

European Commission approves Aubagio® (teriflunomide) as the first oral MS therapy for first-line treatment of children and adolescents living with relapsing-remitting multiple sclerosis

PARIS – June 18, 2021 - The European Commission (EC) has approved Aubagio® (teriflunomide) for the treatment of pediatric patients 10 to 17 years of age with relapsing-remitting multiple sclerosis (RRMS). The EC approval is based on data from the Phase 3 TERIKIDS study. The approval confirms Aubagio as the first oral multiple sclerosis (MS) therapy for first-line treatment of children and adolescents with MS in the European Union.

MS affects an estimated 2.8 million people around the world, with children and adolescents representing at least 30,000 of those impacted.^{1,2} Pediatric MS is a rare condition and onset follows a relapsing-remitting disease course in 98 percent of pediatric patients.^{3,4} Compared with adult-onset MS, pediatric patients often present with higher relapse rates and a greater lesion burden.⁵ Due to the earlier onset of disease, irreversible disability and secondary progression often occur at an earlier age than with adult counterparts.³ The symptoms of MS can impact all aspects of a young person's life from physical health to social development and self-esteem.⁶

“Pediatric multiple sclerosis remains an area of significant unmet medical need,” said Erik Wallström, MD, PhD, Therapeutic Area Head, Neurology Development at Sanofi Genzyme. “The European approval of Aubagio in pediatrics means young people with MS have a new treatment option, and importantly - one that can offer meaningful improvement in managing this serious disease.”

Aubagio was initially approved in the EU in 2013 for the treatment of adult patients with RRMS and the EC approval for the pediatric indication provides an additional year of marketing protection in the European Union.

Aubagio Efficacy and Safety in Pediatric Patients

The Phase 3 TERIKIDS study is a multicenter, randomized, double-blind, placebo-controlled, parallel-group trial that enrolled 166 pediatric patients with relapsing-remitting forms of MS across 22 countries worldwide. The study consisted of a screening period (up to four weeks), followed by a double-blind treatment period (up to 96 weeks after randomization). An open-label TERIKIDS Phase 3 trial extension is ongoing. The primary endpoint was time to first confirmed clinical relapse, with prespecified sensitivity analysis including time to high magnetic resonance imaging (MRI) activity as relapse equivalent. Additionally, patients who completed the double-blind period, or had high MRI activity, were eligible to continue into the open-label extension.

The primary efficacy results and safety and tolerability data from the double-blind core study period (up to 96 weeks after randomization) were initially presented at the 2020 EAN Virtual Congress.

In the study, 109 and 57 patients were randomized to teriflunomide and placebo, respectively.

The primary endpoint was not statistically significant with numerically a lower risk (-34%) of clinical relapse for teriflunomide vs placebo (median time: 75.3 vs 39.1 weeks; HR [95% CI] 0.66 [0.39, 1.1] P=0.29). Switches from double-blind to open-label treatment due to high MRI activity were more frequent than anticipated. Switches were more frequent and earlier in the placebo group vs teriflunomide (26% and 14%, respectively). This decreased study power for the primary endpoint.

In the pre-specified sensitivity analysis of the composite endpoint of time to first clinical relapse or high MRI activity meeting study criteria to switch to open label, teriflunomide significantly reduced the time to clinical relapse or switch due to high MRI activity by 43% relative to placebo (median time: 72.1 vs 37.0 weeks; HR [95% CI] 0.57 [0.37, 0.87] P=0.04).

Key secondary endpoints showed teriflunomide significantly reduced the number of T1 gadolinium (Gd) -enhancing lesions per MRI scan (relative reduction 75%; P<0.0001) as well as the number of new and enlarging T2 lesions per MRI scan (relative reduction 55%, P=0.0006).

In the study, teriflunomide was well tolerated and had a manageable safety profile in the pediatric population. The overall incidences of adverse events (AEs) and serious adverse events (SAEs) were similar in the teriflunomide group and the placebo group (88.1% vs 82.5%, and 11.0% vs 10.5%), respectively. There were no deaths in the study. AEs reported more frequently in the teriflunomide group than the placebo group (with a difference of $\geq 5\%$) included nasopharyngitis, upper respiratory tract infection, alopecia, paresthesia, abdominal pain, and increased blood creatine phosphokinase (≥ 3 times the upper limit of normal). Cases of pancreatitis were reported in 1.8% (2/109) of the teriflunomide-treated patients compared to none in the placebo group, in the double-blind phase. In pediatric patients treated with teriflunomide in the open-label phase of the study, two additional cases of pancreatitis and one case of serious acute pancreatitis (with pseudo-papilloma), were reported.

For more information on the TERIKIDS Phase 3 clinical trial visit www.clinicaltrials.gov.

Multiple Sclerosis: a chronic disease that attacks the central nervous system

Multiple sclerosis is a chronic neurodegenerative disease in which a person's immune system causes damage to the brain and spinal cord. It is an unpredictable disease that affects 2.8 million people around the world, and the latest prevalence statistics across 47 countries estimate that at least 30,000 of those affected are children and teenagers.^{1,2}

About Aubagio® (teriflunomide)

Aubagio is approved in more than 80 countries to treat certain patients with relapsing-remitting multiple sclerosis, with additional marketing applications under review by regulatory authorities globally. Aubagio is supported by one of the largest clinical programs of any MS therapy, with more than 5,000 trial participants in 36 countries, as well as a Phase 4 study program with more than 3,600 patients currently enrolled. There is over 16 years of combined clinical and real-world experience with Aubagio. More than 110,000 patients are currently being treated with Aubagio commercially worldwide.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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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 fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi’s ability to benefit from external growth opportunities, to complete related transactions 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 and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties 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, 2019. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

¹ Walton, C., King, R., Rechtman, L., Kaye, W., Leray, E., Marrie, R., Robertson, N., La Rocca, N., Uitdehaag, B., van der Mei, I., Wallin, M., Helme, A., Angood Napier, C., Rijke, N., & Baneke, P. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Multiple Sclerosis Journal* 2020; 26:14.

² The Multiple Sclerosis International Federation Atlas of MS, 3rd ed, September 2020. <https://www.atlasofms.org>.

³ Renoux C, Vukusic S, Confavreux C. The natural history of multiple sclerosis with childhood onset. *Clin Neurol Neurosurg.* 2008;110(9):897-904.

⁴ Alroughani R, Boyko A. Pediatric multiple sclerosis: a review. *BMC Neurol* 2018; 18:27.

⁵ Pena JA, Lotze TE. Pediatric multiple sclerosis: current concepts and consensus definitions. *Autoimmune Diseases* 2013(3):673947.

⁶ MacAllister WS, Boyd JR, Holland NJ, Milazzo MC, Krupp LB. The psychosocial consequences of pediatric multiple sclerosis. *Neurology.* 2007;68(16 SUPPL. 2):S66–S69.