News Release

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Not intended for UK-based media

ERBITUX® in Combination with FOLFOX or FOLFIRI Approved as First-Line Therapy for Patients in China with RAS Wild-Type Metastatic Colorectal Cancer

- **Approval is for ERBITUX® in combination with FOLFOX or FOLFIRI for first-line treatment, or in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy**
- **Pivotal Phase III evidence shows significant improvements with ERBITUX® in combination with FOLFOX versus FOLFOX alone in response rate, disease progression and survival**
- **This marks a meaningful step forward in Merck KGaA, Darmstadt, Germany's commitment as a global specialty innovator - including bringing innovative medicines to markets with high unmet medical needs**

Darmstadt, Germany, September 27, 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 ERBITUX® (cetuximab) has been granted approval by the National Medical Products Administration (NMPA) of China for the first-line treatment for patients with RAS wild-type (wt) metastatic colorectal cancer (mCRC) in combination with FOLFOX or FOLFIRI, or in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy. The pivotal Phase III evidence from the TAILOR study, on which the approval was based, shows significant benefit in overall response rate (ORR), progression-free survival (PFS) and overall survival (OS) for patients treated with ERBITUX® in combination with FOLFOX, compared to FOLFOX alone, in the first-line setting for this challenging type of cancer.[1,2]

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"ERBITUX®, in combination with chemotherapy, has long been a standard of care for the treatment of RAS wild-type mCRC and the TAILOR study further demonstrates the possibilities it can bring in the first-line setting," said Professor Jin Li, Tongji University Shanghai East Hospital, China and principal investigator in the TAILOR study. "This approval marks an important development for patients in China, who now have the benefit of a new and much needed treatment option."

"ERBITUX® is globally recognized as a first-line standard of care for the treatment of RAS wild-type mCRC. We welcome the National Medical Products Administration's decision to make it available to Chinese patients in the first-line setting," said Chris Round, Head of International Operations and Global Core Franchises, Merck KGaA, Darmstadt, Germany, operating in China. "This approval is a significant step forward in Merck KGaA, Darmstadt, Germany's commitment as a global specialty innovator – including bringing innovative medicines to markets with high unmet medical needs."

As the third most commonly diagnosed cancer, it is estimated that 1.85 million new cases of colorectal cancer (CRC) are diagnosed every year worldwide.[3] Based on this statistic, the global burden of CRC is expected to increase by nearly 20% to more than 2.2 million new cases and approximately 1.1 million deaths by 2030.[4] In China, CRC has the fifth highest incidence among all cancers in men and the fourth in women.[5]

The approval is based on the TAILOR study of 393 randomized patients from China with RAS wt mCRC, which found that adding ERBITUX® to FOLFOX as a first-line treatment for mCRC delays the risk of a PFS event (disease progression or death) occurring by 31% (hazard ratio [HR]: 0.69; p=0.004); reduces the risk of death Tby 24% (HR: 0.76; p=0.02) and achieves an ORR of 61.1% (versus 39.5% with FOLFOX alone; odds ratio [OR]: 2.41; p<0.001). The safety profile of ERBITUX® observed in TAILOR is similar to that seen in prior randomized clinical trials, with no unexpected safety findings.[1]

TAILOR is the first Phase III trial in the Chinese population to prospectively evaluate an anti-epidermal growth factor receptor (EGFR) antibody in the first-line treatment

of patients with RAS wt mCRC and reinforces the value and importance of RAS biomarker testing in clinical practice to provide patients with the right targeted therapy from the start of treatment. The data are consistent with previous international pivotal studies and reaffirm the efficacy of ERBITUX® in combination with FOLFOX as a first-line treatment for patients with RAS wt mCRC.

ERBITUX® has obtained marketing authorization in over 100 countries worldwide for the treatment of RAS wt mCRC and/or squamous cell carcinoma of the head and neck (SCCHN). In the EU, ERBITUX® is indicated as first-line therapy for patients with RAS wt mCRC tumors together with the oxaliplatin-containing regimen FOLFOX, or together with regimens containing irinotecan-based regimens in any line of treatment, or as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan.[6]

About mCRC
Approximately half of patients with mCRC have RAS wild-type tumors and half have RAS mutant tumors.[7] Results from studies assessing RAS mutation status in patients with mCRC have shown that anti-epidermal growth factor receptor (EGFR) monoclonal antibody therapies, such as ERBITUX® (cetuximab), can improve outcomes in patients with RAS wild-type mCRC.[1-2,6] Colorectal cancer (CRC) is the third most common cancer worldwide, with an estimated incidence of more than 1.85 million new cases annually.[3] An estimated 880,000 deaths from CRC occur worldwide every year, accounting for 9.2% of all cancer deaths and making it the second most common cause of death from cancer.[3] Almost 55% of CRC cases are diagnosed in developed regions of the world[8], and incidence and mortality rates are substantially higher in men than in women.[3]

About ERBITUX® (cetuximab)
ERBITUX® is an IgG1 monoclonal antibody targeting the epidermal growth factor receptor (EGFR). As a monoclonal antibody, the mode of action of ERBITUX® is distinct from standard non-selective chemotherapy treatments in that it specifically targets and binds to the EGFR. This binding inhibits the activation of the receptor and the subsequent signal-transduction pathway, which results in reducing both the invasion of normal tissues by tumor cells and the spread of tumors to new sites. It is also believed to inhibit the ability of tumor cells to repair the damage caused by chemotherapy and radiotherapy and to inhibit the formation of new blood vessels inside tumors, which appears to lead to an overall suppression of tumor growth. Based on *in vitro* evidence, ERBITUX® also targets cytotoxic immune effector cells towards EGFR-expressing tumor cells (antibody-dependent cell-mediated cytotoxicity [ADCC]).

ERBITUX® has already obtained market authorization in over 100 countries worldwide for the treatment of RAS wild-type metastatic colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck. Merck KGaA, Darmstadt, Germany licensed the right to market ERBITUX®, a registered trademark of ImClone LLC, outside the U.S. and Canada from ImClone LLC, a wholly owned subsidiary of Eli Lilly and Company, in 1998.

ERBITUX® Important Safety Information from the US FDA-Approved Label
The US Prescribing Information for ERBITUX® includes BOX WARNINGS for infusion reactions and cardiopulmonary arrest. Very commonly (≥25%) reported side effects with ERBITUX® include cutaneous adverse reactions (including acne-like skin rash, pruritus, and nail changes), headache, diarrhea, infection and hypomagnesemia.

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WARNING: INFUSION REACTIONS and CARDIOPULMONARY ARREST
Infusion Reactions: ERBITUX® can cause serious and fatal infusion reactions [see Warnings and Precautions (5.1), Adverse Reactions (6)]. Immediately interrupt and permanently discontinue ERBITUX® for serious infusion reactions [see Dosage and Administration (2.4)].

Cardiopulmonary Arrest: Cardiopulmonary arrest or sudden death occurred in patients with squamous cell carcinoma of the head and neck receiving ERBITUX® with radiation therapy or a cetuximab product with platinum-based therapy and fluorouracil. Carefully consider use of ERBITUX® with radiation therapy, or platinum-based therapy with fluorouracil, in head and neck cancer patients with a history of coronary artery disease, congestive heart failure, or arrhythmias. Monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after ERBITUX® administration [see Warnings and Precautions (5.2, 5.6)].

Please see full US Prescribing Information available at www.accessdata.fda.gov

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 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.