

## **TAKEDA ONCOLOGY** 2020 World Conference on Lung Cancer IR Event



January 29, 2021

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### Today's Presenters







### Agenda



All times in Eastern Daylight Time (EDT)

5:00 – 5:10	<b>Teresa Bitetti, President of Global Oncology Business Unit</b> Introduction
5:10 – 5:30	Chris Arendt, Head of Oncology R&D EGFR Exon20 Insertion+ mNSCLC Overview Mobocertinib Phase 1/2 Data Summary Program Overview
5:30 – 5:35	<b>Teresa Bitetti, President of Global Oncology Business Unit</b> Closing
5:35 – 6:00	Question & Answer Session

We Are Committed to Leveraging Scientific Innovation to Address the Unique and Urgent Needs of People Living with Cancer



**OUR FOUNDATION** 

**OUR FOCUS** 

Demonstrated leadership in the treatment of hematologic cancers and solid tumors 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



VAL <sup>1</sup> FY22	Next Checkp	-Gen Innate &		Cell	Therapy
	Next-Gen Innate & Checkpoint Modulators			Cell Therapy	
evonedistat HR-MDS Unfit AML	<b>TAK-981</b> Multiple cancers	<b>TAK-605</b> Multiple cancers	<b>TAK-676</b> Solid tumors	<b>TAK-007</b> Hematologic malignancies	<b>TAK-940</b> R/R B-Cell malignancie.
				<b>TAK-102</b> Solid tumors	
					<b>TAK-102</b> Solid tumors

DIFFERENTIATED I/O PLATFORMS	AND PARTNERSHIPS
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Innate immunomodulation Novel-scaffold immune checkpoint platforms and oncolytic virus Next-gen cell therapy & immune engager platforms

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

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.<sup>1-2</sup>



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



EGFR Exon20 insertions are more prevalent in mNSCLC patients with adenocarcinoma, **never smokers/light smokers** and Asian populations.<sup>3-4</sup>



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**\*.<sup>5-7</sup>

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

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

**1.** Reiss JW, et al. J Thorac Oncol. 2018;13:1560-1568. **2.** Fang W, et al. BMC Cancer. 2019;19:5951. **3.** Kobayashi Y, Mitsudomi T. Cancer Sci. 2016;107(9):1179-1186. **4.** Yatabe Y, Kerr KM, Utomo A, et al. J Thorac Oncol. 2015;10(3):438-445. **5.** Garon EB, Ciuleanu TE, Arrieta O, et al. Lancet. 2014;384(9944):665-673. **6.** Yang G, Li J, Xu H, et al. Lung Cancer. 2020;145:186-194. **7.** Udagawa H, Matsumoto S, Ohe Y, et al. JTO. 2019;14(1):S224.



## **Mobocertinib Update**



### Design and Patient Cohorts in Phases 1/2 and EXCLAIM





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

<sup>a</sup> Active or measurable (but not both) CNS metastases permitted

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

9 CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *EGFR*, 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

Takeda

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



November Data to Form Basis for Mobocertinib FDA Submission in Platinum Pretreated EGFR Exon20 Patient Population

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

Zhou C. Mobocertinib in NSCLC With EGFR Exon 20 Insertions: Results From EXCLAIM and Platinum-Pretreated Patient Populations. IASLC World Conference on Lung Cancer (WCLC). Jan 28-31, 2020. Singapore. Abstract OA04.03

### Mobocertinib Demonstrated 7.3 Months Median PFS\*





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

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# 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. Mobocertinib Resulted in Clinically Meaningful Improvement in Core Lung Cancer Symptoms (EXCLAIM Cohort)



*Data cutoff: May 29, 2020* 

- 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

EORTC QLQ-LC13, European Organization for Research and Treatment of Cancer 13-item lung cancer-specific questionnaire module

Zhou C. Mobocertinib in NSCLC With EGFR Exon 20 Insertions: Results From EXCLAIM and Platinum-Pretreated Patient Populations. IASLC World Conference on Lung Cancer (WCLC). Jan 28-31, 2020. Singapore. Abstract OA04.03

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# Mobocertinib Safety Profile is Consistent with Known EGFR TKI Profile

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



- 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

Data cutoff: May 29, 2020

- 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



15 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.

Q&A









FY2020 Q3 EARNINGS
CONFERENCE CALL

**FEBRUARY 4, 2021,** THURSDAY 6:00 a.m. ET / 8:00 p.m. JST

**GROWTH & EMERGING MARKETS STRATEGIC UPDATE CALL** 

MARCH 11, 2021, THURSDAY TBD

WAVE 1 PIPELINE MARKET OPPORTUNITY CALL (PART 2)

FY2020 Q4 EARNINGS CONFERENCE CALL APRIL 6, 2021, TUESDAY TBD

**MAY 11, 2021,** TUESDAY TBD



## **THANK YOU FOR ATTENDING!**

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

