



New Analysis Suggests Aubagio® (teriflunomide) Slows Brain Atrophy in People with Relapsing Multiple Sclerosis

- Additional MRI data on brain atrophy from Phase III TEMSO study will be presented at ECTRIMS -

Paris, France - October 7, 2015 - [Sanofi](#) and its subsidiary [Genzyme](#) announced today that magnetic resonance imaging (MRI) data from the Phase III TEMSO study demonstrate that Aubagio® (teriflunomide) significantly slowed brain volume loss (or atrophy) vs. placebo over two years in people with relapsing multiple sclerosis (RMS). In this analysis, MRI data from TEMSO were analyzed utilizing SIENA (structural image evaluation using normalization of atrophy), an alternative methodology than originally used.

Change in brain volume from baseline was assessed in patients treated with Aubagio 14 mg or 7 mg, or placebo. In the MS clinical studies of Aubagio, including TEMSO, the incidence of serious adverse events was similar among Aubagio and placebo-treated patients. These data will be presented on October 10, 2015 at the 31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Barcelona, Spain.

Results to be presented include:

- By month 12, median percent reduction from baseline in brain volume was 0.39, 0.40, and 0.61 for Aubagio 14 mg, 7 mg, and placebo, respectively. This change was lower for both Aubagio groups vs. placebo: 14 mg by 36.9 percent, $p=0.0001$; 7 mg by 34.4 percent, $p=0.0011$.
- The significant difference in reduction of brain atrophy for Aubagio vs. placebo was maintained at month 24. Median percent reduction in brain volume from baseline was 0.90, 0.94, and 1.29 for Aubagio 14 mg, 7 mg, and placebo, respectively. This change was lower for both Aubagio groups vs. placebo: 14 mg by 30.6 percent, $p=0.0001$; 7 mg by 27.6 percent, $p=0.0019$.

Brain atrophy is the result of the destructive pathological processes that occur in MS. It is seen from the earliest stages of disease and leads to irreversible neurological and cognitive impairment.

“Control or prevention of brain atrophy is an important target for MS treatment,” said Prof. Dr. Ludwig Kappos, Neurology Chair, University Hospital Basel, Switzerland. *“These data help provide further insight into teriflunomide’s potential effects in people with RMS.”*

“These results showing the reduction in brain atrophy over two years add to the growing body of data for Aubagio,” said Bill Sibold, Head of Genzyme’s Multiple Sclerosis business. *“We remain committed to furthering the understanding of Aubagio and the potential benefits it could deliver to relapsing MS patients.”*



Aubagio® (teriflunomide) U.S. Indication

Aubagio is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

Important Safety Information About Aubagio

WARNING: HEPATOTOXICITY AND RISK OF TERATOGENICITY

Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. AUBAGIO is contraindicated in patients with severe hepatic impairment and in patients taking leflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for 6 months after starting AUBAGIO. If drug induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or charcoal. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO.

Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy.

Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure after AUBAGIO treatment.

Warnings and Precautions

Patients with pre-existing acute or chronic liver disease, or those with serum ALT >2 times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with AUBAGIO. In clinical trials, if ALT elevation was >3 times the ULN on 2 consecutive tests, patients discontinued AUBAGIO and underwent accelerated elimination. Consider additional monitoring if co-administering AUBAGIO with other potentially hepatotoxic drugs; monitor patients who develop symptoms suggestive of hepatic dysfunction (eg, unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine).

Before starting therapy, use of reliable contraception must be confirmed, and the patient counseled on risks to the fetus. Patients with delayed onset of menses or other reason to suspect pregnancy should immediately see their physician for pregnancy testing. Patients who become pregnant or wish to become pregnant should discontinue treatment, followed by accelerated elimination until plasma concentrations of <0.02 mcg/mL are verified, a level expected to pose minimal risk to the fetus. Women who become pregnant while taking AUBAGIO may enroll in the AUBAGIO pregnancy registry by calling 1-800-745-4447, option 2.

Teriflunomide is eliminated slowly from the plasma—it takes an average of 8 months, or up to 2 years, to reach plasma concentrations <0.02 mcg/mL. Elimination may be accelerated by administration of cholestyramine or charcoal, but this may cause disease activity to return in patients who were responding to AUBAGIO.

Decreases in white blood cell counts, mainly of neutrophils and lymphocytes, and platelets have been reported with AUBAGIO. Obtain a complete blood cell count within 6 months before starting treatment, with further monitoring based on signs and symptoms of bone marrow suppression. AUBAGIO is not recommended for patients with severe immunodeficiency, bone marrow disease, or severe uncontrolled infections. Tuberculosis (TB) has been observed in clinical studies of AUBAGIO. Before starting treatment, screen patients for latent TB infection with a tuberculin test. Treatment in patients with acute or chronic infections should not be started until the infection(s) is resolved. Administration of live vaccines is not recommended.

The risk of malignancy, particularly lymphoproliferative disorders, or infection may be increased with the use of some medications with immunosuppressive potential, including teriflunomide.



Peripheral neuropathy, including polyneuropathy and mononeuropathy, has been reported with AUBAGIO. Age >60 years, concomitant neurotoxic medications, and diabetes may increase the risk. If peripheral neuropathy is suspected, consider discontinuing treatment and performing accelerated elimination.

Interstitial lung disease and rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported with leflunomide; a similar risk would be expected for teriflunomide. If a severe skin reaction develops with AUBAGIO, stop treatment and use accelerated elimination.

Blood pressure increases and hypertension have occurred with AUBAGIO. Measure blood pressure at treatment initiation and manage any elevations during treatment.

Adverse Reactions: The most frequent adverse reactions ($\geq 10\%$ and $\geq 2\%$ greater than placebo) with AUBAGIO 7 mg and 14 mg and placebo, respectively, were headache (18% and 16% vs 15%), ALT increased (13% and 15% vs 9%), diarrhea (13% and 14% vs 8%), alopecia (10% and 13% vs 5%), and nausea (8% and 11% vs 7%).

Drug Interactions: Monitor patients when teriflunomide is coadministered with warfarin, or with drugs metabolized by CYP1A2, CYP2C8, substrates of OAT3 transporters, substrates of BCRP, or OATP1B1/1B3 transporters

Use in Specific Populations: AUBAGIO is detected in human semen. To minimize any possible fetal risk, men not wishing to father a child and their female partners should use reliable contraception. Men wishing to father a child should discontinue therapy and undergo accelerated elimination, with verification of plasma concentrations < 0.02 mcg/mL. Nursing mothers should not use AUBAGIO.

Please click [here](#) for full US Prescribing Information for Aubagio, including Boxed **WARNING**.

About Aubagio® (teriflunomide)

Aubagio is approved in more than 50 countries, with additional marketing applications under review by regulatory authorities globally. More than 40,000 people have been treated with Aubagio worldwide.

Aubagio is an immunomodulator with anti-inflammatory properties. Although the exact mechanism of action for Aubagio is not fully understood, it may involve a reduction in the number of activated lymphocytes in the central nervous system (CNS). Aubagio is supported by one of the largest clinical programs of any MS therapy, with more than 5,000 trial participants in 36 countries.

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.

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About Sanofi

Sanofi, a global 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, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris (EURONEXT: [SAN](#)) and in New York (NYSE: [SNY](#)).

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, the Group's ability to benefit from external growth opportunities, trends in exchange rates and prevailing interest rates, the impact of cost containment policies 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, 2014. 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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