iPSC-Derived, Off-the-Shelf anti-CD19 CAR T cells Deliver Improved Clinical Outcomes in Lupus with Reduced or No Conditioning Chemotherapy

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Introduction

Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy shows extraordinary promise in autoimmune disease, but accessibility is limited

Autologous CAR T-cell therapy is transformative medicine, but has limitations:

- Prolonged time to treatment with pre- and post-apheresis timeline, limited access to authorized treatment centers, drug product inconsistency, high cost, and limited production capacity

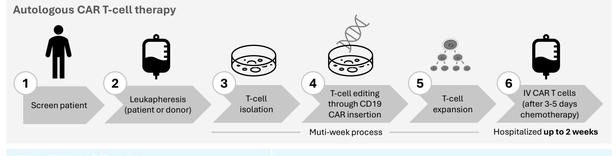
FT819 is an off-the-shelf, CD19-targeting CAR T-cell product:

- Derived from an induced pluripotent stem cell (iPSC) master cell bank (MCB)
- Produced for on-demand availability and unencumbered accessibility

FT819 is designed to improve efficacy and safety:

- Extension of cell effector function without uncontrolled expansion due to a 1XX CAR-signaling domain
- More uniform CAR expression and enhanced potency as a result of CRISPR-targeted integration of the CAR transgene into the T-cell receptor (TCR) alpha chain constant region locus
- Complete bi-allelic disruption of TCR expression to prevent graft-versus-host disease (GvHD)

Figure 1. Autologous CAR T-Cell Therapy vs. FT819 iPSC-derived CAR T-Cell Therapy



- No leukapheresis means patients can stay on current therapy prior to treatment
- Manufactured in large-scale, uniform CAR T-cell drug product
- Available on-demand with broad patient accessibility
- Safety profile allows for shorter hospitalization

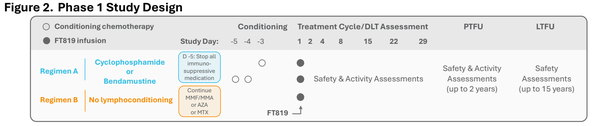
Table 1. Differentiated CAR T-Cell Manufacturing Process

Autologous	Allogeneic	iPSC-derived CAR T cell
Impaired starting material	Healthy starting material	• **Defined clonal MCB:** Single-cell derived, genetically uniform, potency-selected • **Engineered MCB:** One-time edit, donor-independent, scalable • **Modular innovation:** Accelerates development through efficient, multiplexed engineering
Random, variable, per-patient T-cell engineering	Random, variable, per-batch T-cell engineering	• **One-time, uniform iPSC precision engineering:** Modular, multiplexed edits • **Reliable drug product:** Well characterized, >5-year shelf life, ~50,000-dose per year capacity in current GMP space
Complex logistics	Complex logistics	• **Off-the-shelf, streamlined logistics:** Inventory-based supply, antibody-like manufactured and delivery
Single-dose paradigm	Multiple-dose paradigm	• **Multiple-dose paradigm:** Enables repeat dosing, outpatient-enabling
Heterogeneous drug product	Heterogeneous drug product	• **Homogenous drug product:** Genetically uniform, reproducible product • **No donor variability:** Consistent quality across batches
Extended hospitalization	Extended hospitalization	• **Reduced hospitalization:** Low toxicity profile • **Patient-centered:** Outpatient-compatible, easier administration
Prohibitively expensive ($$$$)	Expensive ($$$)	• **Cost effective:** Low cost of goods, estimated at $3,000 per dose

CAR = chimeric antigen receptor; GMP = Good Manufacturing Practice; iPSC = induced pluripotent stem cell; MCB = master cell bank

Methods

Figure 2. Phase 1 Study Design



AZA = azathioprine; DLT = dose-limiting toxicity; LTFU = long-term follow-up; MMF/MPA = mycophenolate mofetil/mycophenolic acid; MTX = methotrexate; PTFU = post-treatment follow-up

A Phase 1 dose-escalation study evaluating the safety, pharmacokinetics, and anti-B-cell activity of FT819 in patients with B-cell mediated autoimmune diseases is ongoing (NCT06308978).

Broad SLE eligibility

- Meet EULAR/ACR 2019 classification criteria for systemic lupus erythematosus (SLE)
- Have at least one of ANA 1:160, anti-dsDNA, or anti-Smith
- Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) ≥8 + 1 British Isles Lupus Assessment Group (BILAG) A or 2 BILAG B scores

Single-dose FT819 administration under 2 regimens

- **Regimen A:** Less intensive conditioning chemotherapy with a single dose of cyclophosphamide or bendamustine daily for 2 days prior to FT819; no use of fludarabine chemotherapy enhances safety profile and provides a more patient-friendly experience
- **Regimen B:** No conditioning chemotherapy with continued stable dose of maintenance therapy, including mycophenolate mofetil (MMF)

Dose levels: DL1: 3.6 × 10^8 viable cells and DL2: 9 × 10^8 viable cells

Patient Enrollment

At baseline, patients had treatment-refractory SLE with a median disease duration of 10 years and up to 10 prior treatment failures

As of 25 September 2025, 10 patients have received a single dose of FT819 across 8 active US sites:

- 8 with fludarabine-free, less-intensive conditioning chemotherapy (Regimen A)
- 2 without conditioning chemotherapy (on background therapy) (Regimen B)

Discussions with ex-US regulatory agencies are ongoing, with first-patient dosing anticipated by year-end 2025.

