

News Release

Your Contacts

Media Relations

gangolf.schrimpf@emdgroup.com

Phone: +49 6151 72-9591

Investor Relations

investor.relations@emdgroup.com

Phone: +49 6151 72-3321

March 25, 2020

Not intended for UK-based media

TEPMETKO® (Tepotinib) Approved in Japan for Advanced NSCLC with *MET*ex14 Skipping Alterations

- **TEPMETKO is the first and only therapy in Japan to be approved for line-agnostic treatment of advanced non-small cell lung cancer with *MET* exon 14 (*MET*ex14) skipping alterations**
- **In Phase II VISION study *MET*ex14 skipping alterations were identified by liquid or tissue biopsy**
- **TEPMETKO has been approved in Japan on the basis of demonstrating meaningful benefit in objective response across different lines of treatment, and is administered as a once-daily oral dose**

Darmstadt, Germany, March 25, 2020 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) has approved TEPMETKO®* (tepotinib) for the treatment of patients with unresectable, advanced or recurrent non-small cell lung cancer (NSCLC) with *MET* exon 14 (*MET*ex14) skipping alterations. TEPMETKO is administered 500 mg once daily as two 250 mg tablets. This is the first regulatory approval globally for an oral MET inhibitor indicated for the treatment of advanced NSCLC harboring *MET* gene alterations. TEPMETKO was previously granted SAKIGAKE 'fast-track' designation and orphan drug designation by the MHLW.



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“With TEPMETKO, we are pleased to offer the first approved MET inhibitor in Japan, and a new option that can change the course of treatment for non-small cell lung cancer harboring *MET*ex14 skipping alterations,” said Belén Garijo, CEO Healthcare and Member of the Executive Board of Merck KGaA, Darmstadt, Germany. “With a focus on identifying these alterations in NSCLC patients with flexibility and precision, the companion diagnostic to TEPMETKO offers both liquid and tissue biopsy testing capabilities to best support the delivery of this targeted therapy to the patients who may benefit.”

The approval of TEPMETKO (tepotinib) in Japan is supported by data from 99 patients (including 15 Japanese patients) with NSCLC with *MET*ex14 skipping alterations enrolled in the ongoing single-arm Phase II VISION study.¹ The primary endpoint, objective response rate as assessed by an Independent Review Committee (IRC), was 42.4% (95% CI: 32.5, 52.8) in patients identified by liquid biopsy (LBx) or tissue biopsy (TBx). The median duration of response based on independent assessment was 12.4 months for both LBx-identified (95% CI: 8.4 months, not evaluable) and TBx-identified patients (95% CI: 9.7 months, NE). In a safety analysis of 130 patients, tepotinib was well-tolerated; the most frequent treatment-related adverse events (TRAEs) of any grade were peripheral edema (53.8%), nausea (23.8%) and diarrhea (20.8%). TRAEs led to permanent discontinuation in 11 patients (8.5%).

“Identifying oncogenic drivers in order to guide the course of treatment for lung cancer patients is a clinical best practice; however, there previously was no approved therapy that specifically targeted *MET* alterations in metastatic NSCLC,” said Hiroshi Sakai, M.D., Director, Division of Thoracic Oncology, Saitama Cancer Center, Saitama, Japan. “With the approval of TEPMETKO, we now have a new treatment option that addresses this need, offering clinical benefit and duration of response with convenient once-daily oral dosing, representing real progress for patients with this aggressive type of lung cancer.”

Lung cancer is the most common type of cancer worldwide, with 2 million cases diagnosed annually,² and is the second most common type of cancer in Japan.³ Alterations of the MET signaling pathway are found in various cancer types, including

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3% to 5% of NSCLC cases, and correlate with aggressive tumor behavior and poor clinical prognosis.⁴⁻⁶

Merck KGaA, Darmstadt, Germany has a strategic partnership with ArcherDX to develop a companion diagnostic featuring both liquid and tissue biopsy capabilities to identify *MET*ex14 skipping alterations among patients with NSCLC with high precision and accuracy prior to treatment. The companion diagnostic received approval by MHLW in March 2020, and it is the first and only companion diagnostic to be approved for the detection of *MET* gene alterations. [ArcherDX](#) is a genomic analysis company dedicated to democratizing precision oncology through a suite of products and services that are accurate, personal, actionable and easy to use in local settings.

Discovered in-house at Merck KGaA, Darmstadt, Germany, tepotinib is an oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, including both *MET*ex14 skipping alterations and *MET* amplifications, or MET protein overexpression.

In September 2019, the US Food and Drug Administration (FDA) granted Breakthrough Therapy Designation for tepotinib in patients with metastatic NSCLC harboring *MET*ex14 skipping alterations who progressed following platinum-based cancer therapy. Merck KGaA, Darmstadt, Germany plans to file tepotinib for regulatory review with the FDA in 2020. Tepotinib is also being investigated in the INSIGHT 2 study (NCT03940703) in combination with the tyrosine kinase inhibitor (TKI) osimertinib in epidermal growth factor receptor (EGFR)-mutated, *MET* amplified, locally advanced or metastatic NSCLC that has acquired resistance to prior EGFR TKI.

**The brand name TEPMETKO® is not approved for use outside of Japan.*

About Non-Small Cell Lung Cancer

With 2 million cases diagnosed annually, lung cancer (including trachea, bronchus and lung) is the most common type of cancer worldwide and the leading cause of cancer-related death, with 1.7 million mortality cases worldwide. Alterations of the MET signaling pathway, including *MET* exon 14 (*MET*ex14) skipping alterations and *MET* amplifications, occur in 3% to 5% of NSCLC cases.

About TEPMETKO®

TEPMETKO® (tepotinib) is approved in Japan for the treatment of unresectable, advanced or recurrent non-small cell lung cancer (NSCLC) with *MET* exon 14 (*MET*ex14) skipping alterations. Tepotinib is an oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene)

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alterations, including both *MET*^{ex14} skipping alterations and *MET* amplifications, or *MET* protein overexpression. Discovered in-house at Merck KGaA, Darmstadt, Germany, it has been designed to have a highly selective mechanism of action,⁷ with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations. Tepotinib is currently under clinical investigation in NSCLC and not yet approved in any markets outside of Japan. Merck KGaA, Darmstadt, Germany is actively assessing the potential of investigating tepotinib in combination with novel therapies and in other tumor indications.

References

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Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 57,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2019, Merck KGaA, Darmstadt, Germany generated sales of € 16.2 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.