New Investigational Data on Six-Year Efficacy of Sanofi Genzyme’s Lemtrada® (alemtuzumab) in Multiple Sclerosis Patients Who Experienced Relapse Between Treatment Courses To Be Presented at AAN

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CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sanofi Genzyme, the specialty care global business unit of Sanofi, announced today positive new six-year investigational data from a post-hoc analysis of the extension study of Lemtrada® (alemtuzumab) in patients with relapsing remitting multiple sclerosis (RRMS). These data will be presented at the 69th American Academy of Neurology (AAN) Annual Meeting.

Lemtrada is 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, twelve months later.

The majority of patients treated with Lemtrada (76%; n=330) in the Phase III pivotal study CARE-MS II did not relapse between their first and second courses of Lemtrada; 24% (n=105) of Lemtrada-treated patients in CARE-MS II relapsed between courses.

Clinical and MRI outcomes in the Lemtrada-treated patients who relapsed between courses markedly improved after their second course. Through six years, the clinical and MRI results observed in these patients were similar to those in the patients who did not relapse between courses:

- Annualized relapse rate (ARR):
  - In patients who relapsed between courses, ARR declined from 1.2 in year 1 to 0.5 in year 2, after they received their second treatment course. ARR continued to decline through year 6 (years 3, 4, 5 and 6: 0.4, 0.4, 0.3, and 0.2, respectively.)
  - In patients who did not relapse between courses, ARR in years 2, 3, 4, 5, and 6 was 0.2, 0.2, 0.2, 0.2 and 0.1, respectively.
- Confirmed disability worsening (CDW), defined as ≥ 1-point Expanded Disability Status Scale (EDSS) increase (or ≥ 1.5 points if baseline EDSS=0) confirmed over six months:
  - The majority of patients who relapsed between courses (80%) were free of CDW in year 2, and 60% remained free of CDW in year 6.
  - The majority of patients who did not relapse between courses (91%) were free of CDW in year 2, and 75% remained free of CDW in year 6.
- Confirmed disability improvement (CDI), defined as ≥ 1-point EDSS decrease from baseline (patients with baseline score ≥ 2.0) confirmed over six months:
  - In year 2, 28% of patients who relapsed between courses achieved CDI, and the proportion achieving CDI in years 3, 4, 5 and 6 was 33%, 34%, 34% and 34%, respectively.
  - In year 2, 31% of patients who did not relapse between courses achieved CDI, and the proportion achieving CDI in years 3, 4, 5 and 6 was 37%, 43%, 44% and 45%, respectively.
- No evidence of disease activity (NEDA), defined as absence of clinical disease activity (relapses and six-month CDW) and MRI disease activity (new Gd-enhancing T1 and new/enlarging T2 hyperintense lesions):
  - In patients who relapsed between courses, the proportion achieving NEDA was 38% in year 2 and 58% in year 6.
  - In patients who did not relapse between courses, the proportion achieving NEDA was 64% in year 2 and 60% in year 6.
- Brain volume loss (BVL), derived by relative change in brain parenchymal fraction:
In patients who relapsed between courses, median percent yearly BVL was -0.10% in year 2, and remained low in years 3, 4, 5 and 6 (-0.07%, -0.19%, -0.29%, and -0.13%, respectively).

In patients who did not relapse between courses, median percent yearly BVL was -0.27% in year 2, and remained low in years 3, 4, 5 and 6 (-0.12%, -0.19%, -0.01% and -0.10%, respectively.)

Retreatment data for both groups of patients is as follows:

- 33% of patients who relapsed between courses received no additional treatment after course two through year six; 53% received retreatment with Lemtrada, 7% percent received retreatment with another disease-modifying therapy (DMT), and 7% received retreatment with Lemtrada and another DMT.

- 55% of patients who did not relapse between courses received no additional treatment after course two through year six; 36% received retreatment with Lemtrada, 4% received retreatment with another DMT, and 5% received retreatment with Lemtrada and another DMT.

Consistent with the CARE-MS I and II full cohorts, through year six the most frequent adverse events (AEs) observed with Lemtrada were infusion-associated reactions; other AEs of interest included autoimmune AEs.

"Relapses are not uncommon following the initiation of disease-modifying therapies for relapsing MS. Approximately 25% to 45% of RMS patients treated with DMTs experience relapses in the first year or two of treatment," said Barry Singer, M.D., Director of The MS Center for Innovations in Care, Missouri Baptist Medical Center, St. Louis, MO. "The new Lemtrada data being presented at AAN suggest that occurrence of relapses in patients after receiving their initial course but before receiving their second course is not an indicator of lack of response to the treatment, and support the importance of administering the full two-course regimen. The 24% of Lemtrada-treated patients in CARE-MS II who relapsed between their first and second courses experienced a marked improvement in clinical and MRI disease activity at year 2, which was maintained through six years. The results observed in these patients through six years were similar to those observed in the 76% of patients who were relapse-free between courses one and two."

The Phase III trials of Lemtrada were randomized, open-label, 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. More than 90 percent of the patients who were treated with Lemtrada in the CARE-MS trials enrolled in the extension study. These patients were eligible to receive additional treatment with Lemtrada during the extension if they experienced at least one relapse or at least two new or enlarging brain or spinal cord lesions. They were eligible to receive treatment with another DMT during the extension at the investigator's discretion.

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 60 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 13,000 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
- trouble swallowing or breathing
- swelling in your neck
- cough that is not caused by a cold
- pain in front of neck
- hoarseness or other voice changes that do not go away

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 gain
• unexplained weight loss
• feeling cold
• eye swelling
• worsening tiredness
• nervousness
• constipation
• fast heartbeat

**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
• dark urine
• fast heartbeat
• yellowing of the skin or whites of the eyes (jaundice)

**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
• chest pain or tightness
• cough
• coughing up blood
• wheezing

**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
• trouble sleeping
• upper respiratory infection
• herpes viral infection
• hives
• itching
• diarrhea
• sinus infection
• mouth pain or sore throat
• tingling sensation
• dizziness
throat
• itching
• dizziness
• nausea
• fungal infection
• joint pain
• pain in your arms or legs
• back pain
• 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 Consumer Healthcare.

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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3 Company data on file

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 regarding the marketing and other potential of the product, or regarding potential future revenues from the product. 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, unexpected regulatory actions or delays, or government regulation generally, that could affect the availability or commercial potential of the product, the absence of guarantee that the product will be commercially successful, the uncertainties inherent in research and development, including future clinical data and analysis of existing clinical data relating to the product, including post marketing, unexpected safety, quality or manufacturing issues, competition in general, risks associated with intellectual property and any related future litigation and the ultimate outcome of such litigation, and volatile economic conditions, as well as those risks 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, 2016. 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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