Press Release

Sanofi provides update on tolebrutinib in primary progressive multiple sclerosis

- PERSEUS phase 3 study in primary progressive multiple sclerosis did not meet its primary endpoint in delaying time to onset of 6-month composite confirmed disability progression compared to placebo
- The safety profile of tolebrutinib was consistent with previous studies

Paris, December 15, 2025. Results from the PERSEUS phase 3 study (clinical study identifier: NCT04458051) showed that tolebrutinib did not meet its primary endpoint in delaying time to 6-month composite confirmed disability progression (cCDP) in participants with primary progressive multiple sclerosis (PPMS), which represents 10% of the overall multiple sclerosis patient population. Based on these results, Sanofi will not pursue regulatory registration for PPMS.

> *"We are disappointed by today's results; however, we do believe that these results will improve our understanding of the underlying disease biology of multiple sclerosis,"* said **Houman Ashrafian**, Executive Vice President, Head of Research & Development at Sanofi. *"We extend our deepest appreciation to the study participants, their families, and healthcare professionals who support our scientific and innovative vision. Our commitment to the multiple sclerosis community remains unchanged, as do our efforts to pursue novel advancements that address existing unmet needs and we remain confident in the value tolebrutinib can bring to those living with non-relapsing secondary progressive multiple sclerosis."*

Preliminary analysis showed the safety profile was consistent with previous tolebrutinib studies. As previously reported, drug-induced liver injury (DILI) is an identified risk of tolebrutinib. Strict adherence to liver monitoring requirements, and prompt management of liver enzyme elevations, are important to mitigate DILI risk. Full safety and efficacy results will be presented at a forthcoming medical meeting.

Tolebrutinib was provisionally approved in the United Arab Emirates in July 2025 for the treatment of non-relapsing secondary progressive multiple sclerosis and to slow disability accumulation independent of relapse activity in adults. It is currently under regulatory review in the EU and other jurisdictions worldwide. Tolebrutinib was previously granted breakthrough therapy designation by the FDA in December 2024.

Financial considerations

Sanofi will conduct an impairment test in accordance with IFRS (IAS 36) on the intangible asset value attached to tolebrutinib with a status to be provided with Q4 and FY 2025 results in January 2026. The outcome of this test will have no impact to the business net income / business EPS and there is no change to the financial guidance for 2025.

About multiple sclerosis

MS is a progressive neurologic disorder characterized by accumulation of disability with shifts in the underlying biology and dominant drivers of disability over time impacting clinical presentation and treatment response.

The clinical presentation of PPMS is characterized by a slow, insidious neurologic decline, often with a predominance of spinal cord involvement, and symptoms gradually worsen over time without periods of improvement.

Secondary progressive multiple sclerosis typically refers to people with a previous diagnosis of relapsing MS who have stopped experiencing relapses but continue to experience disability accumulation, in the absence of relapses.

Addressing disability accumulation remains a significant unmet need in MS, as treatment options are limited.

About PERSEUS

PERSEUS (clinical study identifier: NCT04458051) is a global, double-blind, randomized phase 3 clinical study which evaluated the efficacy and safety of tolebrutinib compared to placebo in participants with PPMS. Participants were randomized (2:1) to receive either an oral daily dose of tolebrutinib or matching placebo for up to approximately 60 months. The inclusion criteria for the study included participants aged 18–55 years old, a diagnosis of PPMS as per the 2017 revised McDonald criteria, an EDSS score ≥2.0 and ≤6.5 at screening, positive cerebrospinal fluid findings (OCBs and/or elevated IgG index) and either no access, intolerance, or perceived lack of efficacy to ocrelizumab.

The primary endpoint was six-month composite confirmed disability progression (cCDP), defined as increase over at least six months of ≥1.0 point from the baseline expanded disability status scale (EDSS) score when the baseline score is ≤5.5, or ≥0.5 points when the baseline EDSS score is >5.5, or ≥20% from the baseline T25-FW, or ≥20% from the baseline 9-HPT. Secondary endpoints included six-month confirmed disability progression, three-month cCDP, number of new/enlarging T2 lesions as detected by MRI, time to confirmed disability improvement, change in brain volume loss, change in cognitive function, quality of life, pharmacokinetics, as well as the safety and tolerability of tolebrutinib.

About tolebrutinib

Tolebrutinib is an investigational, oral, brain-penetrant Bruton's tyrosine kinase inhibitor specifically designed to target smoldering neuroinflammation, a key driver of disability progression in MS. This mechanism addresses the underlying pathology of progressive MS by targeting the inflammatory processes that contribute to neurodegeneration and disability accumulation.

Tolebrutinib represents Sanofi's commitment to developing innovative treatments that address the underlying causes of neurological diseases and potentially transform the treatment landscape. Standing at the intersection of neurology and immunoscience, Sanofi is focused on improving the lives of those living with serious neuro-inflammatory and neuro-degenerative conditions including MS, chronic inflammatory demyelinating polyneuropathy, Alzheimer's disease, Parkinson's disease, and age-related macular degeneration. The neurology pipeline currently has several projects in phase 3 studies across various diseases.

About Sanofi

Sanofi is an R&D driven, AI-powered biopharma company committed to improving people's lives and delivering compelling growth. We apply our deep understanding of the immune system to invent medicines and vaccines that treat and protect millions of people around the world, with an innovative pipeline that could benefit millions more. Our team is guided by one purpose: we chase the miracles of science to improve people's lives; this inspires us to drive progress and deliver positive impact for our people and the communities we serve, by addressing the most urgent healthcare, environmental, and societal challenges of our time.

Sanofi is listed on EURONEXT: SAN and NASDAQ: SNY

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Sanofi forward-looking statement
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 global crises may 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. 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, 2024. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.