Fate THERAPEUTICS

Better Cells For Better Therapies™

Programmed Cellular Immunotherapies

Leading the Development of Off-the-Shelf Cell-based Cancer Immunotherapies using Clonal Master Engineered iPSC Lines

January 2021

Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the Company's research and development activities and its progress, plans and timelines for its manufacture, preclinical development and clinical investigation of its product candidates, the timing for the Company's receipt of data from its clinical trials and preclinical studies, the Company's clinical development and regulatory strategy, and the therapeutic and market potential of the Company's product candidates. These and any other forward-looking statements in this presentation are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that results observed in prior studies of its product candidates will not be observed in ongoing or future studies involving these product candidates, the risk of a delay in the initiation of, or in the enrollment or evaluation of subjects in, any clinical studies, and the risk that the Company may cease or delay manufacture, or preclinical or clinical development, of any of its product candidates for a variety of reasons (including regulatory requirements, difficulties in manufacturing or supplying the Company's product candidates, and any adverse events or other negative results that may be observed during preclinical or clinical development). These statements are also subject to other risks and uncertainties as further detailed in the Company's most recently filed periodic report, and subsequent periodic reports filed by the Company, under the Securities Exchange Act of 1934, as amended, any of which could cause actual results to differ materially from those contained in or implied by the forward-looking statements in this presentation. The Company is providing the information in this presentation as of the date hereof and does not undertake any obligation to update any forward-looking statements contained in this presentation unless required by applicable law.

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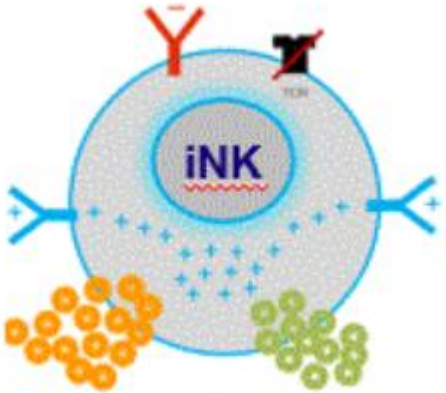
A Remarkable 2-Year Journey of Firsts

Building the Leading Off-the-Shelf NK Cell Cancer Immunotherapy Company

Best-in-Class Lymphoma | Best-in-Class Myeloma | Solid Tumors

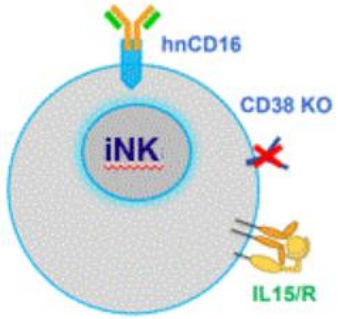
FT500



FT516

FT596

FT538



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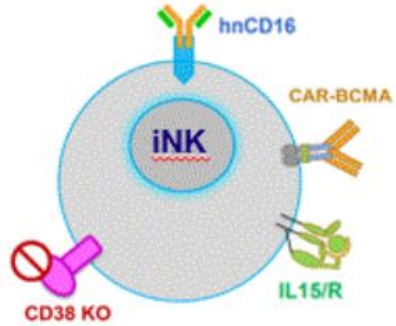

- FT516 + mAbs
- FT538 + mAbs
- CAR MICA/B
- ONO Product 2
- Janssen Targets

July 2018 → Sept 2020

1st IND submission
87 employees
$78M in cash

ONO

janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson

9 Cleared INDs
250+ employees
$930M+ in cash[a]

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[a] *On an as adjusted basis to include January 2021 common stock offering*

Changing the Game in Cell Therapy

Necessary Hurdles to Overcome to Change the Game

1. ***Multiplexed Engineering***. Embed multiple elements of synthetic biology to deliver multiple mechanisms of action, increase therapeutic efficacy and reduce toxicity

2. ***Uniform Product***. Minimize sources of variability (cell source, engineering, production, etc.) to consistently demonstrate identity, purity and potency of cell product

3. ***Mass Production***. Repeatedly operate a GMP manufacturing process that yields hundreds to thousands of doses in single batch to support multi-dose regimens, cost-effective treatment and widespread product availability

4. ***Off-the-shelf Availability***. Cryopreserve cell products in a fill / finish formulation that supports long-term stability, inventory build, and thaw-infuse administration to patients

5. ***Patient Accessibility***. Greatly simplify logistics to enable treatment of many patients on-demand, without delay, and with high convenience

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Changing the Game in Cell Therapy

Universal, Off-the-Shelf Cell Products Derived from Renewable Master Cell Lines

Key Features	Cell Therapy 1.0 and 2.0	Cell Therapy 3.0
Cell Source	Patient and Donor Cells	Renewable Master Cell Line
Genetic Engineering	Random & Variable	Uniform & Complete
Characterization	Imprecise	Well-defined
Product Identity	Heterogeneous	Homogeneous
Manufacturing	Low Yield-to-Cell Dose Ratio	High Yield-to-Cell Dose Ratio
Packaging	Fresh / Short Shelf Life	Cryopreserved / Long Shelf Life
Dosing	Single Dose	Multiple Doses
Delivery	Complex Logistics	Off-the-Shelf
Overall Paradigm	**Process-centric**	**Product-centric**

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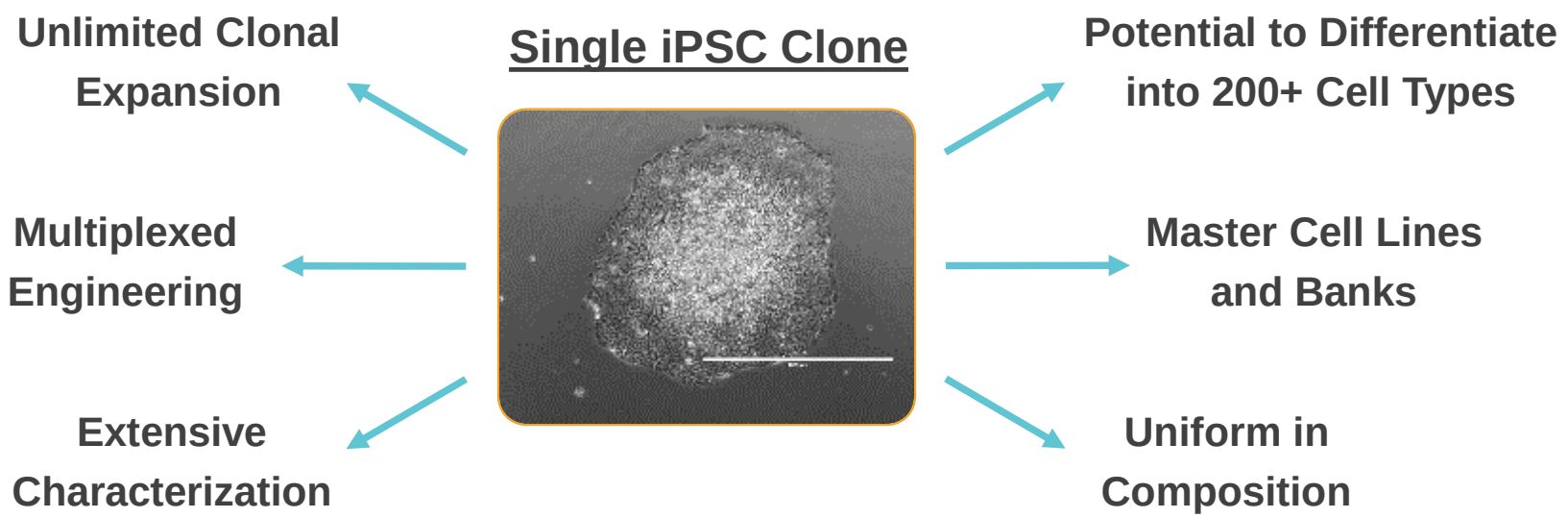
Unique Advantages of Human iPSCs

Single-cell Isolation, Characterization & Selection

A Single Human Induced Pluripotent Stem Cell (iPSC)

A renewable source for making cell products



Fate Therapeutics' iPSC product platform is supported by an IP portfolio of 300+ issued patents and 150+ pending patent applications

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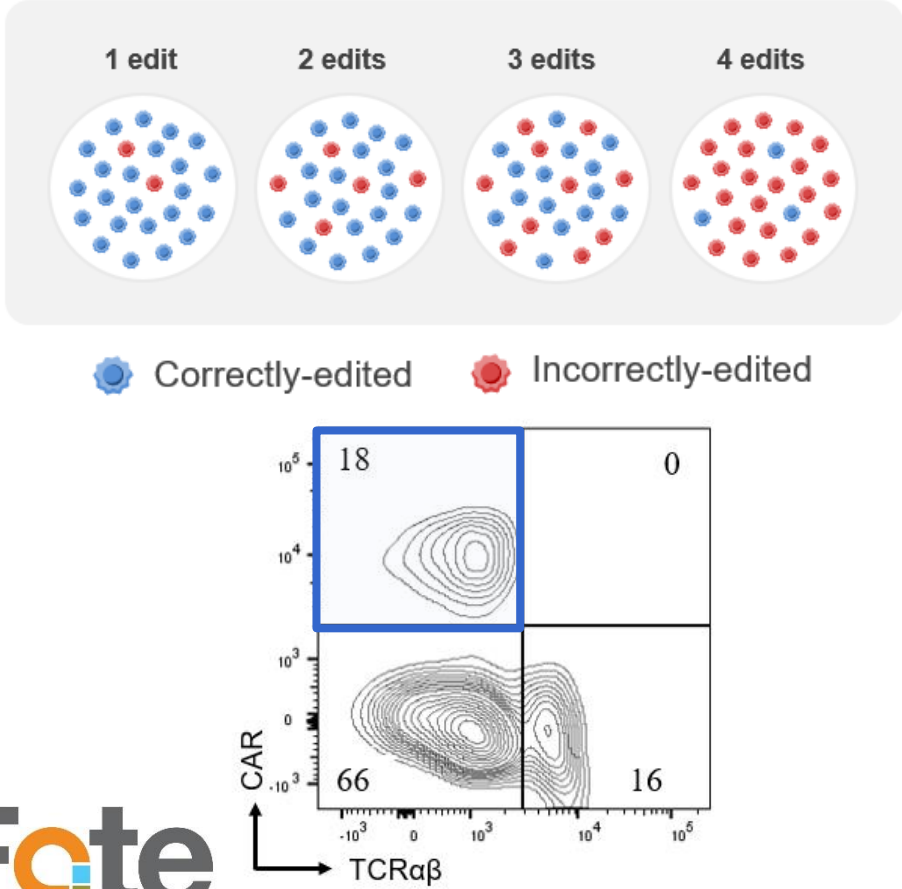
Unique Advantages of Human iPSCs

Creating a Clonal Master Engineered iPSC Line

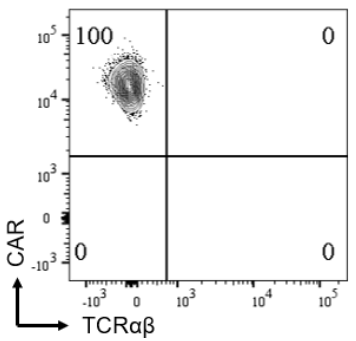
Cell Population Engineering



Single-cell iPSC Isolation, Characterization and Selection

- ✓ *Determination of copy number*
- ✓ *Confirmation of genomic stability*
- ✓ *Confirmation of transgene integration site*
- ✓ *Confirmation of pluripotency and propensity to differentiate*
- ✓ *Confirmation of highly functioning cells*
- ✓ *Confirmation of uniform transgene expression and enhanced function*
- ✓ *A myriad of additional safety and efficacy analyses*

Clonal Master Engineered iPSC Line



4 edits

A Renewable Cell Source for Mass Production of Engineered Immune Cells

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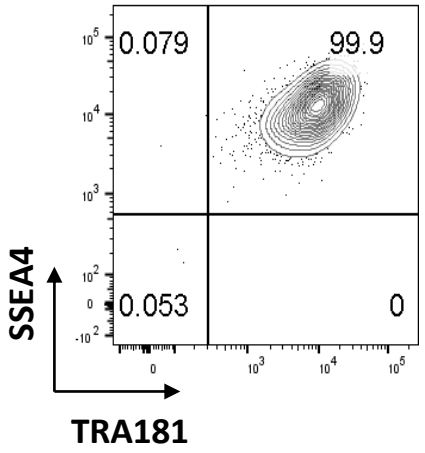
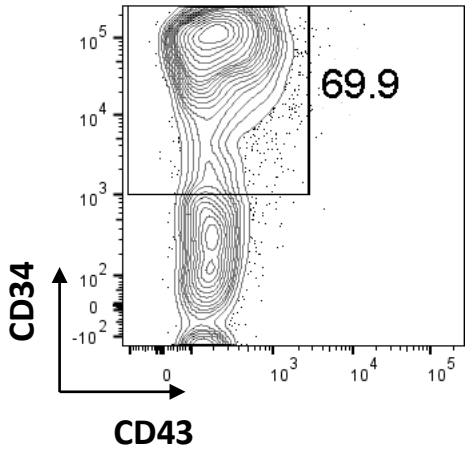
The Making of Bona Fide NK Cells from Clonal Master Engineered iPSC Bank

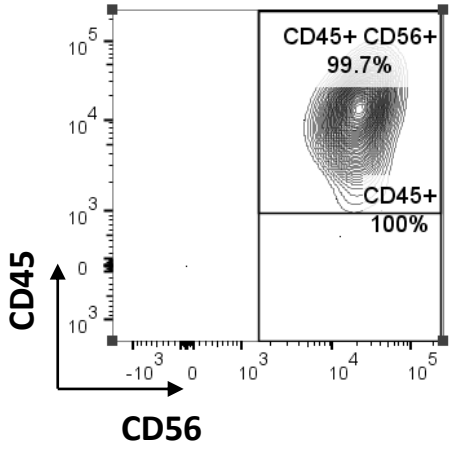
Robust cGMP Process

iPSCs → **iCD34s** → **iNKs**

Day 0 ***Day 10*** ***Day 44[a]***







> 1 million-fold expansion

10^6 iPSCs

> 10^{12} iNKs

- *Homogeneous cell product*
- *100s-1,000s doses per campaign*
- *Low-cost per dose cGMP production*
- *Cryopreserved*
- *High post-thaw viability*

[a] Rezner et al. ASH Annual Meeting 2020

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Off-the-Shelf, iPSC-derived NK Cell Cancer Immunotherapy Franchise

Systematic Build of Industry-Leading iPSC-derived NK Cell Product Pipeline

Universal, Off-the-Shelf NK Cell Cancer Immunotherapy Pipeline

Clonal Master iPSC Line	Synthetic Biology	FT500	FT516	FT596	FT538	FT576	FT536
Multi-faceted Innate Immunity		✓	✓	✓	✓	✓	✓
+ High-Affinity, Non-cleavable CD16	*Augment mAb therapy*		✓	✓	✓	✓	✓
+ IL-15 Receptor Fusion	*Enhance NK cell function*			✓	✓	✓	✓
+ CAR Insertion	*Target tumor antigens*			CD19		BCMA	MICA/B
+ CD38 Knock-out	*Enhance metabolic fitness*				✓	✓	✓
	# of Synthetic Elements	**0**	**1**	**3**	**3**	**4**	**4**

