human epidermal growth factor receptor 2 gene; MRI, magnetic resonance imaging; NSCLC, non–small cell lung cancer; ORR, objective response rate; QD, once daily; PK, pharmacokinetics; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor
Mobocertinib is a First-in-Class Oral Targeted Therapy That Has Shown Clinical Benefit in Platinum Pretreated EGFR Exon20 Patient Population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PPP Cohort (N=114)</th>
</tr>
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<tbody>
<tr>
<td><strong>Data cutoff: November 1, 2020</strong></td>
<td></td>
</tr>
<tr>
<td>Median time on treatment, mo (range)</td>
<td>7.4 [0–34.0]</td>
</tr>
<tr>
<td>Confirmed ORR per investigator, n (%) [95% CI]</td>
<td>40 (35%) [26–45]</td>
</tr>
<tr>
<td>Confirmed ORR per IRC, n (%) [95% CI]</td>
<td>32 (28%) [20–37]</td>
</tr>
<tr>
<td>DCR per IRC, n (%) [95% CI]&lt;sup&gt;a&lt;/sup&gt;</td>
<td>89 (78%) [69–85]</td>
</tr>
<tr>
<td>Median PFS per IRC, mo [95% CI]</td>
<td>7.3 [5.5–9.2]</td>
</tr>
<tr>
<td>Median DoR per IRC, mo [95% CI]&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17.5 [7.4–20.3]</td>
</tr>
</tbody>
</table>

ORR, objective response rate; IRC, independent review committee; CI, confidence interval; DCR, disease control rate; PFS, progression-free survival; DoR, duration of response; PPP, platinum-pretreated patient population

<sup>a</sup> DCR defined as confirmed complete response or partial response, or best response of stable disease for at least six weeks after initiation of study drug

<sup>b</sup> DoR per Kaplan-Meier estimates


November Data to Form Basis for Mobocertinib FDA Submission in Platinum Pretreated EGFR Exon20 Patient Population
Mobocertinib Demonstrated 7.3 Months Median PFS*

Median PFS
in platinum-pretreated population (N=114)

Data cutoff: May 29, 2020

Mobocertinib Demonstrated 7.3 Months Median PFS*

Median PFS 7.3 months (95% CI 5.5-10.2)

Median PFS from the November data cutoff consistent with May at 7.3 months (95% CI 5.5-9.2)

PFS is defined as the time interval from the date of the first dose of the study treatment until the first date at which disease progression is objectively documented per RECIST v1.1, or death due to any cause, whichever occurs first. PFS, progression-free survival; CI, confidence interval; IRC, independent review committee

*Per IRC assessment

Mobocertinib Generated Durable Responses in Platinum Pretreated Population*

For patients with a confirmed CR/PR per RECIST v1.1, DoR is defined as the time interval from the time that the measurement criteria are first met for CR/PR (whichever is first recorded) until the first date that the progressive disease is objectively documented or death.

CR, complete response; PR, partial response; DoR, duration of response; CI, confidence interval; IRC, independent review committee

*Per IRC assessment.


Duration of Response
in platinum-pretreated population (N=114)

Data cutoff: May 29, 2020

Median DoR 17.5 months
(95% CI 8.3-NE)

Median DoR from the November data cutoff consistent with May at 17.5 months
(95% CI 7.4-20.3)
Mobocertinib Resulted in Clinically Meaningful Improvement in Core Lung Cancer Symptoms (EXCLAIM Cohort)

Clinically meaningful improvements (i.e., ≥10-point decrease in EORTC QLQ-LC13 symptom score) were observed for dyspnea (54.4% of patients), coughing (44.4%) and pain in chest (37.8%)

Mean changes from baseline in scores for dyspnea, coughing and pain in chest were evident in cycle 2 and maintained throughout treatment

Data cutoff: May 29, 2020

Mobocertinib Safety Profile is Consistent with Known EGFR TKI Profile

<table>
<thead>
<tr>
<th>n (%)</th>
<th>PPP Cohort (N=114)</th>
</tr>
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<tbody>
<tr>
<td>Any treatment-related AE</td>
<td>113 (99)</td>
</tr>
<tr>
<td>Grade ≥3 treatment-related AE</td>
<td>53 (46)</td>
</tr>
<tr>
<td>Serious treatment-emergent AEs</td>
<td>52 (46)</td>
</tr>
<tr>
<td>AEs leading to dosage reduction</td>
<td>28 (25)</td>
</tr>
<tr>
<td>AEs leading to treatment discontinuation</td>
<td>19 (17)</td>
</tr>
<tr>
<td>Treatment-related AEs leading to death</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

