



Off-the-shelf Cell-based Cancer Immunotherapy

Developing First-of-kind Cell Products using Clonal Master iPSC Lines

June 2020

www.fatetherapeutics.com

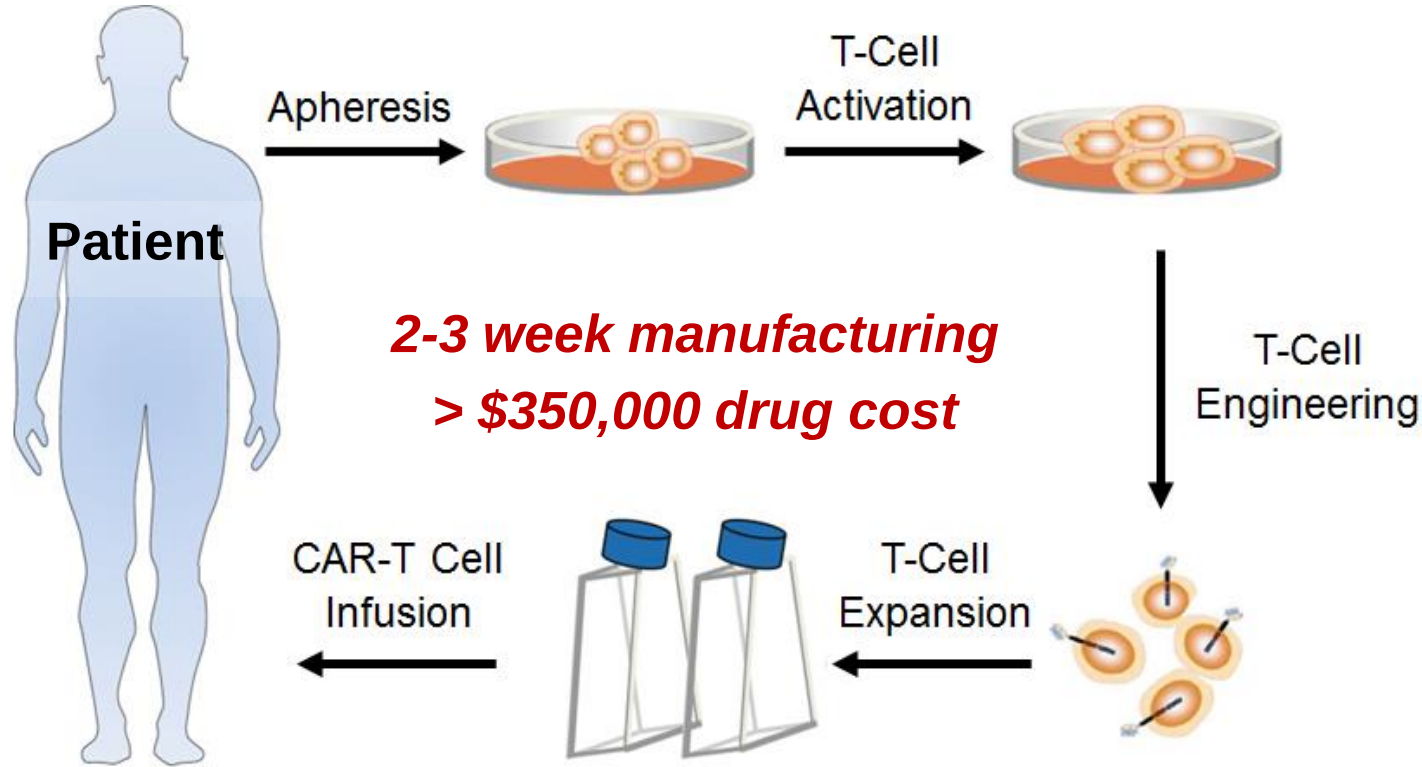
Forward-Looking Statements



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 clinical investigation, preclinical development and manufacture of its product candidates, the timing for the Company's planned submission of regulatory filings and the receipt of data from its clinical trials and preclinical studies, the Company's clinical development and regulatory strategy, the therapeutic and market potential of the Company's product candidates, and the success of, and ability of the Company to receive future payments under, its collaboration agreements. 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.

First Innings of Cell Therapy Development

Patient-derived CAR-T Cell Immunotherapy



"When factoring in all the costs associated with CAR T-cell therapy, hospitals may charge as much as \$1.5 million or more to avoid losing money."

Richard T. Maziarz, MD
Professor of Medicine, Oregon Health & Science University's Knight Cancer Institute

Impaired Starting Material | **Random & Variable** Engineering | **Complex** Logistics
Heterogeneous Drug Product | **Expensive** | **Single-dose** Limitation

Changing the Game in Cell-based Cancer Immunotherapy

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	Limited Dose Availability	Off-the-Shelf Availability
Cost-per-Dose	High	Low
Dosing	Single Dose	Multiple Doses / Multiple Cycles
Overall Paradigm	Process-centric	Product-centric

