Safety and Efficacy of an Off-the-Shelf Anti-CD19 CAR T-Cell Therapy With Reduced Conditioning in SLE: A Phase 1 Study Supporting Same-Day Discharge

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Introduction

Anti-CD19 CAR T-cell therapy shows promise in autoimmune diseases but remains limited by access and scalability. FT819 was developed to overcome these challenges.

Autologous CAR T-cell therapies involve prolonged pre- and post-apheresis timelines, with limited access to treatment centers, drug product inconsistency, high cost, and limited production capacity.

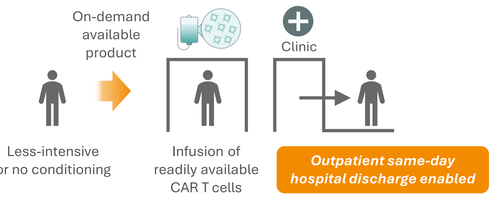
FT819 is an investigational, off-the-shelf CD19-targeting CAR T-cell product derived from an iPSC clonal master cell bank and designed to be mass produced and administered in the outpatient setting.

FT819 is designed to improve efficacy and safety through:

- Extension of T-cell effector function without uncontrolled expansion via a 1XX CAR-signaling domain, balancing safety and efficacy
- CRISPR-targeted integration of the CAR transgene into the TCR alpha chain constant region locus, leading to uniform CAR expression, enhancing product consistency while maintaining CAR expression under control of the T-cell promoter
- Complete bi-allelic disruption of TCR expression at the CAR insertion site, reducing risk of GvHD

FT819 is currently being evaluated in a Phase 1, open-label, dose-finding study (FT819-102; NCT06308978) in patients with B-cell-mediated autoimmune diseases (SLE, SSc, IIM, and AAV).

Figure 1. Off-the-Shelf iPSC derived CAR T-Cell Therapy

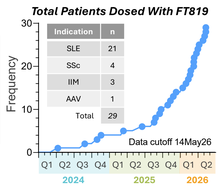


- ✓ Successful outpatient administration of FT819 with same-day discharge was previously demonstrated in the US
- ✓ Off-the-shelf CAR T-cell therapy with reduced or no conditioning therapy and on-demand availability can broaden patient access, including in underserved regions
- ✓ Potential for scalable outpatient and community-based treatment delivery

Methods

This is an ongoing Phase 1 dose-finding study evaluating the safety, pharmacokinetics, and anti-B-cell activity of FT819 in patients with SLE, SSc, IIM, and AAV.

Figure 2. Phase 1 Trial Design



Here, we report findings from the SLE arm in Regimen A:

- Single-dose FT819 administration
- Less-intensive conditioning therapy with a single dose of cyclophosphamide or 2 days of bendamustine prior to FT819 administration on Day 1
- Omission of fludarabine may improve tolerability, reduce risks associated with conditioning chemotherapy, and provide a more patient-friendly experience with improved treatment accessibility

Results

Patient Enrollment

As of May 14, 2026, 16 SLE patients in Regimen A have received a single dose of FT819 across 16 active sites; 13 patients have completed at least 1 month of follow-up. Outpatient administration is enabled in the US.

At baseline, patients were young (mean age 33.8 years), predominantly female (87.5%), and had refractory SLE with median disease duration 7.56 years and 7 prior treatment failures.

Table 1. Baseline Characteristics (SLE; Regimen A)

SLE Parameter	Regimen A (N=16)
Age, y, mean (range)	33.8 (19, 57)
Female, n (%)	14 (87.5)
SLE duration, y, median (range)	7.56 (1.0-33.7)
Anti-dsDNA or anti-Smith positive at baseline, n (%)	13 (81.3)
Prior therapies, n, median (range)*	7 (3-10)
Follow-up, months, median (range)	6.01 (0.3-25.3)
Active lupus nephritis, n (%)	10 (62.5)
Class III ± V	3 (30)
Class IV ± V	6 (60)
Class V	1 (10)
UPCr, mean ± SD	2.80 ± 1.992
BILAG A or B, n (%)	Renal 10 (62.5); Muc 10 (62.5); MSK 7 (43.8); Cardio 5 (31.3); Heme 1 (6.3); Const 1 (6.3)
SLEDAI-2K, mean ± SD	13.6 ± 4.27
PGA, mean ± SD	2.18 ± 0.391
FACIT-Fatigue score, mean ± SD	26.4 ± 13.79

Data cutoff 14 May 2026. All patients had previously received glucocorticoids and hydroxychloroquine. * Includes data entered after data cut-off. Cardio = cardiorespiratory; Const = constitutional symptoms; Heme = hematological; MSK = musculoskeletal; Muc = mucocutaneous.

All Regimen A SLE patients tolerated FT819 without DLT. No Grade >2 CRS; no ICANS, GvHD, or deaths reported in these patients on study.

