

## News Release

January 23, 2009

### **Merck Serono's Oral Investigational Treatment Cladribine Tablets for Multiple Sclerosis Significantly Reduced Relapse Rate in Two-Year Phase III Pivotal Trial**

- **Two-year primary efficacy endpoint of CLARITY trial met: 58% relative reduction in annualized relapse rate in the low total dose treatment group and 55% in the high total dose treatment group**
- **Submission for registration of cladribine tablets planned for mid-2009**
- **Cladribine tablets are the first oral investigational multiple sclerosis treatment to complete a two-year pivotal study**

Geneva, Switzerland, January 23, 2009 – Merck Serono, a division of Merck KGaA, Darmstadt, Germany, announced today that the CLARITY<sup>1</sup> Phase III pivotal trial of its proprietary oral formulation of cladribine (cladribine tablets) met the two-year primary endpoint of clinical relapse rate reduction in patients with relapsing-remitting multiple sclerosis (MS).

The two cladribine tablet treatment groups of the study, assessing different dose regimens, demonstrated a statistically significant reduction in the annualized rate of relapses compared to placebo. Patients from the lower total dose group experienced a 58% relative reduction in annualized relapse rates with respect to placebo (0.14 versus 0.33 for the placebo group;  $p < 0.001$ ). Patients from the higher total dose group experienced a 55% relative reduction in annualized relapse rates with respect to placebo (0.15 versus 0.33;  $p < 0.001$ ).

Overall, the frequencies of adverse events were low in the cladribine tablet treatment groups and were comparable to that observed in the placebo group. Lymphopenia, an

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expected event based on the presumed mechanism of action of cladribine, occurred more frequently in the cladribine tablet treatment groups. With the exception of lymphopenia, the most frequently reported adverse events in the three study groups were headaches and nasopharyngitis.

“We believe the CLARITY data mark an important milestone in the assessment of investigational oral treatments for multiple sclerosis and that cladribine tablets have the potential to make a real difference in the lives of patients,” said Elmar Schnee, President of Merck Serono. “Based on the successful completion of the CLARITY study, we plan to submit cladribine tablets for registration to the EMEA and to the FDA for mid-2009.”

Secondary endpoints of the CLARITY study were also met, including reduction of lesion activity as measured by magnetic resonance imaging (MRI), proportion of subjects relapse-free and disability progression. Full study results will be submitted for presentation at an upcoming scientific meeting.

The CLARITY study was a two-year (96 weeks), randomized, double-blind, placebo-controlled, international trial. It enrolled 1,326 patients with relapsing-remitting MS according to the revised McDonald criteria<sup>2</sup>. Study participants were randomized to one of three different treatment groups consisting of two different dose regimens of cladribine tablets or matching placebo tablets (1:1:1 ratio). Cladribine tablets were given in two or four treatment courses in the first year, with each course consisting of once daily administration for four to five consecutive days, which means study patients took cladribine tablets for only 8 to 20 days during the year. In the second year, two treatment courses were administered to all patient groups. The primary endpoint of the CLARITY study was the qualifying relapse rate at 96 weeks. Secondary endpoints included MRI endpoints<sup>3</sup>, proportion of subjects relapse-free and disability progression at 96 weeks. Out of the 1,326 randomized patients, 90% of patients treated with cladribine tablets completed the study (92% in the lower total dose group and 89% in the higher total dose group) compared to 87% in the placebo group.

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### <sup>1</sup> CLARITY: **CLAdRI**bine Tablets Treating MS Orally

<sup>2</sup> The McDonald criteria are diagnostic criteria for MS. In April 2001 an international panel in association with the National Multiple Sclerosis Society (NMSS) of America recommended revised diagnostic criteria for MS. They make use of advances in MRI imaging techniques and are intended to replace the Poser criteria. The new criteria facilitate the diagnosis of MS in patients who present with signs and symptoms suggestive of the disease. The McDonald criteria for the diagnosis of multiple sclerosis were revised in 2005 to simplify and speed diagnosis, while maintaining adequate sensitivity and specificity.

<sup>3</sup> The exact correlation between MRI findings and the current or future clinical status of patients, including disability progression, is unknown.

### About cladribine tablets

Merck Serono's proprietary oral formulation of cladribine (cladribine tablets) is currently being evaluated in Phase III as a treatment for patients with relapsing forms of multiple sclerosis (MS). Cladribine is a small molecule that may interfere with the behavior and the proliferation of certain white blood cells, particularly lymphocytes, which are thought to be involved in the pathological process of MS.

The clinical development program for cladribine tablets includes:

- The CLARITY (**CLAdRI**bine Tablets Treating MS Orally) extension study: a two-year placebo-controlled extension of the CLARITY study, designed to provide data on the long-term safety and efficacy of extended administration of cladribine tablets for up to four years

- The ORACLE MS (**ORAI CLAdRI**bine in **EARLY MS**) study: a two-year Phase III placebo-controlled trial designed to evaluate the efficacy and safety of cladribine tablets as a monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS). This trial was announced in September 2008.

- The ONWARD (**ORAI CLAdRI**bine Added **ON** To Rebif New Formulation in Patients **With Active Relapsing Disease**) study: a Phase II placebo-controlled trial designed primarily to evaluate the safety and tolerability of adding cladribine tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy. This trial was announced in January 2007.

Cladribine tablets have been granted a fast track designation by the US Food and Drug Administration based on the need for an oral therapy in a subset of patients with relapsing forms of multiple sclerosis.

### About Merck Serono and multiple sclerosis

Merck Serono is a leader in multiple sclerosis (MS) with Rebif<sup>®</sup> (interferon beta-1a), a disease-modifying drug used to treat relapsing forms of MS, which is registered in more than 80 countries worldwide. Full prescribing information for this product can be obtained by contacting the Company or visiting its website. Additional therapeutic options are currently under development at Merck Serono, including cladribine tablets, currently in Phase III and potentially the first oral therapy for MS, as well as several products in early stage development. Merck Serono also is taking a leading role in developing an understanding of the role of genetics in MS.

### About multiple sclerosis

Multiple sclerosis (MS) is a chronic, inflammatory condition of the nervous system and is the most common, non-traumatic, disabling neurological disease in young adults. The World Health Organization estimates that up to 2.5 million people suffer from MS worldwide. While symptoms can vary, the most common symptoms of MS include blurred vision, numbness or tingling in the limbs and problems with strength and coordination. The relapsing forms of MS are the most common.

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### 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 affiliates operate in the United States and Canada as EMD Serono.

Merck Serono has leading brands serving patients with cancer (Erbitux®, cetuximab), multiple sclerosis (Rebif®, interferon beta-1a), infertility (Gonal-f®, follitropin alfa), endocrine and cardiometabolic disorders (Glucophage®, metformin); (Concor®, bisoprolol); (Euthyrox®, levothyroxine); (Saizen® and Serostim®, somatropin). 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 € 7.1 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 appropriated 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)