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Off-the-Shelf, iPSC-derived NK Cell Cancer Immunotherapy Franchise

Initial Clinical Validation

Clinical experience supports the transformative potential of iPSC Product Platform

- **Experience**
  - 35+ patients dosed with 150+ doses of iPSC-derived NK cells (FT500, FT516, FT596, FT538)
  - Treated diseases include lymphoma, AML and solid tumors
- **Safety**
  - Demonstrated ability to administer up to 6 doses safely in an outpatient setting
  - No CRS, ICANS or GvHD at dose levels $\leq$ 300M cells / dose
  - No evidence of anti-product T- or B-cell mediated immunogenicity
- **Activity**
  - Clear evidence of anti-tumor activity at initial low doses
  - Patient responses achieved in heavily pre-treated patients with relapsed / refractory disease

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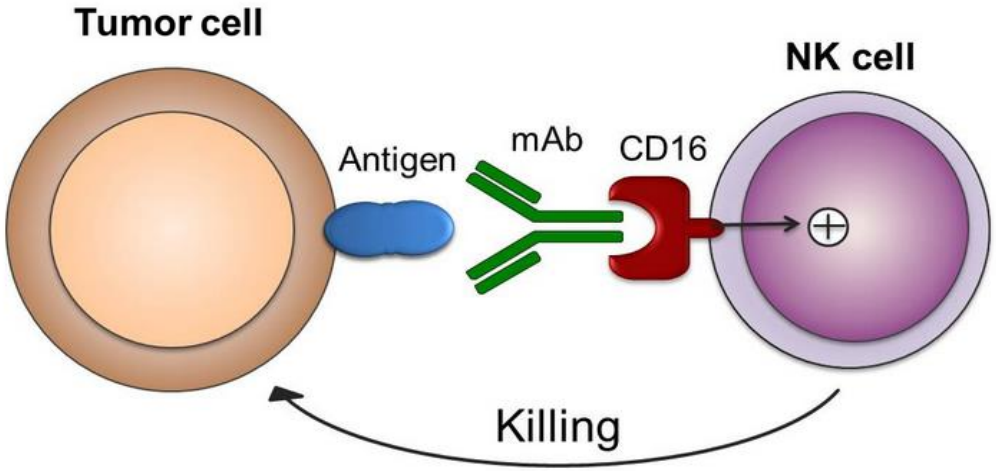
B-cell Malignancy Franchise

FT516: hnCD16 NK Cell Product Candidate

CD16 Fc Receptor Mediates Antibody-Dependent Cellular Cytotoxicity (ADCC)

- **CD16 is an activating receptor expressed on NK cells**
  - Mediates antibody-dependent cellular cytotoxicity (ADCC), a potent anti-tumor mechanism by which NK cells recognize, bind and kill antibody-coated cancer cells
- **CD16 occurs in two variants: high (158V) or low (158F) affinity for the Fc domain of IgG antibodies**
  - Only ~15% of patients are homozygous for 158V
  - Numerous clinical studies with FDA-approved tumor-targeting antibodies have demonstrated that patients homozygous for 158V have improved clinical outcomes
- **The endogenous NK cell compartment of a cancer patient is significantly impaired**
  - Absolute NK cell numbers are low
  - CD16 expression levels are low and shedding inhibits ADCC
  - Tumor suppressive mechanisms contribute to NK cell exhaustion



Rituxan Rituximab · GAZYVA obinutuzumab · DARZALEX (daratumumab) · Herceptin trastuzumab Precision • Power • Promise · ERBITUX Cetuximab · BAVENCIO avelumab Injection

How to bring the 158V CD16 NK cell experience to <u>all</u> patients?

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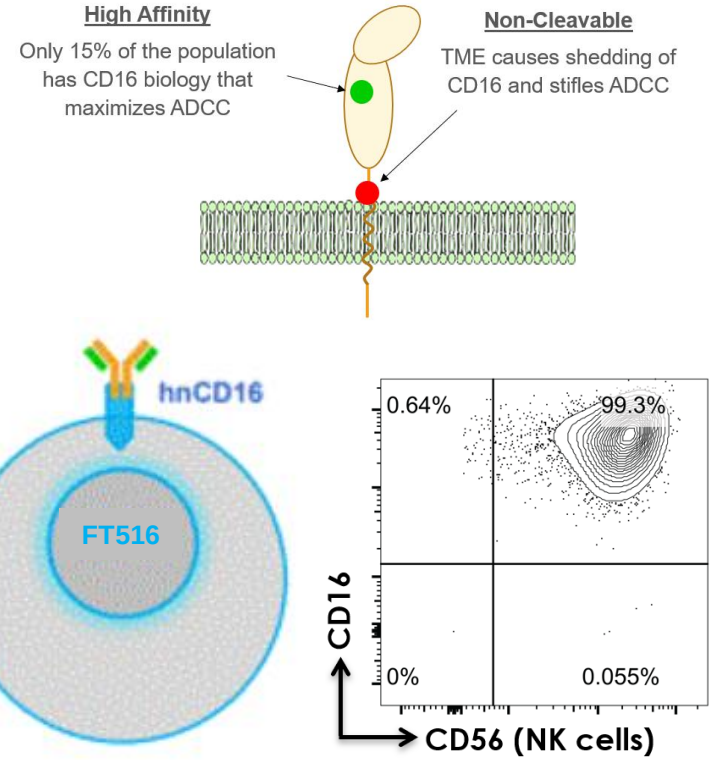
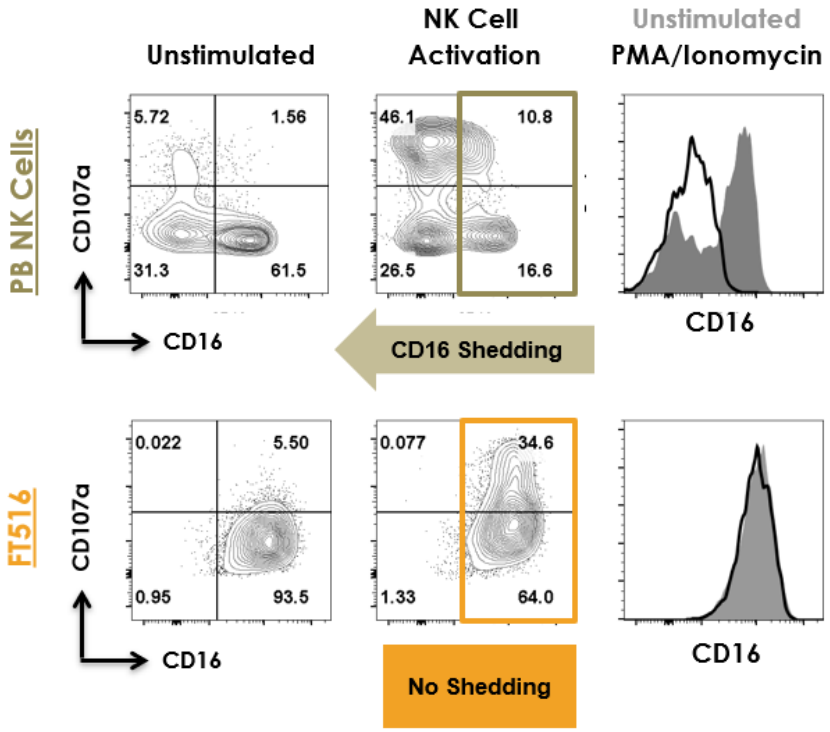
FT516: hnCD16 NK Cell Product Candidate

Our Novel High-Affinity, Non-Cleavable CD16a Fc Receptor for Enhanced ADCC

Proprietary High-affinity, Non-cleavable CD16a (hnCD16) Fc Receptor for Enhanced ADCC

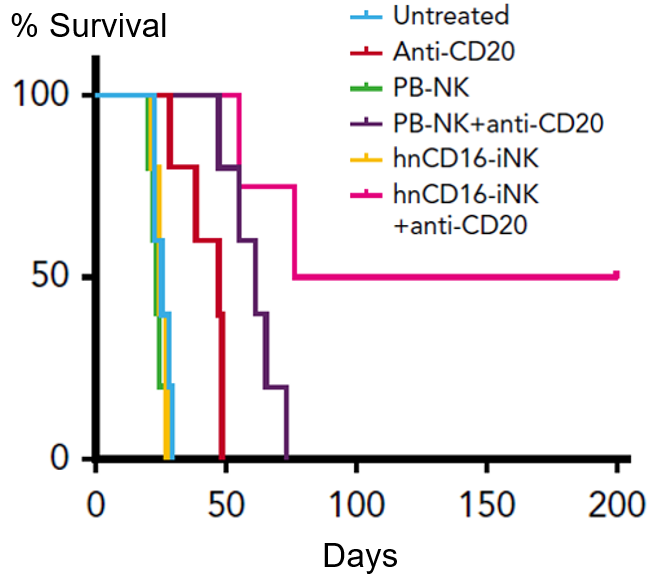


Resistance to Activation-induced Shedding as Compared to Healthy Donor NK Cells



Prolonged Survival In Vivo as Compared to Healthy Donor NK Cells

Raji Cancer Cells in Disseminated Xenograft Model of Lymphoma



Zhu et al. Blood 2020

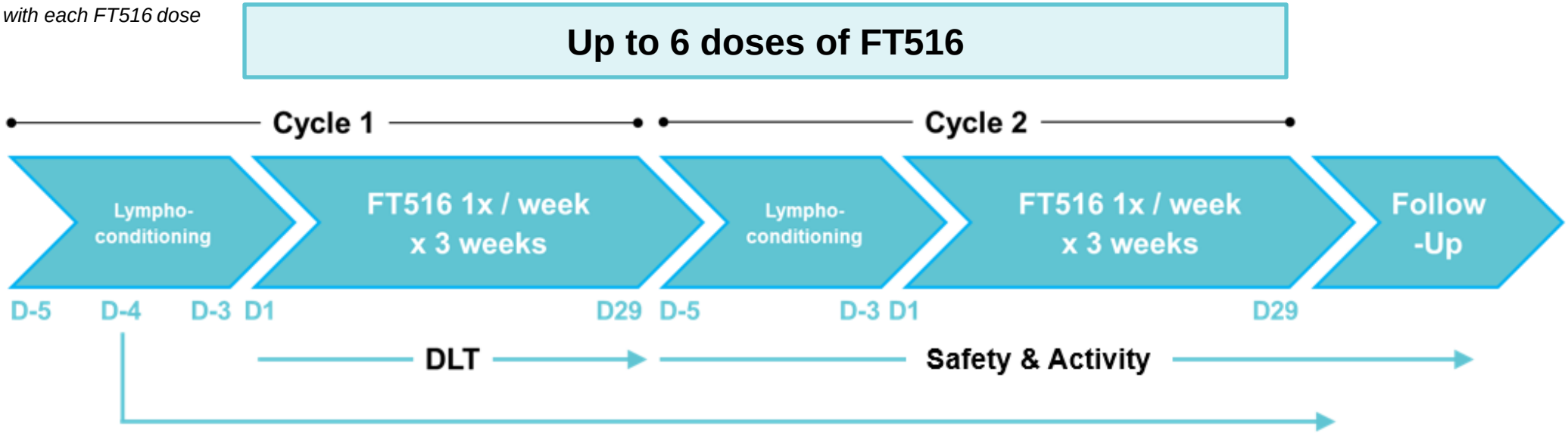
FT516-101: B-Cell Lymphoma in Combination with Rituximab

Phase 1 Study Design: Multiple Doses over Multiple Cycles

Cyclophosphamide: 500 mg/m2 IV x 3 days

Fludarabine: 30 mg/m2 IV x 3 days

IL-2: 6M units sc with each FT516 dose



Rituximab: 1 dose at 375 mg/m^2 IV per cycle

<u>Regimen B</u> – Rituximab Combination

Rituxan Rituximab

- Relapsed / refractory B-cell lymphoma
- Dose Escalation: 30M, 90M, 300M, 900M cells per dose + mAb
- Dose Expansion: up to 15 subjects

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FT516-101: B-Cell Lymphoma in Combination with Rituximab

Phase 1 Study: Patient Baseline Characteristics

FT516 Dose Cohort	Subject #	Age / Sex	Lymphoma Type	Prior Systemic Therapy		
				Regimen	Best Response	DoR
90M cells	2005	50 / M	DLBCL	1) R-CHOP 2) Flu/Cy → Yescarta 3) R-ICE	PR CR PD	1 month 8 months NA
	2006	65 / M	DLBCL	1) R-CEOP/MTX 2) R-DHAX	PD PR	NA <2 months
	2007	62 / M	DLBCL (Double-Hit)	1) R-CHOP 2) R-EPOCH 3) Flu/Cy → R + Yescarta	UNK PD CR	UNK PD 2.5 months
300M cells	2008*	68 / M	FL	1) R 2) R-Bendamustine 3) R 4) R-CHOP	CR CR PR CR	UNK 3 years 13 months 4 months

DLBCL = Diffuse Large B-Cell Lymphoma; **FL** = Follicular Lymphoma; **R** = Rituximab; **CHOP** = cyclophosphamide, doxorubicin, vincristine, prednisone; **ICE** = ifosfamide, carboplatin, etoposide; **CEOP** = cyclophosphamide, etoposide, vincristine, prednisone; **MTX** = methotrexate; **DHAX** = dexamethasone, cytarabine, oxaliplatin; **EPOCH** = etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin; **Flu/Cy** = fludarabine/cyclophosphamide conditioning; **CR** = Complete Response; **PR** = Partial Response; **PD** = Progressive Disease; **NA** = Not Applicable; **UNK** = Unknown; **DoR** = Duration of Response; ***** Information on prior systemic therapies per investigator communication (data not entered into database)

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Note: As of November 16, 2020 database entry. Data subject to cleaning and source document verification.

FT516-101: B-Cell Lymphoma in Combination with Rituximab

Phase 1 Safety, Tolerability and Protocol-Defined Response

FT516 Dose Cohort	Subject #	Prior Systemic Therapy		Bridging Therapy	FT516 Doses	FT516-Related Safety					Immunogenicity[1]		Post-C2 Response[2]
		With Rituximab	Relapsed / Refractory			DLT	Any Grade CRS	Any Grade ICANS	Any Grade GvHD	Grade ≥ 3 AE	T-cell mediated	B-cell mediated	
90M cells	2005	2	Refractory	No	6	No	No	No	No	No	No	No	**CR**
	2006	2	Relapsed	No	6	No	No	No	No	No	Pending	No	**PR**
	2007	3	Relapsed	No	6	No	No	No	No	No	No	No	**PD**
300M cells	2008	4	Relapsed	No	6	No	No	No	No	No	Pending	No	**CR**

AE = adverse event; **DLT** = Dose limiting toxicity; **CRS** = Cytokine release syndrome; **ICANS** = Immune effector cell-associated neurotoxicity syndrome; **GvHD** = Graft-versus-Host Disease; **CR** = Complete response; **PR** = Partial Response; **PD** = Progressive Disease

[1] Host-vs-product alloreactivity measured Day 15 and Day 29 of Cycles 1 and 2 for T cells, and Day 29 of Cycles 1 and 2 for B cells.