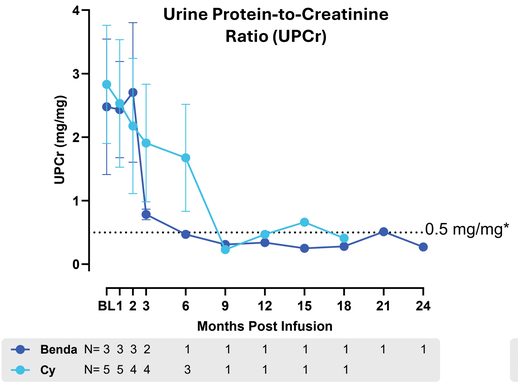
Table 2. Preliminary Safety Data of FT819 in Regimen A SLE: Select AESIs

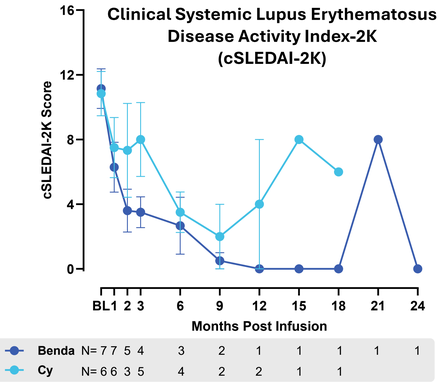
Safety Parameter	Incidence, n (%); (N=16)
CRS (Grades 1 and 2)	4 (25.0)
CRS (Grade ≥3)	0
ICANS	0
GvHD	0
Hypogammaglobinemia	0
Dose-limiting toxicity	0
Grade ≥3 adverse event (any)	6 (37.5)
Infection (Grade ≥3)*	3 (18.8)
Cytopenia (Grade ≥3)†	3 (18.8)

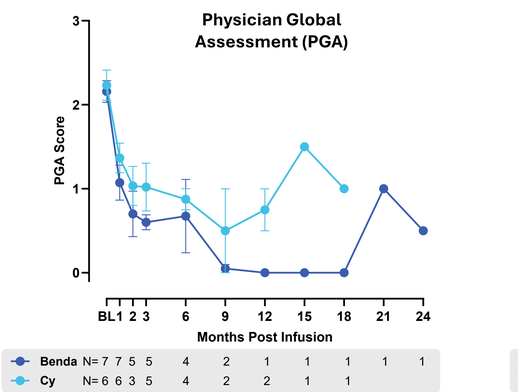
Data cutoff 14 May 2026.
* Infection includes urinary tract infection (2) and tooth abscess (1).
† Cytopenia includes the MedDRA preferred terms anaemia, leukopenia, lymphopenia, and neutropenia, corresponding to haemoglobin decreased, white blood cell count decreased, lymphocyte count decreased, and neutrophil count decreased, respectively.

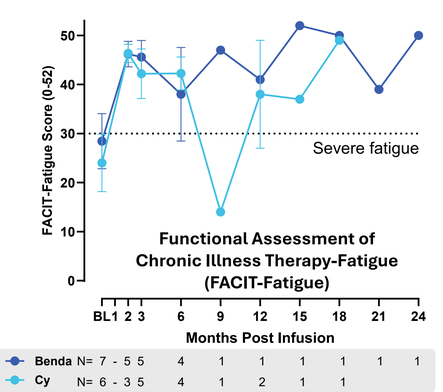
FT819 with less-intensive conditioning demonstrated early and sustained clinical improvement, with a trend toward more favorable responses with bendamustine conditioning, consistent with translational data.

Figure 4. Disease Activity Measures Among SLE Patients in Regimen A With at Least 1-Month Follow-up









Data cutoff 14 May 2026. Mean ± SEM. Notes: FT819 administered on Day 1. Three participants treated with Cy resumed additional immunosuppressive therapy: one mycophenolate at ~7.5 months and voclosporin at ~15.5 months; one (without lupus nephritis) anifrolumab at ~2 months; and one azathioprine at ~3 months. One patient discontinued the study after the Month 1 visit due to inability to meet trial requirements. UPCr at Month 3 (bendamustine) includes data entered after the data cutoff.
* Complete renal response requires UPCr <0.5 mg/mg.

FT819 combined with less-intensive conditioning cooperate to drive deep B-cell depletion with reconstitution of the preferred naïve state and meaningful decrease of top clones.

