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PETACC-8 Study Investigating Erbitux as Adjuvant Treatment in Colon Cancer Completes Recruitment

- **Major pan-European trial investigates potential role of Erbitux in the adjuvant setting for stage III colon cancer patients with KRAS wild-type tumors**
- **The Erbitux cell-targeting mechanism of action is highly active in shrinking tumors, providing hope for study success**

Geneva, Switzerland, November 6, 2009 – Merck Serono, a division of Merck KGaA, Darmstadt, Germany, today announced that recruitment has been completed for the Phase III clinical trial PETACC-8,^a investigating the efficacy of Erbitux[®] (cetuximab) for the treatment of stage III colon cancer in the adjuvant setting. PETACC-8 is a randomized, controlled, multinational trial sponsored and coordinated by the Fédération Francophone de Cancérologie Digestive (FFCD), Paris. The study has successfully recruited the required 2,566 patients throughout Europe since commencing enrollment in 2005.

The PETACC-8 trial is investigating the efficacy of Erbitux plus standard chemotherapy after surgery of the primary tumor (the 'adjuvant' setting) compared with FOLFOX-4 alone, over 6 months in patients with stage III colon cancer whose tumors were KRAS wild-type and have been fully resected (surgically removed). The primary endpoint of PETACC-8 is disease-free survival (DFS).¹

"In almost one-third of stage III colon cancer patients whose tumors have been completely removed by surgery, the cancer will unfortunately recur. Finding new ways to prevent this recurrence is therefore a priority," said Dr. Julien Taïeb from the Groupe

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Hospitalier Pitié-Salpêtrière, Paris, and the PETACC-8 Principal Investigator. “We are hopeful this study will meet its primary endpoint, especially given the consistent efficacy demonstrated by Erbitux in patients with metastatic colorectal cancer whose tumors are KRAS wild-type.”

In the adjuvant setting, the overall goal of treatment is to destroy any cancer cells that may remain after the tumor has been surgically removed. It is hypothesized that because Erbitux directly targets cancer cells via the epidermal growth factor receptor (EGFR), it will be highly active in this setting.

“We expect PETACC-8 to add to the number of exciting developments we have seen recently with Erbitux in metastatic colorectal cancer,” commented Dr. Oliver Kisker, Senior Vice-President, Global Clinical Development Unit Oncology, Merck Serono. “The introduction of standard KRAS status testing at diagnosis in metastatic colorectal cancer brought Erbitux to the forefront of personalized cancer care and led to a significant increase in treatment efficacy for those patients with KRAS wild-type tumors. The success of the personalized approach in the metastatic setting warrants hope for a cure in the adjuvant setting for this disease.”

Colorectal cancer is the third most common malignancy worldwide in terms of new cases.² In Europe alone, more than 413,000 people develop colorectal cancer every year, accounting for 13% of the total cancer burden and around 200,000 deaths.³ In around a quarter of patients diagnosed with colorectal cancer each year the tumor has already spread through the bowel wall and to regional lymph nodes.⁴ Although surgery followed by chemotherapy has significantly improved survival, approximately one-quarter of patients are likely to experience disease recurrence within 3 years.⁵ Therefore, it is essential that new therapies are investigated to decrease the level of recurrence and increase survival rates.

^a **PETACC-8: Pan-European Trial in Alimentary traCt Cancer #8**

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About FFCD

FFCD is a non profit organisation, based in France, involved in the conception, the set up, the analyses and the publication of large clinical trials in digestive oncology.

For more information, please visit www.ffcd.fr

References

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- ² Parkin DM, et al. Int J Cancer 2001;94(2):153-6.
- ³ Ferlay J, et al. Ann Oncol 2007;18:581-92.
- ⁴ NHS Center for Reviews and Dissemination, University of York, UK. Effective Health Care 1997;3(6). ISSN: 0965-0288.
- ⁵ Andre T, et al. N Engl J Med 2004;350:2343-51.

