

## News Release

September 11, 2009

### **New Data from CLARITY Study on Disease Activity in MS Patients Who Received Cladribine Tablets Presented at 25<sup>th</sup> ECTRIMS Congress**

- **Post-hoc analysis from CLARITY study show that short-course oral treatment with Cladribine Tablets significantly increased the proportion of patients who had absence of disease activity compared with placebo**

Düsseldorf, Germany, and Geneva, Switzerland, September 11, 2009 – Merck Serono, a division of Merck KGaA, Darmstadt, Germany, announced new data from a post-hoc analysis of the two-year (96-week) placebo-controlled CLARITY<sup>1</sup> Phase III trial using a short-course of Cladribine Tablets (Merck Serono's proprietary investigational oral formulation of cladribine) to treat patients with relapsing-remitting multiple sclerosis (MS). The data from this post-hoc analysis of the CLARITY study were presented at the 25<sup>th</sup> congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Düsseldorf, Germany.<sup>2</sup>

These data show that over two years of study, 43% and 44% of patients treated with Cladribine Tablets (total dose of 3.5 mg/kg and 5.25 mg/kg respectively) had absence of disease activity, compared with 16% of patients who received placebo ( $p < 0.001$  for both Cladribine Tablets groups). Disease activity was assessed both clinically and radiologically and absence of disease activity was stringently defined as no relapses, no sustained disability progression, no T1 gadolinium-enhancing lesions and no active T2 lesions based on magnetic resonance imaging (MRI) during the study.

"Immune-mediated disorders such as relapsing forms of multiple sclerosis are characterized by periods of disease activity alternating with periods of remission, and a very important goal in treating such disorders is to help patients achieve and maintain

## News Release

disease remission for longer periods of time,” said Dr Peter Rieckmann, Professor of Neurology, Director Department of Neurology, Bamberg Hospital, Germany, UBC Research Chair Vancouver/Canada and an investigator in the CLARITY study. “This CLARITY data analysis is very encouraging, based on the comparison between short-course oral treatment with Cladribine Tablets and placebo with respect to MS patients who had no disease activity, as assessed by both clinical and radiological measures over two years, with only 8-20 days of treatment in the first year of study and only 8-10 days of treatment in the second year of study.”

Merck Serono submitted a marketing authorization application to the European Medicines Agency (EMA) for Cladribine Tablets in July 2009 and will submit further registration applications for Cladribine Tablets in other countries, including the United States, during Q3 2009.

<sup>1</sup> CLARITY: CLAdRIbine Tablets Treating MS Orally

<sup>2</sup> Giovanonni G. et al.ECTRIMS Congress 2009; Poster P 471

### About the CLARITY study

The CLARITY study was a two-year (96-week), randomized, double-blind, placebo-controlled, international trial. It randomized 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 (3.5 mg/kg total dose) or four (5.25 mg/kg total dose) 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 8 to 20 days during the year. In the second year, two treatment courses were administered to all patient groups, meaning that patients took Cladribine Tablets for 8 to 10 days during the year.

All primary and secondary endpoints were met.

Overall, the frequencies of adverse events by MedDRA System Organ Class in both Cladribine Tablets treatment groups from the CLARITY study were comparable to those observed in the placebo group. The most commonly reported adverse events were headaches, upper respiratory tract infection, nasopharyngitis and nausea. Lymphopenia, an expected event based on the presumed mechanism of action of cladribine, occurred more frequently in the Cladribine Tablets treatment groups (low-dose regimen: 21.6%; high-dose regimen: 31.5%; placebo: 1.8%). The overall rate and incidence of infections in patients treated with Cladribine Tablets and placebo were similar. Herpes zoster infections were reported in 2.3% of patients treated with Cladribine Tablets. These herpes infections were localized to the skin and responded appropriately to treatment.

## News Release

### About Cladribine Tablets

Merck Serono is currently seeking registration of its proprietary oral formulation of cladribine (Cladribine Tablets) 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 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 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 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 and is ongoing.

Cladribine Tablets has 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 central nervous system and is the most common, non-traumatic, disabling neurological disease in young adults. It is estimated that more than two million people have 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.

## 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.

For more information, please visit [www.merckserono.com](http://www.merckserono.com) or [www.merck.de](http://www.merck.de)

### 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](http://www.merckserono.com) or [www.merck.de](http://www.merck.de)