[2] Cycle 2 Day 29 protocol-defined response assessment per Lugano 2014 criteria

Dose escalation ongoing at 300M cells / dose

Note: As of November 16, 2020 database entry. Data subject to cleaning and source document verification.

FT516-101: B-Cell Lymphoma in Combination with Rituximab

Initial Clinical Observations

- Up to 6 doses of FT516 were well-tolerated
  - No events *of any grade* of CRS, ICANS, or GvHD
  - No FT516-related Grade 3 or greater adverse events
  - No evidence of anti-product T- or B-cell mediated immunogenicity
- Objective response at post-C2 assessment observed in 3 of 4 patients treated with ≥ 90 million cells / dose
  - **CR** – 2005 (90M): relapsed following CAR19 T-cell therapy, and refractory to last prior rituximab regimen (RR)
  - **PR** – 2006 (90M): refractory to 1L RR, and 2L RR showed PR of minimal duration
  - **CR** – 2008 (300M): four prior RR with progressively shorter durations of response
- Clear evidence that FT516 can drive responses in relapsed / refractory patients
  - All patients previously treated with at least 2 prior rituximab-containing regimens
  - 3 of 4 patients have disease refractory to at least 1 prior rituximab-containing regimen
  - One patient had relapsed after achieving CR of <3 months duration on CAR19 T-cell therapy
- Clinical data strongly suggest that proprietary hnCD16 Fc receptor can effectively synergize with and enhance the MOA of tumor-targeted antibodies

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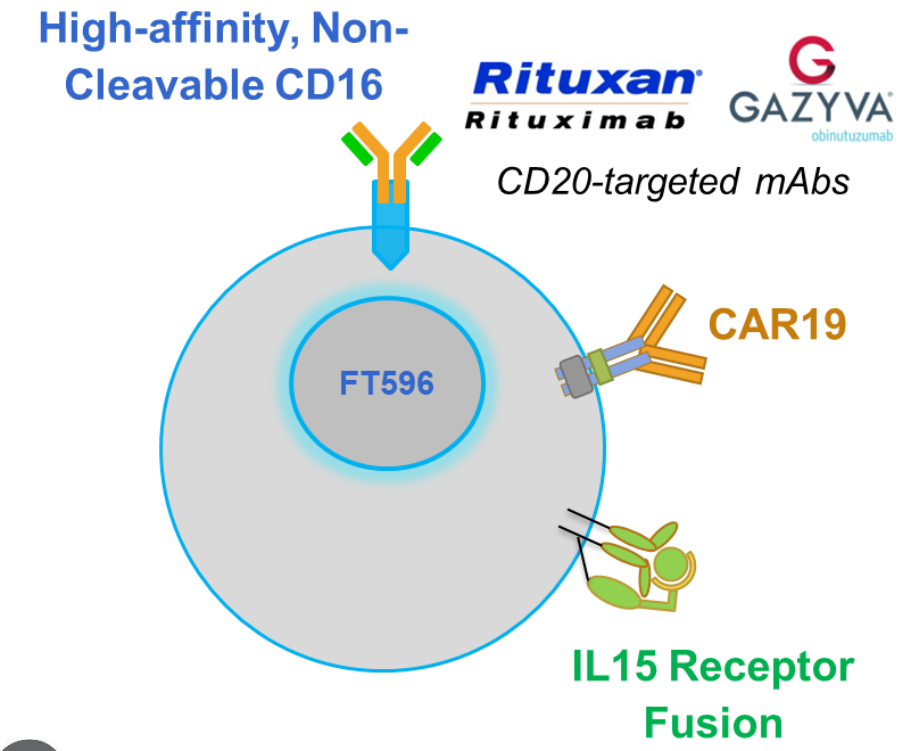
FT596: Multi-antigen Targeted CAR19 NK Cell Product Candidate

Potential Best-in-Class Cell-based Cancer Immunotherapy for B-cell Malignancies

First-ever Cell Therapy Engineered with Three Active Anti-tumor Modalities Cleared for U.S. Clinical Investigation



hnCD16: High-affinity 158V, non-cleavable CD16 Fc receptor that has been modified to augment antibody-dependent cellular cytotoxicity by preventing CD16 down-regulation and enhancing CD16 binding to tumor-targeting antibodies

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CAR19: Chimeric antigen receptor optimized for NK cell biology, which contains a NKG2D transmembrane domain, a 2B4 co-stimulatory domain and a CD3-zeta signaling domain, that targets B-cell antigen CD19

IL-15RF: Interleukin-15 receptor fusion, a potent cytokine complex that promotes survival, proliferation and trans-activation of NK cells and CD8 T cells

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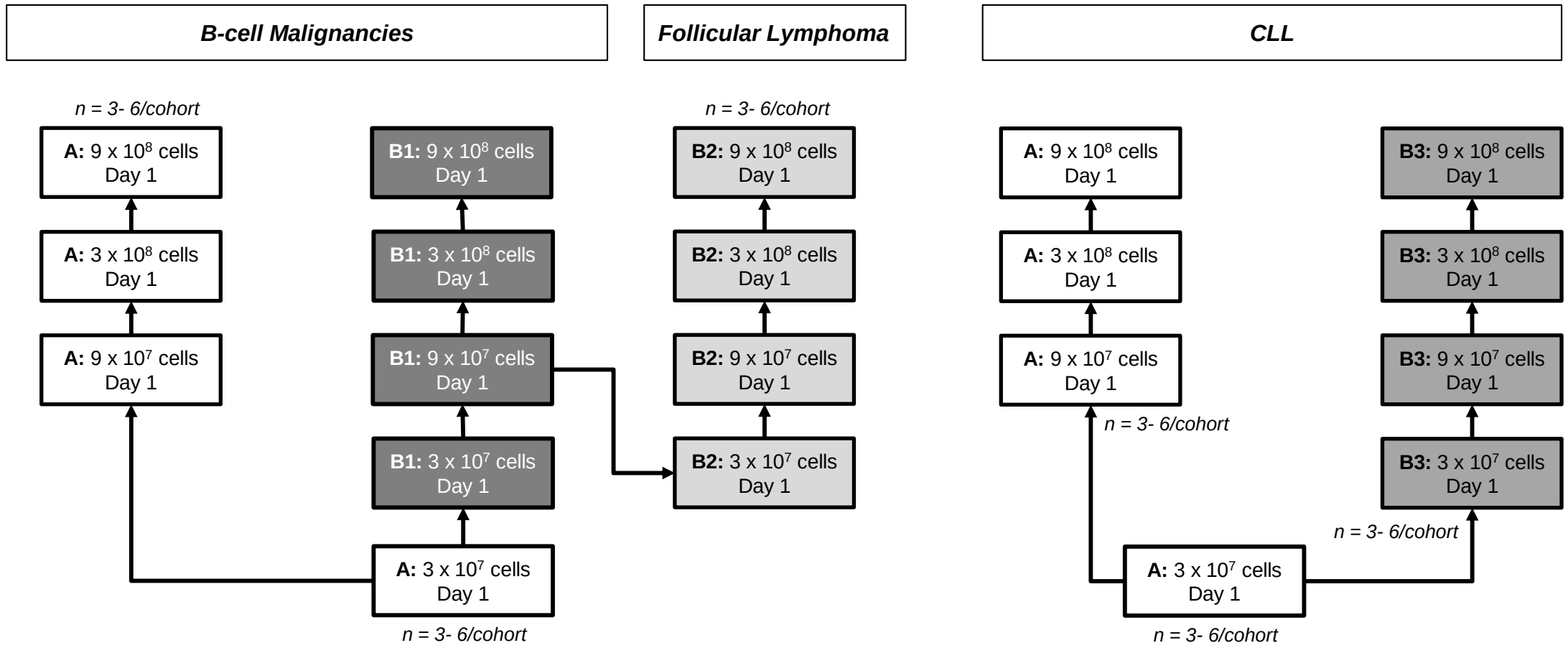
FT596-101: Phase 1 Dose Escalation Schema

Parallel Escalation of Single-dose Mono and mAb Combo in BCL and CLL



Regimen A: FT596 Mono

Regimen B1: FT596 + Rituximab

Regimen B2: FT596 + Obinutuzumab (BCL)

Regimen B3: FT596 + Obinutuzumab (CLL)

FT596-101: Patient 2002 Case Study – Patient History

Dose Cohort 1 Monotherapy (Single dose of FT596 at 30M cells)

76 y/o woman with DLBCL, GCB subtype

- Stage II at study entry (mesenteric mass)
- Medical history notable for COPD, coronary artery disease, fungal pneumonia
- Received 7 prior therapies
  - 5 prior therapies included rituximab
  - 2 prior therapies included Flu / Cy
- Refractory to last therapy
  - Flu / Cy followed by experimental combination therapy of donor-derived NK cell therapy ($16x10^9$ cells), IL-2, and rituximab
- Enrolled in FT596-101 study at first dose level
  - 110 days from last therapy
  - No bridging therapy administered

Prior Regimen		Best Response	Approximate DOR
1	Rituximab, cyclophosphamide, hydroxydaunomycin, oncovin, prednisone (R-CHOP)	CR	2 years
2	Rituximab, carboplatin, etoposide, ifosfamide (R-ICE) Carmustine, etoposide, cytarabine, melphalan (BEAM) followed by ASCT	CR	16 months
3	Rituximab and ADAM17 inhibitor (maintenance)	NA	NA
4	BET inhibitor	PD	-----
5	Gemcitabine and oxaliplatin (GemOx)	PR	<1 month
6	Flu / Cy lympho-conditioning followed by rituximab and ACTR707	CR	4 months
7	Flu / Cy lympho-conditioning followed by *ex vivo* expanded, donor-derived NK cells, IL-2, and rituximab	SD	<2 months

DOR = Duration of Response
ASCT = Autologous stem cell transplant
BET = Bromodomain and extra-terminal motif
NA = Data Not Available
CR complete response
PR partial response
SD stable disease
PD progressive disease

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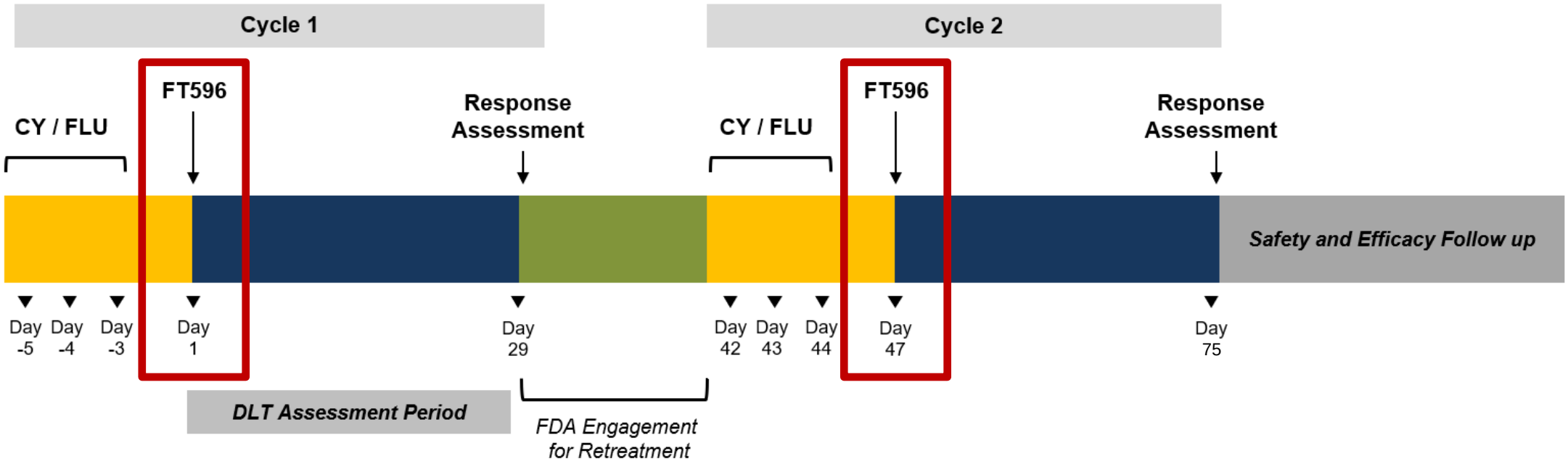
FT596-101: Patient 2002 Case Study – Clinical Course

Dose Cohort 1 Monotherapy (Single dose of FT596 at 30M cells)

- First FT596 Single-dose Treatment Cycle
  - Single-dose monotherapy at 3 x 10^7 cells
- Second FT596 Single-dose Treatment Cycle
  - Single-dose monotherapy at 3 x 10^7 cells
  - Administered following FDA consent based on review of Cycle 1 clinical data



Cyclophosphamide: 500 mg/m2 IV x 3 days; Fludarabine: 30 mg/m2 IV x 3 days

FT596-101: Patient 2002 Case Study – Safety

Dose Cohort 1 Monotherapy (Single dose of FT596 at 30M cells)

Adverse Events of Interest	Cycle 1	Cycle 2
Any Grade		
Cytokine Release Syndrome	No	No
ICANS [1]	No	No
Graft-versus-Host Disease	No	No

[1] ICANS = Immune Effector Cell-Associated Neurotoxicity Syndrome

Anti-Product Immunogenicity	Cycle 1	Cycle 2
B-Cell mediated *Detectable anti-FT596 Class I HLA Antibodies*	0 *Measured D29*	0 *Measured D29*
T-Cell mediated *FT596-specific T-cell IFNg Response by ELISpot*	**Not Detected** *Measured D18, D29*	**Not Detected** *Measured D18, D29*

- No dose-limiting toxicities (DLTs)
- No FT596-related serious adverse events (SAEs)
- Safety profile of adverse events (AEs) of interest was similar between Cycle 1 and Cycle 2
- Grade ≥3 AEs considered probably related to Flu/Cy conditioning and possibly related to FT596 included decreases in neutrophil, white blood cell, and lymphocyte counts
- Grade ≥3 AEs not related to FT596 were consistent with lympho-conditioning chemotherapy, medical history and prior treatment regimens
- No evidence of B- or T-cell mediated anti-product immunogenicity

