News Release

Your Contact
annemarie.eckhardt@emdgroup.com
Phone: +49 6151 72 26560

November 20, 2019

Not intended for UK-based media

Merck KGaA, Darmstadt, Germany, Announces Orphan Drug Designation for Investigational Therapy Tepotinib in Patients with NSCLC Harboring *MET* Gene Alterations

- **Japanese Ministry of Health, Labour and Welfare grants orphan drug designation for diseases that affect fewer than 50,000 patients in Japan, and for which significant unmet medical need exists**
- ***MET* exon 14 (*MET*ex14) skipping alterations and *MET* amplifications are present in 3-5% of non-small cell lung cancer patients and correlate with poor prognosis**
- **In March 2018, tepotinib received SAKIGAKE 'fast-track' regulatory designation in Japan and in September 2019 received Breakthrough Therapy Designation in the US**

Darmstadt, Germany, November 20, 2019 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) has granted orphan drug designation (ODD) for its investigational therapy tepotinib* for patients with non-small cell lung cancer (NSCLC) harboring *MET* gene alterations.

"Advanced NSCLC harboring *MET* gene alterations is associated with aggressive tumor behavior and poor clinical prognosis," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "This orphan drug designation helps to advance this program within Japan and, coupled with the SAKIGAKE 'fast-track' designation received last year, provides important mechanisms,

Frankfurter Strasse 250
64293 Darmstadt · Germany
Hotline +49 6151 72-5000
www.emdgroup.com

Head of Media Relations -6328
Spokesperson: -9591 / -7144 / -8908 / -55707

such as priority review, to quickly deliver this medicine to Japanese patients with this difficult-to-treat disease."

The Japan MHLW ODD program is designed to promote research and development of orphan drugs for diseases that affect fewer than 50,000 patients in Japan, and for which significant unmet medical need exists. An investigational drug can qualify for ODD if there is no approved alternative treatment option or if there is an expectation of high efficacy or safety compared to existing treatment options. Drugs receiving ODD qualify for several benefits intended to support development, such as guidance and subsidies for research and development activities from the MHLW, preferential tax treatment, priority consultation for clinical development, and priority review of applications.

Discovered in-house at Merck KGaA, Darmstadt, Germany, tepotinib is an investigational oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, including both *MET* exon 14 skipping alterations and *MET* amplifications, or MET protein overexpression. It has been designed to have a highly selective mechanism of action,[1] with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations.

Alterations of the MET signaling pathway are found in various cancer types, including 3-5% of NSCLC cases, and correlate with aggressive tumor behavior and poor clinical prognosis.[2-4] Lung cancer is the most common type of cancer worldwide, with two million cases diagnosed annually.[5]

Tepotinib is being investigated in the ongoing VISION study (NCT02864992), which showed preliminary efficacy in patients harboring *MET*ex14 skipping alterations detected by liquid biopsy (LBx) or tissue biopsy (TBx) across different lines of treatment.

Results from the interim analysis of the VISION study were presented in an oral presentation at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting[6] and the 2019 Japan Society of Medical Oncology (JSMO) Annual Meeting.[7] The use of both LBx and TBx to identify patients for the VISION study is intended to support improved patient selection and is consistent with the company's focus on patient-centric drug development.

News Release

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 having acquired resistance to prior EGFR TKI.

In March 2018, the Japan MHLW granted SAKIGAKE 'fast-track' designation for tepotinib in advanced (stage IIIB/IV) NSCLC harboring *MET*ex14 skipping alterations and, in September 2019, the US Food and Drug Administration (FDA) granted Breakthrough Therapy Designation (BTD) for tepotinib in patients with metastatic NSCLC harboring *MET*ex14 skipping alterations who progressed following platinum-based cancer therapy.

[*] *Tepotinib is currently under clinical investigation and not approved for any use anywhere in the world.*

About Non-Small Cell Lung Cancer
With two 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.[5] Alterations of the MET signaling pathway, including *MET* exon 14 skipping alterations and *MET* amplifications, occur in 3-5% of NSCLC cases.[2-4]

About Tepotinib
Tepotinib, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, including both *MET* exon 14 skipping alterations and *MET* amplifications, or MET protein overexpression. It has been designed to have a highly selective mechanism of action,[1] with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations.

Tepotinib is currently being investigated in NSCLC and Merck KGaA, Darmstadt, Germany, is actively assessing the potential of investigating tepotinib in combination with novel therapies and in other tumor indications.

References
1. Bladt, F, et al. Clin Cancer Res 2013;19:2941-2951.
2. Reungwetwattana T, et al. Lung Cancer 2017;103:27-37.
3. Mo HN, et al. Chronic Dis Transl Med 2017; 3(3):148-153.
4. Lutterbach B, et al. Cancer Res 2007;67:2081–8.
5. Bray F, et al. CA Cancer J Clin. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. 2018;68(6):394–424. https://doi.org/10.3322/caac.21492 PMID:30207593
6. Paik P, et al. J Clin Oncol 2019;37: (suppl; abstr 9005).
7. Sakai H, et al. Ann Oncol 2019;30(Suppl_6):Abstract MO2-15-5.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 56,000 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 2018, Merck KGaA, Darmstadt, Germany, generated sales of € 14.8 billion in 66 countries.

News Release

Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 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.