The Development of an Off-the-Shelf CAR T-Cell Therapy Targeting CD19 and CD38 for Broad Application in Autoimmune Disease

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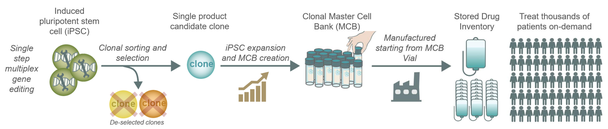
Introduction

Induced Pluripotent Stem Cell (iPSC) derived T cells overcome the challenges associated with autologous CAR T-cell therapies & allow for broad patient access



Platform Advantages

- ✓ **Defined Clonal Master Cell Bank (MCB)**: Single-cell derived, genetically uniform, selected for potency and genomic integrity.
- ✓ **Engineered MCB Starting Material**: One-time edit, highly scalable, donor-independent, and enables consistent high-quality products.
- ✓ **Modular Innovation**: Accelerates development through efficient, multiplexed precision engineering.

iPSC-Derived Cell Therapy Products

- ✓ **Reliable, Scalable Drug Product**: Consistent, well-characterized, >5-year shelf stability; ~50,000-dose GMP-scale capacity at current site.
- ✓ **Cost-Effective & Consistent**: Low COGs, inventory-based economics, and no donor variability.
- ✓ **Patient-Centered Therapy**: Off-the-shelf, antibody-like treatment with repeat dosing, low toxicity, and outpatient-friendly administration.

Autologous CAR T-cell Therapy

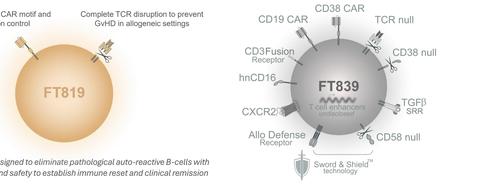
Total therapy time ≥6 weeks

Fate Therapeutics' CAR T-cell Therapy

Total therapy time ~1 week

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

FT819 and FT839 provide unique advantages in targeting pathological B cells and aberrant immune cells to eliminate autoimmune disease



CD19 CAR T-cell designed to eliminate pathological auto-reactive B-cells with balanced efficacy and safety to establish immune reset and clinical remission

Summary & Conclusions

- Autologous CAR T-cell therapy is a transformative medicine, but has limitations with 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 and designed to improve efficacy and safety with broad patient access
- Preliminary data in patients with moderate-to-severe systemic lupus erythematosus (SLE) treated with FT819 combined with less-intensive or no conditioning chemotherapy exhibits promising initial efficacy, durability of response, a differentiated safety profile, effective B-cell depletion, potential for broad patient access, manufactured drug product that is uniform and consistent, on-demand availability and 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 FT819-102 clinical protocol
- FT839 is a next generation off-the-shelf CAR T-cell that uniquely incorporates novel synthetic functional elements that enable multi-antigen targeting to eliminate a range of pathogenic immune cell types without requiring conditioning chemotherapy to treat complex autoimmune diseases

Results

Updated data from FT819 clinical study in SLE shows accelerated enrollment with continued favorable safety profile

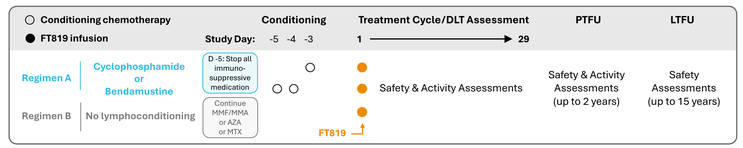


Figure 1. FT819-102 Study Treatment Schema. A Phase 1 dose-escalation study evaluating the safety, pharmacokinetics, and anti-B-cell activity of FT819 in patients with B-cell mediated autoimmune diseases is ongoing (NCT06308978). AZA = azathioprine; DLT = dose-limiting toxicity; LTFU = long-term follow-up; MMF/MPA = mycophenolate mofetil/mycophenolic acid; MTX = methotrexate; PTFU = post-treatment follow-up. Panel on right depicts the frequency of activated sites that are enrolling patients and the number of patients enrolled as of November 25, 2025.

Study FT819-102 Patient Enrollment & Safety Summary

- As of November 25, 2025, 13 patients have received a single dose of FT819 across 11 active sites in the US and 3 in the UK: 11 patients with fludarabine-free, less-intensive conditioning chemotherapy (Regimen A) and 2 without conditioning chemotherapy (on background therapy; Regimen B).
  - Baseline clinical characteristics for the 12 patients with systemic lupus erythematosus (SLE) are summarized in Table 1.
  - At baseline, the single patient with systemic sclerosis (SSc) is a 31-year-old female with 5 years of diffuse SSc and interstitial lung disease, with prior therapies including hydroxychloroquine (HCQ), MTX, MMF/MPA, IV immunoglobulin, rituximab, tocilizumab, and prednisone (concurrent at baseline). This patient is pending the 1-month follow-up visit.
- Among patients with at least 1 month of follow-up, no high-grade CRS, ICANS, GvHD, or DLTs were observed (Table 2).