Note: As of September 24, 2020 data cut

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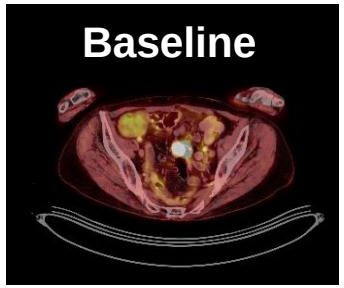
FT596-101: Patient 2002 Case Study – Activity & Pharmacokinetics

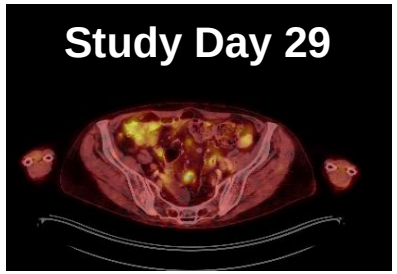
Dose Cohort 1 Monotherapy (Single dose of FT596 at 30M cells)

- Partial response at Study Day 29 following first FT596 single-dose cycle
- Deepening of response at Study Day 75 following second FT596 single-dose cycle
- DoR = 3.7 months, comparable to that of auto CD19 CAR-T cell therapy among patients who achieve PR as BOR
- FT596 demonstrated consistent, detectable PK in peripheral blood following each single-dose treatment cycle



SPD
1292 mm^2

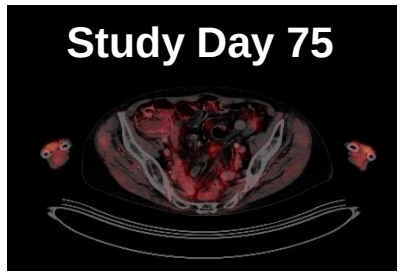
SUV
28



SPD
624 mm^2

SUV
6.6

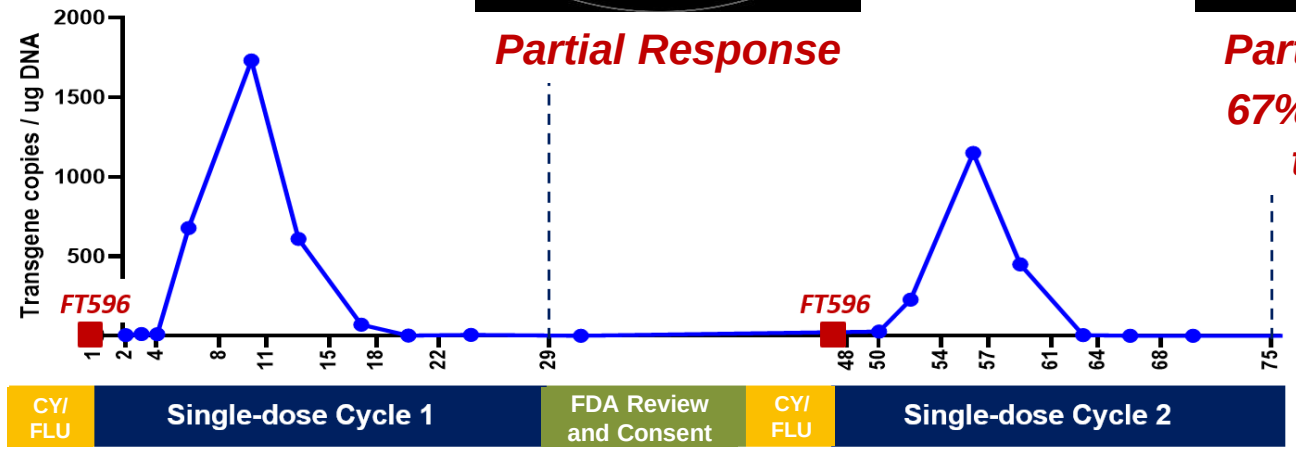
Partial Response



SPD
420 mm^2

SUV
2.6

Partial Response
67% reduction in tumor size



SPD: Sum of the Product of the Diameters
SUV: Standardized Uptake Value

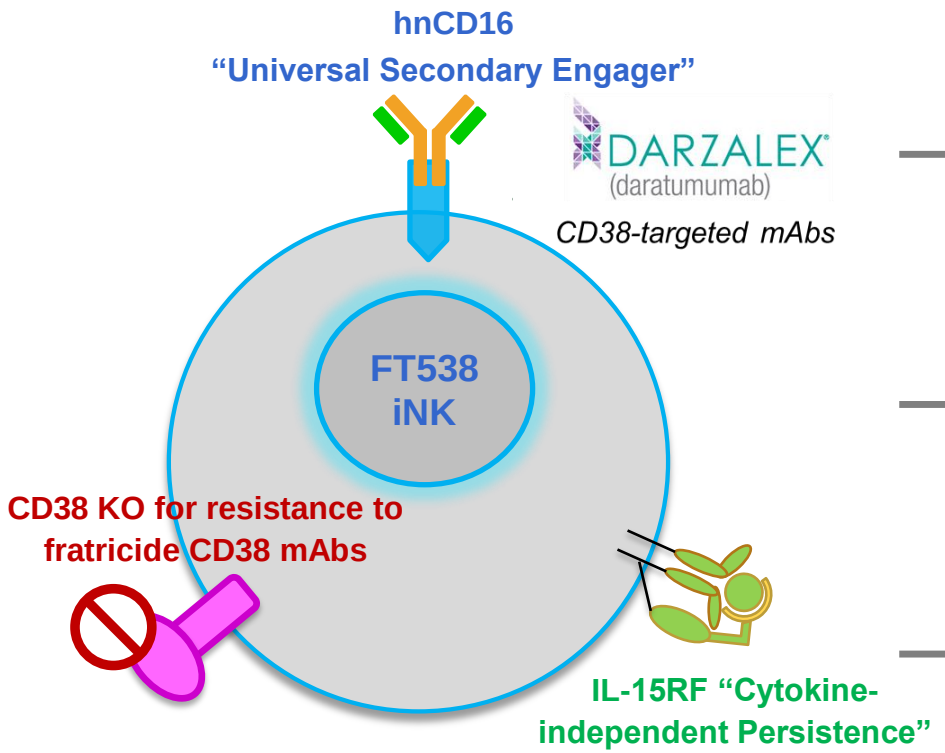
Note: As of September 24, 2020 data cut

Multiple Myeloma Franchise

FT538: hnCD16 + IL-15RF + CD38KO NK Cell Product Candidate

First-ever CRISPR-edited iPSC-derived Cell Therapy

Engineered with Three Components to Enhance Multiple Mechanisms of Innate Immunity



hnCD16: High-affinity 158V, non-cleavable CD16 Fc receptor that has been modified to augment antibody-dependent cellular cytotoxicity by preventing CD16 down-regulation and enhancing CD16 binding to tumor-targeting antibodies

---

CD38KO: Deletion of CD38 to eliminate anti-CD38 antibody mediated NK cell fratricide. Also shown to improve NK cell biology and potency through optimization of metabolic signaling

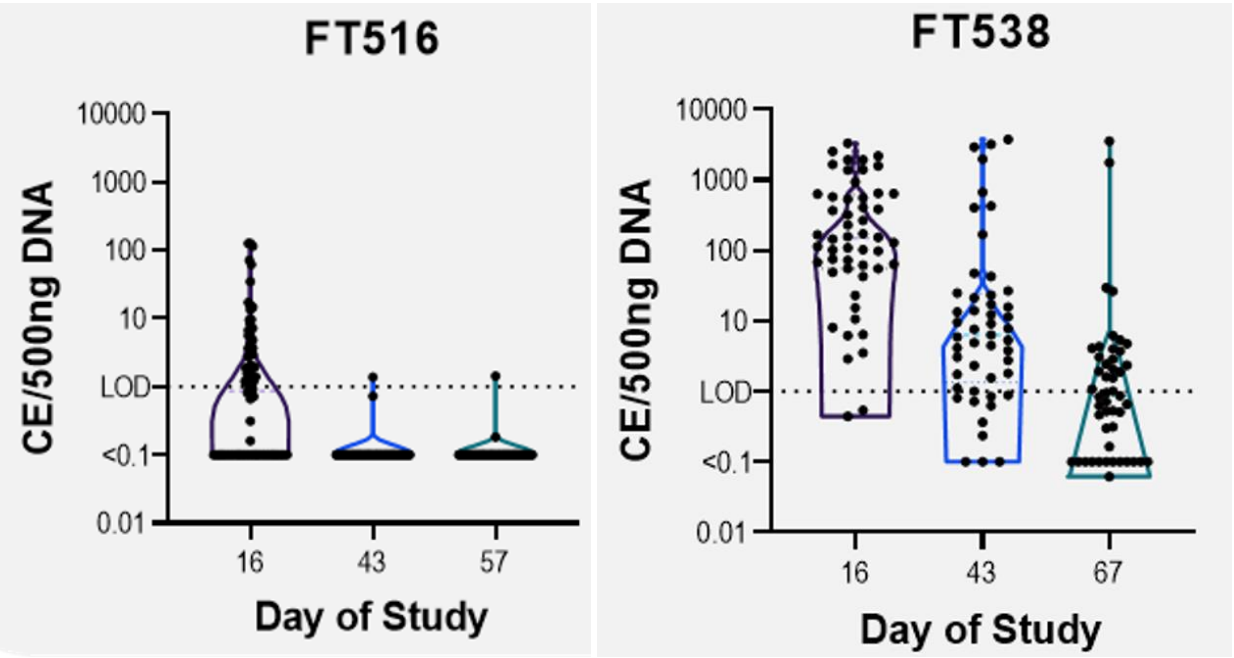
---

IL-15RF: Interleukin-15 receptor fusion, a potent cytokine complex that promotes survival, proliferation and trans-activation of NK cells and CD8 T cells

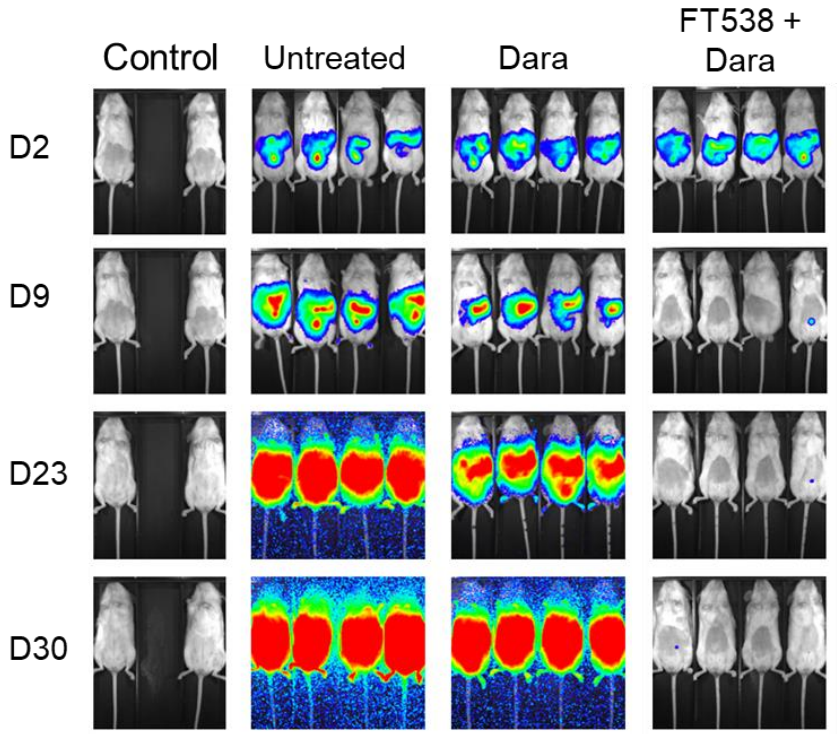
FT538: hnCD16 + IL-15RF + CD38KO NK Cell Product Candidate

Enhancing Multiple Mechanisms of Innate Immunity

Enhanced NK Cell Persistence & Metabolic Fitness



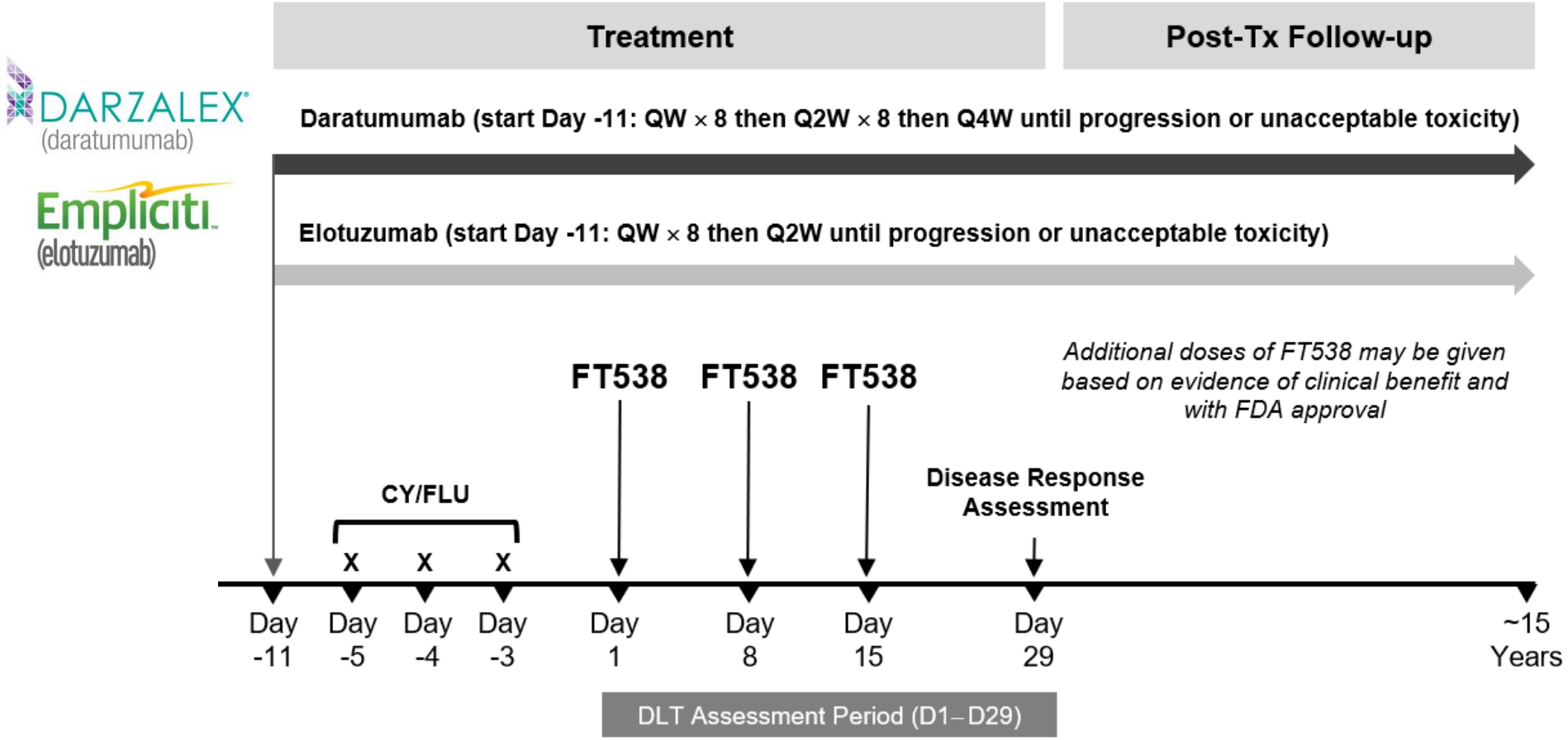
Enhanced NK Cell ADCC[a]



