



## Genzyme Announces Successful Phase III Results for Alemtuzumab (LEMTRADA™) in Multiple Sclerosis

***-Significant efficacy of alemtuzumab over interferon beta-1a (Rebif®) observed on both relapse and disability co-primary endpoints in treatment-experienced MS patients -***

***- Genzyme confirms Q1 2012 regulatory submission objective -***

**Paris, France - November 14, 2011** - Sanofi (EURONEXT: SAN and NYSE: SNY) and its subsidiary Genzyme report today that the Phase III CARE-MS II trial met both of its co-primary endpoints. Relapse rate and sustained accumulation (worsening) of disability (SAD) were significantly reduced in multiple sclerosis patients receiving alemtuzumab (LEMTRADA™) as compared with Rebif® (44 mcg subcutaneous interferon beta-1a). Results for both of these co-primary endpoints were highly statistically significant. CARE-MS II is the randomized Phase III clinical trial comparing the investigational drug alemtuzumab to interferon beta-1a in patients with relapsing-remitting multiple sclerosis (RRMS). Patients were required to have experienced a relapse while on a prior therapy to be eligible for CARE-MS II. Genzyme is developing alemtuzumab in MS in collaboration with Bayer HealthCare.

In this randomized trial involving 840 patients, a 49 percent reduction in relapse rate was observed in patients treated with alemtuzumab 12 mg compared to interferon beta-1a over two years of study ( $p < 0.0001$ ). Importantly, there was also a 42 percent reduction in the risk of sustained accumulation (worsening) of disability as measured by the Expanded Disability Status Scale (EDSS) ( $p = 0.0084$ ). Analysis of the full CARE-MS II data is ongoing and results will be presented at a forthcoming scientific meeting.

*"CARE-MS II represents the culmination of many years of clinical and laboratory research aimed at demonstrating the potential for alemtuzumab as a highly effective treatment for MS and understanding mechanisms involved in the complex natural history of the disease,"* said Professor Alastair Compston, Chair of the Steering Committee overseeing the conduct of the study and head of the Department of Clinical Neurosciences at the University of Cambridge, United Kingdom. *"Taken together, the Phase II and III clinical trial data illustrate the promise that alemtuzumab holds as a transformative treatment for people with relapsing MS."*

The CARE-MS II trial compared treatment with alemtuzumab 12 mg given daily as an IV administration for 5 days, and then again for 3 days one year later, to treatment with interferon beta-1a 44 mcg administered by injection three times per week throughout the two years of study.

*"The superior efficacy results for alemtuzumab, particularly the slowing of disability, are very promising since this was a head-to-head comparison trial with high dose subcutaneous interferon beta-1a,"* said Dr. Jeffrey Cohen, Professor of Medicine (Neurology), Cleveland Clinic Lerner College of Medicine; Director of Experimental Therapeutics, Mellen Center for MS Treatment and Research; and a member of the Steering Committee overseeing the conduct of the study. *"These results suggest alemtuzumab's potential to offer patients with MS a new and effective treatment option."*



The safety profile observed in the trial was consistent with previous alemtuzumab use in MS and adverse events continued to be manageable. The most common types of adverse events associated with alemtuzumab in the CARE-MS II study were infusion-associated reactions, the symptoms of which most commonly included headache, rash, nausea, hives, fever, itching, insomnia, and fatigue. Infections were common in both groups with a higher incidence in the alemtuzumab group. The most common infections in patients receiving alemtuzumab included upper respiratory and urinary tract infections, sinusitis and herpes simplex infections. Infections were predominantly mild to moderate in severity and there were no treatment-related life-threatening or fatal infections.

Approximately 16 percent of alemtuzumab-treated patients developed an autoimmune thyroid-related adverse event and approximately one percent developed immune thrombocytopenia during the two-year study period. These cases were detected early through a monitoring program and managed using conventional therapies. Patient monitoring for immune cytopenias and thyroid or renal disorders is incorporated in all Genzyme-sponsored trials of alemtuzumab for the investigational treatment of MS.

*“We are very pleased with the results of the CARE-MS II study which are unprecedented,” said David Meeker, M.D., President and Chief Executive Officer, Genzyme. “We believe that LEMTRADA™, with its impressive efficacy, novel dosing regimen and manageable safety profile, could make a very important contribution to the MS treatment landscape, where a significant unmet need still exists for many patients. Based on these positive results, we are on track to submit LEMTRADA™ for review to US and EU regulatory authorities in the first quarter of 2012.”*

Alemtuzumab has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA). The FDA's Fast Track program is designed to expedite the review of new drugs that are intended to treat serious or life-threatening conditions and demonstrate the potential to address unmet medical needs. Under Fast Track designation, alemtuzumab for MS is eligible for Priority Review. Since it is not yet approved for the treatment of MS, alemtuzumab must not be used in MS patients outside of a formal, regulated clinical trial setting in which appropriate patient monitoring measures are in place.