Baseline Parameter	Overall (N=13) Regimen A, n=11; Regimen B, n=2
SSc, n	**1**
SLE, n – Clinical Characteristics	**12**
Age, y, mean (range)	30.8 (19-57)
Female, n (%)	11 (92)
SLE duration, y, median (range)	8.7 (1-34)
Prior therapies, n, median (range)	7 (3-10)
Follow-up, month, median (range)	4 (0-19.5)
SLEDAI-2K, median (range)	14 (8-20)
Lupus nephritis, n (%)	7 (58)
UPCr, mean ± SD*	2.6 ± 1.8
PGA, mean ± SD	2.3 ± 0.4
FACIT-Fatigue score, mean ± SD	23 ± 13

Table 1. Baseline Characteristics of SLE Patients Treated with FT819. All patients had previously received glucocorticoids (GC) and HCQ. * Measured in patients with lupus nephritis. FACIT = Functional Assessment of Chronic Illness Therapy; PGA = Physician's Global Assessment; SD = standard deviation; SLE = systemic lupus erythematosus; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SSc = systemic sclerosis; UPCr = urine protein-to-creatinine ratio.

Safety Parameter	Incidence, n (%) Among Patients with ≥1 Month Follow-up (N=10)
CRS, Grade 1-2	3 (30)
CRS, Grade ≥3	0
ICANS/neurotoxicity	0
GvHD	0
DLT	0
Grade ≥3 AEs (any)	3 (30)
Infection, Grade ≥3*	2 (20)
Cytopenia, Grade ≥3†	2 (20)
Hypogammaglobulinemia	0

Table 2. Preliminary Clinical Safety Data: Select Adverse Events of Interest. All patients with ≥1 month of follow-up had SLE. Regimen A, n=8; Regimen B, n=2. Data cutoff date 22 Oct 2025.
* Infection includes influenza and urinary tract infection.
† Cytopenia includes any PTs of anaemia, leukopenia, neutropenia, neutrophil count decreased, lymphopenia, pancytopenia, and thrombocytopenia.
AE = adverse event; CRS = cytokine release syndrome; DLT = dose-limiting toxicity; GvHD = graft-versus-host-disease; ICANS = immune effector cell-associated neurotoxicity syndrome; SLE = systemic lupus erythematosus.

Early and sustained improvement in SLE disease activity following FT819 treatment is further supported with preliminary data suggestive of a potential dose response trend in enhancing the kinetics of disease reduction

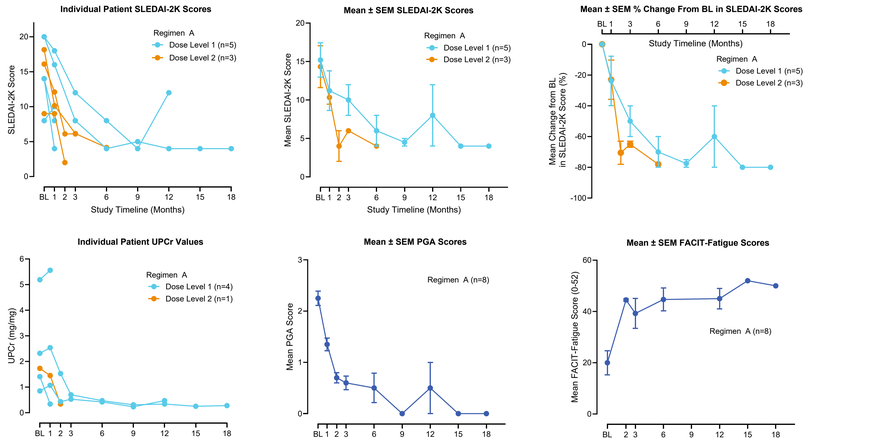


Figure 2. SLEDAI-2K, PGA, UPCr, and FACIT-Fatigue Assessed at Baseline (Pre-FT819) and Study Time Points. Includes study visits up to 22 Oct 2025. BL = baseline; FACIT = Functional Assessment of Chronic Illness Therapy; PGA = Physician's Global Assessment; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; UPCr = urine protein-to-creatinine ratio. SEM is represented by error bars.