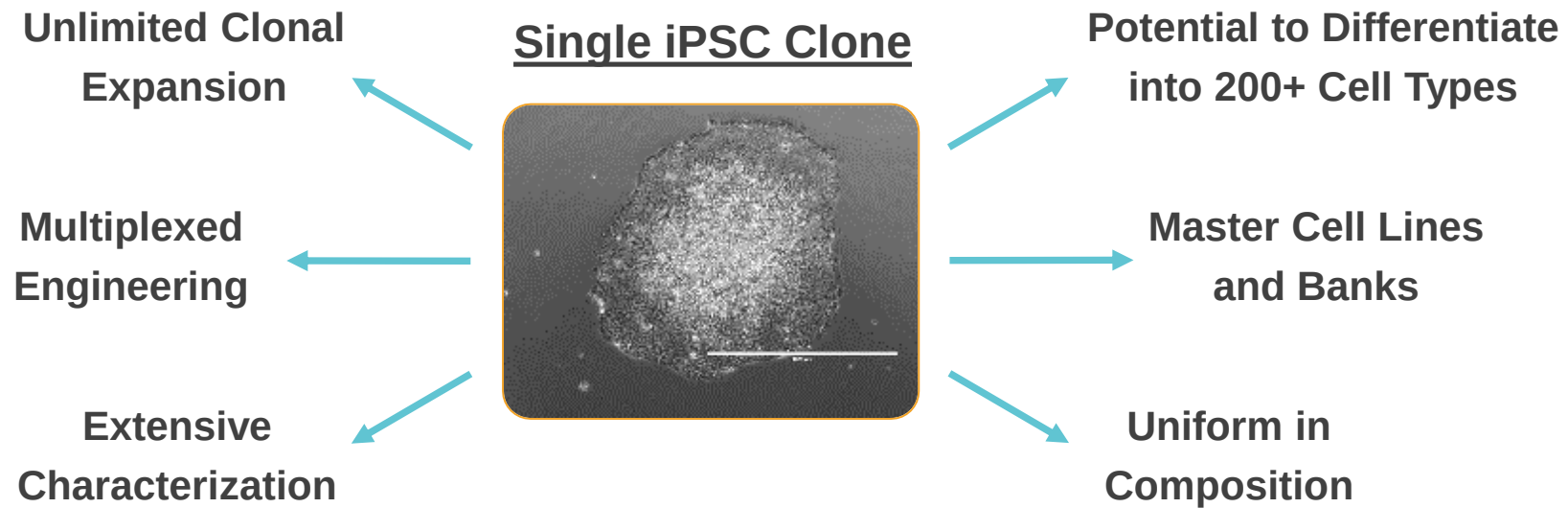
Unique Advantages of Human iPSCs

Single-cell Isolation, Characterization & Selection



A Single Human Induced Pluripotent Stem Cell (iPSC)

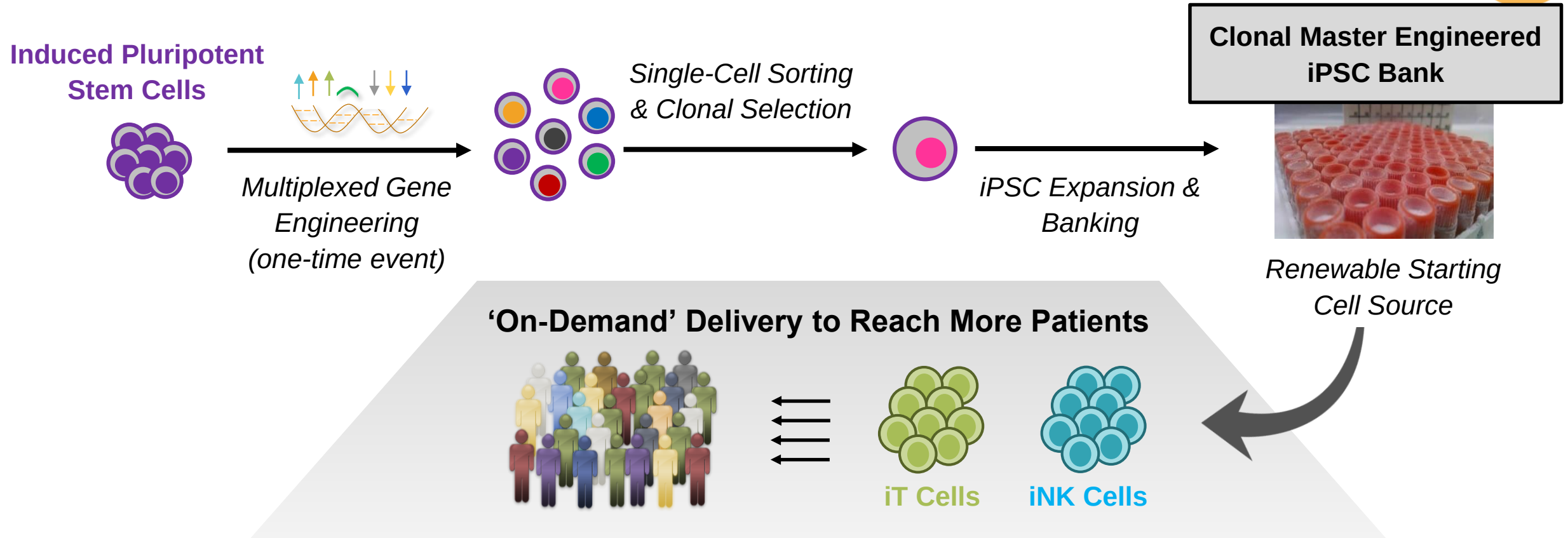
A renewable source for making cell products



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

iPSC Product Platform

Disruptive Approach Enabling Mass Production of Universal NK Cell and T-Cell Products



Clonal master iPSC lines are a renewable cell source that can be repeatedly used to mass produce homogeneous, cryopreserved cell product in a cost-effective manner

iPSC Product Platform

Ownership and Full Control of cGMP Manufacturing



Launched First Facility in 3Q19 / Second Facility Under Construction

FT500 Cell Product		
Identity, CD45+	100%	
Identity, CD45+CD56+	98%	
Viability	80%	
Residual iPSCs	Not detected	
Packaging	Cryopreserved	
Availability	On-site	
Administration	Thaw-and-infuse 'on demand'	
Delivery	Outpatient setting	



Uniformly-engineered cell product Cryopreserved with high post-thaw viability

Potential for thousands of doses per campaign Low-cost per dose cGMP production

On-demand availability for broad patient accessibility



iPSC-derived NK Cell Franchise

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



Product	Cell Type	Engineered Functionality	Indication	R&D	Preclinical	Clinical
Hematologic Malignancies						
FT516	iNK	hnCD16	AML			
FT516	iNK	hnCD16	BCL + mAb			
FT596	iNK	hnCD16 + IL15-RF + CAR19	BCL and CLL ± mAb			
FT538	iNK	hnCD16 + IL15-RF + CD38-KO	AML			
FT538	iNK	hnCD16 + IL15-RF + CD38-KO	MM + mAb			
FT576	iNK	hnCD16 + IL15-RF + CD38-KO + CAR-BCMA	MM ± mAb			
FT819	iT	TRAC-targeted CAR19 + TCR-KO	Hematologic Malignancies			
Advanced Solid Tumors						
FT500	iNK	Non-engineered	Advanced Solid Tumors + CPB			
FT516	iNK	hnCD16	Advanced Solid Tumors + mAb			
FT###	<u>iNK</u> and <u>iT</u>	Multiplexed engineered CAR-MICA/B	Advanced Solid Tumors			
Cancer Immunotherapy Collaborations						
Janssen	iNK and iT	Multiplexed engineered CAR-targeted	Up to 4 cancer antigens			
ONO	iT	Multiplexed engineered CAR-targeted	Up to 2 cancer antigens			
iPSC = induced pluripotent stem cell <u>iNK</u> = iPSC-derived NK cell <u>iT</u> = iPSC-derived T cell hnCD16 = high-affinity, non-cleavable CD16 Fc receptor IL15-RF = IL-15/IL-15 receptor fusion CD38-KO = CD38 knock-out CAR = chimeric antigen receptor <u>mAb</u> = monoclonal antibody CPB = checkpoint blockade therapy AML = Acute myelogenous leukemia BCL = B-cell lymphoma CLL = Chronic lymphocytic leukemia MM = Multiple myeloma						

