Press Release

Update on the US regulatory review of tolebrutinib in non-relapsing, secondary progressive multiple sclerosis

Paris, September 22, 2025. The US Food and Drug Administration (FDA) has extended by three months the target action date of its review of the new drug application (NDA) of tolebrutinib, an oral and brain-penetrant investigational Bruton's tyrosine kinase (BTK) inhibitor to treat non-relapsing, secondary progressive multiple sclerosis (nrSPMS) and to slow disability accumulation independent of relapse activity in adult patients.

Based on the submission of additional analyses during the review, the FDA has determined that the additional information constituted a major amendment to the NDA and extended the target action date accordingly. The revised target action date for the FDA decision is December 28, 2025.

Sanofi is confident in the potential positive impact tolebrutinib can provide and will continue to collaborate closely with the FDA during the review period.

Tolebrutinib was the first brain-penetrant BTK inhibitor in nrSPMS to be designated as a breakthrough therapy by the FDA.

The FDA review of tolebrutinib is based on pivotal data from the global, double-blinded randomized HERCULES and GEMINI 1 and 2 phase 3 studies evaluating the efficacy and safety of tolebrutinib in patients with nrSPMS and relapsing MS (RMS), respectively.

The safety and efficacy of tolebrutinib have not been established by the FDA, and it remains under review by regulatory authorities worldwide, including in the EU. In addition to the completed HERCULES and GEMINI 1 and 2 studies, the PERSEUS phase 3 study in primary progressive MS is ongoing with study results anticipated in H2 2025.

About multiple sclerosis

Multiple sclerosis is a chronic, immune-mediated neurodegenerative disease of the central nervous system (CNS) that may result in accumulation of irreversible disabilities over time. The physical and cognitive disability impairments translate into gradual deterioration of health status, impacting patients' care and quality of life. Disability accumulation remains a significant unmet medical need in MS. Currently, the primary target of currently approved medicines has been peripheral B and T cells, while innate immunity within the CNS which is believed to drive disability accumulation remains largely unaddressed.

People living with nrSPMS refers to people with MS who have stopped experiencing relapses but continue to accumulate disability, experienced as symptoms such as fatigue, cognitive impairment, balance and gait impairment, loss of bowel and/or bladder function, sexual dysfunction, amongst others.

About HERCULES

HERCULES (clinical study identifier: NCT04411641) was a double-blinded, randomized phase 3 clinical study evaluating the efficacy and safety of tolebrutinib in patients with nrSPMS. At baseline, nrSPMS was defined as having a SPMS diagnosis with an expanded disability status scale (EDSS) between 3.0 and 6.5, no clinical relapses for the previous 24 months and documented evidence of disability accumulation in the previous 12 months. Participants were randomized (2:1) to receive either an oral daily dose of tolebrutinib or matching placebo for up to approximately 48 months.

The primary endpoint was six-month confirmed disability progression (CDP) defined as the increase of ≥1.0 point from the baseline EDSS score when the baseline score is ≤5.0, or the increase of ≥0.5 point when the baseline EDSS score was >5.0. Secondary endpoints included time to onset of three-month CDP as assessed by EDSS score, total number of new or enlarging T2 hyperintense lesions as detected by MRI, time to onset of confirmed disability improvement, 3-month change in 9-hole peg test and timed 25-foot walk (T25-FW) test, as well as the safety and tolerability of tolebrutinib.

About GEMINI 1 and 2

GEMINI 1 (clinical study identifier: NCT04410978) and GEMINI 2 (clinical study identifier: NCT04410991) were double-blinded, randomized phase 3 clinical studies evaluating the efficacy and safety of tolebrutinib compared to teriflunomide, an oral disease modifying medicine, in patients with RMS. Participants were randomized in both studies (1:1) to receive either tolebrutinib and placebo daily or 14 mg teriflunomide and placebo.

The primary endpoint for both studies was the annualized relapse rate for up to approximately 36 months defined as the number of confirmed adjudicated protocol defined relapses. Secondary endpoints included time to onset of confirmed disease worsening, confirmed over at least six months, defined as an increase of ≥1.5 points from the baseline EDSS score when the baseline score is 0, an increase of ≥1.0 point from the baseline EDSS score when the baseline score is 0.5 to ≤5.5 or an increase of ≥0.5 point from the baseline EDSS score when the baseline score was >5.5 in addition to the total number of new and/or enlarging T2 hyperintense lesions as detected by MRI from baseline through the end of study, the total number of Gd-enhancing T1 hyperintense lesions as detected by MRI from baseline through the end of study, and the safety and tolerability of tolebrutinib.

About tolebrutinib

Tolebrutinib is an 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, age-related macular degeneration, and other neurological diseases. 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

Media Relations

Sandrine Guendoul | +33 6 25 09 14 25 | sandrine.guendoul@sanofi.com
Evan Berland | +1 215 432 0234 | evan.berland@sanofi.com
Léo Le Bourhis | +33 6 75 06 43 81 | leo.lebourhis@sanofi.com
Victor Rouault | +33 6 70 93 71 40 | victor.rouault@sanofi.com
Timothy Gilbert | +1 516 521 2929 | timothy.gilbert@sanofi.com
Léa Ubaldi | +33 6 30 19 66 46 | lea.ubaldi@sanofi.com

Investor Relations

Thomas Kudsk Larsen | +44 7545 513 693 | thomas.larsen@sanofi.com
Alizé Kaisserian | +33 6 47 04 12 11 | alize.kaisserian@sanofi.com
Felix Lauscher | +1 908 612 7239 | felix.lauscher@sanofi.com
Keita Browne | +1 781 249 1766 | keita.browne@sanofi.com
Nathalie Pham | +33 7 85 93 30 17 | nathalie.pham@sanofi.com
Tarik Elgoutni | +1 617 710 3587 | tarik.elgoutni@sanofi.com
Thibaud Châtelet | +33 6 80 80 89 90 | thibaud.chatelet@sanofi.com
Yun Li | +33 6 84 00 90 72 | yun.li3@sanofi.com

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 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.

All trademarks mentioned in this press release are the property of the Sanofi group.