FT819 treatment induces a dose dependent depletion of CD19+ B-cells and reemergence of naïve B cell subsets

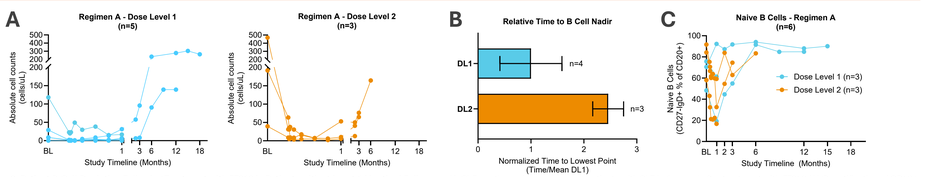


Figure 3. Patient B-Cell Depletion Following Treatment with FT819 in Patients with at Least 1 Month of Follow-up. (A-C) From the peripheral blood of patients with SLE before and after treatment with FT819 **(A)** Quantification of CD19+ B cells; **(B)** Relative time to B cell nadir presented as mean ± SE of values normalized to the average day of the DL1 nadir; and **(C)** Proportion of naive B cells. Reference: Greene T, et al. ACR Convergence 2025; Poster #2454.

FT839: A next generation CAR T cell designed to eliminate multiple immune cell types in complex disease settings

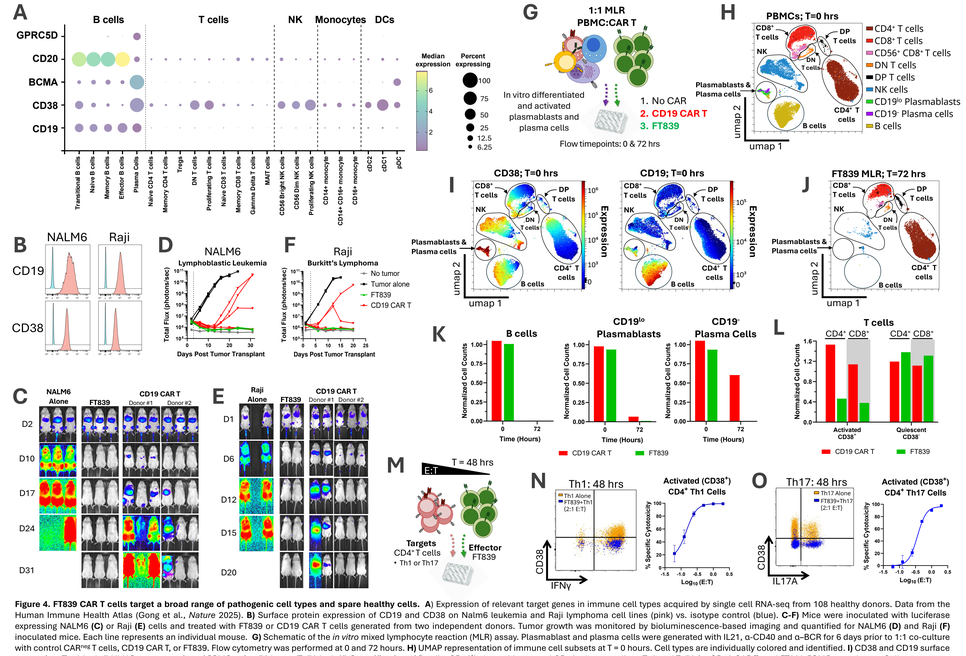


Figure 4. FT839 CAR T cells target a broad range of pathogenic cell types and spare healthy cells. A) Expression of relevant target genes in immune cell types acquired by single cell RNA-seq from 108 healthy donors. Data from the Human Immune Health Atlas (Gong et al., *Nature* 2025). **B)** Surface protein expression of CD19 and CD38 on Nalm6 leukemia and Raji lymphoma cell lines (pink) vs. isotype control (blue). **C-F)** Mice were inoculated with luciferase expressing NALM6 **(C)** or Raji **(E)** cells and treated with FT839 or CD19 CAR T cells generated from two independent donors. Tumor growth was monitored by bioluminescence-based imaging and quantified for NALM6 **(D)** and Raji **(F)** inoculated mice. Each line represents an individual mouse. **G)** Schematic of the *in vitro* mixed lymphocyte reaction (MLR) assay. Plasmablast and plasma cells were generated with IL21, α-CD40 and α-BCR for 6 days prior to 1:1 co-culture with control CAR^{neg} T cells, CD19 CAR T, or FT839. Flow cytometry was performed at 0 and 72 hours. **H)** UMAP representation of immune cell subsets at T = 0 hours. Cell types are individually colored and identified. **I)** CD38 and CD19 surface expression (T = 0 hrs). **J)** UMAP representation of PBMCs after 72 hours (T=72 hrs). **K)** Quantification of B cells, CD19^{lo} plasmablasts, and CD19^{-} plasma cells at T=0 and T=72 for CD19 CAR T- and FT839-PBMC co-cultures. Cell counts were normalized to control CAR^{neg} T cell-PBMC co-cultures. **L)** Quantification of CD38^{+} and CD38^{-}, CD4^{+} and CD8^{+} T cells at T=72 hrs. Cell counts were normalized to the CAR^{neg} T cell-PBMC co-cultures. **M)** Schematic of 48-hour co-culture with FT839 and polarized CD4^{+} cells. Representative flow cytometry plots and % specific cytotoxicity are shown for FT839 co-cultures with **N)** Th1 and **O)** Th17 target cells.

