CAR T cells Targeting pan-Tumor Antigens MICA/B can be Uniquely Combined with SOC Treatments without Conditioning Chemotherapy for Broad and Effective Therapeutic Application in Cancer

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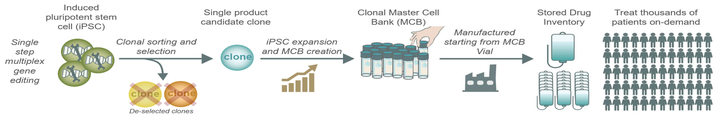
INTRODUCTION

Broad patient access with highly engineered allogeneic CAR T cells derived from induced pluripotent stem cells (iPSC)



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.
- ✓ **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

Removal or tapering of existing medicines → Collect white blood cells in the hospital → Isolate patient's T cells and edit through CD19 CAR insertion → Manufacture CAR T cells for single/ limited doses → Intensive conditioning therapy → Infusion of CAR T cells; Hospitalization ≥2 weeks

Total therapy time ≥6 weeks

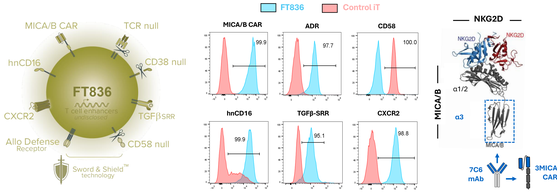
Fate Therapeutics' CAR T-cell Therapy

Infusion of readily available CAR T cells → Clinic → Opportunity for same-day discharge and limited hospitalization

- No leukapheresis or complicated manufacturing logistics
- Manufactured at large scale to produce uniform and reproducible CAR T-cell drug product
- Available on-demand for broad patient accessibility
- Potential for shorter or no hospitalization without conditioning chemotherapy

Total therapy time ≥6 weeks

Unique engineering profile of FT836 supports rational combination with standard of care therapeutics for both hematological and solid tumors



- MICA/B is broadly expressed in many human cancers
- Shedding of MICA/B is a common escape mechanism
- α3 targeting prevents MICA/B shedding
- FT836 targets the α3 domain and is resistant to suppression by soluble MICA/B

Summary & Conclusions

FT836 is a next generation, iPSC derived CAR T-cell, uniquely designed for pan-tumor targeting of both solid tumors and hematological malignancies and engineered to eliminate the need for conditioning chemotherapy and thereby productively combine with standard of care therapeutics

- ✓ **Pan-tumor targeting**: Unique recognition of highly conserved α3 domain of MICA/B; synergistic with standard of care treatments (*e.g.* IMIDs, radiotherapy, and chemotherapy) that enhance MICA/B expression.
- ✓ **Multi-Antigen targeting:** Engineered to express hnCD16 to enable ADCC when combined with therapeutic monoclonal antibodies to combat tumor heterogeneity and antigen escape.
- ✓ **Resistance to host immune cell-mediated rejection:** Sword & Shield™ technology consisting of CD58 knockout ($CD58^{KO}$) for immune **evasion** and alloimmune defense receptor (ADR) to **selectively eliminate** allogeneic immune responses.
- ✓ **Elimination of lymphodepleting preconditioning**: Sword & Shield™ (ADR and $CD58^{KO}$) dual-resistance strategy enabling administration without the need for pre-conditioning chemotherapy eliminating the toxicity risks of lymphodepletion and can rationally combined with standard of care treatments to enhance performance, increase specific trafficking to tumors, and resist the immunosuppressive tumor microenvironment.
- ✓ **Off-the-shelf**: Manufactured from an iPSC master cell bank that is derived from a fully characterized and multiplex-engineered clonal iPSC line, delivering uniform expression of functional elements at a large scale to support on-demand delivery.

FT836 was awarded TRAN1 grant from CIRM in January of 2025 to support its clinical translation. Phase 1 clinical trial for FT836 for advanced solid tumors without conditioning chemotherapy is open for enrollment (NCT07216105).

RESULTS

Universal anti-tumor activity of FT839 via novel MICA/B CAR or in combination with therapeutic monoclonal antibodies to mitigate antigen heterogeneity

