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News Release

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FDA Accepts Filing of New Drug Application for Tepotinib for the Treatment of Patients with Metastatic NSCLC with METex14 Skipping Alterations

- **Tepotinib granted Priority Review and is being evaluated under FDA Real-Time Oncology Review (RTOR) pilot program**
- **Tepotinib is a highly targeted inhibitor of c-MET that is administered as a once-daily oral tablet**
- **Data show robust, consistent and durable clinical response across different lines of therapy, including in patients with brain metastases, and as assessed by liquid biopsy or tissue biopsy**

Darmstadt, Germany, August 25, 2020 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the US Food and Drug Administration (FDA) has accepted and granted Priority Review to the new drug application (NDA) for once-daily, orally-dosed tepotinib* for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition exon 14 (*MET*ex14) skipping, as detected by an FDA-approved test. Tepotinib was granted Priority Review and is being reviewed by the FDA under its Real-Time Oncology Review (RTOR) pilot program, which is intended to create a more efficient review process to bring safe and effective treatments to patients as early as possible.[1] Priority Review is intended to accelerate evaluation of applications for drugs that could offer improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.[2] Tepotinib

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was granted Breakthrough Therapy Designation by the FDA in September 2019 for the treatment of patients with metastatic NSCLC harboring *MET*ex14 skipping alterations who progressed following platinum-based cancer therapy.

The application is based on results from the pivotal ongoing, single-arm Phase II VISION study (NCT02864992) evaluating tepotinib as monotherapy in patients with advanced NSCLC with *MET* exon 14 (*MET*ex14) skipping alterations prospectively assessed by liquid and/or tissue biopsy. Results demonstrate consistent response rate and durable anti-tumor activity across lines of treatment including in patients with brain metastases and in patients assessed by both liquid biopsy (LBx) and tissue biopsy (TBx). Data from the primary analysis of the VISION study were published in *The New England Journal of Medicine (NEJM)* on May 29, 2020 and presented during the American Society of Clinical Oncology (ASCO) ASCO20 Virtual Scientific Program.[3]

"*MET*ex14 skipping alterations drive a particularly aggressive form of NSCLC in a patient population that is generally elderly, facing poor clinical prognosis and in urgent need of new therapeutic options," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "With this acceptance and review under the RTOR program, we look forward to working with FDA and to making this precision medicine available to patients in the U.S. as soon as possible."

In the US in 2020, there were approximately 228,000 new cases of lung cancer and more than 135,000 deaths from lung cancer.[4] 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.[5-7] Patients with NSCLC harboring *MET*ex14 skipping tend to be older than those with NSCLC harboring other alterations.[8] 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, tepotinib became the first oral MET inhibitor indicated for the treatment of advanced NSCLC harboring *MET* gene alterations to receive a regulatory approval globally, with the Japanese Ministry of Health, Labour and

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Welfare (MHLW) approval for the treatment of patients with unresectable, advanced or recurrent NSCLC with *MET*ex14 skipping alterations.

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

References

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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 1.9 million mortality cases worldwide.[9] 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.[5-7]

About Tepotinib

Tepotinib is an oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations. Discovered and developed in-house at Merck KGaA, Darmstadt, Germany, it has been designed to have a highly selective mechanism of action[10], with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations. In March 2020, tepotinib became the first oral MET inhibitor indicated for the treatment of advanced NSCLC harboring *MET* gene alterations to receive a regulatory approval globally, with the Japanese Ministry of Health, Labour and Welfare (MHLW) approval 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 whose disease progressed following platinum-based cancer therapy. Tepotinib is also being investigated in the Phase II INSIGHT 2 study in combination with osimertinib in *MET* amplified, advanced or metastatic NSCLC harboring activating *EGFR* mutations that has progressed following first-line treatment with osimertinib.

About VISION

VISION is Phase II, pivotal, multi-center, multi-cohort, single-arm, open-label study investigating tepotinib as a monotherapy for advanced (locally advanced or metastatic) non-small cell lung cancer (NSCLC) with *MET* exon 14 (*MET*ex14) skipping alterations or *MET* amplification identified by liquid or tissue biopsy. The primary outcome measure is objective response as assessed by independent review committee (IRC) and according to Response Evaluation Criteria in Solid Tumors (RECIST). Secondary outcome measures include objective response, duration of response, objective disease control, progression free survival, overall survival and other measures. The trial is ongoing and continuing to enroll patients.

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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.