[a] Bjordahl et al. ASH Annual Meeting 2019

FT538-101: Relapsed / Refractory Multiple Myeloma

Multi-dose Combination with CD38-targeted and SLAMF7-targeted mAb



DL1 = 100M cells / dose

DL2 = 300M cells / dose

DL3 = 1.0B cells / dose

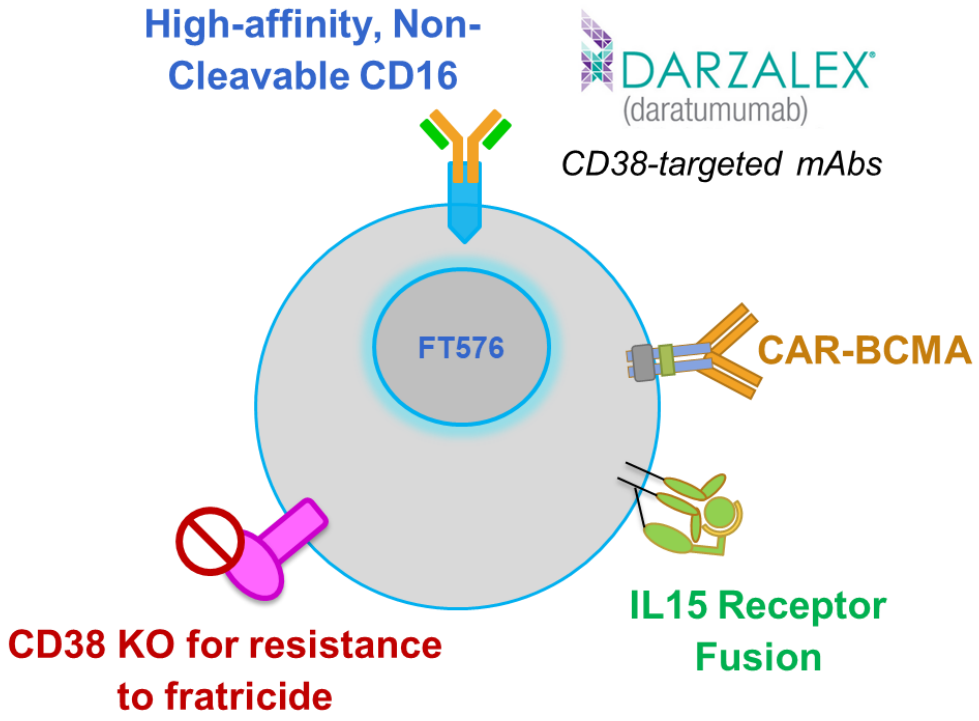
DL4 = 1.5B cells / dose

Fate THERAPEUTICS

FT576: Multi-antigen Targeted CAR-BCMA NK Cell Product Candidate

Potential Best-in-Class Cell-based Cancer Immunotherapy for Multiple Myeloma

Engineered with Four Anti-tumor Modalities for Multiple Myeloma



hnCD16: High-affinity 158V, non-cleavable CD16 Fc receptor that has been modified to augment antibody-dependent cellular cytotoxicity by preventing CD16 down-regulation and enhancing CD16 binding to tumor-targeting antibodies

---

CAR-BCMA: Chimeric antigen receptor optimized for NK cell biology, which contains a NKG2D transmembrane domain, a 2B4 co-stimulatory domain and a CD3-zeta signaling domain, that targets B-cell maturation antigen

---

IL-15RF: Interleukin-15 receptor fusion, a potent cytokine complex that promotes survival, proliferation and trans-activation of NK cells and CD8 T cells

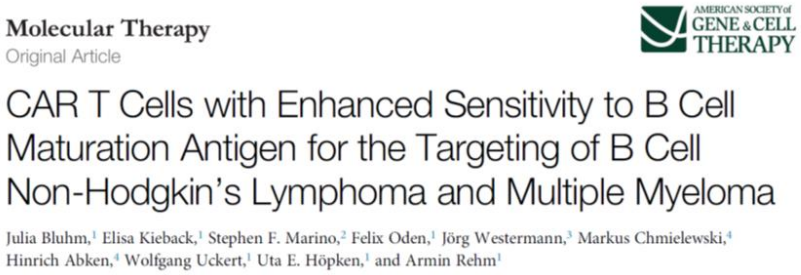
---

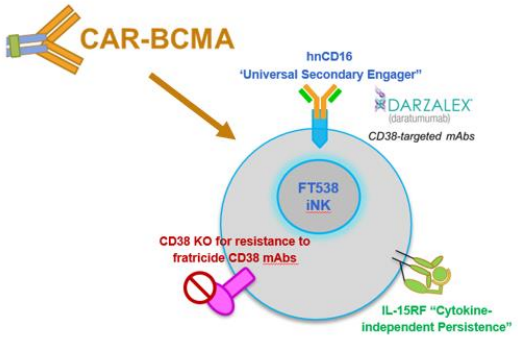
CD38 KO: Deletion of CD38 to eliminate anti-CD38 antibody mediated NK cell fratricide. Also shown to improve NK cell biology and potency through optimization of metabolic signaling

IND Allowed in December 2020

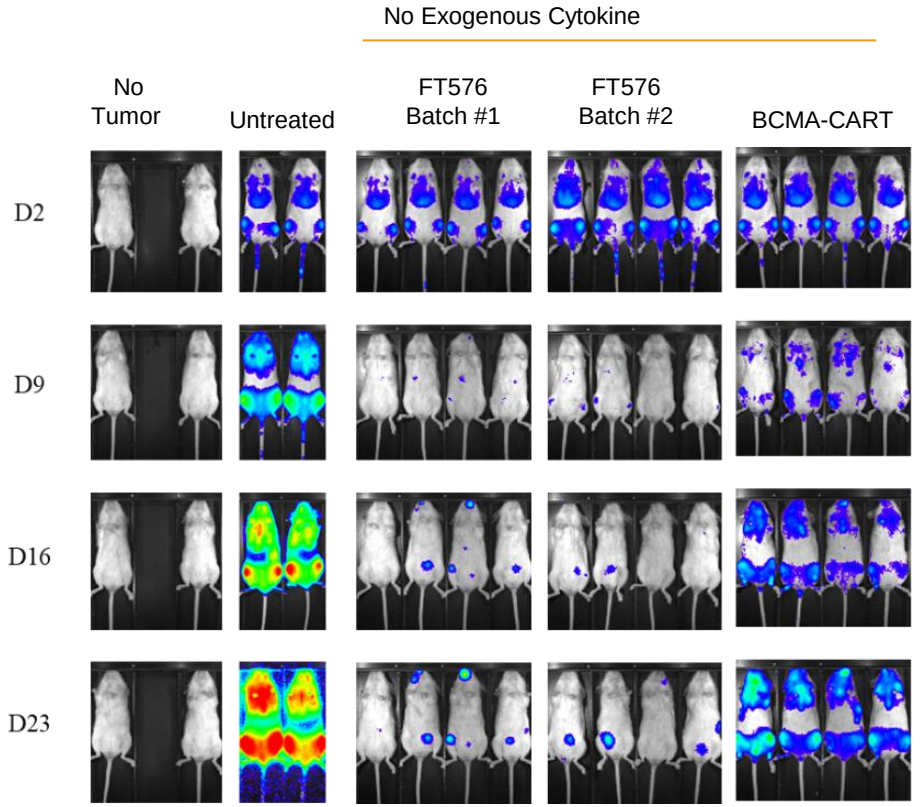
FT576: Multi-antigen Targeted CAR-BCMA NK Cell Product Candidate

BCMA Binding Domain with Differentiated Activation Threshold





- ✓ Validated CAR BCMA in diffuse large B cell lymphoma, follicular lymphoma, mantle cell lymphoma, and chronic lymphocytic leukemia
- ✓ BCMA CAR T cells triggered target cell lysis with an activation threshold in the range of 100 BCMA molecules, which allowed for an efficient eradication of B-NHL cells in vitro and in vivo
- ✓ Potential novel therapeutic option for patients where BCMA is expressed at low abundance or where anti-BCMA immunotherapies have failed due to antigen loss



MM.1S-Luc cells

Miller et al. ASH Annual Meeting 2020

AML Franchise

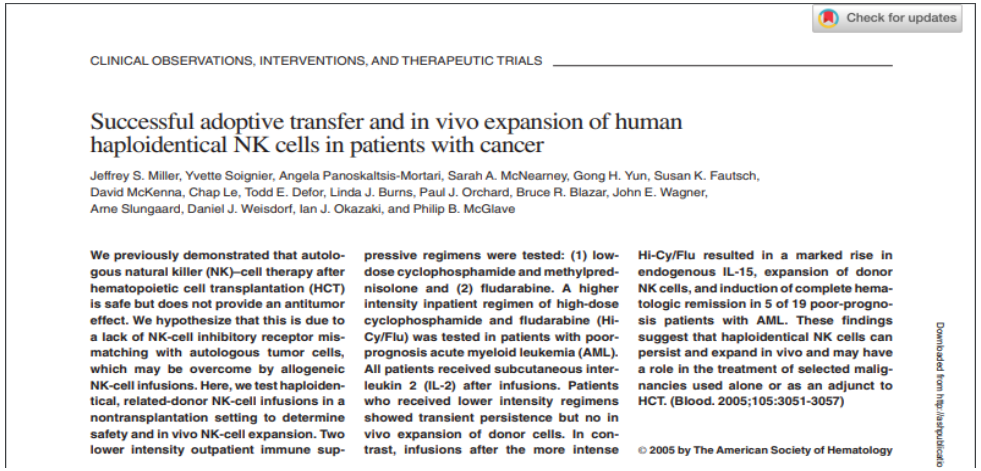
Rationale for NK Cell Therapy in AML

Clinical Precedent with Non-Engineered Allogeneic NK Cell Therapy

Jeffrey S. Miller, MD

UNIVERSITY OF MINNESOTA
Driven to Discover℠

Seminal 2005 Manuscript, >1,000 citations



Check for updates

CLINICAL OBSERVATIONS, INTERVENTIONS, AND THERAPEUTIC TRIALS

Successful adoptive transfer and in vivo expansion of human haploidentical NK cells in patients with cancer

Jeffrey S. Miller, Yvette Soignier, Angela Panoskaltsis-Mortari, Sarah A. McNearney, Gong H. Yun, Susan K. Fautsch, David McKenna, Chap Le, Todd E. Defor, Linda J. Burns, Paul J. Orchard, Bruce R. Blazar, John E. Wagner, Arne Slungaard, Daniel J. Weisdorf, Ian J. Okazaki, and Philip B. McGlave

We previously demonstrated that autologous natural killer (NK)–cell therapy after hematopoietic cell transplantation (HCT) is safe but does not provide an antitumor effect. We hypothesize that this is due to a lack of NK-cell inhibitory receptor mismatching with autologous tumor cells, which may be overcome by allogeneic NK-cell infusions. Here, we test haploidentical, related-donor NK-cell infusions in a nontransplantation setting to determine safety and in vivo NK-cell expansion. Two lower intensity outpatient immune suppressive regimens were tested: (1) low-dose cyclophosphamide and methylprednisolone and (2) fludarabine. A higher intensity inpatient regimen of high-dose cyclophosphamide and fludarabine (Hi-Cy/Flu) was tested in patients with poor-prognosis acute myeloid leukemia (AML). All patients received subcutaneous interleukin 2 (IL-2) after infusions. Patients who received lower intensity regimens showed transient persistence but no in vivo expansion of donor cells. In contrast, infusions after the more intense Hi-Cy/Flu resulted in a marked rise in endogenous IL-15, expansion of donor NK cells, and induction of complete hematologic remission in 5 of 19 poor-prognosis patients with AML. These findings suggest that haploidentical NK cells can persist and expand in vivo and may have a role in the treatment of selected malignancies used alone or as an adjunct to HCT. (Blood. 2005;105:3051-3057)

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Downloaded from http://ashpublicatio

- 300+ AML/MDS patients treated with allogeneic NK cells[a]
- Numerous clinical studies in relapsed / refractory AML have shown[a]:
  - CR rates = 25-35%
  - No GvHD
  - Minimal CRS / neurotoxicity
- Unmet need in AML remains high
  - ~21,000 newly diagnosed patients in the US alone every year[b]
  - 5-year survival rate ~28%[b]
  - Significant opportunity for more effective, less toxic therapies
    - <50% of elderly patients respond to initial therapy[c]
    - 20-40% of younger patients fail to respond to initial therapy[c]
    - ~50% of patients who attain an initial CR eventually relapse[d]

Fate THERAPEUTICS

[a] *Fate Therapeutics, Internal Literature Review*
[b] *National Cancer Institute Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: AML. 2015.*
[c] *Mangan J and Luger S. Salvage therapy for relapsed or refractory acute myeloid leukemia. Ther Adv Hematol. 2011; 2(2):73-82.*
[d] *Leopold LH, Willemeze R. The Treatment of Acute Myeloid Leukemia in First Relapse: A Comprehensive Review of the Literature. Leuk Lymphoma. 2002; 43(9); 1715-1727*

Off-the-Shelf, iPSC-derived NK Cell Cancer Immunotherapy Franchise

Multiple Ongoing Phase 1 Studies in Relapsed / Refractory AML

Program	FT516 Monotherapy	FT538 Monotherapy	FT538 + anti-CD38 mAb
Dose	Three dose levels ranging from 90-900 million cells / dose	Four dose levels ranging from 100-1,500 million cells / dose	Four dose levels ranging from 100-1,500 million cells / dose
Schedule	Lympho-conditioning [1] 3 once-weekly doses + IL-2 2 cycles	Lympho-conditioning [1] 3 once-weekly doses Cycle 2 with FDA consent	Lympho-conditioning [2] 3 once-weekly doses Cycle 2 with FDA consent
Assessment	C1D30 Safety C2D30 Anti-tumor response	C1D30 Safety C1D30 Anti-tumor response	C1D30 Safety C1D30 Anti-tumor response
Status	Dose escalation ongoing	First patient treated	IND allowed (UMN IIT)

