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

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Background

Anti-CD19 CAR T-cell therapy shows promise in autoimmune diseases, but accessibility is limited.

Autologous CAR T-cell therapy represents a potentially transformative therapy in autoimmune disease, but has challenges:

- Prolonged pre- and post-apheresis timelines, 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 designed to address these challenges:

- Derived from an iPSC master cell bank
- Produced for on-demand availability and unencumbered accessibility

FT819 is designed to improve efficacy and safety through the following mechanisms:

- 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 and enhanced product consistency and quality, while maintaining CAR expression under control of the endogenous T-cell promoter
- Complete bi-allelic disruption of TCR expression at the CAR insertion site, reducing risk of GvHD

FT819 is under study in a Phase 1, open-label, dose-escalation trial (NCT06308978) in patients with B-cell-mediated autoimmune diseases. Here, we describe the study design and present initial data in adults with SLE.

Figure 1. Unique Platform for Delivery of Off-the-Shelf Cellular Therapies

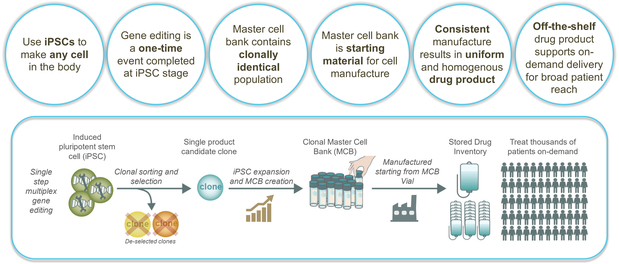
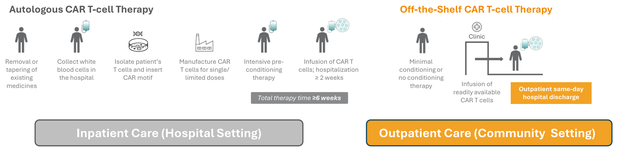


Figure 2. Autologous Versus Off-the-Shelf CAR T-cell Therapy

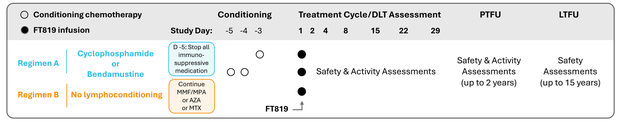


- ✓ Successfully dosed FT819 in an outpatient setting with same-day discharge
- ✓ Outpatient or same-day discharge with reduced or no conditioning chemotherapy and on-demand availability facilitates broad patient access
- ✓ Off-the-shelf CAR T-cell therapy in community hospital-based settings reduces healthcare infrastructure burden and supports a viable, scalable, and practical therapeutic paradigm

Methods

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

Figure 3. Phase 1 Trial Design



Single-dose FT819 administration under 2 regimens in patients aged 12-70 years:

- **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 (MTX, MMF/MPA, or AZA)

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

Patient Enrollment

At baseline, patients were young (mean age 31 years); 92% female and had treatment-refractory SLE, with a median disease duration of 8.8 years and a median of 7 prior treatment failures.

As of 23 December 2025, 14 patients have received a single dose of FT819 across 11 active sites in the United States and 3 in the United Kingdom:

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

Baseline characteristics for the 13 patients with SLE are shown below.

Table 1. Baseline Characteristics of SLE Patients Treated With FT819

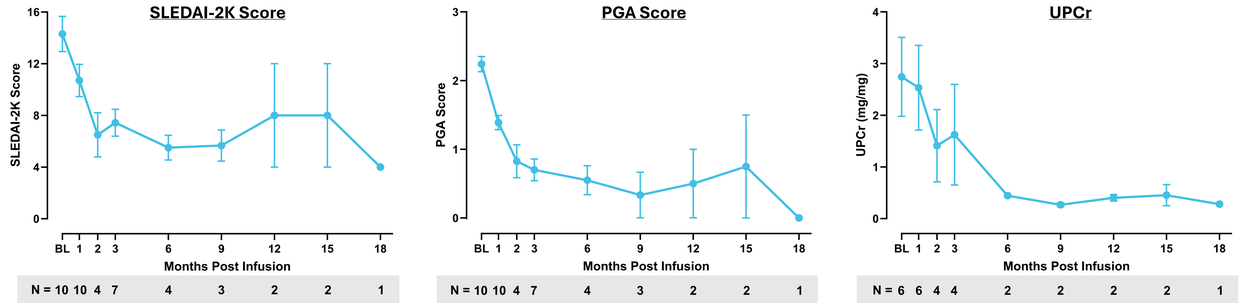
SLE Parameter	SLE Population (N=13)
Regimen, n	Regimen A: n=10; Regimen B: n=3
Age, y, mean (range)	31.2 (19-57)
Female, n (%)	12 (92.3)
SLE duration, y, median (range)	8.8 (1.0-33.7)
Positive anti-dsDNA or anti-Smith, n (%)	11 (84.6)
Prior therapies, median (range)	7 (3-10)
Follow-up, months, median (range)	4.21 (0.5-20.7)
Active lupus nephritis, n (%)*	7 (53.8)
Class III ± V	2 (28.6)
Class IV ± V	5 (71.4)
UPCr, mean (SD)†	2.55 (1.78)
SLEDAI-2K, median (range)	14.0 (8-20)
PGA, mean (SD)	2.15 (0.36)
FACIT-Fatigue score, mean (SD)	24.2 (12.94)

Data cutoff 23 Dec 2025.
* Regimen A, n=6; Regimen B, n=1
† Measured in patients with active lupus nephritis at baseline.
All patients had previously received glucocorticoids and hydroxychloroquine.