\*LEMTRADA™ is the proprietary name submitted to health authorities for the company's investigational multiple sclerosis agent alemtuzumab.

#### **About the CARE-MS II Trial**

CARE-MS II (The Comparison of Alemtuzumab and Rebif® Efficacy in Multiple Sclerosis) trial was designed to evaluate whether the investigational MS therapy alemtuzumab could achieve meaningful efficacy and safety improvements over the approved, active comparator interferon beta-1a, a standard treatment for relapsing MS.

CARE-MS II was a Phase III, global, randomized clinical trial comparing treatment with alemtuzumab to treatment with subcutaneous interferon beta-1a (44 mcg administered by injection three times per week) in 840 patients who relapsed despite receiving prior MS treatment. Patients enrolled in the trial had to have experienced at least two relapses within the two years prior to entering the trial, with at least one of these relapses occurring within one year prior to enrollment and at least one relapse occurring while on MS therapy.

The CARE-MS II trial had two co-primary endpoints: reduction in relapse rate and six months sustained accumulation of disability (SAD)\*\*. Secondary outcome measures include: Percentage of relapse-free patients at year two; Expanded Disability Status Scale (EDSS) change from baseline; percent change in magnetic/resonance imaging (MRI)-T2-hyperintense lesion volume at year two; and Multiple Sclerosis Functional Composite (MSFC) change from baseline. Disability assessments



were performed at regularly scheduled visits by independent, evaluating neurologists who were blinded to the patients' treatment assignments. Relapse was determined by a blinded committee.

\*\* Sustained Accumulation of Disability – Clinical representation of the worsening of a patient's level of disability; CARE-MS II monitored this endpoint over the course of six months.

### **About Alemtuzumab**

Alemtuzumab is a humanized monoclonal antibody being studied as a potential therapy for relapsing MS. Alemtuzumab targets the cell-surface glycoprotein CD52, which is highly expressed on T- and B-lymphocytes. Preliminary research suggests that alemtuzumab initially depletes the T- and B-cells that may be responsible for the cellular damage in MS. This depletion of T- and B-cells is followed by a distinctive pattern of lymphocyte repopulation. Alemtuzumab appears to have little or no effect on other cells of the immune system. In addition to the completed CARE-MS II study, another Phase III trial, CARE-MS I, evaluated alemtuzumab against interferon beta-1a in relapsing-remitting MS patients naive to prior treatment and found a statistically significant reduction in relapse rate with alemtuzumab.

Genzyme has the worldwide rights to alemtuzumab and has primary responsibility for the development and commercialization of alemtuzumab in MS. Bayer HealthCare has been co-developing alemtuzumab in MS with Genzyme. Bayer HealthCare retains an option to co-promote alemtuzumab in MS and upon regulatory approval and commercialization would receive contingent payments based on sales revenue.

### **About Genzyme, a Sanofi Company**

Genzyme has pioneered the development and delivery of transformative therapies for patients affected by rare and debilitating diseases for over 30 years. We accomplish our goals through world-class research and with the compassion and commitment of our employees. With a focus on rare diseases and multiple sclerosis, we are dedicated to making a positive impact on the lives of the patients and families we serve. That goal guides and inspires us every day. Genzyme's portfolio of transformative therapies, which are marketed in countries around the world, represents groundbreaking and life-saving advances in medicine. As a Sanofi company, Genzyme benefits from the reach and resources of one of the world's largest pharmaceutical companies, with a shared commitment to improving the lives of patients. Learn more at [www.genzyme.com](http://www.genzyme.com).

### **About Sanofi**

Sanofi, a global and diversified healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth platforms: diabetes solutions, human vaccines, innovative drugs, rare diseases, consumer healthcare, emerging markets and animal health. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

### **About Bayer HealthCare**

The Bayer Group is a global enterprise with core competencies in the fields of health care, nutrition and high-tech materials. Bayer HealthCare, a subgroup of Bayer AG with annual sales of more than EUR 16.913 billion (2010), is one of the world's leading, innovative companies in the healthcare and medical products industry and is based in Leverkusen, Germany. The company combines the global activities of the Animal Health, Consumer Care, Medical Care and Pharmaceuticals divisions. Bayer HealthCare's aim is to discover and manufacture products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 55,700 employees and is represented in more than 100 countries. Find more information at [www.bayerhealthcare.com](http://www.bayerhealthcare.com).

### **Sanofi Forward Looking Statements**

*This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include*



projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words “expects”, “anticipates”, “believes”, “intends”, “estimates”, “plans” and similar expressions. Although Sanofi’s management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of such products candidates, the absence of guarantee that the products candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, the Group’s ability to benefit from external growth opportunities as well as those discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under “Risk Factors” and “Cautionary Statement Regarding Forward-Looking Statements” in Sanofi’s annual report on Form 20-F for the year ended December 31, 2010. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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