Evaluate Vantage

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Sanofi tries a new mechanism in multiple sclerosis

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The notion of flipping an immuno-oncology mechanism on its head to treat an autoimmune disorder was highlighted last week by the mid-stage success of Lilly's arthritis project peresolimab; this week it is Sanofi's turn. A hit with the anti-CD40L antibody frexalimab (SAR441344) in multiple sclerosis, also in phase 2, adds to a resurgence in this mechanism's popularity. The CD40/CD40L costimulatory pathway is thought to regulate immune cell function; blocking it has yielded a recent win for Horizon in Sjögren's syndrome. Other projects include Novartis's iscalimab, being trialled in Sjögren's as well as hidradenitis suppurativa among other indications. UCB and Biogen are further advanced, with their agent dapirolizumab pegol having started phase 3 in lupus. Sanofi will push frexalimab, which it licensed from Immunext in 2017, into phase 3 in MS next year. Sanofi could do with another late-stage asset: its BTK inhibitor tolebrutinib remains on partial US clinical hold. The opposite mechanism, CD40 agonism, is being investigated by several companies for various cancers, though one of these groups, Apexigen, bit the dust in March.

Ph2 (NCT04879628) data on Sanofi's frexalimab		
	Frexalimab high-dose	Frexalimab low-dose
Reduction in new gadolinium-enhancing T1-hyperintense lesions, vs pbo, at 12wk*	89%	79%
p value	0.0004	0.0021
Freedom from new GdE T1-lesions at 24wk	96%	Undisclosed
**Primary endpoint. Source: company release.*		