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
Multi-faceted Innate Immunity		✓	✓	✓	✓	✓
+ High-Affinity, Non-cleavable CD16	<i>Augment mAb therapy</i>		✓	✓	✓	✓
+ IL-15 Receptor Fusion	<i>Enhance NK cell function</i>			✓	✓	✓
+ CAR Insertion	<i>Target tumor-associated antigen</i>			CD19		BCMA
+ CD38 Knock-out	<i>Resist CD38-mediated fratricide</i>				✓	✓
	Total # of Synthetic Elements	0	1	3	3	4

Six INDs Allowed by FDA for FT500, FT516, FT596 and FT538

IND Submission for FT576 Planned for 4Q20

FT500 Off-the-Shelf NK Cell Product Candidate

Phase 1 Dose Escalation Clinical Objectives



Assessment of Safety & Tolerability of Novel Cell Therapy Treatment Paradigm

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

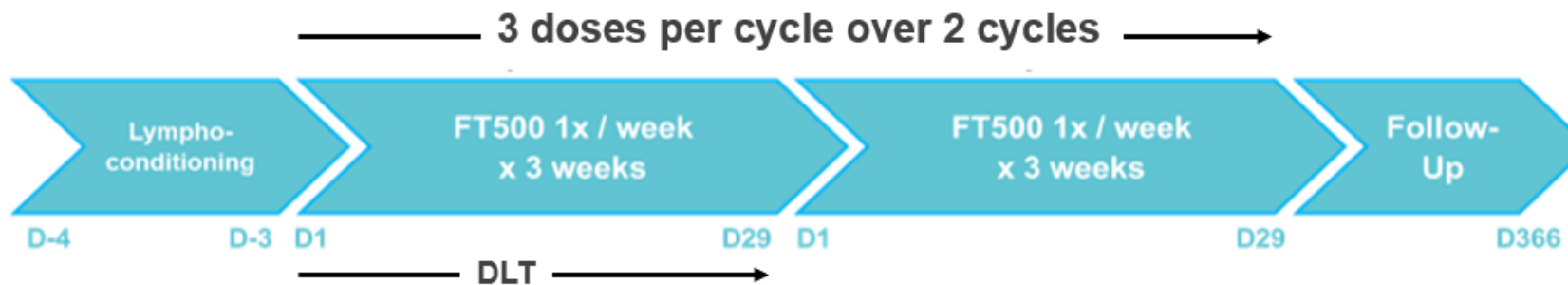
- Immune cell recovery
- Endogenous cytokine response (GvHD, CRS)
- Anti-product immunogenicity

FT500 Off-the-Shelf NK Cell Product Candidate

Phase 1 Dose Escalation in Advanced Solid Tumors

Phase 1 Dose Escalation Design in Advanced Solid Tumors

Cy: 300 mg/m² IV x 2 days
Flu: 25 mg/m² IV x 2 days
Prior to Cycle 1 only



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

FT500 Phase 1 Dose Escalation – Key Clinical Read-outs

Regimen A Monotherapy – Safety, Tolerability, Best ORR, and Disposition



Cohort / Cell Dose	Subject #	# Lines of Prior Therapy	FT500 Doses Received	Safety			Best Overall Response *	Disposition	
				Dose Limiting Toxicities	Related Grade ≥ 3 AEs	Related SAEs		Days on Study	Reason for Study Discontinuation
A1 100M cells / dose	1	3	6	None	None	None	SD	94	Clinical Progression
	2	2	6	None	None	None	iUPD	94	iCPD
	3	6	6	None	None	None	SD	83	iUPD
A2 300M cells / dose	1	4	6	None	None	None	SD	70	iUPD
	2	1	5	None	None	None	SD	55	Clinical Progression
	3	2	3	None	None	None	iUPD	33	iUPD
	4	4	6	None	None	None	iUPD	72	Clinical Progression
	5	4	6	None	None	None	iUPD	90	iCPD

* Per iRECIST SD = stable disease iUPD = immune unconfirmed progressive disease iCPD = immune confirmed progressive disease

FT500 Phase 1 Dose Escalation – Key Clinical Read-outs

Regimen B CI Combination – Safety, Tolerability, Best ORR, and Disposition



Cohort / Cell Dose	Subject #	# Lines of Prior Therapy	FT500 Doses Received	Safety			Best Overall Response *	Disposition	
				Dose Limiting Toxicities	Related Grade ≥ 3 AEs	Related SAEs		Days on Study	Reason for Study Discontinuation
B1^a 100M cells / dose	1	7	3	None	None	None	SD	76	Patient decision
	2	4	6	None	None	None	SD	98	iUPD
	3	2	6	None	None	None	iUPD	85	iCPD
B2^b 300M cells / dose	1	4	6	None	None	None	SD	On-study	n/a
	2	14	4	None	None	None	iUPD	61	Clinical Progression
	3	5	6	None	None	None	iUPD	72	iUPD

* Per iRECIST SD = stable disease iUPD = immune unconfirmed progressive disease iCPD = immune confirmed progressive disease

^a B1 As of 28 November 2019 data cutoff.

^b B2 Not included in 28 November 2019 data cutoff; as reported by investigator.

Database is not locked and final data are subject to change.