For more information on Erbitux in colorectal, head & neck and non-small cell lung cancer, please visit: www.globalcancernews.com.

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 5% of patients, hypersensitivity reactions may occur during treatment with Erbitux; about half of these reactions are severe.

Erbitux has already obtained market authorization in 77 countries. It has been approved for the treatment of colorectal cancer in 77 countries and for the treatment of squamous cell carcinoma of the head and neck (SCCHN) in 72 countries:

- December 2003 (Switzerland), February 2004 (USA), June 2004 (EU) and followed by other countries: for use in combination with irinotecan in patients with EGFR-expressing mCRC (metastatic colorectal cancer) who have failed prior irinotecan therapy. In addition, Erbitux is also approved for single-agent use in further countries.
- April 2006 (EU) and followed by other countries: for use in combination with radiotherapy for the treatment of locally advanced squamous cell carcinoma of the head and neck (SCCHN). In further countries, Erbitux is also approved as monotherapy in patients with recurrent and/or metastatic SCCHN who failed prior chemotherapy.
- July 2008 (EU): license was updated for the treatment of patients with epidermal growth factor receptor (EGFR) expressing, KRAS wild-type mCRC in combination with chemotherapy and as a single agent in patients who have failed oxaliplatin-and irinotecan-based therapy and who are intolerant to irinotecan.

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- July 2008 (Japan): for use in combination with irinotecan in patients with EGFR-expressing mCRC who have failed prior irinotecan therapy
- In November 2008 (EU): license was updated for the use in combination with platinum-based chemotherapy in patients with recurrent and/or metastatic SCCHN

Merck Serono licensed the right to market Erbitux outside the US and Canada from ImClone Systems, a wholly-owned subsidiary of Eli Lilly and Company, in 1998. In Japan, ImClone Systems, Bristol-Myers Squibb Company and Merck Serono jointly develop and commercialize Erbitux. Merck Serono 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 Serono 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.

Merck Serono 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 Serono obtained the exclusive worldwide licensing rights from Oncothyreon Inc., Seattle, Washington, USA.

In addition, Merck Serono is developing cilengtide, which is the first in a new class of investigational anti-cancer therapies called integrin inhibitors to reach Phase III of development; it is currently being investigated for the treatment of glioblastoma, SCCHN and NSCLC. Integrin inhibitors are thought to work by targeting the tumor and its vasculature.

About Merck Serono

Merck Serono is the division for innovative prescription pharmaceuticals of Merck KGaA, Darmstadt, Germany, a global pharmaceutical and chemical company. Headquartered in Geneva, Switzerland, Merck Serono discovers, develops, manufactures and markets innovative small molecules and biopharmaceuticals to help patients with unmet medical needs. In the United States and Canada, EMD Serono operates through separately incorporated affiliates.

Merck Serono has leading brands serving patients with cancer (Erbitux[®], cetuximab), multiple sclerosis (Rebif[®], interferon beta-1a), infertility (Gonal-f[®], follitropin alpha), endocrine and metabolic disorders (Saizen[®] and Serostim[®], somatropin), (Kuvan[®], sapropterin dihydrochloride) as well as cardiometabolic diseases (Glucophage[®], metformin), (Concor[®], bisoprolol), (Euthyrox[®], levothyroxine). Not all products are available in all markets.

With an annual R&D expenditure of around € 1bn, Merck Serono is committed to growing its business in specialist-focused therapeutic areas including neurodegenerative diseases, oncology, fertility and endocrinology, as well as new areas potentially arising out of research and development in autoimmune and inflammatory diseases.

About Merck

Merck is a global pharmaceutical and chemical company with total revenues of € 7.6 billion in 2008, a history that began in 1668, and a future shaped by approximately 33,000 employees in 60 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 an approximately 70% interest and free shareholders own the remaining approximately 30%. In 1917 the U.S. subsidiary Merck & Co. was appropriated and has been an independent company ever since.

For more information, please visit www.merckserono.com or www.merck.de