Results

Early and sustained improvement was observed in SLEDAI-2K, UPCr, PGA, and FACIT-Fatigue following treatment with FT819 with less-intensive conditioning.

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



Data cutoff 23 Dec 2025. Mean ± SEM. Notes: FT819 administered on Day 1. One patient resumed mycophenolate at ~7.5 months, having received this therapy for >4 years prior to CAR T-cell therapy. One patient (without lupus nephritis) resumed anifrolumab at ~2 months, after ~3 years of prior treatment before CAR T-cell therapy. One patient discontinued the study after the Month 1 visit due to inability to meet trial requirements.

Clinically meaningful improvements were observed in disease activity and patient-reported outcome measures (Figure 4):

- **SLEDAI-2K**: Scores decreased by 13 points from baseline at Month 6 (mean ± SEM)
- **PGA**: Scores decreased by 1.75 points from baseline at Month 6 (mean ± SEM)
- **UPCr**: Levels decreased by 0.90 and 1.14 mg/mg from baseline at Months 3 and 6, respectively (mean ± SEM)
- **FACIT-Fatigue**: Scores improved by 23.4 ± 5.98, 24.3 ± 3.07, and 25.0 ± 3.00 points from baseline at Months 3, 6, and 12, respectively (mean ± SEM; data not shown)

These improvements were observed early following treatment with FT819 using less-intensive conditioning chemotherapy in Regimen A (≥1-month follow-up) and were maintained over time.

All patients tolerated FT819 without DLT. No Grade >2 CRS, ICANS, GvHD, or deaths were reported on study.

Table 2. Preliminary Safety Data of FT819 in SLE and SSc: Select AESIs

Safety Parameter	Incidence, n (%); (N=14)
CRS (Grades 1 and 2)	3 (21.4)
CRS (Grade ≥3)	0
ICANS	0
GvHD	0
Hypogammaglobinemia	0
Dose-limiting toxicity	0
Grade ≥3 adverse event (any)	4 (28.6)
Infection (Grade ≥3)*	2 (14.3)
Cytopenia (Grade ≥3)†	3 (21.4)

Data cutoff 23 Dec 2025. Safety population (N=14) includes all dosed patients (13 with SLE; 1 with SSc).
* Infections include influenza and urinary tract infection.
† Cytopenia includes any anaemia, haemoglobin decreased, pancytopenia, leukopenia, white blood cell count decreased, lymphopenia, lymphocyte count decreased, neutropenia, neutrophil count decreased, thrombocytopenia, and platelet count decreased.

Conclusion

Preliminary data in patients with moderate-to-severe SLE treated with FT819 combined with less-intensive conditioning chemotherapy demonstrated:

- **Favorable safety and tolerability**
- **Encouraging efficacy, including clinically meaningful and persistent reduction in UPCr**
- **Effective B-cell depletion**
- **Successful administration in an outpatient setting**

Collectively, these results support further clinical development of FT819 in SLE, with a potential path to a registrational trial and continued evaluation in other B-cell mediated autoimmune diseases (ANCA-associated vasculitis, idiopathic inflammatory myositis, and systemic sclerosis).

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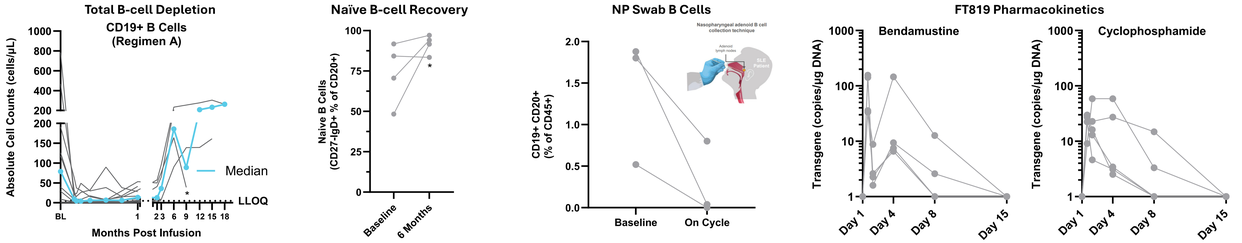
FT819 induced host CD19+ B-cell depletion and a predominantly naïve B-cell phenotype upon recovery.



Deep initial B-cell depletion in periphery followed by recovery between 1 and 6 months

Post-recovery naïve B cells dominate and increase in proportion.

Secondary lymphoid tissue depletion (sampled on Day 8 or 15)

Bendamustine associates with greater expansion of FT819 (expansion is associated with response in oncology).

* Patient resumed anifrolumab (~2 months); later discontinued hydroxychloroquine and anifrolumab at approximately Month 8 (per investigator).

Abbreviations: AAV = ANCA-associated vasculitis; AESI = adverse event of special interest; AZA = azathioprine; 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; PGA = Physician Global Assessment; MMF/MPA = mycophenolate mofetil/mycophenolic acid; MTX = methotrexate; PK = pharmacokinetics; PTFU = post-treatment follow-up; SLE = systemic lupus erythematosus; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SSc = systemic sclerosis; TCR = T-cell receptor; UPCr = urine protein-to-creatinine ratio.

Disclosures: J Medlin: Nothing to disclose; A BitMansour: Fate Therapeutics, Inc. (Employee and stockholder).