FT500 Phase 1 Dose Escalation – Key Clinical Read-outs

Summary Findings



Treatment with Universal, Off-the-Shelf, iPSC-derived NK Cell Cancer Immunotherapy Showed Favorable Safety and Was Well Tolerated

As of a November 28, 2019 data cutoff:

- All patients received ≥ 3 doses of FT500 in outpatient setting
- No DLTs
- No FT500-related SAEs or Grade ≥ 3 AEs
- No immune-related AEs (e.g., CRS, neurotoxicity, or GVHD)
- No treatment discontinuations due to AEs

FT500 Phase 1 Dose Escalation – Key Translational Questions

Assess Patient's Immunological Response to Novel Cell Therapy Treatment Paradigm



FT500 is a Universal, Off-the-Shelf, iPSC-derived NK Cell Cancer Immunotherapy administered with Multiple Doses to Patients without Matching

- Immune cell recovery
 - Do iNK cells negatively impact hematopoietic recovery following lympho-conditioning?
- Endogenous cytokine response
 - Is there molecular evidence of immunotoxicity (e.g., CRS, neurotoxicity and/or GvHD)?
- Anti-product immunogenicity
 - T-cell mediated: Do anti-product T-cell clones expand and become dominant?
 - B-cell mediated: Are anti-product antibodies raised?

FT500 Phase 1 Dose Escalation – Key Molecular Read-outs

Summary Findings



Administration of Multiple Doses of FT500 to Patients without Matching Was Safe and Well Tolerated without Eliciting Host Immune Rejection

As of a November 28, 2019 data cutoff:

- Healthy endogenous immune cell recovery following multi-dose FT500 treatment
- No biomarker evidence of sub-clinical CRS, neurotoxicity, or GvHD
- Endogenous T-cell response to FT500 is not indicative of T-cell mediated immune rejection
- Anti-FT500 antibody assessment is not indicative of B-cell mediated immune rejection

Outpatient lympho-conditioning regimen: Cy (300 mg/m²) x Flu (25 mg/m²) x 2 days prior to Cycle 1 only

FT500 Phase 1 Dose Expansion

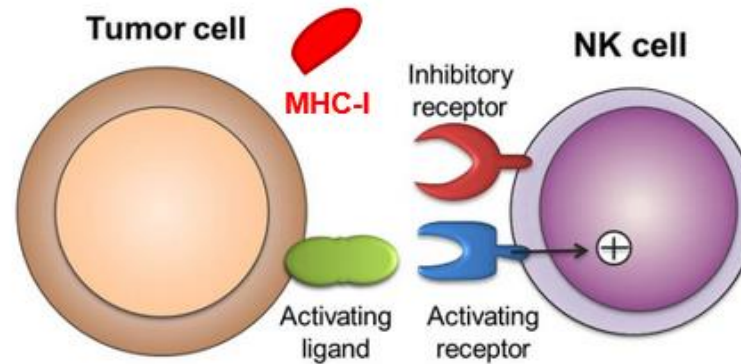
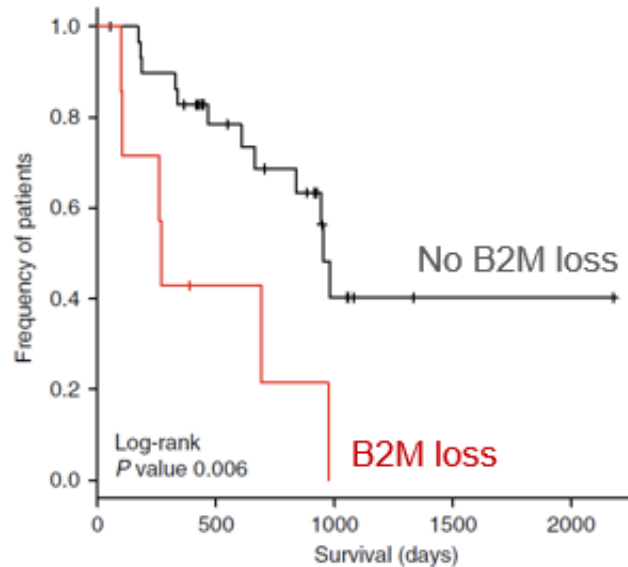
Overcome Resistance to Checkpoint Inhibitor Therapy in Non-Small Cell Lung Cancer

Target Loss of MHC-I Tumor Escape Mechanism in Regimen B2 (n=15)



DOI: 10.1038/s41467-017-01062-w

Resistance to checkpoint blockade therapy through inactivation of antigen presentation



NK cells have the unique ability to recognize and kill cancer cells that have down-regulated MHC Class I, a major tumor escape mechanism

- Loss or down-regulation of MHC Class I is a major tumor escape mechanism in patients having progressed / failed checkpoint inhibitor therapy
- Several tumor cell mutations, including in B2M gene, disrupt MHC Class 1 expression
- B2M mutations are enriched in patients who are resistant to checkpoint blockade (~30%) and are associated with poor survival

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

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



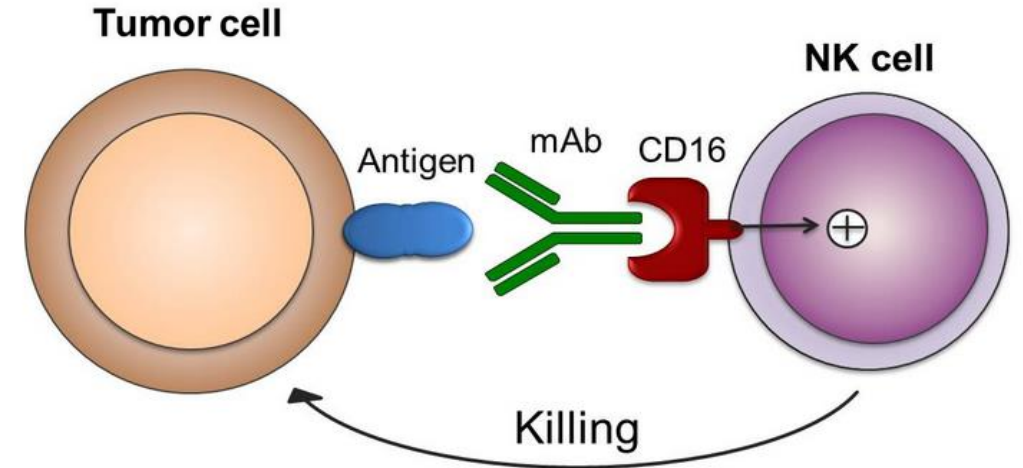
Universal, Off-the-Shelf NK Cell Cancer Immunotherapy Pipeline

