Telitacicept as a Novel BAFF/APRIL-Targeted Therapy for Sjögren's Disease

Sambhawana Bhandari,[1] Himanshu Patel,[2] Jeremy Sokolove,[2] Alfred HJ Kim[1]

[1]Division of Rheumatology, Department of Medicine, Washington University School of Medicine, St. Louis, MO, USA
[2]Vor Biopharma Inc., Boston, MA, USA

Title: 65 characters excluding spaces (max 120 characters excluding spaces)

Abstract length: 2496 characters excluding spaces (max 2500 characters excluding spaces)

Background (Character Count: 796 excluding spaces)

Sjögren's disease (SjD) is a systemic autoimmune disease characterized by lymphocytic infiltration of exocrine glands, causing xerostomia, keratoconjunctivitis sicca, fatigue, and potential systemic manifestations. Pathologic B-cell and plasma cell activation drive tissue injury through autoantibody production, immune complex formation, and antibody-independent pathology, including T-cell activation and cytokine production, contributing to disease progression, systemic complications, and increased lymphoma risk. Despite the disabling impact of SjD on health-related quality of life, treatment remains largely symptomatic with non-selective immunosuppression, highlighting the need for targeted therapies. Telitacicept, a B-cell–directed biologic immunomodulator, is entering phase 3 evaluation in a global SjD population, and this work characterizes a part of its pharmacodynamics (PD).

Methods (Character Count: 563 excluding spaces)

Telitacicept is a novel, fully human transmembrane activator and calcium-modulator and cyclophilin-ligand interactor (TACI)-Fc fusion protein that targets and neutralizes B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL), 2 cytokines essential for B-cell maturation, differentiation, and survival. By neutralizing BAFF and APRIL, telitacicept modulates B cells upstream in their development, lowering antibody production and modulating B-cell activity. Telitacicept has previously demonstrated efficacy and safety in phase 2 (NCT04078386) and 3 (NCT05673993) studies in adults with primary SjD (pSjD) in China.

Results (Character Count: 855 excluding spaces)

In a phase 2 study, telitacicept was associated with reductions in serum immunoglobulin (Ig)G, IgA, and IgM, and CD19+ B-cell counts compared with placebo (Table 1). A PD effect was observed starting at week 4, and at week 24 IgG levels reduced from 19.6 to 15.6 g/L, IgA from 3.0 to 1.5 g/L, and IgM from 1.2 to 0.5 g/L, while circulating CD19+ B-cell counts decreased from 157.8 to 81.7 cells/μL. Despite submaximal reduction in Ig and CD19+ B-cell counts, the primary endpoint was met with statistically significant improvement in EULAR Sjögren's Syndrome Disease Activity Index. As recently presented at ACR 2025, the efficacy of telitacicept was replicated across multiple endpoints in a phase 3 randomized, controlled study conducted in China with 380 participants with similar changes in PD. A global, multicenter, randomized, double-blind, placebo-controlled phase 3 study evaluating the efficacy and safety of telitacicept in adult patients with active pSjD is currently planned (NCT07404865).

Conclusions (Character Count: 282 excluding spaces)

BAFF/APRIL inhibition may provide meaningful clinical benefit in SjD while largely preserving overall B-cell and Ig compartments, consistent with selective modulation of pathogenic B-cell populations. Results from a global adult pSjD population will further characterize the efficacy and safety of telitacicept.

References:

1. Baldini C, Chatzis LG, Fulvio G, et al. Pathogenesis of Sjögren's disease: one year in review 2024. *Clin Exp Rheumatol.* 2024;42(12):2336-2343.
2. Maslinska M, Kostyra-Grabczak K. Immunoglobulin G4 in primary Sjögren's syndrome and IgG4-related disease - connections and dissimilarities. *Front Immunol*. 2024;15:1376723.
3. Verstappen GM, Pringle S, Bootsma H, Kroese FGM. Epithelial-immune cell interplay in primary Sjögren syndrome salivary gland pathogenesis. *Nat Rev Rheumatol*. 2021;17(6):333-348.
4. Zeng L, Yang K, Wu Y, et al. Telitacicept: a novel horizon in targeting autoimmunity and rheumatic diseases. *J Autoimmun*. 2024;148:103291.
5. Ji L, Geng Y, Zhang X, et al. B cell pathway dual inhibition for systemic lupus erythematosus: a prospective single-arm cohort study of telitacicept. *MedComm (2020)*. 2024;5(4):e515.
6. European Patent Application EP3868403A1.
7. ClinicalTrials.gov identifier: NCT07404865. Updated February 12, 2026. Accessed February 23, 2026. https://clinicaltrials.gov/study/NCT07404865.
8. Xu D, Fang J, Zhang S, et al. Efficacy and safety of telitacicept in primary Sjögren's syndrome: a randomized, double-blind, placebo-controlled, phase 2 trial. *Rheumatology (Oxford)*. 2024;63(3):698-705.
9. Xu D, Zhang S, Qiao L, et al. Efficacy and safety of telitacicept in patients with Sjögren's disease: results from a multicenter, randomized, double-blind, placebo-controlled, phase 3 clinical study. Presented at: American College of Rheumatology Convergence 2025; October 24-29, 2025; Chicago, IL.

Table 1. Mean change in immunoglobulins (Ig) and CD19+ B-cell counts at week 24 compared with baseline.

Mean (SD)	Placebo		Telitacicept 160 mg	
	Baseline	Week 24	Baseline	Week 24
IgG, g/L	16.3 (4.6)	16.9 (6.3)	19.6 (6.1)	15.6 (5.4)*
IgA, g/L	3.5 (1.6)	3.7 (1.7)	3.0 (1.2)	1.5 (0.6)*
IgM, g/L	1.3 (0.7)	1.0 (0.7)	1.2 (0.4)	0.5 (0.3)*
CD19+ B cells, /μL	193.7 (112.5)	211.6 (118.0)	157.8 (83.2)	81.7 (35.3)

*Statistically significant compared with placebo (P<0.001).

Disclosures:
1. Sambhawana Bhandari disclosures: None.

2. Himanshu Patel is an employee of Vor Biopharma Inc. and owns company stock.

3. Jeremy Sokolove is an employee of Vor Biopharma Inc. and owns company stock.

4. Alfred HJ Kim receives grant support from AstraZeneca, Bristol Myers Squibb, CRISPR Therapeutics, and Novartis. AHJK also receives consulting fees from AbbVie, AstraZeneca, Aurinia Pharmaceuticals, Biogen, Exagen Diagnostics, Genentech/Roche, GlaxoSmithKline, Hinge Bio, Invivyd, Johnson & Johnson, Kymera Therapeutics, Kypha, Miltenyi Biomedicine, Novartis, and Zenas Biopharma. AHJK is a patent beneficiary with Kyhpa (US patent 10029318B2).