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Merck Serono Considers Appealing CHMP Opinion on Erbitux Treatment for Non-Small Cell Lung Cancer

- **Merck Serono is evaluating potential appeal options requesting that the CHMP re-examine data demonstrating clinical relevant benefit to patients**
- **Erbitux is the first and only new targeted compound in clinical development in more than 10 years that increases overall survival in a NSCLC patient population including all histologies**

Geneva, Switzerland, July 23, 2009 – The Committee for Medicinal Products for Human Use (CHMP), the scientific committee of the European Medicines Agency (EMA), has adopted a negative opinion for the use of Erbitux[®] (cetuximab) in combination with platinum-based chemotherapy for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, advanced or metastatic non-small cell lung cancer (NSCLC). Merck Serono, a division of KGaA (Darmstadt, Germany), is evaluating potential appeal options requesting that the CHMP re-examine data demonstrating clinical relevant benefits to patients.

Merck Serono respects the decision and will work closely with the CHMP to find ways to make Erbitux available to lung cancer patients. The company is convinced Erbitux will play a major role in NSCLC as it is the first and only compound in clinical development in more than 10 years to increase overall survival in a patient population including all histologies.¹

Erbitux has generated great interest in the oncology community based on the Phase III study FLEX, which showed a significant survival advantage:

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- The data from the FLEX study were highlighted as one of the three most important results presented during the 2008 annual meeting of the American Society of Clinical Oncology (ASCO) – the worldwide leading cancer congress.²
- The *Journal of Clinical Oncology* named Erbitux as one of the major research advances in this difficult-to-treat cancer.³
- In addition, Erbitux is already recommended for the first-line therapy of NSCLC by US Clinical Practice Guidelines issued by the independent National Comprehensive Cancer Network (NCCN).⁴
- A recent publication in one of the leading medical journals in Europe (*The Lancet*) concludes that Erbitux “added to platinum-based chemotherapy can be regarded as a new standard first-line treatment option for patients with EGFR-expressing advanced non-small cell lung cancer”.¹

^a FLEX: First-Line Erbitux in lung cancer

About FLEX

In the randomized, multinational Phase III FLEX^a study, the overall survival was significantly prolonged for patients receiving Erbitux in first-line therapy. The FLEX study included a patient population (1,125 patients) comprising all histological NSCLC subtypes, who received either standard platinum-based chemotherapy plus Erbitux or chemotherapy alone. Adding Erbitux to chemotherapy significantly prolonged median overall survival regardless of histology compared to chemotherapy alone (11.3 vs. 10.1 months, respectively; $p=0.04$). Across the study population, the addition of Erbitux to platinum-based chemotherapy was tolerated with manageable side effects.¹

For such a broad patient population, Erbitux is the first and only new targeted compound in clinical development in more than 10 years to increase overall survival.

About lung cancer

In Europe, lung cancer is the leading cause of death from cancer – 20% of all cancer deaths (28% in men and 10% in women).⁵ NSCLC accounts for approximately 80% of all lung cancer cases.⁶ At diagnosis, most patients with NSCLC present with advanced, inoperable (unresectable) disease, which is associated with a very poor prognosis.⁷ The overall 5-year survival rate for lung cancer is about 10%, compared to 81% for melanoma and 75% for breast cancer.⁸

Merck Serono submitted an application to the EMEA to license Erbitux for first-line treatment of NSCLC in September 2008. Erbitux is currently a first-line treatment for both metastatic colorectal cancer (mCRC) in patients with KRAS wild-type tumors and squamous cell carcinoma of the head and neck (SCCHN).

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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 76 countries. It has been approved for the treatment of colorectal cancer in 76 countries and for the treatment of squamous cell carcinoma of the head and neck (SCCHN) in 71 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.
- 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

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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 Impetreve[™] (cilengitide), 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 32,700 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 expropriated and has been an independent company ever since.

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