



Treatment Effects Maintained Over Six Years in Patients with Relapsing Remitting Multiple Sclerosis who Received Sanofi Genzyme's Lemtrada[®] (alemtuzumab) in Clinical Trials

– At six years in the extension of two Phase III pivotal studies, 64 and 55 percent of Lemtrada-treated patients received no additional Lemtrada in the prior five years –

– Consistent effects seen across relapse, disability, brain atrophy and MRI lesion activity –

Paris, France - September 16, 2016 - [Sanofi](#) and its specialty care global business unit [Sanofi Genzyme](#) announced today positive new six-year investigational data from the extension study of Lemtrada[®] (alemtuzumab) in patients with relapsing remitting multiple sclerosis (RRMS). These results will be presented today at the 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in London.

In RRMS patients treated with Lemtrada in the CARE-MS Phase III pivotal studies, the effects described below observed in the two-year trials were maintained through four additional years in the extension study. More than 90 percent of the patients who were treated with Lemtrada in the CARE-MS trials enrolled in the extension. These patients were eligible to receive additional treatment with Lemtrada in the extension if they experienced at least one relapse or at least two new or enlarging brain or spinal cord lesions.

After the initial two courses of treatment in the CARE-MS trials, which were given at month zero and at month 12, 64 percent of Lemtrada patients from CARE-MS I and 55 percent from CARE-MS II did not receive additional Lemtrada treatment during the following five years, through month 72.

- The low annualized relapse rates observed in patients who received Lemtrada in the Phase III studies CARE-MS I (0.16) and CARE-MS II (0.28) remained consistent throughout the extension (0.12 and 0.15 at year six.)
- Through year six, 77 percent and 72 percent of patients who received Lemtrada in CARE-MS I and CARE-MS II, respectively, did not experience worsening of six-month confirmed disability as measured by the Expanded Disability Status Scale (EDSS).
- Through year six, 34 percent and 43 percent of patients who had disability before receiving Lemtrada in CARE-MS I and CARE-MS II, respectively, had improvement in EDSS score confirmed over at least six months as compared with pre-treatment baseline.
- Through year six, patients who received Lemtrada in CARE-MS I and II experienced a slowing of brain atrophy as measured by brain parenchymal fraction on magnetic

resonance imaging (MRI). In years three through six, the median yearly brain volume loss was -0.20 percent or less, which was lower than what was observed in the Lemtrada-treated patients during the two-year pivotal studies (CARE-MS I: -0.59 percent in year one; -0.25 percent in year two; CARE-MS II: -0.48 percent in year one; -0.22 percent in year two).

- In each of years three, four, five and six, most patients had no evidence of MRI disease activity, defined as no new gadolinium-enhancing T1 lesions and no new or enlarging T2 lesions (66 – 72 percent, CARE-MS I; 68 – 70 percent, CARE-MS II).

Through year six, the yearly incidence of most adverse events during the extension study was comparable or reduced compared with the pivotal studies. The frequency of thyroid adverse events was highest in year three and declined thereafter.

“The Lemtrada data being presented at ECTRIMS from the ongoing extension study illustrate that more than half of patients experienced sustained effects of treatment on disease activity, despite receiving their last treatment course five years previously,” said Dr. Alasdair Coles, Professor, Department of Clinical Neurosciences, University of Cambridge. *“It is very promising to see these consistent effects over time across relapse, disability and MRI measures.”*

The Phase III trials of Lemtrada were randomized, rater-blinded, two-year pivotal studies comparing treatment with Lemtrada to high-dose subcutaneous interferon beta-1a in patients with RRMS who had active disease and were either new to treatment (CARE-MS I) or who had an inadequate response to another therapy (CARE-MS II). Active disease was defined as at least two relapses in the previous two years and at least one in the previous year. The protocol called for Lemtrada to be administered as two annual treatment courses, with the first treatment course administered via intravenous infusion on five consecutive days, and the second course administered on three consecutive days, 12 months later.

In clinical trials, serious side effects associated with Lemtrada included infusion reactions, autoimmune disorders (such as thyroid disease, autoimmune cytopenias, and nephropathies), infections and pneumonitis. Lemtrada may cause an increased risk of malignancies. Risk management programs incorporating education and monitoring help support early detection and management of key identified and potential risks. The most common side effects of Lemtrada are rash, headache, pyrexia, nasopharyngitis, nausea, urinary tract infection, fatigue, insomnia, upper respiratory tract infection, herpes viral infection, urticaria, pruritus, thyroid gland disorders, fungal infection, arthralgia, pain in extremity, back pain, diarrhea, sinusitis, oropharyngeal pain, paresthesia, dizziness, abdominal pain, flushing, and vomiting. (See Important Safety Information below.)

