Merck KGaA
Darmstadt, Germany

News Release

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ASCO Abstract #
Tepotinib (MET kinase inhibitor): 9005

Not intended for UK-based media

Merck KGaA, Darmstadt, Germany Presents Updated Results for Investigational Therapy Tepotinib Demonstrating Durable Clinical Response in Patients with Advanced NSCLC with *MET*ex14 Skipping Mutations

- **Alterations of the MET signaling pathway are present in 3-5% of non-small cell lung cancer patients and correlate with poor prognosis**
- **New interim data from Phase II VISION study (all lines of treatment) show tepotinib induced objective responses, as assessed by independent review, in 50.0% of patients identified by liquid biopsy (LBx) and 45.1% of patients identified by tissue biopsy (TBx)**
- **Median duration of response was 12.4 months for LBx-identified patients and 15.7 months for TBx-identified patients**
- **Safety results for tepotinib are consistent with those reported in previous studies; most treatment-related adverse events (TRAEs) were Grade 1 and 2, and no Grade 4 or 5 TRAEs were observed**

Darmstadt, Germany, June 3, 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 presented updated results from the

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potentially registrational Phase II VISION study, showing durable anti-tumor clinical activity for the investigational targeted therapy tepotinib* across different lines of treatment in advanced non-small cell lung cancer (NSCLC) patients harboring *MET* exon 14 skipping mutations detected by liquid biopsy (LBx) or tissue biopsy (TBx). Data were shared in an oral presentation today at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL, US.

"Tepotinib has been designed to potentially improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "Tepotinib is an important part of our strategic focus on precision medicine, and both the proportion of patients responding and the duration of anti-tumor clinical activity demonstrate the potential of this investigational therapy."

Discovered in-house at Merck KGaA, Darmstadt, Germany, tepotinib is an investigational, highly potent and selective[1] oral MET kinase inhibitor that is designed to inhibit the oncogenic signaling caused by *MET* (gene) alterations, including both *MET* exon 14 skipping mutations and *MET* amplifications, or MET protein overexpression. 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]

"Patients with this NSCLC molecular subtype lack treatment options that have the potential to significantly improve clinical outcomes," said Paul K. Paik, M.D., primary study investigator and Clinical Director, Thoracic Oncology Service, Memorial Sloan Kettering Cancer Center. "It is noteworthy to see data that are consistent with tepotinib's previously reported efficacy findings in this patient population, and that also provide valuable new insight into its durable clinical activity across various treatment lines."

Results from the ongoing Phase II VISION study in 73 efficacy-evaluable patients with NSCLC with *MET* exon 14 skipping mutations identified by LBx or TBx 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).

The use of both liquid and tissue biopsies to identify patients for the VISION trial is intended to support improved patient selection and is consistent with the company's focus on patient-centric drug development.

Tepotinib is currently being investigated in NSCLC in two different settings: in NSCLC harboring *MET* alterations (*MET* exon 14 skipping mutations and *MET* amplifications) as monotherapy, as well as in combination with the tyrosine kinase inhibitor (TKI) osimertinib in epidermal growth factor receptor (EGFR) mutated *MET* amplified NSCLC having acquired resistance to prior EGFR TKI. Additional information on these clinical trials can be found at ClinicalTrials.gov using the identifiers NCT02864992 and NCT03940703, respectively. Merck, KGaA, Darmstadt, Germany is also actively assessing the potential of investigating tepotinib in combination with novel therapies for other tumor indications.

[*] *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.*

Notes to Editors

Tepotinib oral session:

Title	Lead Author	Abstract #	Presentation Date / Time (CDT)	Location
Tepotinib				
Oral Session				

News Release

Phase II study of tepotinib in NSCLC patients with *MET*ex14 mutations	P.K. Paik	9005	Mon, Jun 3, 8:00 AM – 11:00 AM (9:24 AM – 9:36 AM lecture time)	Hall B1

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.[5] Alterations of the MET signaling pathway, including *MET* exon 14 skipping mutations 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 mutations 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. 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

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.