

News Release

September 18, 2008

Merck Serono Announces Initiation of the ORACLE MS Trial to Evaluate Cladribine Tablets in Patients at Risk of Developing Multiple Sclerosis

- **ORACLE MS Phase III trial will assess effectiveness of cladribine tablets in preventing conversion to definite multiple sclerosis in addition to the fully enrolled Phase III pivotal trial – the CLARITY study – for treatment of relapsing forms of multiple sclerosis**

Geneva, Switzerland, September 18, 2008 – Merck Serono, a division of Merck KGaA, Darmstadt, Germany, announced today the initiation of a Phase III trial to evaluate the therapeutic effects of its proprietary oral formulation of cladribine (cladribine tablets) in patients at risk of developing multiple sclerosis (MS).

The trial, called ORACLE MS (ORAI CLadribine in Early MS) will evaluate the safety and efficacy of two dosage regimens of cladribine tablets versus placebo in the treatment of patients who have experienced a first clinical event suggestive of MS. Cladribine tablets are currently also being evaluated in a fully enrolled Phase III pivotal trial – the CLARITY¹ study – for treatment of relapsing forms of MS. As announced in January 2007, CLARITY was the first pivotal trial among all Phase III oral compounds in development for MS to complete enrollment. Cladribine tablets have been granted a fast track designation by the US Food and Drug Administration.

“There is increasing evidence supporting the initiation of treatment with a disease-modifying drug in patients who have experienced a first clinical event suggestive of multiple sclerosis, an initial stage of the disease when clinical manifestations are not necessarily pronounced but where the potential exists for irreversible neurological damage to take place,” said Dr. Thomas Leist, Associate Professor of Neurology and



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Director of the Comprehensive MS Center at Thomas Jefferson University, Philadelphia, PA, and an investigator in the ORACLE MS study. “The ORACLE MS study will evaluate the effectiveness and safety of cladribine tablets in preventing conversion to definite multiple sclerosis.”

“As a leader in multiple sclerosis treatments, we are committed to providing new options that can further improve the course of the disease and the quality of life for people living with this disease,” said Dr. Richard Douge, Executive Vice President, Global Marketing, Merck Serono. “The initiation of the ORACLE MS study further demonstrates our commitment to continue to build a solid portfolio of products for use in a broad multiple sclerosis patient population. We believe that our proprietary oral formulation of cladribine has the potential to address an important unmet medical need at a critical time of disease development.”

The ORACLE MS study is a randomized, double-blind, placebo-controlled, international trial. It will involve more than 600 patients considered at risk of developing MS due to a recently experienced isolated demyelinating event (e.g. optic neuritis, myelopathy or brainstem syndrome) and having MRI brain scans consistent with early signs of MS. Study participants will be randomized in one of the three arms of the study to receive one of two different dosage regimens of cladribine tablets or matching placebo tablets (1:1:1 ratio).

Patients will be treated for a period of two years (96 weeks), or up to the time when they experience a second attack leading to a diagnosis of clinically definite MS, in which case they would be offered open-label treatment with Rebif[®] 44 mcg three times a week for a 96-week maintenance treatment period. Patients who do not convert to clinically definite MS within the initial 96-week period of the study will be eligible to enroll in a 96-week long-term follow-up treatment period. These maintenance and long-term follow-up periods of the study are intended to assess the effect of early treatment with cladribine tablets on relapses and subsequent treatment response to disease-modifying therapy for relapsing-remitting MS and to evaluate the sustained effect of cladribine tablets in delaying the development of definite MS.

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In the study, cladribine tablets are given in two or four treatment cycles in the first year, with each cycle consisting of once daily administration for four to five consecutive days, which means study patients take cladribine tablets for only 8 to 20 days during that year. In the second year, two treatment cycles are administered to all patient groups.

The primary endpoint of the ORACLE MS trial is time to conversion to MS, according to the McDonald criteria. Other endpoints include time to conversion to clinically definite MS according to the Poser criteria (the main secondary endpoint), assessments of MRI brain scans, and disability progression.

Approximately 200 medical centers globally are expected to participate in this trial.

¹ CLARITY: CLAdRIbine Tablets Treating MS Orally

About cladribine tablets

Merck Serono's proprietary oral formulation of cladribine 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.

About Rebif®

Rebif® (interferon beta-1a) is a disease-modifying drug used to treat relapsing forms of multiple sclerosis (MS) and is similar to the interferon beta protein produced by the human body. The efficacy of Rebif® in chronic progressive MS has not been established. Interferons are thought to help modulate the body's immune system and reduce inflammation. The exact mechanism is unknown.

Rebif®, which was approved in Europe in 1998 and in the US in 2002, is registered in more than 80 countries worldwide. Rebif® has been proven to delay the progression of disability, reduce the frequency of relapses and reduce MRI lesion activity and area*. Rebif® is available in a 22 microgram and 44 microgram ready-to-use pre-filled syringe and a titration pack (8.8 micrograms).

Rebif® should be used with caution in patients with a history of depression, liver disease and seizures. Most commonly reported side effects are flu-like symptoms, injection site disorders, elevation of liver enzymes and blood cell abnormalities. Patients, especially those with depression, seizure disorders, or liver problems, should discuss treatment with Rebif® with their doctors. For more information about Rebif®, please visit www.ms lifelines.com for prescribing information.

* The exact correlation between MRI findings and the current or future clinical status of patients, including disability progression, is unknown.

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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 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.

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 (Erbitux®), multiple sclerosis (Rebif®), infertility (Gonal-f®), endocrine and cardiometabolic disorders (GlucoPhage®, Concor®, Euthyrox®, Saizen®, Serostim®), as well as psoriasis (Raptiva®).

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 31,946 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.net or www.merck.de