FT839 uniquely exhibits functional persistence in allogeneic settings in the absence of conditioning chemotherapy and shows enhanced capacity for selective elimination of aberrant immune subsets in autoimmune patient derived PBMCs

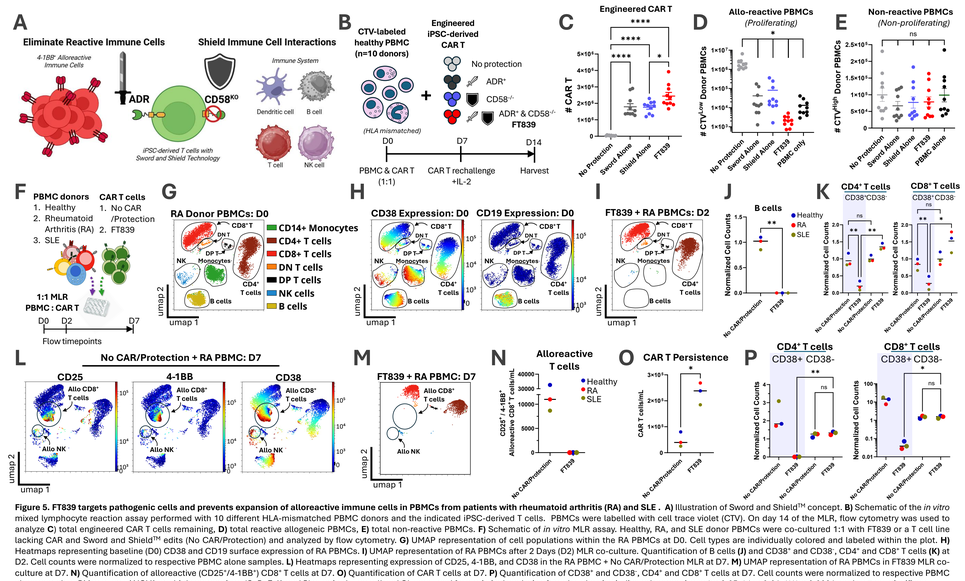


Figure 5. FT839 targets pathogenic cells and prevents expansion of alloreactive immune cells in PBMCs from patients with rheumatoid arthritis (RA) and SLE . A) Illustration of Sword and Shield™ concept. **B)** Schematic of the *in vitro* mixed lymphocyte reaction assay performed with 10 different HLA-mismatched PBMC donors and the indicated iPSC-derived T cells. PBMCs were labelled with cell trace violet (CTV). On day 14 of the MLR, flow cytometry was used to analyze **C)** total engineered CAR T cells remaining, **D)** total reactive allogeneic PBMCs, **E)** total non-reactive PBMCs. **F)** Schematic of *in vitro* MLR assay. Healthy, RA, and SLE donor PBMCs were co-cultured 1:1 with FT839 or a T cell line lacking CAR and Sword and Shield™ edits (No CAR/Protection) and analyzed by flow cytometry. **G)** UMAP representation of cell populations within the RA PBMCs at D0. Cell types are individually colored and labelled within the plot. **H)** Heatmaps representing baseline (D0) CD38 and CD19 surface expression of RA PBMCs. **I)** UMAP representation of RA PBMCs after 2 Days (D2) MLR co-culture. Quantification of B cells **(J)** and CD38^{+} and CD38^{-}, CD4^{+} and CD8^{+} T cells **(K)** at D2. Cell counts were normalized to respective PBMC alone samples. **L)** Heatmaps representing expression of CD25, 4-1BB, and CD38 in the RA PBMC + No CAR/Protection MLR at D7. **M)** UMAP representation of RA PBMCs in FT839 MLR co-culture at D7. **N)** Quantification of alloreactive (CD25^{+}/4-1BB^{+}) CD8^{+} T cells at D7. **O)** Quantification of CAR T cells at D7. **P)** Quantification of CD38^{+} and CD38^{-}, CD4^{+} and CD8^{+} T cells at D7. Cell counts were normalized to respective PBMC alone samples. *RM one-way ANOVA, multiple comparison (C, D, E, K, and P) or paired t-tests (J and O) were used for statistical analysis of graphs, showing indicated comparisons *p<0.05, **p<0.01, ***p<0.0001, and ns = not significant.*