News Release

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Merck KGaA, Darmstadt, Germany Provides Update on Tepotinib Phase II Results in Advanced Hepatocellular Carcinoma

- **Primary endpoints met in two clinical trials for investigational targeted therapy, tepotinib, as a monotherapy in MET-positive, advanced hepatocellular carcinoma (HCC) with Child-Pugh Class A liver function**
- **These data provide further evidence of tepotinib activity in patients with MET-positive advanced cancers**
- **Given evolving standard of care in HCC, Merck KGaA, Darmstadt, Germany will assess the potential of tepotinib in combination for further clinical development**

Darmstadt, Germany, June 11, 2018– Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced positive results from two Phase II clinical trials of its investigational, targeted oncology molecule tepotinib* in MET-positive, advanced hepatocellular carcinoma (HCC) with Child-Pugh Class A liver function. Both studies met their primary endpoint. The trials evaluated the efficacy, safety and pharmacokinetics of tepotinib in patients with HCC as a first-line (NCT01988493) and second-line therapy (NCT02115373). Tepotinib is an important investigational therapy for Merck KGaA, Darmstadt, Germany and plays a key role in the company's strategic focus on innovative precision medicines.

"These results, together with the interim data seen in patients with advanced non-small cell lung cancer harboring *MET* exon 14 skipping mutations presented at ASCO, provide further evidence of the potential of tepotinib as an innovative

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precision medicine," said Luciano Rossetti, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany. "While this is a positive result, given the evolving standard of care in HCC, we will assess the possibility of pursuing tepotinib in this indication as a combination therapy versus a single-agent treatment."

Both tepotinib HCC trials recruited patients with advanced, MET-positive tumors and Child-Pugh Class A liver function. Study NCT01988493 is a multi-center, randomized Phase Ib/II trial investigating tepotinib as a first-line therapy versus sorafenib in Asian patients (Phase II part: tepotinib 45 patients; sorafenib 45 patients randomized, respectively). The primary endpoint for the Phase II part of the trial was time to progression as assessed by independent review committee (RECIST Version 1.1). Study NCT02115373 is a multi-center, single-arm, Phase Ib/II trial investigating tepotinib as a second-line therapy in patients who failed treatment with sorafenib (Phase II part: tepotinib 49 patients treated). The primary endpoint for the Phase II part of NCT02115373 was progression-free survival status at 12 weeks (as assessed by the investigator according to RECIST Version 1.1).

The safety data for tepotinib in these two trials are consistent with that observed in Phase Ib parts of the HCC studies[1,2]; no new safety signals were identified. The HCC data will be shared in more detail at an upcoming scientific conference later in the year.

Tepotinib, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational inhibitor of the c-Met receptor tyrosine kinase. Alterations of the c-Met signaling pathway are found in various cancer types and correlate with aggressive tumor behavior and poor clinical prognosis. Tepotinib has been designed with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific mutations.

As part of the ongoing clinical program, Merck KGaA, Darmstadt, Germany is investigating tepotinib in a Phase II trial in patients with advanced non-small cell lung cancer (NSCLC) harboring *MET* exon 14 skipping mutations. *MET* exon 14 skipping is a targetable gene alteration.[3] Interim data from this study were recently presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting

and showed anti-tumor clinical activity in this patient group and a safety profile consistent with that observed in previous studies.

In March, the Japanese Ministry of Health, Labour and Welfare granted SAKIGAKE 'fast-track' designation to tepotinib in patients with NSCLC harboring *MET* exon 14 skipping mutations.

**Tepotinib is the recommended International Nonproprietary Name (INN) for the c-Met kinase inhibitor (MSC 2156119J). Tepotinib is currently under clinical investigation and not approved for any use anywhere in the world.*

About Hepatocellular Carcinoma
HCC is the most common type of primary liver cancer, accounting for 75–90% of all liver cancer cases.[4,5] c-Met-positive tumors occur in approximately 45% of HCC patients.[6] It occurs predominantly in patients with underlying chronic liver disease and cirrhosis.[5] HCC is the third leading cause of cancer death worldwide, with over 500,000 people affected.[7] Chronic liver disease due to hepatitis B virus or hepatitis C virus and alcohol accounts for the majority of HCC cases.[8] HCC is frequently diagnosed at advanced stages and has a high mortality rate.[9] Patients with HCC have limited treatment options and both the incidence and mortality of this disease has increased over the past 10 years.[6,9]

About Non-Small Cell Lung Cancer
Globally, lung cancer is the most common cause of cancer-related deaths in men and the second most common in women,[10] responsible for more deaths than colon, breast and prostate cancer combined.[11] NSCLC is the most common type of lung cancer, accounting for 80 to 85% of all lung cancers.[12] *MET* exon 14 skipping mutations occur in 3-4% of lung cancers.[13,14] The five-year survival rate for people diagnosed with lung cancer that has spread (metastasized) to other areas of the body is 1%.[15]

About Tepotinib
Tepotinib is an investigational, small-molecule inhibitor of the c-Met receptor tyrosine kinase discovered in-house at Merck KGaA, Darmstadt, Germany. Alterations of the c-Met signaling pathway are found in various cancer types and correlate with aggressive tumor behavior and poor clinical prognosis. Tepotinib is currently being investigated in a Phase II study in NSCLC.

About SAKIGAKE
SAKIGAKE designation is granted by the Japanese Ministry of Health, Labour and Welfare, promoting research and development in Japan and aiming at early practical application for innovative pharmaceutical products, medical devices and regenerative medicines. SAKIGAKE designation can reduce a drug's review period down from 12 months to a target of 6 months.

The system's objective is to designate drugs that have the potential of prominent effectiveness against serious and life-threatening diseases in order to make them available to patients in Japan ahead of the rest of the world.

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About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Almost 53,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany, holds the global rights to the „Merck" name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.