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News Release

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Merck KGaA: Erbitux Meets Primary Endpoint in First-Line Phase III Metastatic Colorectal Cancer Study

Darmstadt, Germany, January 10, 2007 – Merck KGaA announced today that a Phase III study of Erbitux® (cetuximab) plus irinotecan-based therapy met the primary endpoint of increasing median duration of progression-free survival in patients with previously untreated metastatic colorectal cancer (mCRC). This randomized Phase III international trial, known as CRYSTAL*, studied patients treated with Erbitux plus FOLFIRI (irinotecan-based chemotherapy) compared with FOLFIRI alone.

"We are delighted with these results. The data from this controlled clinical trial of an EGFR-targeting monoclonal antibody demonstrate an improvement in progression-free survival in the first-line treatment setting," said Dr Wolfgang Wein, Senior Vice President, Global Oncology Commercialization at Merck KGaA. "They demonstrate the benefit of adding Erbitux to chemotherapy in initial, first-line treatment."

In the CRYSTAL study, more than 1000 patients[1] from around the world were recruited to detect a difference in progression-free survival for the Erbitux plus FOLFIRI arm compared with the FOLFIRI arm alone. Results have been submitted for presentation at the 2007 American Society of Clinical Oncology Annual Meeting in Chicago in June..

CRC is a major health concern, with more than 370,000 people developing colorectal cancer in Europe per year, accounting for 13 percent of the total cancer burden and around 200,000 deaths.[2] Approximately 25 percent of patients present with metastatic disease.[3] Five-year survival rates for patients with mCRC are as low as 5 percent.[4]

* **C**etuximab combined with i**R**inotecan in first line therap**Y** for meta**ST**atic colorect**AL** cancer

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Notes for editors

About the study
CRYSTAL is a randomized Phase III study comparing Erbitux plus FOLFIRI to FOLFIRI alone in epidermal growth factor receptor-expressing mCRC patients who have not previously been treated. Patients were randomized to one of two arms:

- Arm 1. Patients received an initial dose of Erbitux (400mg/m^2) followed by a weekly dose of Erbitux (250mg/m^2), and FOLFIRI.
- Arm 2. Patients received FOLFIRI alone.

The primary endpoint was progression-free survival. The secondary endpoints are overall survival, response rate, disease control rate, quality of life and safety. The study is carried out in centers across Europe, Australia, Asia, South Africa and Latin America.

About ERBITUX
ERBITUX® is a first-in-class and highly active 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. The most commonly reported side effect with Erbitux is an acne-like skin rash that seems to be correlated with a good response to therapy. In approximately five percent of patients, hypersensitivity reactions may occur during treatment with Erbitux; about half of these reactions are severe.

Erbitux has already obtained market authorization in 59 countries. It has been approved for the treatment of colorectal cancer in 58 countries so far: Argentina, Australia, Bulgaria, Canada, Chile, China, Colombia, Croatia, Ecuador, El Salvador, the European Union, Guatemala, Hong Kong, Iceland, India, Israel, Lebanon, Malaysia, Mexico, Montenegro, New Zealand, Nicaragua, Norway, Panama, Peru, the Philippines, Romania, Serbia, Singapore, South Korea, Switzerland, Taiwan, the US and Venezuela for use in combination with irinotecan in patients with EGFR-expressing mCRC who have failed prior irinotecan therapy. Erbitux is also approved for single-agent use in: Argentina, Australia, Canada, Chile, Colombia, Ecuador, El Salvador, Guatemala, Hong Kong, Lebanon, Mexico, New Zealand, Nicaragua, Panama, Peru, the Philippines, Singapore, the US and Venezuela.

In addition, Erbitux in combination with radiotherapy has been approved for the treatment of locally advanced squamous cell carcinoma of the head and neck (SCCHN) in 44 countries: Argentina, Brazil, Bulgaria, Chile, Colombia, the European Union, Hong Kong, Iceland, India, Israel, Malaysia, Mexico, Montenegro, Norway, the Philippines, Romania, Serbia, Switzerland, Taiwan and the US. In Argentina, Chile, Israel, Mexico, the Philippines and the US, and Erbitux is also approved as monotherapy in patients with recurrent and/or metastatic SCCHN who failed prior chemotherapy.

About Merck KGaA
Merck KGaA, Darmstadt, Germany, licensed the right to market Erbitux outside the US and Canada from ImClone Systems Incorporated of New York in 1998. In Japan, Merck KGaA has co-exclusive marketing rights with ImClone Systems.

Merck KGaA has an ongoing commitment to the advancement of oncology treatment and is currently investigating novel therapies in highly targeted areas, such as the use of Erbitux in colorectal cancer, squamous cell carcinoma of the head and neck and non-small cell lung cancer. Merck KGaA has also acquired the rights for the cancer treatment UFT® (tegafur-uracil) – an oral chemotherapy administered with folinic acid (FA) for the first-line treatment of metastatic colorectal cancer.

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Merck KGaA is also investigating among other cancer treatments the use of Stimuvax® (formerly referred to as BLP25 Liposome Vaccine) in the treatment of non-small cell lung cancer. The vaccine was granted fast-track status in September 2004 by the FDA. Merck obtained the exclusive worldwide licensing rights from Biomira Inc. of Edmonton, Alberta, Canada, with the exception of Canada where the companies share rights.

References:

1. Lang I et al. ASCO 2006, abstract No. 3555
2. Ferlay J et al. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide IARC Cancer Base No. 5. version 2.0, IARC Press, Lyon, 2004.
3. Cunningham D et al. *Eur J Cancer* 1993; 29A: 2007–2079.
4. MacDonald JS. *CA Cancer J Clin* 1999; 49 (4): 202–219.

Merck is a global pharmaceutical and chemical company with sales of EUR 5.9 billion in 2005, a history that began in 1668, and a future shaped by about 35,000 employees (including Merck Serono) in 56 countries. Its success is characterized by innovations from entrepreneurial employees. Merck's operating activities come under the umbrella of Merck KGaA, in which the Merck family holds a 73% interest and free shareholders own the remaining 27%. In 1917 the U.S. subsidiary Merck & Co. was expropriated and has been an independent company ever since.