

Sanofi's Cenrifki (tolebrutinib) approved in the EU as the first disability-targeting medicine for secondary progressive multiple sclerosis without relapses

- Cenrifki represents a significant advancement for people living with SPMS by targeting disability progression
- Approval based on the HERCULES phase 3 study in nrSPMS with supporting data from the GEMINI 1 and 2 phase 3 studies in RMS

Paris, June 23, 2026. The European Commission has approved Cenrifki (tolebrutinib) for the treatment of secondary progressive multiple sclerosis (SPMS) without relapses in the last two years. This follows the [positive opinion](#) by the European Medicines Agency's Committee for Medicinal Products for Human Use.

The approval is based on results from the HERCULES phase 3 study (clinical study identifier: [NCT04411641](#)) in non-relapsing SPMS (nrSPMS), with supporting data from the GEMINI 1 (clinical study identifier: [NCT04410978](#)) and GEMINI 2 (clinical study identifier: [NCT04410991](#)) phase 3 studies in relapsing multiple sclerosis (RMS). The HERCULES study demonstrated that Cenrifki significantly delayed the onset of disability progression in nrSPMS.

The safety profile of Cenrifki has been consistent across the clinical program. The most common adverse events were COVID-19 and upper respiratory tract infections. Significant liver enzyme elevations were also observed. Drug-induced liver injury (DILI) is an identified safety risk of Cenrifki. Strict adherence to liver monitoring requirements, and prompt management of liver enzyme elevations, are important to mitigate DILI risk.

Sanofi will make Cenrifki commercially available in Germany this year in close collaboration between local medical teams, treating MS specialists and their patients, all supported by the required Risk Management Program and robust Patient Support Program. This reflects Sanofi's commitment to a careful approach to introducing this innovative, first-in-class medicine for people living with SPMS without relapses.

About secondary progressive multiple sclerosis

SPMS is a debilitating stage of MS where patients experience continuous accumulation of disability, including fatigue, cognitive impairment, mobility difficulties, and loss of independence – often without available treatment options. Across major European economies, the yearly cost of MS-related disability surpasses the average annual income per person. As disability accumulates, many are forced to reduce working hours or leave the workforce entirely – while up to 82% of those living with severe MS rely on informal caregiving, extending the strain far beyond the individual. Addressing disability progression remains one of the most significant unmet needs in MS care.

About HERCULES

HERCULES (clinical study identifier: [NCT04411641](#)) was a double-blind, 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 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-blind, 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 Cenrifki

Cenrifki (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 unique mechanism of action addresses the underlying biology of progressive MS by targeting the inflammatory processes that contribute to disability accumulation. Cenrifki is the first disease-targeting therapy designed to address the underlying process of MS disability accumulation approved in the EU for adults with SPMS without relapses in the last two years.

Cenrifki is administered once daily with a meal, and treatment should be initiated and supervised by a physician experienced in the management of multiple sclerosis.

Cenrifki is also approved in Australia for the treatment of nrSPMS and to slow disability accumulation in the absence of relapse activity with SPMS and in the United Arab Emirates for the treatment of SPMS without relapses in the last two years.

Cenrifki 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

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