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November 16, 2009

Erbix recognized by ASCO as a 2009 Major Cancer Advance as First SCCHN Treatment to Improve Survival in 30 Years

- **Erbix acknowledged by ASCO for the second year as a major advance in cancer treatment**
- **Coincides with *Lancet Oncology* publication of long-term survival data for Erbix in locally advanced SCCHN demonstrating half of patients were alive at 5 years**

Geneva, Switzerland, November 16, 2009 – The American Society of Clinical Oncology (ASCO) has once again recognized Erbix[®] (cetuximab) as one of the major clinical cancer advances of 2009. This year Erbix was selected by ASCO for providing the first significant increase in survival for 30 years in the treatment of patients with 1st-line recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN).¹

ASCO Clinical Advances Report¹

The ASCO report, 'Clinical Cancer Advances 2009: Major Research Advances in Cancer Treatment, Prevention and Screening', published this week in the *Journal of Clinical Oncology*, is an independent assessment of the most significant clinical cancer research studies of the past year.

Erbix was singled out for the pivotal 1st-line SCCHN study, EXTREME^a, the first randomized trial in 30 years to identify a regimen that increases survival for patients with recurrent and/or metastatic SCCHN. The report commented that, "The ability to improve overall survival with chemotherapy has proven elusive over the last 30 years in several randomized trials comparing different chemotherapy regimens in this setting.

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Thus, the results of this [EXTREME] trial are particularly noteworthy and are changing clinical practice.”

This is the second consecutive year that Erbitux has featured in the ASCO ‘Advances’ list.³ In 2008 it was recognized for extending survival in the 1st-line treatment of NSCLC and for the role of KRAS tumor status in predicting whether patients with newly diagnosed metastatic colorectal cancer will respond to Erbitux.²

“Merck Serono is honored that Erbitux is recognized by ASCO two years in a row, and across three different disease areas – colorectal cancer, lung cancer and now head and neck cancer, as a major clinical advance,” commented Dr. Wolfgang Wein, Executive Vice President, Oncology, Merck Serono, a division of Merck KGaA, Darmstadt, Germany. “This latest acknowledgement from ASCO is a tribute to the role Erbitux now plays as a gold standard therapy in 1st-line recurrent and/or metastatic SCCHN”.

The EXTREME study demonstrated that SCCHN patients treated with Erbitux plus chemotherapy experienced the following improvements, compared to chemotherapy alone:³

- Median overall survival (OS) increased by nearly 3 months (10.1 vs. 7.4 months; $p=0.04$), equating to a 20% reduction in the risk of death (Hazard Ratio [HR] 0.80) during the study period
- 46% increase in median progression-free survival (5.6 vs. 3.3 months; $p<0.001$)
- Almost doubling of response rate (36% vs. 20%; $p<0.001$)
- Based on the EXTREME study, the ESMO Guidelines Working Group earlier this year recommended Erbitux as the only treatment with a grade of recommendation ‘A’ and level of evidence ‘I’⁴

Long-Term Survival Results in Locally Advanced SCCHN

Also this week, the 5-year survival data from the Bonner trial for Erbitux in locally advanced (LA) SCCHN were published in the *Lancet Oncology*. The Phase III Bonner trial formed the basis for the initial Erbitux LA SCCHN license, granted in Europe in

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2006. This new long-term analysis provides further support for the combination of Erbitux and radiotherapy in the treatment of LA SCCHN, demonstrating:⁵

- Almost half of patients receiving Erbitux plus radiotherapy are still alive at 5 years – in contrast to only one third of patients receiving radiotherapy alone (45.6% vs. 36.4%; p=0.018)
- Adding Erbitux to radiotherapy leads to a sustained survival benefit (OS 49.0 vs. 29.3 months; HR 0.725; p=0.018)
- The development of prominent skin rash is associated with an additional survival benefit leading to a reduction in the risk of death of 51%

Head and Neck Cancer

Head and neck cancer includes cancers of the tongue, mouth, salivary glands, pharynx, larynx, sinuses and other sites located in the head and neck area. It is estimated that there are around 143,000 new cases of head and neck cancer and more than 68,000 deaths due to the disease in Europe each year.⁶ About 90% of head and neck cancers are of the squamous cell variety⁷ and nearly all express the epidermal growth factor receptor which is critical for tumor growth.⁸ About 40% of patients with head and neck cancer have recurrent and/or metastatic SCCHN.⁹ At least 75% of all head and neck cancers are attributed to two major risk factors, smoking and alcohol consumption.¹⁰

^aEXTREME: ErbituX in 1st-line Treatment of REcurrent or MEtastatic head and neck cancer

References

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

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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.
- 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 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 or www.merck.de