Clonal Master iPSC Line	Synthetic Biology	FT500	FT516	FT596	FT538	FT576
Multi-faceted Innate Immunity		✓	✓	✓	✓	✓
+ High-Affinity, Non-cleavable CD16	<i>Augment mAb therapy</i>		✓	✓	✓	✓
+ IL-15 Receptor Fusion	<i>Enhance NK cell function</i>			✓	✓	✓
+ CAR Insertion	<i>Target tumor-associated antigen</i>			CD19		BCMA
+ CD38 Knock-out	<i>Resist CD38-mediated fratricide</i>				✓	✓
	Total # of Synthetic Elements	0	1	3	3	4

FT516 Off-the-Shelf 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 IgG1 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
- **CD16 shedding in the tumor microenvironment can significantly limit NK cell anti-tumor activity**



Rituxan
Rituximab

GAZYVA
obinutuzumab

DARZALEX
(daratumumab)

Herceptin
trastuzumab
Precision • Power • Promise

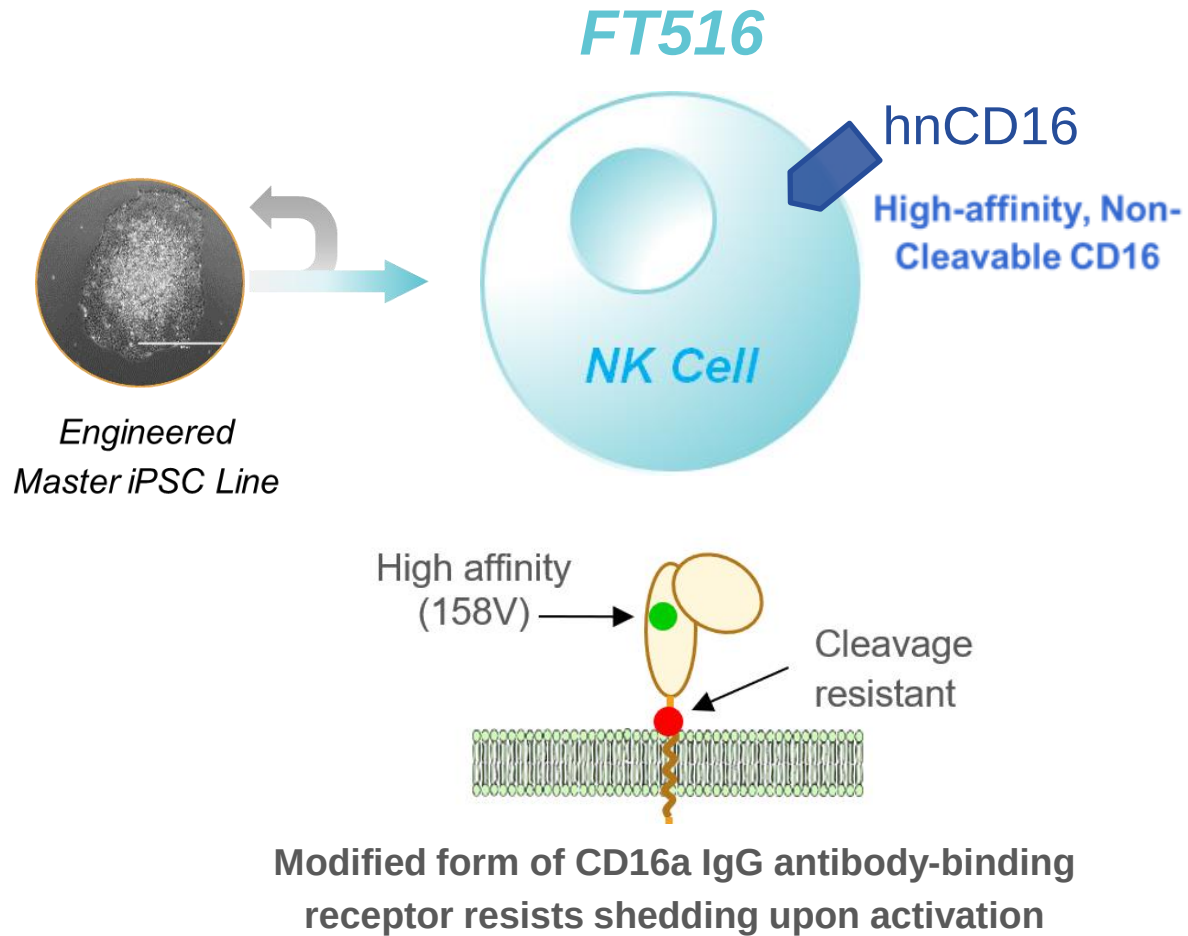
ERBITUX
Cetuximab

BAVENCIO
avelumab Injection

How to bring the 158V CD16 NK cell experience to all patients?

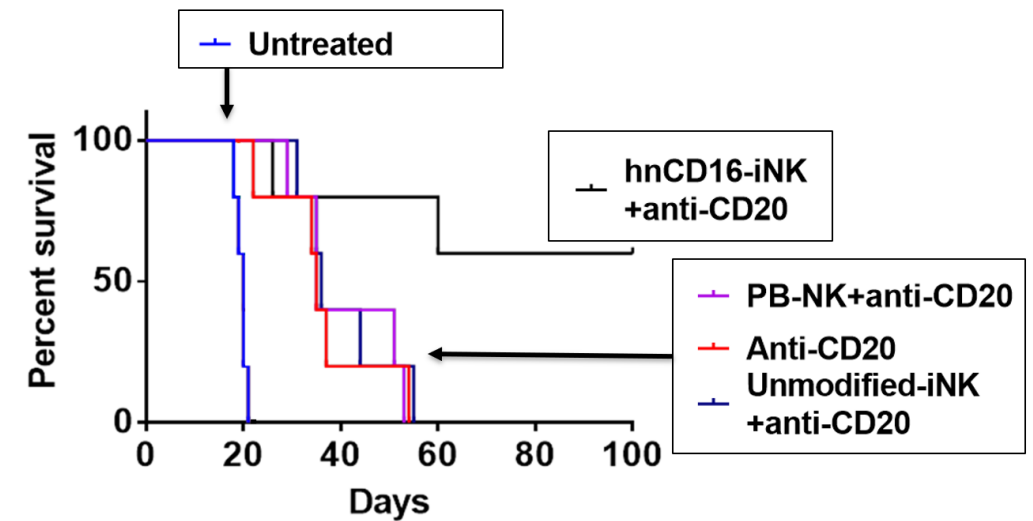
FT516 Off-the-Shelf hnCD16 NK Cell Product Candidate