[1] Cy 500 mg/m2 x Flu 30 mg/m2 x 3 days

[2] Cy 300 mg/m2 x Flu 30 mg/m2 x 2 days

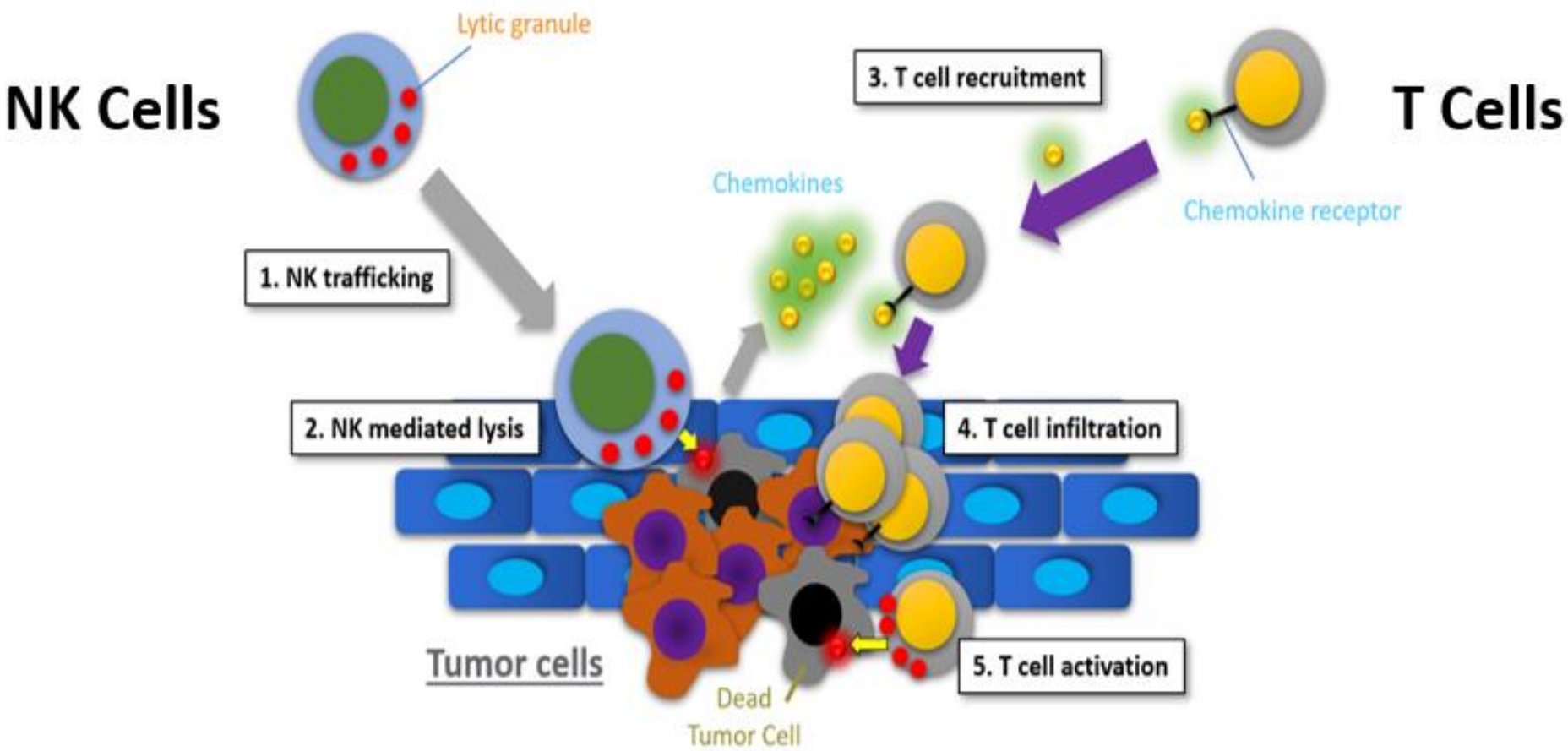
Fate THERAPEUTICS

Solid Tumor Franchise

Off-the-Shelf, iPSC-derived NK Cell Cancer Immunotherapy Franchise

The NK-Cell-Mediated Cancer Immunity Cycle

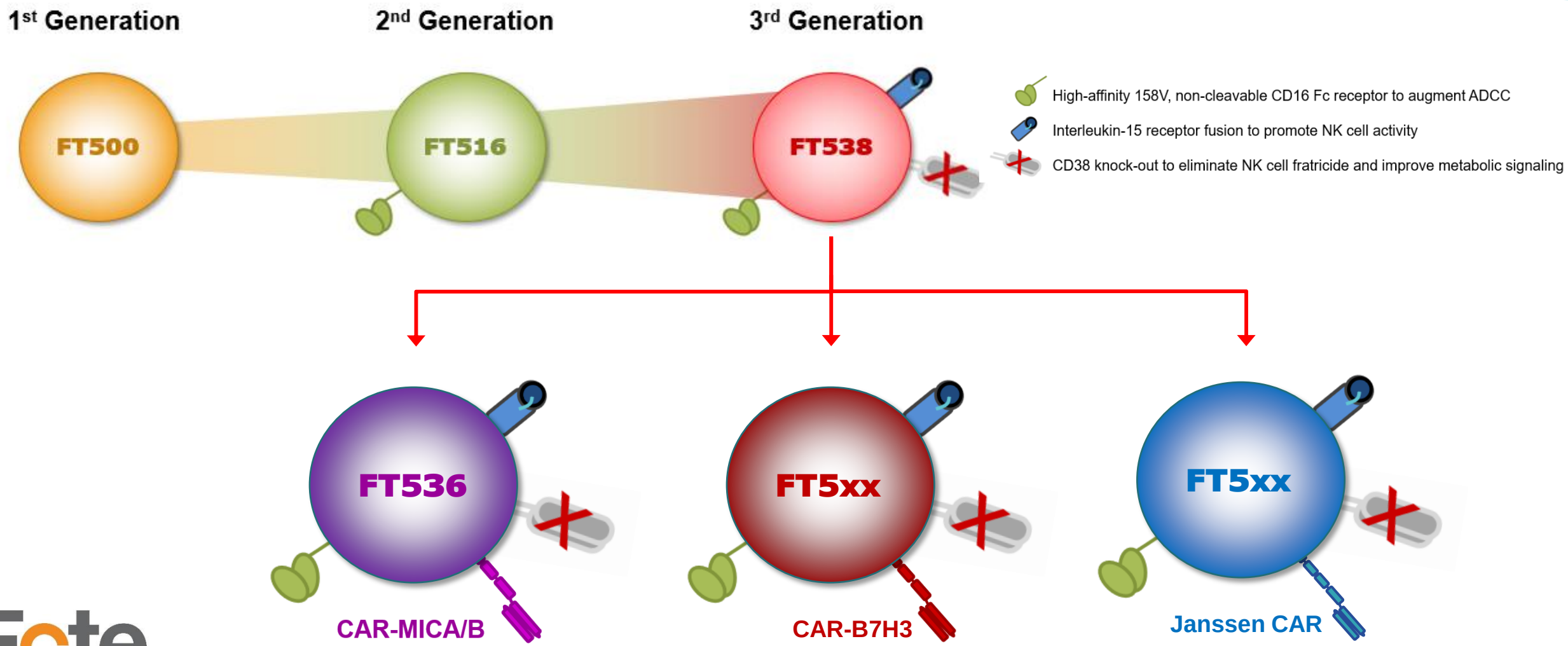
Bridging Innate and Adaptive Immunity



Fate THERAPEUTICS

Off-the-Shelf, iPSC-derived NK Cell Cancer Immunotherapy Franchise

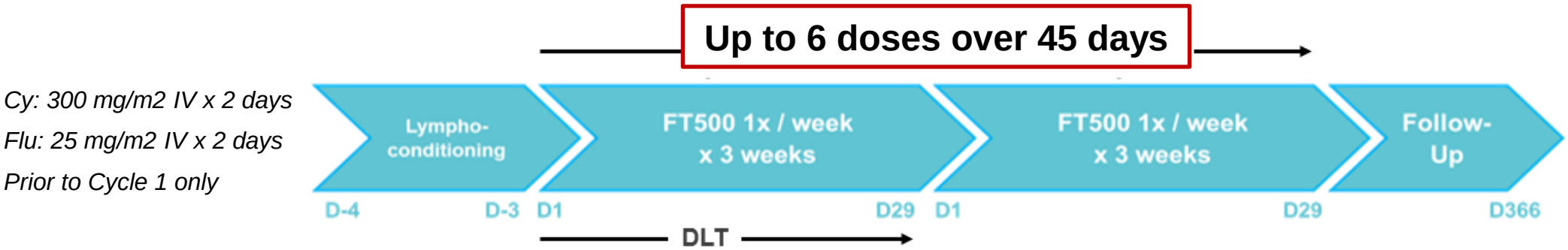
Multi-antigen Targeting: Enhanced Innate Immunity + CAR



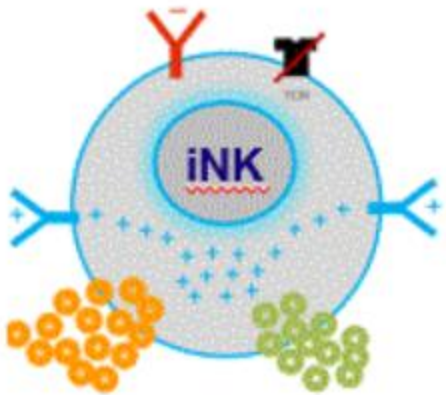
Fate THERAPEUTICS

FT500-101: First-ever U.S. Clinical Study of iPSC-derived Cell Product

Phase 1 Dose Escalation in Advanced Solid Tumors



FT500



- **Regimen A**: Monotherapy (n=9)
  - Salvage setting with patients having progressed or failed all FDA-approved therapies
- **Regimen B**: Combination with immune checkpoint inhibitor (ICI) therapy (n=6)
  - Tumor types where ICIs are approved
  - Salvage setting with patients having progressed or failed ICIs
- **Two dose levels**
  - 100M cells / dose and 300M cells / dose x up to 6 doses

Fate THERAPEUTICS

FT500-101: First-ever U.S. Clinical Study of iPSC-derived Cell Product

Clinical Objectives

Assessment of Safety & Tolerability as Monotherapy and in Combination with Checkpoint Inhibitor

Assess Novel Paradigm

- First-ever U.S. clinical study of iPSC-derived cell
- Universal starting material (e.g., no patient matching)
- Multi-dose, multi-cycle treatment strategy
- One-time, outpatient lympho-conditioning
- No exogenous cytokine support

Key Clinical Read-outs

- FT500 safety and tolerability (DLTs, AEs)
- Immune-mediated toxicities (GvHD, CRS)

Key Molecular Read-outs

- Immune cell recovery
- Endogenous cytokine response (GvHD, CRS)
- Anti-product immunogenicity

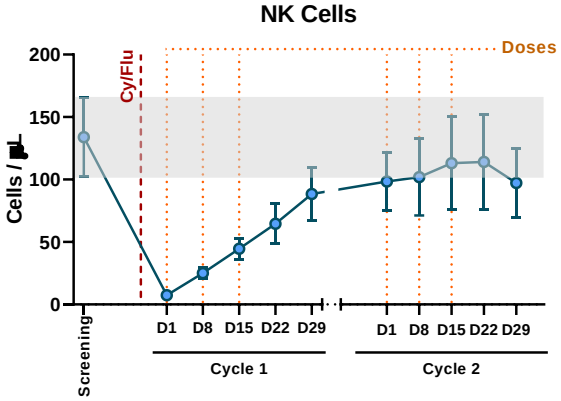
Fate THERAPEUTICS

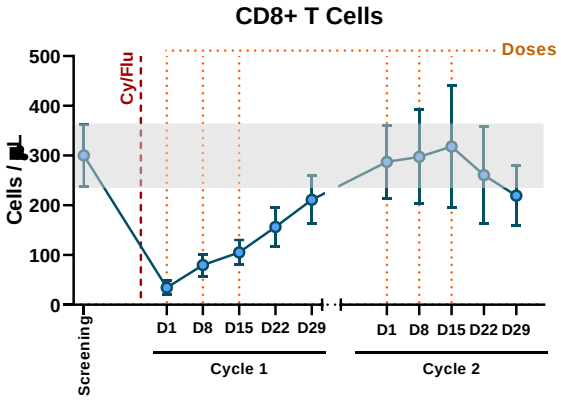
FT500-101: Dose Escalation Clinical Results

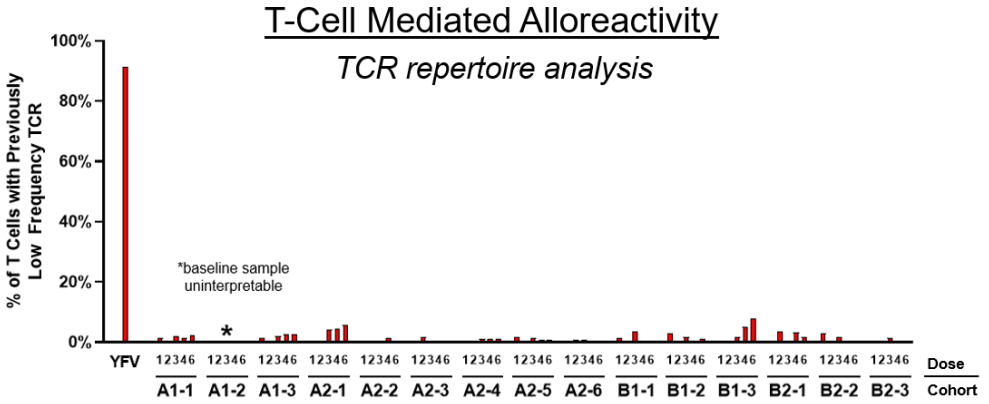
Phase 1 Dose Escalation in Advanced Solid Tumors

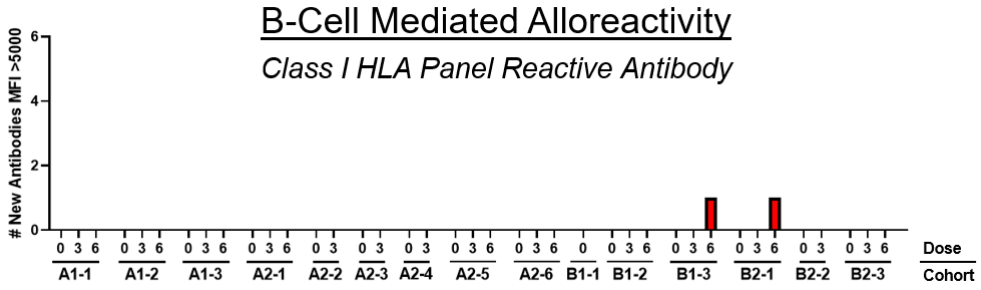
Multi-dosing

- All 15 patients completed Cycle 1 (3 doses)
- 13 patients advanced to Cycle 2, with 11 of 13 patients completing Cycle 2 (3 additional doses)
- Among the 13 patients who initiated Cycle 2 treatment, dose discontinuation was due to disease progression
- 81 total doses of FT500 were administered to patients in the outpatient setting
- No B-cell or T-cell mediated anti-product responses observed despite post-conditioning immune recovery









