

## News Release

August 1/2, 2009

### **Merck Serono Presented New Data On the Combination of Erbitux with Standard First-Line Therapy in Patients with NSCLC**

- **Results reported from a meta-analysis including 2,018 NSCLC patients show a benefit across all efficacy endpoints for adding Erbitux to standard first-line therapy<sup>1</sup>**
- **Erbitux is the first and only targeted compound in clinical development in more than 10 years to increase overall survival in a NSCLC patient population including all histologies<sup>2</sup>**

San Francisco, CA, USA / Geneva, Switzerland, August 1/2, 2009 – Merck Serono, a division of Merck KGaA (Darmstadt, Germany), announced today that new data from a meta-analysis of trials evaluating the addition of Erbitux<sup>®</sup> (cetuximab) to standard first-line chemotherapy in patients with non-small cell lung cancer (NSCLC) was presented today at the International Association for the Study of Lung Cancer's 13<sup>th</sup> World Conference on Lung Cancer (WCLC) in San Francisco.

The meta-analysis included four randomized Phase II/III clinical trials with a total of 2,018 patients across all histologies.<sup>1,2,3,4,5</sup> The analysis showed the benefit of Erbitux when added to standard first-line platinum-based chemotherapy for overall survival progression free survival and overall response rate (overall survival p=0.010; progression-free survival p=0.036, overall response rate p<0.001) compared to chemotherapy alone.<sup>1</sup>

"The meta-analysis showed the benefit for Erbitux for all investigated endpoints across a broad patient population in the first-line NSCLC setting," said Professor Nick Thatcher, Christie Hospital NHS Trust, Manchester, UK. "The survival benefit, seen

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irrespective of which standard chemotherapy regimen was used, shows Erbitux may have an important role in the treatment of NSCLC.”

“This meta-analysis shows significant results across all efficacy endpoints, including response rate, progression-free survival and overall survival, in trials that include all histological types of NSCLC for Erbitux in combination with standard platinum doublets adding further evidence to the already published results of the FLEX<sup>a</sup> study,” said Dr. Wolfgang Wein, Executive Vice President Oncology of the division Merck Serono.

In Europe, lung cancer is the leading cause of death from cancer, accounting for 20% of all cancer deaths (28% in men and 10% in women).<sup>6</sup> NSCLC accounts for approximately 80% of all lung cancer cases.<sup>7</sup> At diagnosis, most patients with NSCLC present with advanced, non-operable (also called unresectable) disease, which is associated with a very poor prognosis.<sup>8</sup> The overall 5-year survival rate for lung cancer is about 10%, compared to 81% for melanoma and 75% for breast cancer.<sup>9</sup>

Erbitux is already established as a standard in the treatment of metastatic colorectal cancer and squamous cell carcinoma of the head and neck.

Merck Serono has submitted an application to the European Medicines Agency (EMA) to license Erbitux for first-line treatment of NSCLC. Following the negative decision of the CHMP Merck Serono has requested re-examination of this opinion.

<sup>a)</sup> **FLEX: First-Line ErbituX** in lung cancer

### References

- 1) Thatcher N, et al. WCLC 2009. Abstract No. A3.7.
- 2) Pirker R, et al. Lancet 2009;373:1525-31.
- 3) Butts C, et al. J Clin Oncol 2007;25:5777-84.
- 4) Rosell R, et al. Ann Oncol 2008;19:362-9.
- 5) Lynch T. et al. J Thorac Oncol 2007;2 (Suppl. 4):S340-41.
- 6) European Lung Foundation. [www.european-lung-foundation.org/index.php?id=65](http://www.european-lung-foundation.org/index.php?id=65).
- 7) D’Addario G & Felip E. Ann Oncol 2008;19(Suppl 2):ii39-40.
- 8) Bunn PA & Thatcher N. Oncologist 2008;13(Suppl 1):1-4.
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For more information on Erbitux in colorectal, head & neck and non-small cell lung cancer, please visit: [www.globalcancernews.com](http://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
- 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 USA 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<sup>®</sup> (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<sup>®</sup> (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 Oncocyte Inc., Seattle, Washington, USA.

In addition, Merck Serono is developing 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.

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### **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 expropriated and has been an independent company ever since.

For more information, please visit [www.merckserono.com](http://www.merckserono.com) or [www.merck.de](http://www.merck.de)