High-Affinity 158V, Non-Cleavable CD16 Fc Receptor for Enhanced ADCC



Enhanced Survival *In Vivo* with Rituximab

Mouse model of human lymphoma (Raji cells)



Median survival time for FT516 + anti-CD20 was not reached at Day 100

Pluripotent stem cell-derived NK cells with high-affinity noncleavable CD16a mediate improved antitumor activity

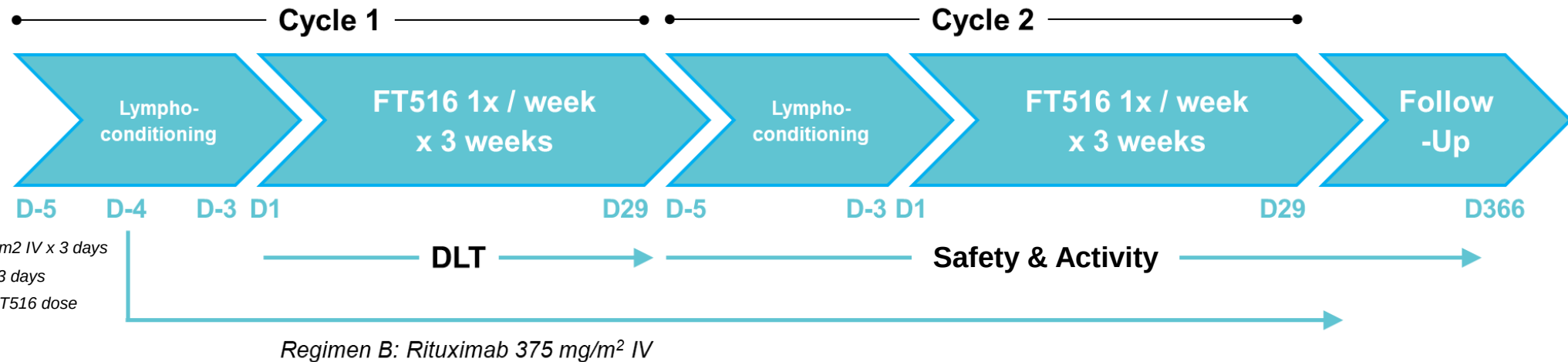
Huang Zhu,¹ Robert H. Blum,¹ Ryan Bjordahl,² Svetlana Gaidarova,² Paul Rogers,² Tom Tong Lee,² Ramzey Abujaour,² Gregory B. Bonello,² Jianming Wu,³ Pei-Fang Tsai,² Jeffrey S. Miller,⁴ Bruce Walcheck,³ Bahram Valamehr,² and Dan S. Kaufman¹



FT516 Off-the-Shelf hnCD16 NK Cell Product Candidate

Phase 1 Study Design: Multiple Doses over Multiple Cycles for AML & Lymphoma

First-ever Clinical Trial in World of Engineered iPSC-derived Cell Therapy



Regimen A – Monotherapy

- Relapsed / refractory AML
- Dose Escalation: 90M, 300M, 900M cells per dose
- Dose Expansion: up to 15 subjects

Regimen B – 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

FT516 Off-the-Shelf hnCD16 NK Cell Product Candidate

First Clinical Observations in Regimen A for Patients with AML



Patient 1

- Refractory to multiple lines of therapy
- Early disease assessment following the first three doses of FT516 with IL-2 cytokine support showed:
 - No morphologic evidence of leukemia in the bone marrow
 - Recovery of neutrophils (>1,000 per μL)
- Protocol-defined response assessment following completion of the second 30-day cycle of FT516 showed stable disease
 - Patient successfully bridged to haploidentical HSCT

Patient 2

- Received three prior lines of therapy and was most recently refractory to experimental therapy
- Protocol-defined response assessment following completion of the second 30-day cycle of FT516 showed stable disease

No DLTs, no FT516-related SAEs, and no events of cytokine release syndrome, neurotoxicity, or graft-versus-host disease were reported by investigators in either patient

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
Multi-faceted Innate Immunity		✓	✓	✓	✓	✓
+ High-Affinity, Non-cleavable CD16	<i>Augment mAb therapy</i>		✓	✓	✓	✓
+ IL-15 Receptor Fusion	<i>Enhance NK cell function</i>			✓	✓	✓
+ CAR Insertion	<i>Target tumor-associated antigen</i>			CD19		BCMA
+ CD38 Knock-out	<i>Resist CD38-mediated fratricide</i>				✓	✓
	Total # of Synthetic Elements	0	1	3	3	4

FT596 Off-the-Shelf Multi-Targeted CAR 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**