FT500-101: Dose Escalation Clinical Results

Phase 1 Dose Escalation in Advanced Solid Tumors

Safety

- No dose-limiting toxicities, and no SAEs or Grade ≥ 3 AEs considered related to FT500, were observed
- No cases of cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, or graft-versus-host disease were observed
- No treatment-related discontinuations or deaths were observed

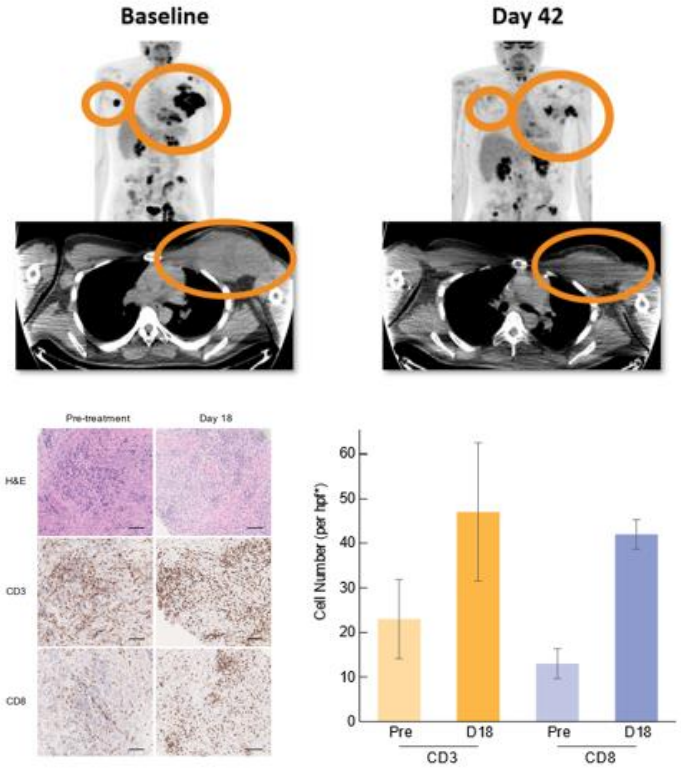
Efficacy

- Among 15 heavily pre-treated patients (10 who were refractory to prior therapy), 11 had a best overall response of SD

Patient Case Study - r/r cHL Resistant to anti-PD1 Therapy

- 29 y/o male with relapsed / refractory classical Hodgkin lymphoma (cHL)
- 14 prior therapies including multiple regimens containing FDA-approved ICI therapies; refractory to last prior regimen containing experimental anti-PD-1 therapy
- 84% reduction in size of a lymphonodal mass and a 58% reduction in size of all target lesions following three doses of FT500 plus anti-PD-1 therapy, however, new bone lesion was observed

Patient Case Study
(300M FT500 cells combined with ICI)



IHC staining of the lymphonodal mass demonstrated post-treatment increases in the number of CD3+ and CD8+ cells and in the ratio of CD3+ and CD8+ cells to tumor cells, indicative of T-cell trafficking to the responding tumor bed.

Fate THERAPEUTICS

FT500-101: Phase 1 Dose Expansion Ongoing

Targeting Solid Tumors Amendable to NK Cell Accessibility, Recognition, and Killing

Overcoming Resistance to Checkpoint Inhibitor Therapy in Advanced Solid Tumors

Patient who progressed on prior ICI

FT500 + IL2 + ICI

KEYTRUDA® (pembrolizumab) Injection 100 mg

OPDIVO® (nivolumab)

TECENTRIQ® atezolizumab

FT500 mediates both direct tumor lysis and T-cell recruitment / activation to re-sensitize ICI-resistant tumors

Dose Expansion Strategy	Rationale
Tumor Enrichment • NSCLC • cHL	• High % of tumor mutations leading to low / null MHC Class I expression • NSCLC: NK cell trafficking • cHL: POC in dose-escalation phase • Accessible tumor biopsies
Add IL-2 Support	• IL-2 known to enhance NK cell function and persistence

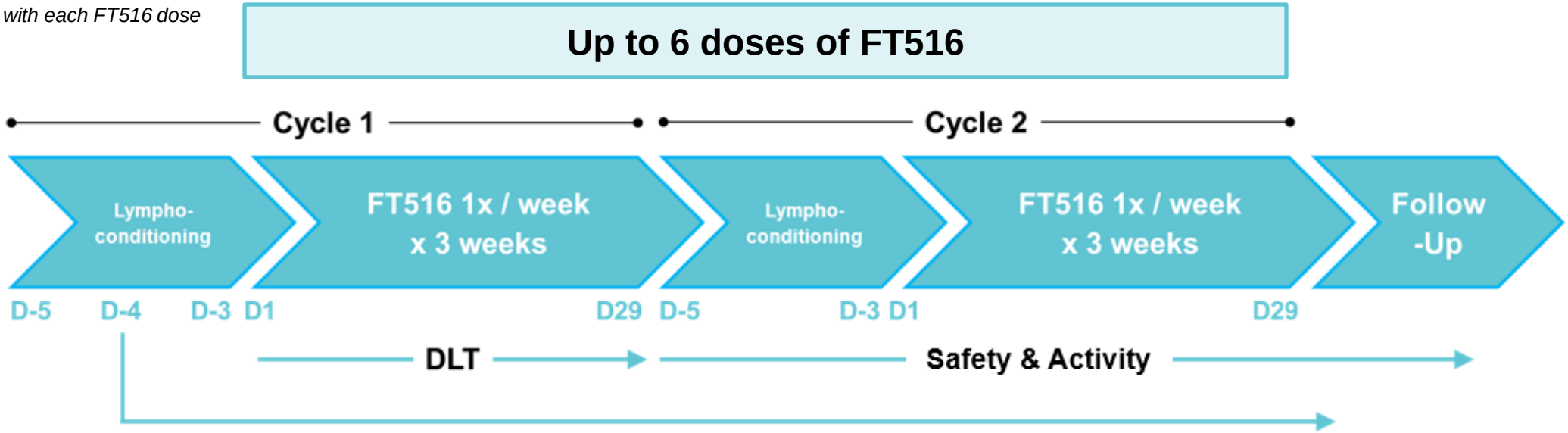
FT500 Dosing: Up to six doses; three once-weekly doses at 300M cells / dose x 2 cycles

Fate THERAPEUTICS

FT516-102: hnCD16 NK Cell Product Candidate for Advanced Solid Tumors

First Patient Treated in Combination with PD-L1-targeted mAb

Cyclophosphamide: 500 mg/m2 IV x 3 days
Fludarabine: 30 mg/m2 IV x 3 days
IL-2: 6M units sc with each FT516 dose



Avelumab: 800 mg every 2 weeks IV until disease progression or unacceptable toxicity

BAVENCIO® avelumab Injection

Avelumab Arm

- Advanced solid tumors for which anti-PD-L1 mAb is approved
- Dose Escalation: 90M, 300M, 900M cells per dose + avelumab
- Dose Expansion: up to 30 patients in two 15-patient expansion cohorts

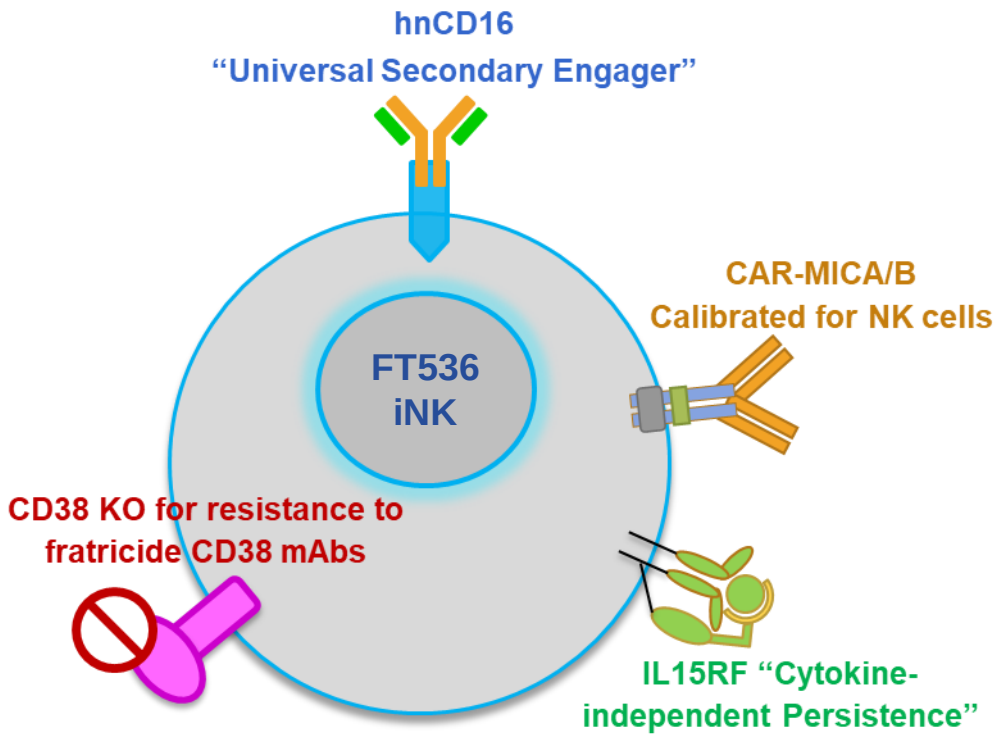
Combination arms with PD1-, HER2-, EGFR-targeted mAbs are also allowed under IND

Fate THERAPEUTICS

FT536: Multi-antigen Targeted CAR-MICA/B NK Cell Product Candidate

Pan-tumor Targeting Strategy for Solid Tumors

Engineered with Four Anti-tumor Modalities for Solid Tumors



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CAR-MICA/B: Chimeric antigen receptor optimized for NK cell biology, which contains a NKG2D transmembrane domain, a 2B4 co-stimulatory domain and a CD3-zeta signaling domain, the conserved α3 domain of MICA/B

IL-15RF: Interleukin-15 receptor fusion, a potent cytokine complex that promotes survival, proliferation and trans-activation of NK cells and CD8 T cells

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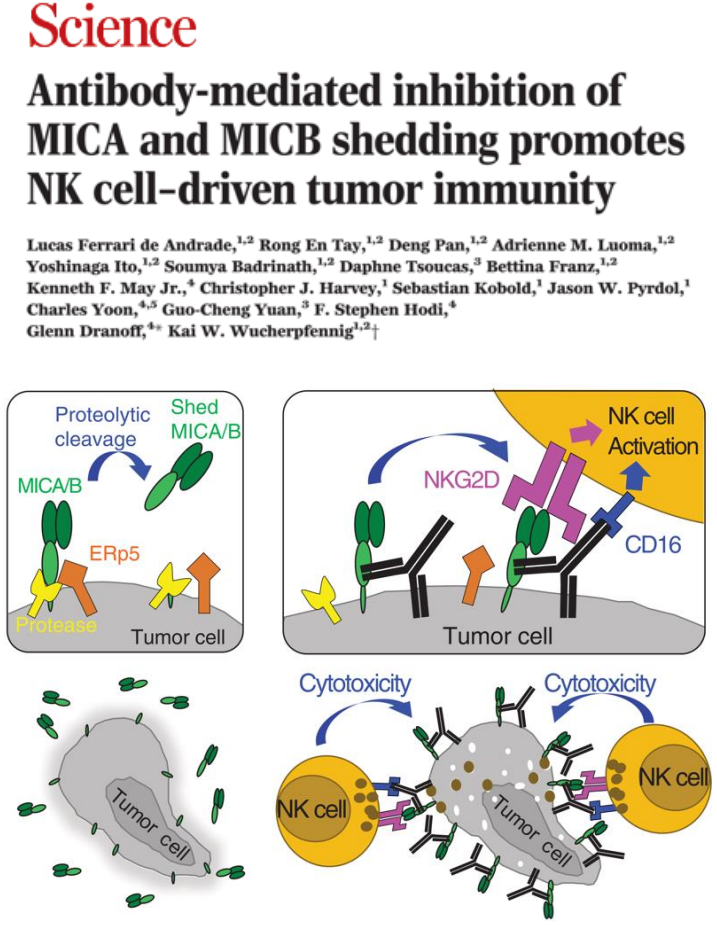
CD38 KO: Deletion of CD38 to eliminate anti-CD38 antibody mediated NK cell fratricide. Also shown to improve NK cell biology and potency through optimization of metabolic signaling

IND Submission Anticipated in 2021

FT536: Multi-Targeted CAR-MICA/B NK Cell Product Candidate

Novel Pan-tumor Targeting Strategy for Solid Tumors



- ✓ MICA/B are induced by cellular stress and transformation, and their expression has been reported for many cancer types
- ✓ NKG2D, an activating receptor expressed on NK and T cells, targets the membrane-distal α1 and α2 domains of MICA/B, activating a potent cytotoxic response
- ✓ Advanced cancer cells frequently evade immune cell recognition by proteolytic shedding of the α1 and α2 domains of MICA/B, which can significantly reduce NKG2D function and the cytolytic activity
- ✓ Therapeutic antibodies targeting the membrane-proximal α3 domain inhibited MICA/B shedding, resulting in a substantial increase in the cell surface density of MICA/B and restoration of immune cell-mediated tumor immunity
- ✓ We have developed a novel CAR targeting the conserved α3 domain of MICA/B (CAR-MICA/B)
- ✓ By uniquely targeting the α3 domain, FT536 prevents shedding and directly targets one of the most highly-expressed stress ligands on a broad range of tumors

Fate THERAPEUTICS

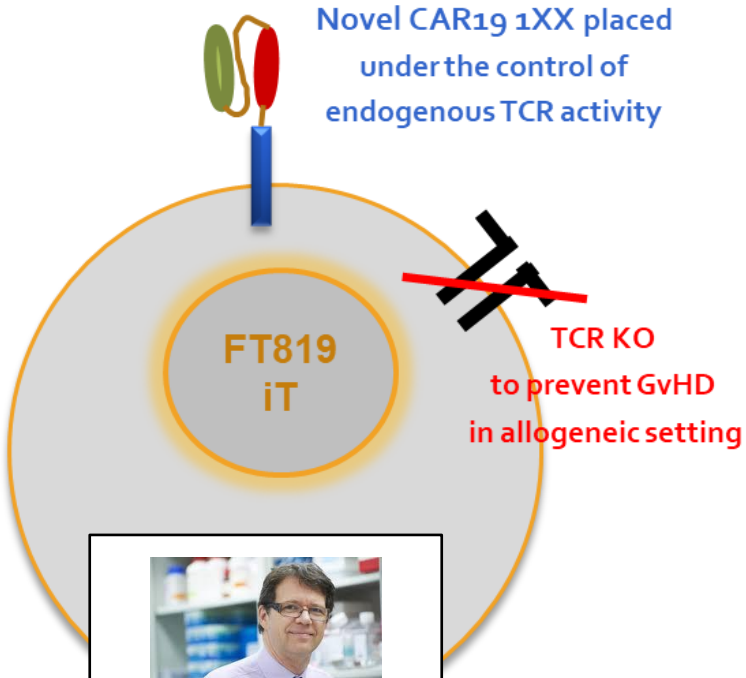
Dana-Farber Cancer Institute

iPSC-derived CAR T Cells

FT819: Off-the-Shelf CAR19 T-Cell Product Candidate

Collaboration with Memorial Sloan Kettering Cancer Center

First-of-Kind Off-the-Shelf CAR T-cell Therapy Derived from Renewable Master iPSC Line Engineered to Uniformly Express Novel 1XX CAR19 and Knock-out TCR