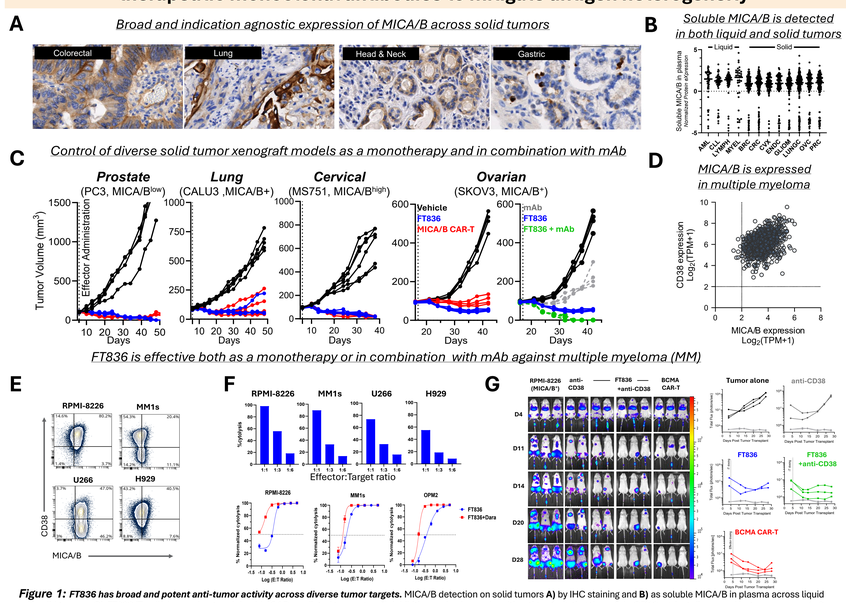


Figure 1: *FT836 has broad and potent anti-tumor activity across diverse tumor targets.* MICA/B detection on solid tumors **A)** by IHC staining and **B)** as soluble MICA/B in plasma across liquid and solid tumors. **C)** *FT836 iT cells have robust and durable CAR-mediated tumor growth inhibition and enhanced multi-antigen targeting through hnCD16 against diverse subcutaneous xenograft models.* **D)** MICA/B and CD38 gene expression on MM targets from COMMPASS database. **E)** Flow cytometry staining of CD38 and MICA/B expression on MM cell lines. FT836 mediated cytotoxicity on MM targets as monotherapy **F)** top panel and combination with mAb, bottom panel in-vitro and **G)** in-vivo on a MM (RPMI8226 $MICA/B^{High}$) *liquid tumor model, comparable to 1st CAR T cell control. A single dose of FT836 was combined with a single dose of Herceptin (SKOV3 model) or Daratumumab (RPMI8226) for mAb combination arm.*

Sword & Shield™ technology eliminates the need for conditioning chemotherapy, selectively eliminating allogeneic immune cells and supportingg the functional persistence of FT839

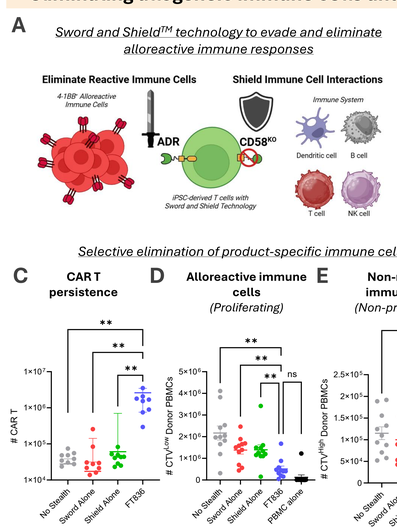
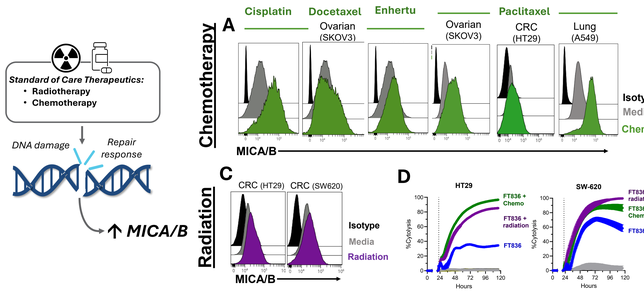


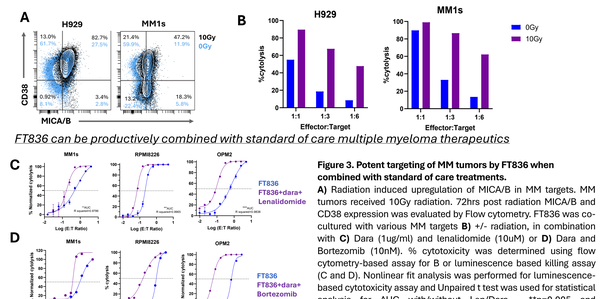
Figure 2. The Sword and Shield™ (ADR and CD58KO) technology protects iPSC-derived T cells from allorejection, prevents expansion of highly reactive allo-PBMC while sparing non-reactive allo-PBMC. **A)** Illustration of Sword and Shield™ concept. **B)** Schematic of the *in vitro* mixed lymphocyte reaction performed with 10 different allogeneic PBMC donors and the indicated iPSC-derived T cells. On day 14 of the MLR, flow cytometry was used to analyze **C)** total engineered CAR T cells remaining, **D)** total reactive allogeneic PBMC, and **E)** total non-reactive PBMCs. **F)** 3D Tri-cultures were set up to test the ability of Sword & Shield™ iT cells to resist primed alloreactive PBMC rejection in comparison to iT cells without Sword & Shield™ protection. **G)** FT836 mediated cytolysis of tumor spheroids was measured in a serial restimulation over two rounds of killing compared to no protection CAR T with/without primed PBMCs. **H)** Flow cytometric analysis of the indicated iT cells present at the end of each round. *One-way ANOVA, multiple comparison was used for statistical analysis of all graphs, showing indicated comparisons with *p<0.05, **p<0.001, ***p<0.0001, and ns = not significant.*

