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Cilengitide Study Provides Long-Term Follow-up Data in Glioblastoma Patients Receiving Investigational Drug for More Than 4 Years

- **No treatment-related severe adverse events were observed during long-term treatment in a randomized Phase II study**

Chicago/Rockland, Massachusetts, June 5 2010 – EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany, announced today that long-term follow-up data of a randomized Phase II study of two cilengitide doses in recurrent glioblastoma were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. The data showed that treatment of 15 patients with the investigational integrin-inhibitor for more than six months and for up to 4.5 years did not result in any treatment-related severe adverse events (Grade 3/4). In addition, 37% of patients who received the higher dose of cilengitide (2,000 mg) were still alive after one year and 22% after two years.¹ The current prognosis of patients with recurrent glioblastoma is poor with median overall survival (OS) between 4-7 months and one year survival rates of approximately 20%.^{2,3}

Treatment-related adverse events (AEs) usually occurred within the first six months of receiving cilengitide and the most common (>1 patient) was fatigue (n = 3). The most common non-treatment-related grade 3/4 serious AE was convulsion (n = 2).

“The prognosis for patients with recurrent glioblastoma is extremely poor and additional treatment options have been desperately needed for some time,” said Dr. Karen Fink, Baylor University Medical Center, Dallas. “We are excited about the results of this study, in that patients were able to receive cilengitide beyond six months with no treatment-related severe adverse events. Moreover, 10% of patients were still alive after four years.”

The randomized Phase II study also supports the Phase I study finding of activity with cilengitide monotherapy⁴ and indicates that cilengitide efficacy is dose-dependent with OS and long-term survival

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rates consistently higher for the 2,000 mg treatment group compared to the 500 mg group during more than four years of follow-up:

- The one-, two-, and four-year survival rates for patients treated with twice-weekly 2,000 mg cilengitide compared to twice-weekly 500 mg cilengitide were 37% vs. 22%, 22% vs. 12%, and 10% vs. 2%, respectively¹
- In the original Phase II study publication, cilengitide efficacy was dose-dependent with the median OS higher with twice-weekly 2,000 mg than with twice-weekly 500 mg.⁵ Median OS was 9.9 months vs. 6.5 months in the high- and low-dose cilengitide groups, respectively⁵

“These positive long-term data once again support our ongoing Phase III study program of cilengitide in patients with this devastating disease. We believe that cilengitide may play a valuable part in the future care of glioblastoma patients,” said Dr. Wolfgang Wein, Executive Vice President, Oncology, Merck KGaA. .

Developed in Merck KGaA’s own laboratories, cilengitide is the first in the new class of anti-cancer therapies called integrin inhibitors to reach Phase III of development.* A pivotal Phase III trial – CENTRIC^a – is underway in patients with newly diagnosed glioblastoma. The study design of CENTRIC will be presented at this year’s ASCO meeting.⁶ Also presented at the annual meeting will be CENTRIC’s Phase II companion trial investigating cilengitide in glioblastoma (CORE^b).⁷ Other randomized cilengitide trials are currently underway in non-small cell lung cancer (CERTO^c) and squamous cell carcinoma of the head and neck (ADVANTAGE^d).

The ongoing clinical development program for cilengitide is part of EMD Serono’s oncology portfolio that may provide novel treatment options, and therefore new hope, for patients with aggressive cancers, such as non-small cell lung cancer, head and neck cancer and glioblastoma. As such, EMD Serono continues to invest in research to uncover potentially innovative treatments to further change the landscape of cancer management.

About Cilengitide

Cilengitide, an investigational $\alpha\beta3$ and $\alpha\beta5$ integrin inhibitor, has been shown to have anti-angiogenic and direct anti-tumor effects in laboratory studies.⁸⁻⁹ Integrins have been demonstrated to play a role in cancer progression, specifically in tumor cell survival, tumor angiogenesis, and metastasis.⁸⁻⁹

* Cilengitide has not been approved for commercial distribution

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- ^a**CENTRIC:** Cilengitide in combination with Temozolomide and Radiotherapy In newly diagnosed glioblastoma Phase III randomized Clinical trial
- ^b**CORE:** Cilengitide in subjects with newly diagnosed glioblastoma multiforme and unmethylated MGMT gene promoter
- ^c**CERTO:** Cilengitide and cetuximab in combination with platinum-based chemotherapy as first-line treatment for subjects with advanced non-small cell lung cancer.
- ^d**ADVANTAGE:** Open-label, randomized, controlled Phase I/II study of cilengitide to evaluate the safety and efficacy of the combination of different regimens of cilengitide added to cisplatin, 5-FU, and cetuximab in subjects with recurrent/metastatic squamous cell cancer of the head and neck

For more information on studies with cilengitide log on to www.clinicaltrials.gov.

References:

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About cilengitide

Cilengitide is currently being developed by Merck KGaA. Cilengitide is the first in a new class of investigational anti-cancer therapies called integrin inhibitors in 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 blood supply.

Integrins are cell surface receptors that are improperly regulated in many cancer types. This lack of regulation enables them to enhance tumor growth, survival and invasiveness. Integrins are fundamental in the process of angiogenesis (blood vessel growth) – a process that is essential for tumors as it enables them to grow past a finite size.

In addition to the Merck KGaA -sponsored studies, the U.S. National Cancer Institute (NCI) is sponsoring a number of clinical trials under a Cooperative Research and Development Agreement (CRADA) with Merck KGaA for the development of cilengitide. In the United States and Canada, cilengitide is being developed by EMD Serono, an affiliate of Merck KGaA, Darmstadt, Germany.

About EMD Serono, Inc.

EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany, is a leader in the US biopharmaceutical arena, integrating cutting-edge science with unparalleled patient support systems to improve people's lives. The company has strong market positions in neurodegenerative diseases, with Rebif® (interferon beta-1a), as well as in endocrinology, with Saizen® (somatropin (rDNA origin) for injection) and Serostim® (somatropin (rDNA origin) for injection). EMD Serono is a leader in reproductive health, with Gonal-f® (follitropin alfa for injection), Luveris® (lutropin alfa for injection) and Ovidrel® Prefilled Syringe (choriogonadotropin alfa injection). In addition, EMD Serono is growing its expertise and presence in the area of oncology, with more than 10 projects currently in development. With a clear focus on the patient and a leadership presence in the biopharmaceutical industry, EMD Serono's US footprint continues to grow, with more than 1100 employees around the country and fully integrated commercial, clinical and research operations in the company's home state of Massachusetts. For more information, please visit www.emdserono.com

About Merck KGaA

Merck KGaA is a global pharmaceutical and chemical company with total revenues of € 7.7 billion in 2009, a history that began in 1668, and a future shaped by approximately 33,600 employees in 64 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