News Release

Your Contacts
Media Relations
friederike.segeberg@emdgroup.com
Phone: +49 6151 72-6328

Investor Relations
investor.relations@emdgroup.com
Phone: +49 6151 72-3321

September 11, 2019

Not intended for UK-based media

Merck KGaA, Darmstadt, Germany, Announces FDA Breakthrough Therapy Designation for Investigational Therapy Tepotinib in Patients with Metastatic NSCLC with *MET*ex14 Skipping Alterations

- **Investigational oral MET inhibitor has previously received SAKIGAKE 'fast-track' regulatory designation in Japan**
- ***MET* exon 14 skipping alterations and *MET* amplifications are present in 3-5% of non-small cell lung cancer patients and correlate with poor prognosis**
- **The designation is based on data from the ongoing VISION study, which showed preliminary clinical evidence for tepotinib in metastatic NSCLC harboring *MET*ex14 skipping alterations**

Darmstadt, Germany, September 11, 2019 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, which operates its biopharmaceutical business as EMD Serono in the US and Canada, today announced that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for the investigational targeted therapy tepotinib* in patients with metastatic non-small cell lung cancer (NSCLC) harboring *MET* exon 14 skipping alterations who progressed following platinum-based cancer therapy.

"Tepotinib was associated with robust objective responses with durability that has not previously been seen in patients with metastatic NSCLC harboring MET exon 14 skipping alterations, selected by either tissue or liquid biopsy approaches," said Luciano Rossetti, Global Head of Research & Development for the Biopharma

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

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

business of Merck KGaA, Darmstadt, Germany. "This breakthrough therapy designation further underscores the potential of tepotinib, and we aim to advance this program and deliver this medicine as quickly as possible to NSCLC patients who may benefit."

Lung cancer is the most common type of cancer worldwide, with 2 million cases diagnosed annually.[1] 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]

Discovered in-house at Merck KGaA, Darmstadt, Germany, tepotinib is an investigational oral MET kinase inhibitor that is designed to be highly potent and selective[5] and to inhibit the oncogenic signaling caused by *MET* (gene) alterations, including both *MET* exon 14 skipping alterations and *MET* amplifications, or MET protein overexpression.

In March 2018, tepotinib's potential was recognized by the Japanese Ministry of Health, Labour and Welfare (MHLW), which granted SAKIGAKE 'fast-track' designation for tepotinib in advanced NSCLC harboring *MET* exon 14 skipping alterations. SAKIGAKE designation promotes research and development in Japan, aiming at early practical application for innovative pharmaceutical products, medical devices and regenerative medicines.

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.

The Breakthrough Therapy Designation is based on data from the ongoing VISION study (NCT02864992), showing preliminary clinical evidence that tepotinib may

offer an improvement over available therapy in patients with metastatic NSCLC harboring *MET* exon 14 skipping alterations detected by liquid biopsy (LBx) or tissue biopsy (TBx) across different lines of treatment.

Results from an interim analysis of the ongoing VISION study in 73 efficacy-evaluable patients with NSCLC with *MET* exon 14 skipping alterations identified by LBx or TBx testing demonstrate overall objective response rate (ORR) of 50.0% for LBx-identified patients as assessed by Independent Review Committee (IRC), and 55.3% as assessed by investigators. The ORR for TBx-identified patients was 45.1% and 54.9%, respectively. The overall median duration of response (DOR) was 12.4 months and 17.1 months among LBx-identified patients, as assessed by IRC and investigators, respectively, while among TBx-identified patients, 15.7 and 14.3 months were observed, respectively.

Most treatment-related adverse events (TRAEs) were Grade 1 and 2. No Grade 4 or 5 TRAEs were observed. Any grade TRAEs reported by ≥10% of 87 patients evaluable for safety were peripheral edema (48.3%), nausea (23.0%) diarrhea (20.7%) and increased blood creatinine (12.6%). Other relevant TRAEs of any grade include increased lipase (4.6%), fatigue (3.4%) and vomiting (3.4%). TRAEs led to permanent discontinuation in four patients (two patients due to peripheral edema, one due to interstitial lung disease, one due to diarrhea and nausea).

Results from this study were presented in an oral presentation at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting.[6] 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.

[*] *Tepotinib is the recommended International Nonproprietary Name (INN) for the MET kinase inhibitor (MSC2156119J). Tepotinib is currently under clinical investigation and not approved for any use anywhere in the world.*

News Release

About Breakthrough Therapy Designation
Breakthrough Therapy Designation is designed to expedite the development and review of drugs which are intended to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s). The FDA's granting of the Breakthrough Therapy Designation for advanced NSCLC does not alter the standard regulatory requirement to establish the safety and effectiveness of a drug through adequate and well-controlled studies to support approval.

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.[1] 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, 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. 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
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. Bladt, F, et al. Clin Cancer Res 2013;19:2941-2951.
6. Paik P, et al. J Clin Oncol 2019;37: (suppl; abstr 9005).

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 52,000 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.

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 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.