FT836 platform is compatible with and enables rational combinations with standard of care therapeutics across solid and liquid tumors

Chemotherapy and radiotherapy upregulate MICA/B expression in solid tumors, enhancing FT836 anti-tumor activity



Radiotherapy upregulates MICA/B & CD38 expression in MM, enhancing FT836 anti-tumor activity



FT836 can be productively combined with standard of care multiple myeloma therapeutics

Figure 3. Potent targeting of MM tumors by FT836 when combined with standard of care treatments.
A) Solid tumor targets treated with different chemotherapeutic agents and MICA/B expression was evaluated 48hrs post treatment by Flow cytometry. **B)** FT836 was co-cultured with various tumor targets +/- multiple chemotherapy agents for 72hrs and cytotoxicity was measured using xCelligence instrument. 3 representative cytolysis plots of SKOV3 tumors treated with ADC agent (Enhertu), Docetaxel and Paclitaxel. **C)** Representative flow cytometry plots for MICA/B expression changes post radiation (10Gy). **D)** MICA/B targeting by FT836 was evaluated on multiple solid tumor targets 72hrs post +/- radiation (10Gy) or +/- paclitaxel treatment (10nM) at 1:4 Effector to Target ratio using xCelligence system.

Enhanced FT836 trafficking to TME and anti-tumor activity by upregulation of CXCR2 ligand, CXCL8 (IL8) expression on targets following chemo preconditioning

Chemo/radiotherapy upregulate CXCR2 ligands (CXCL8), correlating with enhanced tumor control and effector infiltration

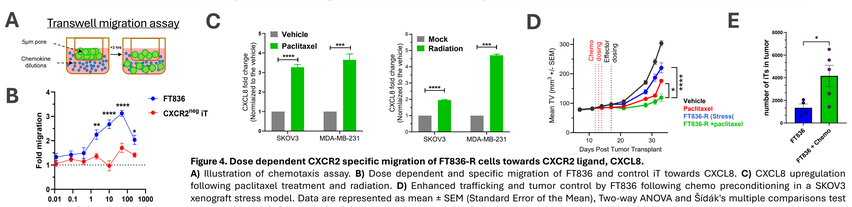
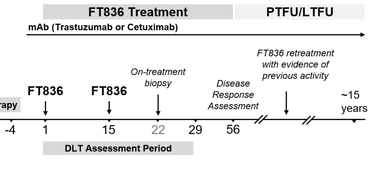


Figure 4. Dose dependent CXCR2 specific migration of FT836-R cells towards CXCR2 ligand, CXCL8.
A) Illustration of chemotaxis assay. **B)** Dose dependent and specific migration of FT836 and control iT towards CXCL8. **C)** CXCL8 upregulation following paclitaxel treatment and radiation. **D)** Enhanced trafficking and tumor control by FT836 following chemo preconditioning in a SKOV3 xenograft stress model. Data are represented as mean ± SEM (Standard Error of the Mean), Two-way ANOVA and Šídák's multiple comparisons test were used for statistical analysis of dose response curve (* p=0.046 ** p=0.0016, **** p<0.0001). 0.005 (**) and p<0.05(*).

FT836 Phase 1 Clinical Trial and Translational Research



Regimens:
A: *FT836 Monotherapy*
B: *Paclitaxel chemotherapy followed by FT836*
C: *FT836 + Cetuximab*
D: *Paclitaxel chemotherapy followed by FT836 + Cetuximab*
E: *FT836 + Trastuzumab*
F: *Paclitaxel chemotherapy followed by FT836 + Trastuzumab*

This is a phase 1 study of FT836 administered in participants with advanced solid tumors. The primary objectives of the study are to evaluate the safety and tolerability of FT836 with or without paclitaxel and/or trastuzumab or cetuximab, and to determine the recommended phase 2 dose (RP2D) of FT836 in combination with trastuzumab or cetuximab; each objective will be assessed with or without paclitaxel chemotherapy. 3 patients enrolled in FT836-101 Ph1 pan-solid-tumor trial. Multiple Myeloma IIT initiated, with FPI anticipated in Q1 2026.