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News Release

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# *New England Journal of Medicine* Publishes Primary Analysis of VISION Data for Tepotinib in Advanced NSCLC with *MET*ex14 Skipping Alterations

- **First publication of primary analysis shows robust and durable clinical response in patients with advanced non-small cell lung cancer (NSCLC) with *MET* exon 14 (*MET*ex14) skipping alterations; data also presented during ASCO 2020**
- **Meaningful clinical benefit was shown to be consistent across different lines of treatment with or without brain metastases, and in patients with *MET*ex14 skipping as assessed by liquid biopsy or tissue biopsy**
- **First patient-reported quality-of-life outcomes in NSCLC with *MET*ex14 skipping alterations show quality of life was maintained on treatment with once-daily, orally available tepotinib**

Darmstadt, Germany, May 29, 2020—Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that updated data from the ongoing, single-arm Phase II VISION study evaluating tepotinib* as a single agent in patients with advanced non-small cell lung cancer (NSCLC) with *MET* exon 14 (*MET*ex14) skipping alterations were published in *The New England Journal of Medicine (NEJM)*. Results from the primary analysis of data from 99 patients with at least 9 months of follow-up demonstrate consistent response rate and durable anti-tumor activity across lines of treatment in patients assessed by both liquid biopsy (LBx) and tissue biopsy (TBx). Results from the VISION study were also presented at the American Society of Clinical Oncology (ASCO) ASCO20 Virtual Scientific Program on May 29, including data from the primary analysis (Abstract #9556) and

including patient-reported outcomes (PROs) of health-related quality of life (HRQoL) (Abstract #9575). Tepotinib is designed to be a highly selective[1] oral MET inhibitor that is administered once daily and is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations.

"*MET* exon 14 skipping is a primary oncogenic driver, but until recently there have been no approved treatment options targeting this genetic alteration in NSCLC," said Paul K. Paik, M.D., primary study investigator, lead author and Clinical Director, Thoracic Oncology Service, Memorial Sloan Kettering Cancer Center. "These new findings highlight the importance of routine next-generation sequencing to identify *MET*ex14 skipping alterations and demonstrate tepotinib's durable anti-tumor activity in patients who are typically elderly, and whose cancers are often harder to treat."

This new analysis of data from 99 patients in the fully enrolled Cohort A with at least 9 months of follow-up was published by *The New England Journal of Medicine* on May 29. Results demonstrate objective response rate (ORR) of 46% (95% CI, 36–57) among patients with *MET*ex14 skipping alterations identified by either LBx or TBx as assessed by Independent Review Committee (IRC), and 56% (95% CI, 45–66) as assessed by investigators. The median duration of response (DOR) was 11.1 months (95% CI, 7.2–could not be estimated (NE)) among patients with *MET*ex14 skipping alterations identified by either LBx or TBx as assessed by IRC, and 14.0 months (95% CI, 9.7–18.3) as assessed by investigators. Results were consistent across different lines of treatment and in patients assessed by LBx or TBx. Additional endpoints were progression-free survival (PFS) and overall survival (OS).

Patients with brain metastases at baseline (n=11) benefitted similarly from treatment. In these patients, systemic ORR as assessed by independent review was 55% (95% CI, 23–83), with a median DOR of 9.5 months (95% CI, 6.6–NE) and a median PFS of 10.9 months (95% CI, 8.0–NE).

Results also include the first patient-reported quality-of-life outcomes in patients with NSCLC with *MET*ex14 skipping alterations. Quality of life was maintained over time of treatment with tepotinib, with symptoms of dyspnea remaining stable and cough symptoms improving. The first longitudinal on-treatment biomarker data

from LBx samples were also reported, showing high concordance between molecular circulating free DNA response (defined as *MET*ex14 depletion) and clinical response based on measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST).

Out of 152 patients evaluable for safety, treatment-related adverse events (TRAEs) of all grades were reported in 135 patients (89%). Grade 3 TRAEs were reported in 38 patients (25%), and 3 patients (2%) experienced Grade 4 TRAEs. One death was considered by the investigator to be treatment-related and occurred in a 79-year-old patient with respiratory failure and dyspnea, secondary to interstitial lung disease. The most common Grade ≥3 TRAE was peripheral edema, which occurred in 11 patients (7%). Serious TRAEs were reported in 23 patients (15%). Permanent tepotinib discontinuations due to TRAEs were reported in 17 patients (11%), and 50 patients (33%) required a dose reduction due to TRAEs. Peripheral edema was the most common TRAE leading to a dose reduction (25 patients, 16%) or dose interruption (28 patients, 18%); permanent discontinuation was uncommon (7 patients, 5%).

"Designed to have a highly selective mechanism of action, tepotinib has the potential to make a difference in the treatment and lives of people living with non-small cell lung cancer harboring *MET*ex14 skipping alterations," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "Following on the recent approval of tepotinib in Japan as the first therapy for the treatment of advanced NSCLC harboring *MET* gene alterations, the publication of these data underscores our commitment to advancing scientific understanding and potential therapeutic options for this challenging cancer."

The ongoing Phase II VISION (NCT02864992) clinical trial is a single-arm, open-label, multi-cohort study investigating the safety and efficacy of tepotinib as a single agent in patients with advanced or metastatic NSCLC with *MET*ex14 skipping alterations identified by LBx and/or TBx. 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.

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Lung cancer is the most common type of cancer worldwide, with 2 million cases diagnosed annually.[2] Alterations of the MET signaling pathway are found in various cancer types, including 3% to 5% of NSCLC cases, and correlate with aggressive tumor behavior and poor clinical prognosis.[3-5] Patients with NSCLC harboring *MET*ex14 skipping tend to be older than those with NSCLC harboring other alterations.[6] In the Phase II VISION study, the patient population is generally characterized as elderly, with a median age of 74.0 years, and as having poor clinical prognosis typical of NSCLC with *MET*ex14 skipping alterations.

In March 2020, the Japanese Ministry of Health, Labour and Welfare (MHLW) approved tepotinib for the treatment of patients with unresectable, advanced or recurrent NSCLC with *MET*ex14 skipping alterations. 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.

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.

[*] *Tepotinib is currently under clinical investigation and not yet approved in any markets outside of Japan.*

*Dr. Paik has provided compensated advisory services to Merck KGaA, Darmstadt, Germany.*

**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.[2] 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.[3-5]

**About Tepotinib**
Tepotinib is an oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations. Discovered in-house at Merck KGaA, Darmstadt, Germany, 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

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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**About Merck KGaA, Darmstadt, Germany**

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 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.