

## News Release

December 1, 2008

### **Merck Serono: European Commission Approves Erbitux for First-Line Use in Head and Neck Cancer**

- **Erbitux approved for first-line use in combination with platinum-based chemotherapy in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck in Europe**
- **Approval based on the results of the EXTREME study, which showed first significant overall survival benefit in this setting in 30 years**

Geneva, Switzerland, December 1, 2008 – Merck Serono, a division of Merck KGaA, Darmstadt, Germany, announced today that it has received approval from the European Commission to extend the use of its targeted therapy Erbitux<sup>®</sup> (cetuximab) to include first-line treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN). Erbitux was previously approved for use in combination with radiotherapy for locally advanced disease.

The approval is based primarily upon the results of the EXTREME<sup>a</sup> study, published in the *New England Journal of Medicine* in September 2008. The EXTREME study established that adding Erbitux to platinum-based chemotherapy significantly prolonged median overall and progression-free survival, and also significantly increased response rate.<sup>1</sup>

Patients treated with Erbitux plus chemotherapy experienced the following improvements compared to chemotherapy alone:<sup>1</sup>

- Median overall survival increase of nearly three months (10.1 vs. 7.4 months;  $p=0.04$ ), equating to a 20% reduction in the risk of death (HR: 0.80) during the study period

## News Release

- 70% increase in median progression-free survival (5.6 vs. 3.3 months;  $p < 0.001$ )
- 80% relative increase in response rate (36% vs. 20%;  $p < 0.001$ )

“To receive approval for Erbitux in the first-line treatment of recurrent and/or metastatic SCCHN is fantastic news. We hope that patients and specialists are equally encouraged by this first significant advance in this treatment setting in 30 years,” said Wolfgang Wein, Executive Vice President, Oncology, Merck Serono. “This latest approval recognizes the impressive potential of Erbitux to extend patients' lives and further confirms the high activity of Erbitux against difficult to treat cancers.”

In Europe alone, it is estimated that there are around 143,000 cases of head and neck cancer, and more than 68,000 deaths due to the disease, each year.<sup>2</sup> About 40% of patients with head and neck cancer have recurrent and/or metastatic SCCHN.<sup>3</sup> Head and neck cancer is the sixth-most common cancer worldwide<sup>4</sup> and includes cancers of the tongue, mouth, salivary glands, pharynx, larynx, sinuses, and other sites located in the head and neck area. Erbitux targets the epidermal growth factor receptor (EGFR). About 90% of head and neck cancers are of the squamous cell variety<sup>5</sup> and nearly all express the EGFR, which is critical for tumor growth.<sup>6</sup>

<sup>a</sup> EXTREME: **ErbituX** in 1<sup>st</sup>-line Treatment of **RE**current or **ME**tastatic head and neck cancer

### References

1. Vermorken JB, et al. N Engl J Med 2008;359:1116-27.
2. GLOBOCAN 2002 ([www-dep.iarc.fr](http://www-dep.iarc.fr)), accessed November 2008.
3. Lefebvre J-L. Ann Oncol 2005;16(Suppl 6):vi7-vi12.
4. Hunter KD, et al. Nat Rev Cancer 2005;5(2):127-35.
5. Vermorken J. Ann Oncol 2005;16(Suppl 2):ii258-ii264.
6. Grandis JR & Tweardy DJ. Cancer Res 1993;53(15):3579-84.

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

## News Release

### About Erbitux

Erbitux<sup>®</sup> 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 75 countries so far: Argentina, Australia, Belarus, Canada, Chile, China, Colombia, Costa Rica, Croatia, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Hong Kong, Iceland, India, Indonesia, Israel, Japan, Kazakhstan, Kuwait, Lebanon, Liechtenstein, Malaysia, Mexico, Moldova, New Zealand, Nicaragua, Norway, Oman, Pakistan, Panama, Peru, the Philippines, Qatar, Russia, Serbia, Singapore, South Africa, South Korea, Switzerland, Taiwan, Thailand, Ukraine, Uruguay, the US, and Venezuela for use in combination with irinotecan in patients with EGFR-expressing mCRC who have failed prior irinotecan therapy. In the European Union, the license was updated in July 2008 for the treatment of patients with epidermal growth factor receptor (EGFR) expressing, KRAS wild-type mCRC (metastatic colorectal cancer) 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. Apart from the European Union label, Erbitux is also approved for single-agent use in: Argentina, Australia, Canada, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Hong Kong, Iceland, Japan, Lebanon, Liechtenstein, Mexico, Moldova, New Zealand, Nicaragua, Norway, Panama, Peru, the Philippines, Russia, Singapore, Thailand, 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 70 countries: Argentina, Australia, Belarus, Brazil, Canada, Chile, Colombia, Costa Rica, Croatia, El Salvador, the European Union, Guatemala, Hong Kong, Iceland, India, Indonesia, Israel, Kazakhstan, Kuwait, Lebanon, Liechtenstein, Malaysia, Mexico, Moldova, New Zealand, Nicaragua, Norway, Oman, Pakistan, Panama, Peru, the Philippines, Qatar, Russia, Serbia, Singapore, South Africa, South Korea, Switzerland, Taiwan, Ukraine, Uruguay, the US, and Venezuela. In Argentina, Chile, Costa Rica, El Salvador, Guatemala, Hong Kong, Israel, Lebanon, Mexico, Moldova, Nicaragua, Peru, the Philippines, Russia, and the US, Erbitux is also approved as monotherapy in patients with recurrent and/or metastatic SCCHN who failed prior chemotherapy. In the European Union, the license was updated in November 2008 for the first-line use in combination with platinum-based chemotherapy in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck.

Merck licensed the right to market Erbitux outside the US and Canada from ImClone Systems Incorporated of New York in 1998. In Japan, ImClone Systems Incorporated, Bristol-Myers Squibb Company and Merck jointly develop and commercialize Erbitux. Merck 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 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 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 obtained the exclusive worldwide licensing rights from Oncothyreon Inc., Bellevue, Washington, USA.

## News Release

### About Merck Serono

Merck Serono is the division for innovative prescription pharmaceuticals of Merck, a global pharmaceutical and chemical group. Headquartered in Geneva, Switzerland, Merck Serono discovers, develops, manufactures and markets innovative small molecules and biopharmaceuticals to help patients with unmet medical needs. Its North American business operates in the United States and Canada as EMD Serono.

Merck Serono has leading brands serving patients with cancer (Erbitux®), multiple sclerosis (Rebif®), infertility (Gonal-f®), endocrine and cardiometabolic disorders (Glucophage®, Concor®, Euthyrox®, Saizen®, Serostim®), as well as psoriasis (Raptiva®).

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 € 7.1 billion in 2007, a history that began in 1668, and a future shaped by 32,458 employees in 59 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.net](http://www.merckserono.net) or [www.merck.de](http://www.merck.de)