

New 48-week frexalimab phase 2 data support potential for high sustained efficacy in multiple sclerosis

- * Data support frexalimab as a potential first-in-class, high-efficacy, non-lymphocyte depleting treatment for relapsing multiple sclerosis
- * 96% of participants receiving high-dose intravenous frexalimab had no new Gd+ T1 lesions and an annualized relapse rate of 0.04 after 48 weeks
- * Sanofi has initiated global phase 3 studies of frexalimab in relapsing MS and non-relapsing secondary progressive MS

Paris, April 17, 2024. Sanofi's CD40L antibody, frexalimab, demonstrated sustained reduction of disease activity and favorable tolerability after nearly one year in participants with relapsing multiple sclerosis. These data will be presented today at the American Academy of Neurology (AAN) 2024 Annual Meeting in Denver, Colorado, US. Results from the 12-week double-blind study period were previously [published](#) in *The New England Journal of Medicine*.

Patrick Vermersch, MD, PhD

University of Lille, CHU Lille, France

"These 48-week data showed that treatment with frexalimab resulted in further decreases in the number of lesions and a sustained reduction in disease activity. The preliminary clinical results are promising with a very low annual relapse rate. This strengthens the rationale for targeting CD40L in MS and supports further development of frexalimab as a potential high-efficacy therapy in relapsing MS."

From the initial 12-week double-blind period, 97% (125/129) of study participants entered the open-label extension (OLE) of the phase 2 study. Of all participants receiving frexalimab, both on high- and low-dose regimens and participants who switched from placebo at the start of the open-label extension period (week 12), 87% (112/129) remained in the study at the 48-week cut-off. During the OLE, participants in the high- (n=50) and low-dose (n=49) arms continued to receive frexalimab 1200 mg intravenously every four weeks, or frexalimab 300 mg subcutaneously every two weeks, respectively, while those initially receiving placebo switched to the aforementioned high or low dose frexalimab treatment arms (n=12 and n=14, respectively).

Erik Wallström, MD, PhD

Global Head of Neurology Development, Sanofi

"Frexalimab represents a novel potential first-in-class treatment mechanism in multiple sclerosis designed to tackle the aspects of this disease where unmet medical needs still exist. We are applying our deep expertise to address the full spectrum of neuroinflammation and neurodegeneration to improve the lives of people living with multiple sclerosis."

Results of the phase 2 OLE at week 48 showed:

- 96% of patients who continued receiving high-dose frexalimab and 87% of those who continued receiving low-dose frexalimab were free of Gd+ T1 lesions at week 48, respectively. Additionally, among patients who switched from placebo to high and low-dose frexalimab at the start of the OLE at week 12, declines were seen at Week 24, and 90% and 92% were free of Gd+ T1 lesions at week 48, respectively.
- The number of Gd+ T1-lesions (mean [SD]) remained low in participants who continued receiving frexalimab (high dose: 0.0 [0.2]; low dose: 0.2 [0.5]) and continued to decline in those who switched from placebo to frexalimab at week 12 (high dose: 0.2 [0.6]; low dose: 0.1 [0.3]).

- Number of and volume change of new or enlarging Gd+ T2-lesions remained low for all frexalimab treatment groups through week 48, and lymphocyte counts remained stable.
- Participants who continued receiving high-dose frexalimab experienced a low annualized relapse rate (ARR) of 0.04 (95% CI: 0.01, 0.18) over the 48-week treatment period with 96% being free of relapses. ARR in the initial low-dose arm was 0.22, and ARR in patients who switched to high and low-dose frexalimab were 0.09 and 0.40, respectively, through week 48.

Frexalimab was generally well-tolerated through week 48. The most common adverse events ($\geq 10\%$) amongst all subgroups of patients receiving frexalimab during OLE until cut-off at week 48 from baseline were nasopharyngitis (n=14 [11%]), headache (n=14 [11%]) and COVID-19 (n=13 [10%]).

About the phase 2 study

The phase 2 study was a randomized, double-blind, placebo-controlled study evaluating frexalimab in participants with relapsing MS. Participants were randomized (4:4:1:1) to receive either high (frexalimab 1200 mg intravenously every four weeks, with an initial 1800 mg loading dose) or low (frexalimab 300 mg subcutaneously every two weeks, with an initial 600 mg loading dose) doses of frexalimab or matching placebo for 12 weeks (Part A). The primary endpoint was the reduction in the number of new Gd+ T1 MRI brain lesions at week 12. Secondary endpoints included additional MRI-based efficacy measures as well as the safety, tolerability and pharmacokinetics of frexalimab. After week 12, participants receiving placebo switched to respective frexalimab arms and entered the open-label Part B, which is currently ongoing.

About frexalimab

Frexalimab (SAR441344) is a potentially first-in-class second generation investigational anti-CD40L antibody that blocks the costimulatory CD40/CD40L pathway which is important for activation and function of adaptive (T and B cells) and innate (macrophages/microglia and dendritic cells) immunity. Through this unique upstream mechanism of action, frexalimab has the potential to address both acute and chronic neuroinflammation in MS, without causing lymphocyte depletion. Sanofi is developing frexalimab under an exclusive license from ImmuNext Inc. Frexalimab is being evaluated in phase 3 clinical studies for Multiple Sclerosis and phase 2 clinical studies for immunology indications and Type 1 Diabetes, and its safety and efficacy have not been reviewed by any regulatory authority. For more information on frexalimab clinical trials, please visit .

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across the world, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Sanofi is listed on Euronext: SAN and NASDAQ: SNY

Media Relations

Sandrine Guendoul | + 33 6 25 09 14 25 | sandrine.quendoul@sanofi.com

Sally Bain | + 1 617 834 6026 | sally.bain@sanofi.com

Victor Rouault | +3333 6 70 93 71 40 | victor.rouault@sanofi.com

Timothy Gilbert | + 1 516 521 2929 | timothy.gilbert@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

Arnaud Delépine | + 33 6 73 69 36 93 | arnaud.delepine@sanofi.com

Corentine Driancourt | + 33 6 40 56 92 21 | corentine.driancourt@sanofi.com

Felix Lauscher | + 1 908 612 7239 | felix.lauscher@sanofi.com

Nathalie Pham | + 33 7 85 93 30 17 | nathalie.pham@sanofi.com

Tarik Elgoutni | + 1 617 710 3587 | tarik.elgoutni@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 pandemics or other 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, 2023. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.