About Lemtrada® (alemtuzumab)

Lemtrada is approved in more than 50 countries, with additional marketing applications under review by regulatory authorities globally. Lemtrada is supported by a comprehensive and extensive clinical development program that involved nearly 1,500 patients worldwide and 5,400 patient-years of follow-up. More than 9,200 patients have been treated with Lemtrada commercially worldwide.

The precise mechanism by which alemtuzumab exerts its therapeutic effects in MS is unknown. Alemtuzumab is a monoclonal antibody that targets CD52, a protein abundant on T and B cells. Circulating T and B cells are thought to be responsible for the damaging inflammatory process in MS. Lemtrada depletes circulating T and B lymphocytes after each treatment course. Lymphocyte

counts then increase over time with a reconstitution of the lymphocyte population that varies for the different lymphocyte subtypes.

Sanofi Genzyme holds the worldwide rights to alemtuzumab and has responsibility for its development and commercialization in multiple sclerosis. Bayer Healthcare receives contingent payments based on global sales revenue.

Lemtrada® (alemtuzumab) U.S. Indication

LEMTRADA is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS). Because of its risks, LEMTRADA is generally used in people who have tried 2 or more MS medicines that have not worked well enough. It is not known if LEMTRADA is safe and effective for use in children under 17 years of age.

Do not receive LEMTRADA if you are infected with human immunodeficiency virus (HIV).

IMPORTANT SAFETY INFORMATION

LEMTRADA can cause serious side effects including:

Serious autoimmune problems: Some people receiving LEMTRADA develop a condition where the immune cells in your body attack other cells or organs in the body (autoimmunity), which can be serious and may cause death. Serious autoimmune problems may include:

- Immune thrombocytopenia, which is when reduced platelet counts in your blood cause severe bleeding that, if not treated, may cause life-threatening problems. Call your healthcare provider right away if you have any of the following symptoms: easy bruising; bleeding from a cut that is hard to stop; heavier menstrual periods than normal; bleeding from your gums or nose that is new or takes longer than usual to stop; small, scattered spots on your skin that are red, pink, or purple
- Kidney problems called anti-glomerular basement membrane disease, which can, if untreated, lead to severe kidney damage, kidney failure that needs dialysis, a kidney transplant, or death. Call your healthcare provider right away if you have any of the following symptoms: blood in the urine (red or tea-colored urine); swelling of legs or feet; coughing up blood

It is important for you to have blood and urine tests before you receive, while you are receiving and every month, for 4 years or longer, after you receive your last LEMTRADA infusion.

Serious infusion reactions: LEMTRADA can cause serious infusion reactions that may cause death. Serious infusion reactions may happen while you receive, or up to 24 hours or longer after you receive LEMTRADA.

- You will receive your infusion at a healthcare facility with equipment and staff trained to manage infusion reactions, including serious allergic reactions, and urgent heart or breathing problems. You will be watched while you receive, and for 2 hours or longer after you receive, LEMTRADA. If a serious infusion reaction happens while you are receiving LEMTRADA, your infusion may be stopped.

Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion, and after you have left the healthcare facility:

- swelling in your mouth or throat
- trouble breathing
- weakness
- fast, slow, or irregular heartbeat
- chest pain
- rash

To lower your chances of getting a serious infusion reaction, your healthcare provider will give you a medicine called corticosteroids before your first 3 infusions of a treatment course. You may also be given other medicines before or after the infusion to try to reduce your chances of having these reactions or to treat them after they happen.

Certain cancers: Receiving LEMTRADA may increase your chance of getting some kinds of cancers, including thyroid cancer, skin cancer (melanoma), and blood cancers called lymphoproliferative disorders and lymphoma. Call your healthcare provider if you have the following symptoms that may be a sign of thyroid cancer:

- new lump
- swelling in your neck
- pain in front of neck
- hoarseness or other voice changes that do not go away
- trouble swallowing or breathing
- cough that is not caused by a cold

Have your skin checked before you start receiving LEMTRADA and each year while you are receiving treatment to monitor for symptoms of skin cancer.

Because of risks of autoimmunity, infusion reactions, and some kinds of cancers, LEMTRADA is only available through a restricted program called the LEMTRADA Risk Evaluation and Mitigation Strategy (REMS) Program.