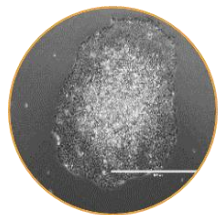
**High-affinity, Non-
Cleavable CD16**

Rituxan[®]
Rituximab

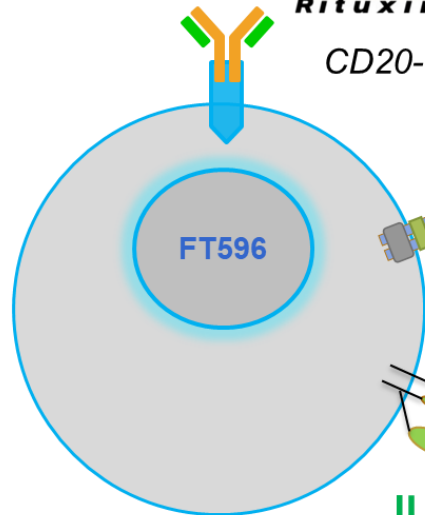
GAZYVA[®]
obinutuzumab

CD20-targeted mAbs

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



Engineered
Master iPSC Line



CAR19

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

**IL15 Receptor
Fusion**

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

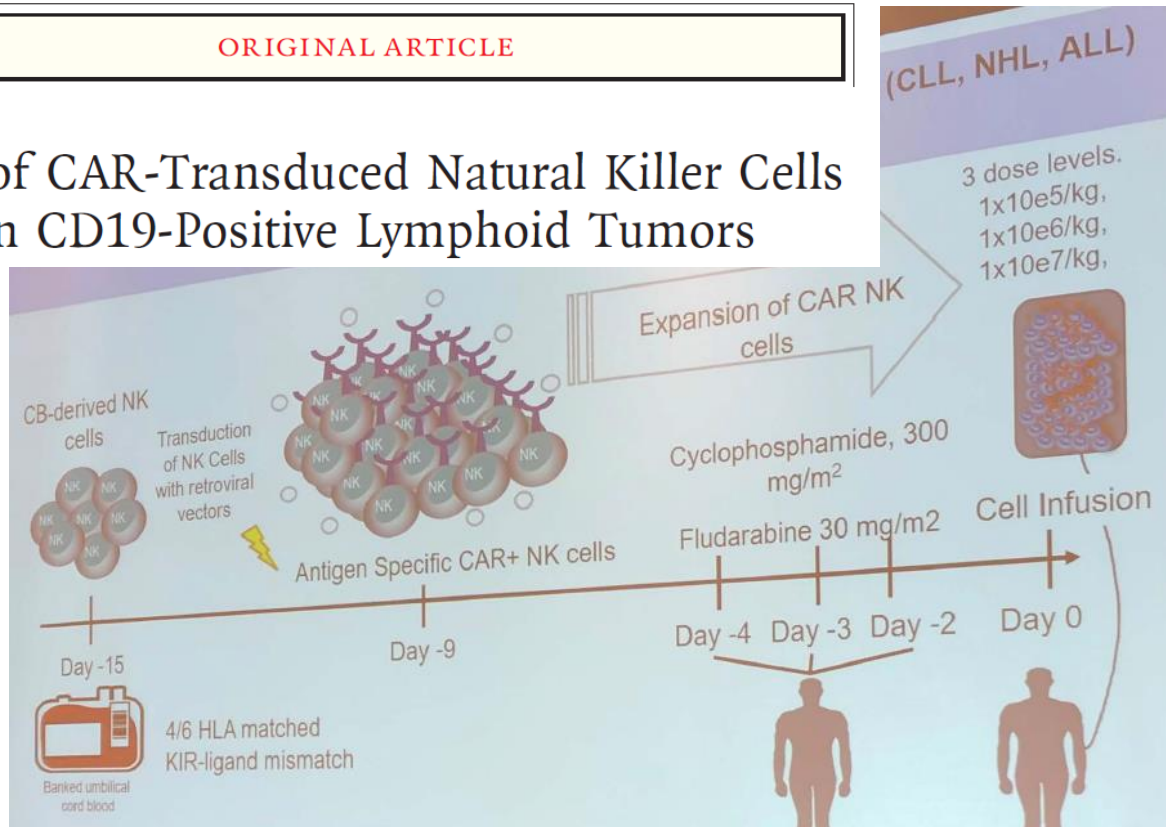
FT596 Supported by Clinical POC with Donor-derived CAR19 NK Cells

M.D. Anderson Cancer Center, Katy Rezvani, M.D., Ph.D. (NCT03056339)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Use of CAR-Transduced Natural Killer Cells in CD19-Positive Lymphoid Tumors



NEJM 2020;382:545-53.

- First-in-human clinical trial testing the safety and efficacy of cord blood-derived CAR NK cells
 - Transduced with CAR19 (28z) / IL15 (secreted) / iCas9 (suicide)
- Treated 11 patients with r/r B-cell malignancies
 - 3 dose levels (0.1M, 1.0M, 10M cells / kg)
- CR in 8/11 patients
 - CRs observed at all dose levels
 - CRs observed across all disease sub-types
- No CRS / neurotoxicity

FT596 Uniformly-engineered, Well-characterized Product Profile

Derived from Clonal Master Engineered iPSC Line



High-affinity, Non-
Cleavable CD16

Rituxan
Rituximab

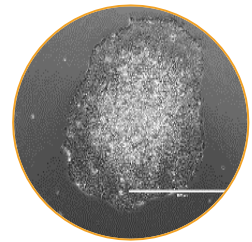
GAZYVA
obinutuzumab

CD20-targeted mAbs

CAR19

IL15 Receptor
Fusion

FT596

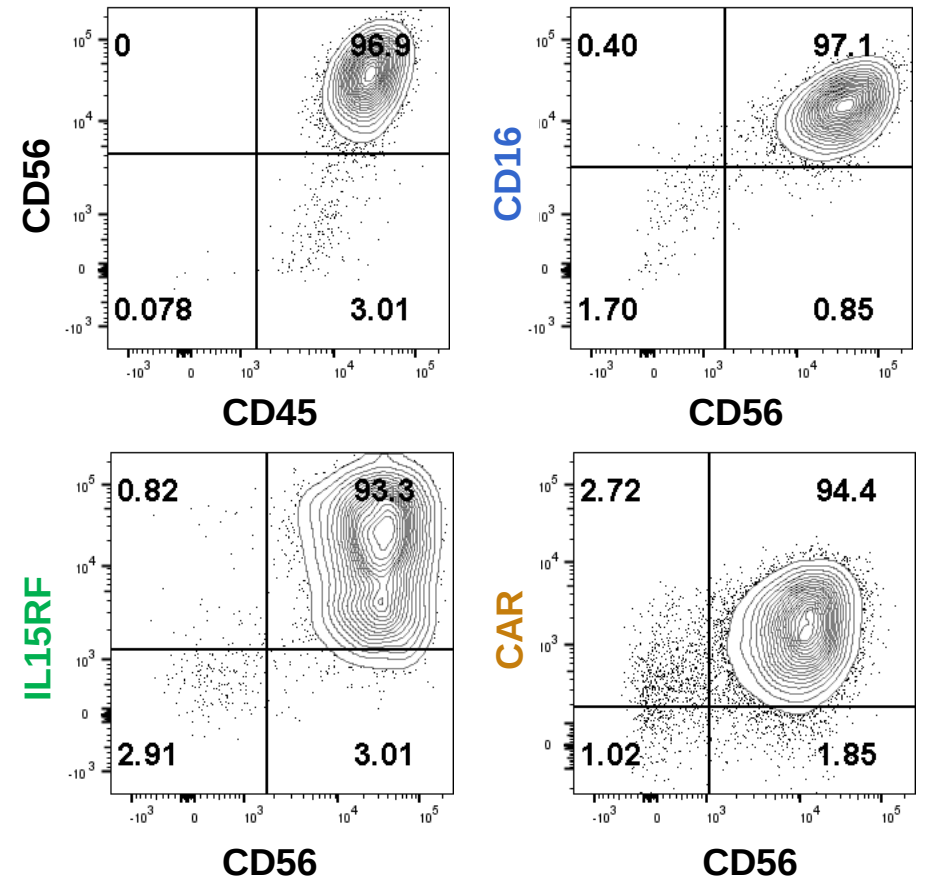


Clonal Master iPSC Line
derived from a single iPSC
engineered with three
functional elements