- The most common AEs leading to treatment discontinuation were nausea (4%), diarrhea (4%), vomiting (2%), decreased appetite (2%), and stomatitis (2%)
- One treatment-related death occurred due to cardiac failure in a platinum-pretreated patient in the EXCLAIM cohort
- The safety profile from the November data cutoff was consistent with that of the May data cutoff

To improve the gastrointestinal tolerability of mobocertinib, Takeda amended the clinical study protocol to include diarrhea management guidelines.
- Full implementation of the amendment did not take place until the trial was nearly enrolled, so the Phase 1/2 results reported thus far are not entirely reflective of these changes.
- In subsequent clinical studies, these guidelines have been fully implemented and are being utilized.

AE, adverse event; PPP, platinum-pretreated patients

Mobocertinib Has Potential to Establish a New Class of EGFR Exon20 Insertion Mutation-Directed Therapy and Become Standard of Care

Following FY20 progress, mobocertinib is positioned to become first approved oral therapy designed to selectively target EGFR Exon20 insertion+ mNSCLC in FY21

**Areas of Investigation**
- Previously treated patients with EGFR Exon20 insertion+ mNSCLC
- First-line EGFR Exon20 insertion+ mNSCLC

**Ongoing Studies**
- Phase 1/2 study (including EXCLAIM cohort) evaluating mobocertinib in patients with EGFR Exon20 insertion+ mNSCLC
  - Single-arm monotherapy cohorts in relapsed/refractory patients
  - Dose-escalation study in combination with carboplatin + pemetrexed
- Phase 3 EXCLAIM-2 trial evaluating mobocertinib versus platinum-based chemotherapy in the first-line treatment of patients with EGFR Exon20 insertion+ mNSCLC
- Phase 1/2 J-EXCLAIM study evaluating mobocertinib as a first-line treatment for Japanese patients with EGFR Exon20 insertion+ mNSCLC

**Companion Diagnostics**
- Partnerships with ThermoFisher and Foundation Medicine to develop CDx for mobocertinib

Takeda has decided to no longer pursue the investigation of mobocertinib to treat HER2 Exon20 mutations.
Key Takeaways

- Mobocertinib is a **first-in-class oral TKI specifically designed to selectively target EGFR Exon20 insertions** in patients with mNSCLC, who currently have **no approved targeted options available**.

- In previously treated patients with EGFR Exon20 insertions, current treatment options provide **limited clinical benefit**.

- Mobocertinib has shown **clinically meaningful and durable responses** in these patients.
  - ORR of 35% per investigator and 28% per IRC
  - Median PFS of 7.3 months per IRC
  - DoR of 17.5 months per IRC

- Mobocertinib has a **manageable safety profile** consistent with existing EGFR TKI targeted therapies.

- Takeda looks forward to **submitting these data to the U.S. FDA** and other regulatory agencies around the globe.
### Upcoming Investor Events

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<tr>
<th>Event Description</th>
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<td><strong>FY2020 Q3 EARNINGS CONFERENCE CALL</strong></td>
<td><strong>FEBRUARY 4, 2021, THURSDAY</strong></td>
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<td></td>
<td>6:00 a.m. ET / 8:00 p.m. JST</td>
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<tr>
<td><strong>GROWTH &amp; EMERGING MARKETS STRATEGIC UPDATE CALL</strong></td>
<td><strong>MARCH 11, 2021, THURSDAY</strong></td>
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<tr>
<td><strong>WAVE 1 PIPELINE MARKET OPPORTUNITY CALL (PART 2)</strong></td>
<td><strong>APRIL 6, 2021, TUESDAY</strong></td>
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<tr>
<td><strong>FY2020 Q4 EARNINGS CONFERENCE CALL</strong></td>
<td><strong>MAY 11, 2021, TUESDAY</strong></td>
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<td>TBD</td>
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THANK YOU FOR ATTENDING!

If further questions (or if not answered), please send an email to takeda.ir.contact@takeda.com