Thyroid problems: Some patients taking LEMTRADA may get an overactive thyroid (hyperthyroidism) or an underactive thyroid (hypothyroidism). Call your healthcare provider if you have any of these symptoms:

- excessive sweating
- unexplained weight loss
- eye swelling
- nervousness
- fast heartbeat
- unexplained weight gain
- feeling cold
- worsening tiredness
- constipation

Low blood counts (cytopenias): LEMTRADA may cause a decrease in some types of blood cells. Some people with these low blood counts have increased infections. Call your doctor right away if you have symptoms of cytopenias such as:

- weakness
- chest pain
- yellowing of the skin or whites of the eyes (jaundice)
- dark urine
- fast heartbeat

Serious infections: LEMTRADA may cause you to have a serious infection while you receive and after receiving a course of treatment. Serious infections may include:

- **Herpes viral infections.** Some people taking LEMTRADA have an increased chance of getting herpes viral infections. Take any medicines as prescribed by your healthcare provider to reduce your chances of getting these infections.
- **Tuberculosis.** Your healthcare provider should check you for tuberculosis before you receive LEMTRADA.
- **Hepatitis.** People who are at high risk of, or are carriers of, hepatitis B (HBV) or hepatitis C (HCV) may be at risk of irreversible liver damage.

These are not all the possible infections that could happen while on LEMTRADA. Call your healthcare provider right away if you have symptoms of a serious infection such as fever or swollen glands. Talk to your healthcare provider before you get vaccinations after receiving LEMTRADA. Certain vaccinations may increase your chances of getting infections.

Swelling of lung tissue (pneumonitis): Some people have had swelling of the lung tissue while receiving LEMTRADA. Call your healthcare provider right away if you have the following symptoms:

- shortness of breath
- cough
- wheezing
- chest pain or tightness
- coughing up blood

Before receiving LEMTRADA, tell your healthcare provider if you:

- are taking a medicine called Campath® (alemtuzumab)
- have bleeding, thyroid, or kidney problems
- have HIV
- have a recent history of infection
- have received a live vaccine in the past 6 weeks before receiving LEMTRADA or plan to receive any live vaccines. Ask your healthcare provider if you are not sure if your vaccine is a live vaccine
- are pregnant or plan to become pregnant. LEMTRADA may harm your unborn baby. You should use birth control while receiving LEMTRADA and for 4 months after your course of treatment
- are breastfeeding or plan to breastfeed. You and your healthcare provider should decide if you should receive LEMTRADA or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. LEMTRADA and other medicines may affect each other, causing side effects. Especially tell your healthcare provider if you take medicines that increase your chance of getting infections, including medicines used to treat cancer or to control your immune system.

The most common side effects of LEMTRADA include:

- rash
- headache
- thyroid problems
- fever
- swelling of your nose and throat
- nausea
- urinary tract infection
- feeling tired
- trouble sleeping
- upper respiratory infection
- herpes viral infection
- hives
- itching
- fungal infection
- joint pain
- pain in your arms or legs
- back pain
- diarrhea
- sinus infection
- mouth pain or sore throat
- tingling sensation
- dizziness
- stomach pain
- sudden redness in face, neck, or chest
- vomiting



Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of LEMTRADA.

You are encouraged to report side effects of prescription drugs to the FDA. Visit <http://www.fda.gov/medwatch> or call 1-800-FDA-1088

Please see full U.S. [Prescribing Information](#), including boxed WARNING and [Medication Guide](#).

About Sanofi

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi is organized into five global business units: Diabetes and Cardiovascular, General Medicines and Emerging Markets, Sanofi Genzyme, Sanofi Pasteur and Merial. Sanofi is listed in Paris (EURONEXT: [SAN](#)) and in New York (NYSE: [SNY](#)).

Sanofi Genzyme focuses on developing specialty treatments for debilitating diseases that are often difficult to diagnose and treat, providing hope to patients and their families. Learn more at www.sanofigenzyme.com

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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 labelling and other matters that could affect the availability or commercial potential of such product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic conditions, the impact of cost containment initiatives and subsequent changes thereto, the average number of shares outstanding 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, 2015. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

Contacts:

Sanofi Genzyme Media Relations

Erin Pascal

Tel: + 1 857 248 0874

E-mail: erin.pascal@genzyme.com



Sanofi Media Relations

Jack Cox

Tel: +33 (0) 1 53 77 46 46

E-mail: mr@sanofi.com

Sanofi Investor Relations

George Grofik

Tel: +33 (0) 1 53 77 45 45

E-mail: ir@sanofi.com