Table 2. Baseline Characteristics of SLE Patients Treated with FT819 (N=10)

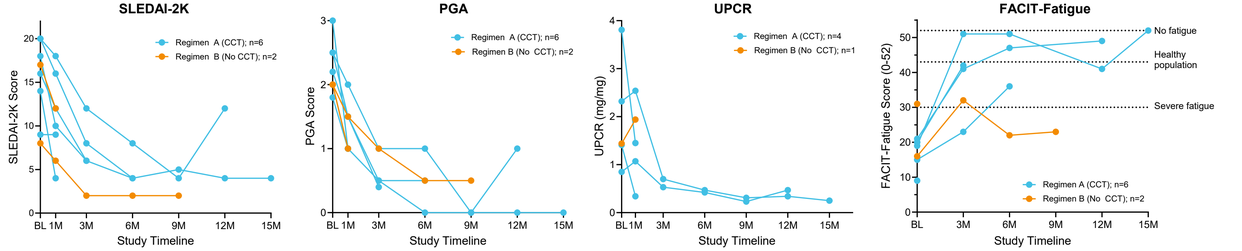
	Regimen A								Regimen B	
Patient	**A1-DL1**	**A2-DL1**	**A3-DL1**	**A4-DL1**	**A5-DL1**	**A1-DL2**	**A2-DL2**	**A3-DL2**	**B1-DL1**	**B2-DL1**
Age, sex	28 F	22 F	29 F	57 F	32 F	28 F	19 F	41 F	23 F	23 F
BILAG domain for inclusion	Renal	Renal	Heme, Renal	MSK, Mucocut	Renal	MSK, Mucocut	Cardioresp, MSK, Mucocut	Constitut, Mucocut, Renal	Cardioresp	Renal
LN classification	III	IV	IV	NA	IV	NA	NA	III + V	NA	IV
Disease duration	~11 y	~4 y	~24 y	~34 y	~4 y	~9 y	~1 y	~19 y	~5 y	~16 y
Baseline SLEDAI-2K	20	20	14	14	8	18	16	9	8	17
Concomitant SLE therapies	GC, HCQ	HCQ	GC, HCQ	GC	GC, HCQ	HCQ	GC, HCQ	HCQ	GC, HCQ, MMF	GC, HCQ, MMF
Prior Therapies *B-cell targeted therapy **bolded**	7 AZA, **BEL**, GC, HCQ, MMF, **RTX**, TAC	8 ANI, **BEL**, CY, GC, HCQ, MMF, MTX, **RTX**	8 AZA, **BEL**, CY, GC, HCQ, MMF, MTX, **RTX**	4 **BEL**, GC, HCQ, MMF	7 CY,GC, HCQ, MMF, **OBI**, **RTX**, TAC	10 ANI, AZA, **BEL**, CY, GC, HCQ, IVIG, MMF, MTX, UST	3 ANI, GC, HCQ	7 AZA, **BEL**, CY, GC, HCQ, IVIG, MTX	5 CY, GC, HCQ, MMF, **RTX**	8 AZA, **BEL**, CY, GC, HCQ, MMF, **OBI**, VOC
Conditioning	Benda	CY	CY	Benda	CY	CY	Benda	CY	None	None

ANI = anifrolumab; AZA = azathioprine; BEL = belimumab; Benda = bendamustine; BILAG = British Isles Lupus Assessment Group; Cardioresp = cardiorespiratory; Constitut = constitutional; CY = cyclophosphamide; DL = dose level; F = female; GC = glucocorticoids; HCQ = hydroxychloroquine; Heme = hematological; IVIG = intravenous immunoglobulin; LN = lupus nephritis; MMF = mycophenolate mofetil; MSK = musculoskeletal; MTX = methotrexate; Mucocut = mucocutaneous; NA = not applicable; OBI = obinutuzumab; RTX = rituximab; SLE = systemic lupus erythematosus; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; TAC = tacrolimus; UST = ustekinumab; VOC = voclosporin. Data cutoff date 25 Sep 2025.