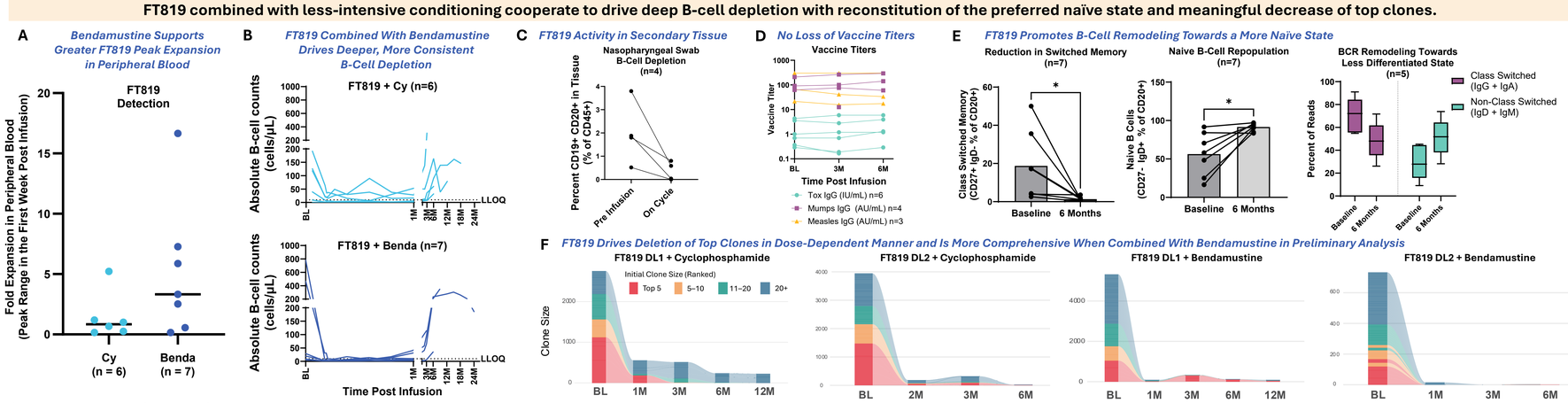


Figure 3. FT819 treatment drives remodeling of the B-cell compartment in synergy with bendamustine. **(A)** Bendamustine conditioning therapy (n=7) associates with greater expansion of FT819 cells between Days 2 and 4 post-treatment than cyclophosphamide (n=6) in patients with SLE. **(B)** B-cell depletion with FT819 is more consistent and complete in patients treated with bendamustine (n=7) compared to those treated with cyclophosphamide (n=6). **(C)** B-cell depletion is also observed in nasopharyngeal swab samples of secondary lymphoid tissue with either conditioning chemotherapy (CCT) modality. **(D)** Titers of tetanus toxoid IgG, measles IgG, and mumps IgG did not change following treatment (n=6); samples shown combined for patients treated with either CCT modality with screening and >3M follow up. Screening data from first 5 Regimen A patients were not collected. **(E)** B-cell remodeling is observed following FT819 treatment, exemplified by reduced switched memory proportion (left) increased naïve proportion (middle) by flow cytometry 6 months after treatment, as well as a shift towards fewer class-switched BCR (right). Data shown as combination of patients from both CCT modalities with >6M follow up. **(F)** Plots of top 50 clone persistence in patients treated with FT819 in combination with either cyclophosphamide or bendamustine for FT819 with dose level 1 (n=1 cyclophosphamide, n=1 bendamustine), or dose level 2 (n=1 cyclophosphamide, n=1 bendamustine). BCR = B-cell receptor.

Abbreviations: AAV = ANCA-associated vasculitis; AESI = adverse event of special interest; AZA = azathioprine; BILAG = British Isles Lupus Assessment Group; BL = baseline; CAR = chimeric antigen receptor; CRISPR = clustered regularly interspaced short palindromic repeats; CRS = cytokine-release syndrome; D = Day; DLT = dose-limiting toxicity; DL = dose level; GvHD = graft-versus-host disease; FACIT = Functional Assessment of Chronic Illness Therapy; IIM = idiopathic inflammatory myositis; ICANS = immune effector cell-associated neurotoxicity syndrome; iPSC = induced pluripotent stem cell; LTFU = long-term follow-up; M = Month; PGA = Physician Global Assessment; MMF/MPA = mycophenolate mofetil/mycophenolic acid; MTX = methotrexate; PTFU = post-treatment follow-up; SLE = systemic lupus erythematosus; cSLEDAI-2K = clinical Systemic Lupus Erythematosus Disease Activity Index 2000; SSc = systemic sclerosis; TCR = T-cell receptor; UPCr = urine protein-to-creatinine ratio.

Conclusion

- **Favorable safety and tolerability:** Preliminary results from this study in patients with moderate-to-severe SLE treated with FT819 support outpatient administration (enabled in the US).
- **Clinically meaningful improvement:** Persistent reductions in UPCr, cSLEDAI, PGA, and FACIT-fatigue were observed with less-intensive conditioning therapy.
- **Robust activity against B cells:** Effective B-cell depletion with reconstitution of naïve B-cell subtypes and elimination of top clones best supported by FT819 at dose level 2 and bendamustine; vaccination titers maintained.
- **On-demand accessibility:** Large-scale manufacturing enables production of off-the-shelf drug product inventory, including potential availability in underserved regions.
- **Supports Phase 2 advancement:** Collectively, these results support advancement into a planned, potentially registrational Phase 2 study of FT819 with bendamustine conditioning in patients with refractory moderate-to-severe SLE with lupus nephritis.
- **Broader development potential:** The observed safety, clinical activity, and outpatient feasibility also support further evaluation of FT819 combined with less-intensive or no conditioning in SLE and continued investigation across other B-cell mediated autoimmune diseases, including SSc, IIM, and AAV.

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