Dr. Michel Sadelain, MD, PhD
Director, Center for Cell Engineering
Memorial Sloan Kettering Cancer Center

1XX CAR19: Novel chimeric antigen receptor consisting of CD28 costimulatory domain and modified CD3z signaling domain for optimal effector cell persistence and anti-tumor potency

---

TRAC targeted CAR: Chimeric antigen receptor integrated into the T Cell Receptor Alpha Constant region to be regulated by endogenous control of TCR expression for optimal CAR performance

---

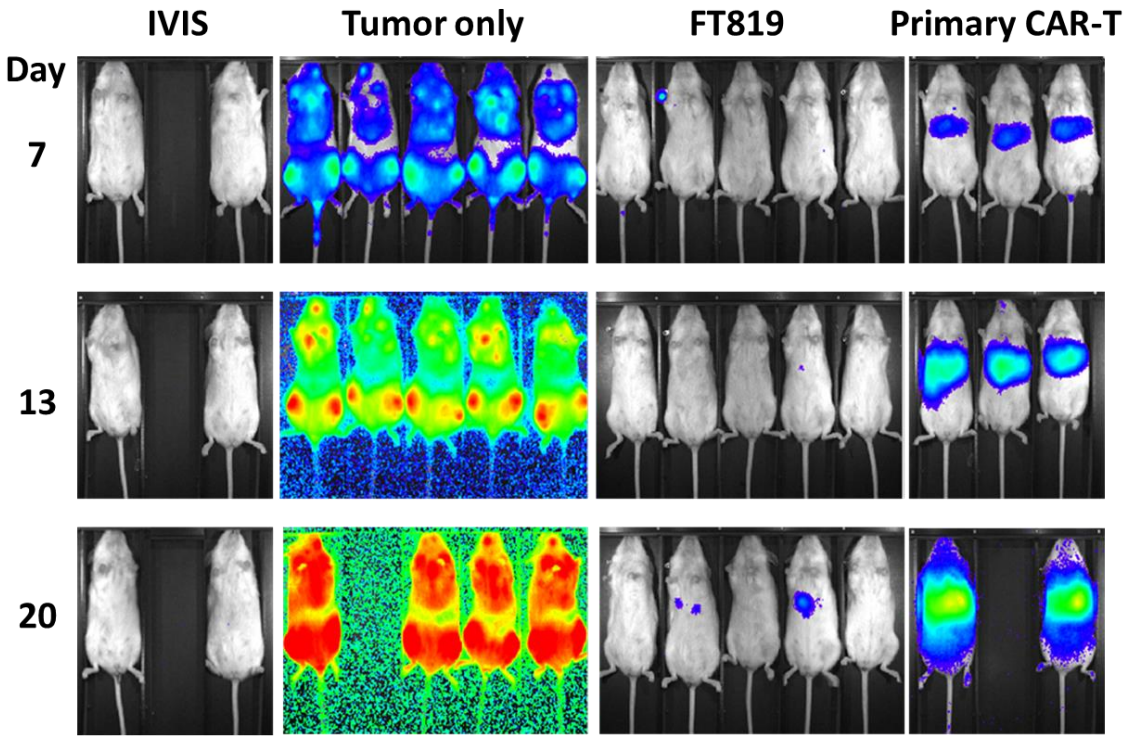
TCR null: Bi-allelic disruption of TRAC at the clonal level for complete removal of TCR expression and the elimination for the possibility of GvHD in allogeneic setting

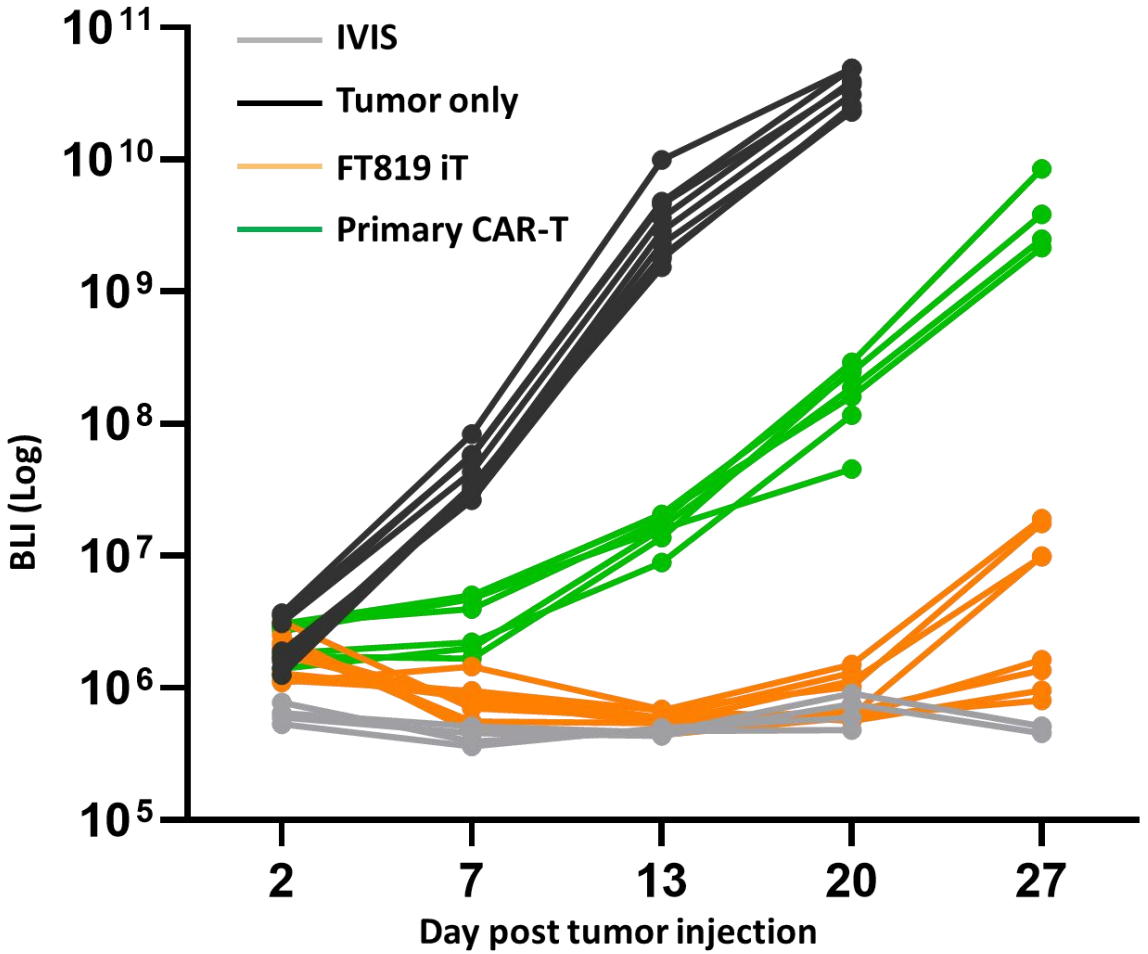
IND Allowed by FDA for BCL, CLL and pre-B ALL

Fate THERAPEUTICS

FT819: Enhanced Tumor Control vs. Primary CAR T Cells

Disseminated Xenograft Model of Lymphoblastic Leukemia



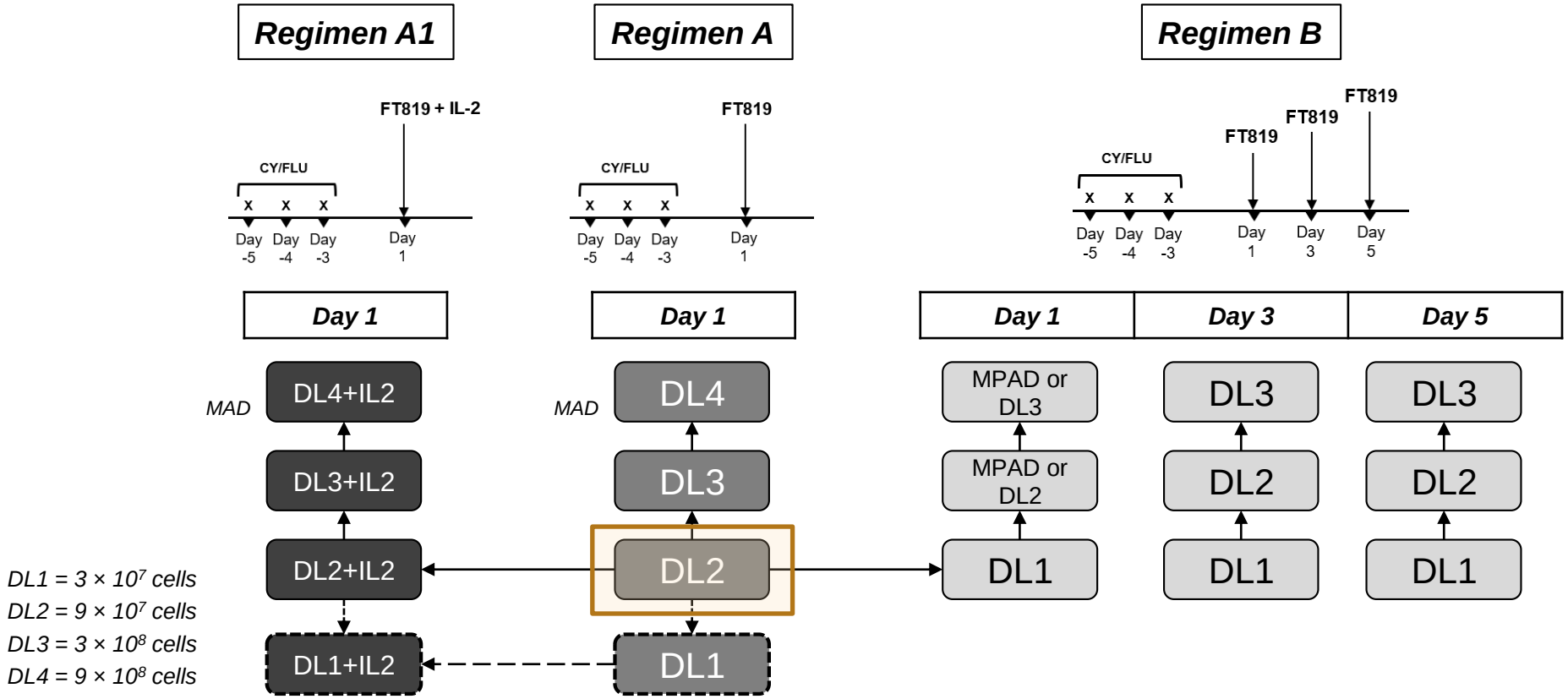


Valamehr et al. Festival of Biologics Annual Meeting 2020

FT819-101: Phase I Dose Escalation Schema

Concurrent and Independent Dose Escalation in BCL, CLL and pre-B ALL

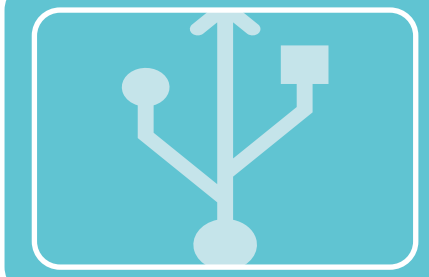
3 Indications x 3 Treatment Regimens



Collaborations

Janssen Cancer Immunotherapy Collaboration (April 2020)

Off-the-shelf, iPSC-derived CAR NK Cell and CAR T-Cell Collaboration

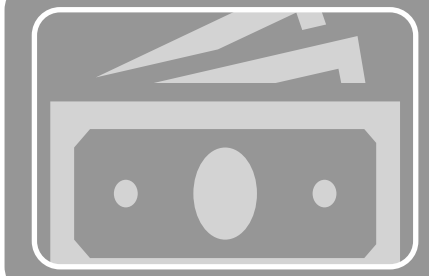


Oncology Innovation

- Proprietary antigen domains contributed by Janssen
- Up to 4 targets including hematologic malignancies and solid tumors
- Substantial investment in next-generation cellular features / functionality

Strategic Collaboration

- FATE leads preclinical development to IND submission
- Janssen option to global clinical development and commercialization
- FATE retains option to 50-50 US commercialization



Significant Economics

- $100m upfront (+$50m equity put)
- Janssen pays for all collaboration costs
- $3+ billion in milestones, double-digit royalties

ONO Cancer Immunotherapy Collaboration (September 2018)

Off-the-shelf, iPSC-derived CAR T-Cell Collaboration

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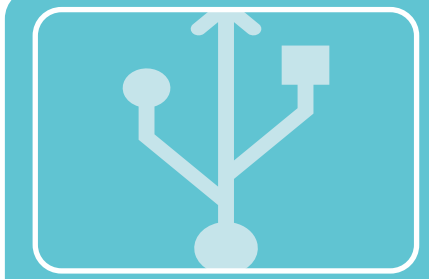
ONO PHARMACEUTICAL CO.,LTD.

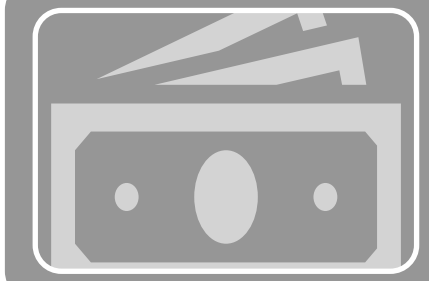


Oncology Innovation

- Proprietary antigen domain contributed by Ono
- Targeting solid tumors
- Potential to include additional antigen binding domains

Strategic Collaboration

- FATE leads preclinical development to pre-IND milestone
- Ono option to global development and commercialization
- FATE retains option to 50-50 worldwide rights ex Asia



Financial Terms

- $10m upfront
- 50-50 cost sharing to pre-IND milestone
- Up to $895 million in milestones, mid-single to low double-digit royalties

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Financials

Financial Summary

As reported in Company's Consolidated Financial Statements

Three Months Ended September 30, 2020	
Revenue	$7.6M
Operating Expense	$39.0M
Cash & Cash Equivalents[1]	$934M
Employees	250+
Total Shares Outstanding[2]	100.9M

[1] On an as adjusted basis to include January 2021 common stock offering

[2] Includes 14.0M shares of common stock from conversion of non-voting preferred stock.

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Better Cells For Better Therapies™