Results

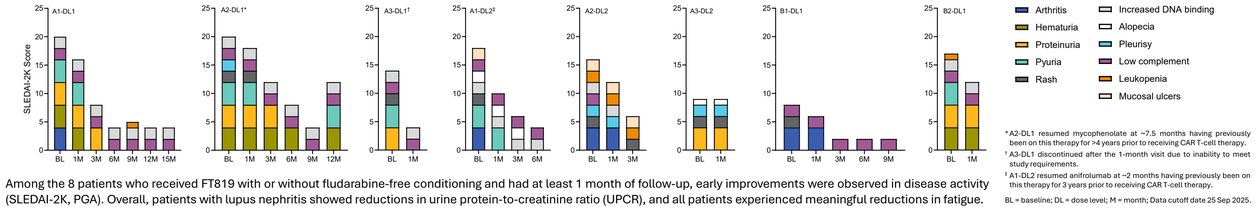
Early and sustained improvement in SLE disease activity following treatment with FT819 with less-intensive or no conditioning chemotherapy (CCT)

Figure 3. SLEDAI-2K, PGA, UPCR, and FACIT-Fatigue Assessed at Baseline (Pre-FT819) and Study Time Points



BILAG = British Isles Lupus Assessment Group; BL = baseline; CCT = conditioning chemotherapy; FACIT = Functional Assessment of Chronic Illness Therapy; M = month; PGA = Physician Global Assessment; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR = urine protein-to-creatinine ratio. Data cutoff date 25 Sep 2025.

Figure 4. SLEDAI-2K Scores for Each Patient at Baseline (Pre-FT819) and Study Time Points



Among the 8 patients who received FT819 with or without fludarabine-free conditioning and had at least 1 month of follow-up, early improvements were observed in disease activity (SLEDAI-2K, PGA). Overall, patients with lupus nephritis showed reductions in urine protein-to-creatinine ratio (UPCR), and all patients experienced meaningful reductions in fatigue.

* A2-DL1 resumed mycophenolate at ~7.5 months having previously been on this therapy for >4 years prior to receiving CAR T-cell therapy.
† A3-DL1 discontinued after the 1-month visit due to inability to meet study requirements.
‡ A1-DL2 resumed anifrolumab at ~2 months having previously been on this therapy for 3 years prior to receiving CAR T-cell therapy.

BL = baseline; DL = dose level; M = month; Data cutoff date 25 Sep 2025.

No high-grade CRS, ICANS, GvHD, or DLTs observed in FT819-treated patients with at least 1 month follow-up

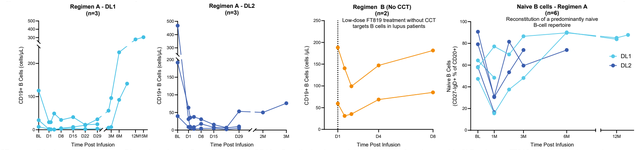
Table 3. Preliminary Clinical Safety Data: Select Adverse Events of Interest (n=8)

	Regimen A						Regimen B	
Patient (conditioning)	**A1-DL1 (Benda)**	**A2-DL1 (CY)**	**A3-DL1 (CY)**	**A1-DL2 (CY)**	**A2-DL2 (Benda)**	**A3-DL2 (CY)**	**B1-DL1 (none)**	**B2-DL1 (none)**
CRS	-	-	-	Grade 2	Grade 1	Grade 1	-	-
Cytopenia*	Grade 2	Grade 4	-	Grade 4	-	-	Grade 2	-
Infection Grade ≥3†	-	-	-	Grade 3	-	-	Grade 3	-

Benda = bendamustine; CRS = cytokine release syndrome; CY = cyclophosphamide; DL = dose level; DLT = dose-limiting toxicity; GvHD = graft-versus-host-disease; ICANS = immune effector cell-associated neurotoxicity syndrome. Patients having more than one AE within a preferred term (PT) are counted only once for that PT at the maximum severity.
* Cytopenia includes any PTs of anaemia, leukopenia, neutropenia, neutrophil count decreased, lymphopenia, pancytopenia, and thrombocytopenia.
† Infection includes influenza and urinary tract infection. Data cutoff date 25 Sep 2025.

FT819 induces host CD19+ B-cell depletion

Figure 5. Host B-Cell Depletion Following Treatment with FT819 in Patients with at Least 1 Month of Follow-up



CCT = conditioning chemotherapy; DL = dose level. Quantification of CD19+ B cells in the peripheral blood of patients with SLE prior to FT819 infusion and at subsequent time points.
Reference: Greene T, et al. Longitudinal analysis of B cell remodeling in systemic lupus erythematosus following iPSC-derived CAR T-cell therapy [poster]. Presented at: ACR Convergence 2025; October 24–29, 2025; Chicago, IL. Poster #2454.

Summary

Preliminary data in patients with moderate-to-severe SLE treated with FT819 combined with less-intensive or no conditioning chemotherapy show:

- **Promising initial efficacy**
- **Durability of response**
- **Differentiated safety profile in line with FT819 used in B-cell malignancies (n=54)**
- **Effective B-cell depletion**
- **Demonstration of broad patient access**
- **Consistently manufactured drug product**
- **On-demand availability**
- **Reduced hospitalization requirements**

These findings support the continued evaluation of FT819 in SLE with a potential path to a registrational trial and the opportunity to treat other B-cell mediated autoimmune diseases (ANCA-associated vasculitis, idiopathic inflammatory myositis, and systemic sclerosis) that are now included in the FT819 protocol.

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