

News Release

June 22, 2009

New Data from CLARITY Study Presented at 19th ENS Meeting Show Rapid and Sustained MS Relapse Reduction for Cladribine Tablets

- **The effect of short-course oral treatment with Cladribine Tablets on annualized relapse rate was significant as early as 12 weeks after initiation of treatment and sustained through to the 96 weeks of the study**

Milan, Italy and Geneva, Switzerland, June 22, 2009 – Merck Serono, a division of Merck KGaA, Darmstadt, Germany, announced today new data from post-hoc analyses of the 2-year (96-week) placebo-controlled CLARITY^a Phase III trial using Cladribine Tablets (Merck Serono's proprietary investigational oral formulation of cladribine) to treat patients with relapsing-remitting multiple sclerosis. These data show that short-course oral treatment with Cladribine Tablets resulted in rapid and sustained improvements in clinical and magnetic resonance imaging (MRI) outcomes, which were accompanied by rapid and sustained effects on blood-cell subtypes implicated in the pathogenesis of multiple sclerosis. The data will be presented at the 19th Meeting of the European Neurological Society (ENS) in Milan, Italy.^{1,2,3,4}

"The early impact on relapse reduction, together with the evidence for sustained benefits over 96 weeks as shown in the CLARITY study, support the short-course annual dosing regimen for Cladribine Tablets," said Prof. Giancarlo Comi, Professor of Neurology at the University Vita-Salute San Raffaele in Milan, Italy and an investigator for the CLARITY study. "Short-course oral treatment with Cladribine Tablets has the potential to make a meaningful difference in the lives of people with multiple sclerosis and their families."

News Release

A total of 1,326 patients were randomized to one of three different arms of the CLARITY study, consisting of two different dose regimens of Cladribine Tablets or matching placebo tablets (1:1:1 ratio). Cladribine Tablets were given in two (low-dose regimen) or four (high-dose regimen) treatment courses in the first year, with each course consisting of once daily administration for four to five consecutive days (depending on patient weight), 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.

In the CLARITY study, Cladribine Tablets significantly reduced the annualized relapse rate compared with placebo (primary endpoint). This effect was significant (as indicated by non-overlap of 95% confidence intervals versus placebo) as early as 12 weeks after initiation of treatment for patients treated with the low-dose regimen of Cladribine Tablets (low-dose regimen: 0.20; placebo: 0.49), and 16 weeks after initiation of treatment for both Cladribine Tablets treatment groups (low-dose regimen: 0.19; high-dose regimen: 0.21; placebo: 0.44). Effects were sustained through to the 96 weeks of the study with relative reductions in annualized relapse rates greater than 50% for patients treated with Cladribine Tablets with respect to placebo (low-dose regimen: 0.14; high-dose regimen: 0.15; placebo: 0.33, $p < 0.001$ for both treatment groups).

Lower mean numbers of different types of brain lesions (as measured by pre-specified key MRI endpoints) were observed for both Cladribine Tablets treatment groups by the first assessment point (24 weeks) and were sustained through the 96-week evaluation period, achieving high levels of statistical significance (all $p < 0.001$). The pre-specified key MRI secondary endpoints were T1 gadolinium-enhanced, active T2 lesions and combined unique lesions.

The effects of Cladribine Tablets on clinical and MRI measures were accompanied by rapid and sustained effects on blood-cell subtypes implicated in the pathogenesis of multiple sclerosis, such as T cells (CD3+, CD4+ and CD8+), and more transiently B cells (CD19+).

News Release

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.

Merck Serono plans to submit Cladribine Tablets for registration to the European Medicines Agency (EMA) and to the US Food and Drug Administration (FDA) during summer 2009.

^a CLARITY: CLAdRIbine Tablets Treating MS Orally

References:

¹ G. Giovannoni et al. Clinical efficacy of cladribine tablet therapy in patients with relapsing-remitting multiple sclerosis: results from the CLARITY study, a 96-week, Phase III, double-blind, placebo-controlled trial

² P. Soelberg-Sørensen et al. Haematological profiles in patients treated with cladribine tablets for relapsing-remitting multiple sclerosis: results from the CLARITY study, a 96-week, Phase III, double-blind, placebo-controlled trial

³ G. Comi et al. Magnetic resonance imaging (MRI) outcomes in patients with relapsing-remitting multiple sclerosis treated with cladribine tablets: results from the CLARITY study, a 96-week, Phase III, double-blind, placebo-controlled trial

⁴ P. Vermersch et al. Rapid and sustained efficacy with cladribine tablet treatment in relapsing-remitting multiple sclerosis: results from the CLARITY study, a 96-week, Phase III, double-blind, placebo-controlled trial

News Release

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 criteria². 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 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, proportion of subjects qualifying 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.

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 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 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[®] (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, 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 business operates in the United States and Canada as EMD Serono.

Merck Serono has leading brands serving patients with cancer (Erbix[®], 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 or 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 32,700 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