ECCO/ESMO Abstract Numbers: 6LBA, 6077, 6079

News Release

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Initial COIN Study Results Presented at European Oncology Congress

- **Results inconsistent with data from all Erbitux pivotal studies**
- **Further analyses planned by the Medical Research Council that conducted the independent COIN study**

Berlin, Germany and Geneva, Switzerland, September 23, 2009 – The Medical Research Council (MRC), a UK-based, publicly-funded organization dedicated to improving human health, today presented the initial results of the independent Phase III COIN[a] study, which did not meet its primary endpoint of overall survival (OS).[1] These findings were presented today at the joint 15th Congress of the European Cancer Organisation (ECCO) and 34th Congress of the European Society for Medical Oncology (ESMO) in Berlin, Germany.

The COIN study was designed to evaluate whether the addition of Erbitux® (cetuximab) to one of two oxaliplatin-based chemotherapy regimens significantly improved outcomes in previously untreated metastatic colorectal cancer (mCRC) patients with KRAS wild-type tumors. The median OS was not statistically significant at 17.0 months in the Erbitux treatment arm compared to 17.9 months for the chemotherapy-alone group (hazard ratio [HR] 1.038; p=0.68).[1]

“Imbalances in the chemotherapy administered between the different study arms were reported previously in the interim safety analysis,” explained Dr. Wolfgang Wein, Executive Vice President, Oncology, Merck Serono. “Further analysis of the dose intensity and 2nd-line treatment, and other factors, such as the advanced disease of patients in the study, are ongoing to determine why the COIN results are not aligned

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News Release

with existing evidence from the other randomized, 1st-line studies, including the significant increase in overall survival achieved with the CRYSTAL study."

Results from the pivotal Phase III CRYSTAL[b] trial also presented earlier today demonstrated that the addition of Erbitux to the standard 1st-line FOLFIRI chemotherapy regimen significantly improved OS in patients with KRAS wild-type tumors (23.5 vs. 20.0 months, HR 0.796, p=0.0094).[2] In addition, results from the Phase II OPUS[c] study, which investigated the benefit of adding Erbitux to the FOLFOX regimen in KRAS wild-type patients, demonstrated:

- Significant improvement in progression-free survival (8.3 vs. 7.2 months, HR 0.567, p=0.0064)
- Significant improvement of response rate (57,3% vs. 34,0%, p=0.0027)
- OS was 22.8 vs. 18.5 months (HR 0.855, p=0.3854).[3]

[a] **COIN:** A Phase III trial comparing either **CO**ntinuous chemotherapy plus cetuximab or **IN**termittent chemotherapy with standard continuous palliative combination chemotherapy with oxaliplatin and a fluoropyrimidine in first line treatment of metastatic colorectal cancer

[b] **CRYSTAL:** **C**etuximab combined with i**R**inotecan in first line therap**Y** for meta**ST**atic colorect**AL** cancer

[c] **OPUS:** **O**xali**P**latin and cet**U**ximab in fir**S**t-line treatment of mCRC

References

1. Maughan TS, et al. ECCO/ESMO Congress 2009. Abstract No: 6LBA. Updated information presented at meeting.
2. Van Cutsem E, et al. ECCO/ESMO Congress 2009. Abstract No: 6077. Updated information presented at meeting.
3. Bokemeyer C, et al. ECCO/ESMO Congress 2009. Abstract No: 6079. Updated information presented at meeting.

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

News Release

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 Oncothyreon 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.

News Release

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 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