1×10^6 iPSCs

1×10^{12} iNKs

FT596 Product Profile



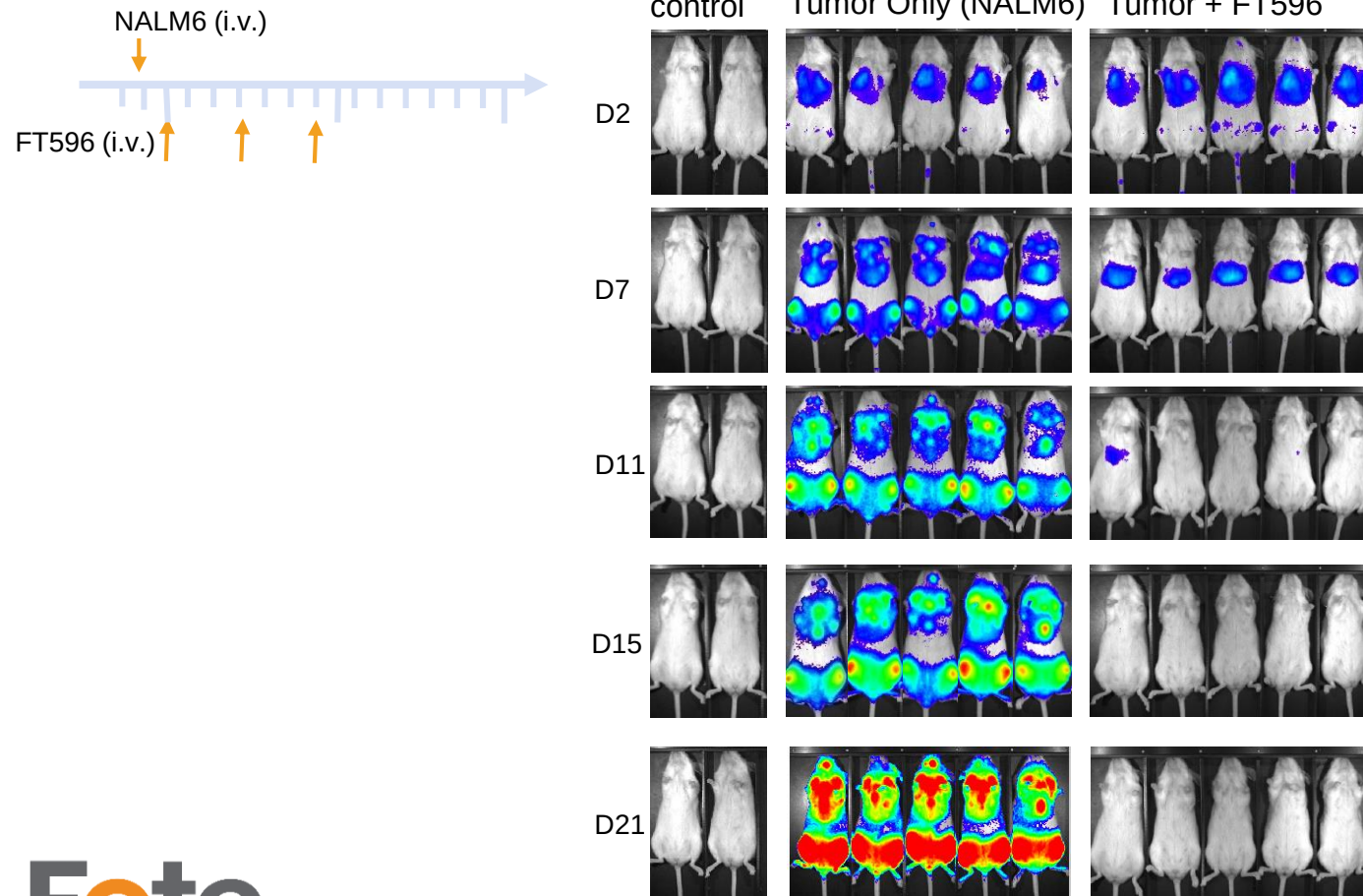
FT596 Monotherapy Anti-tumor Activity *In Vivo*

Durable Anti-Leukemia and Anti-Lymphoma Activity in Various Xenograft Mouse Models

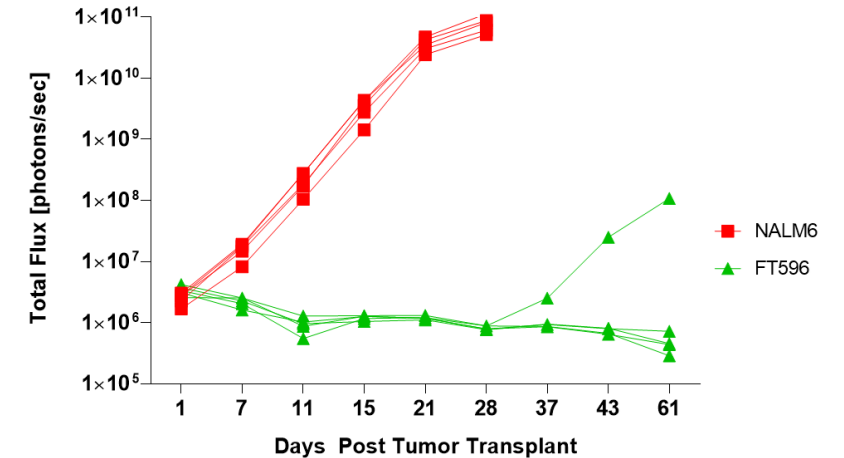


Monotherapy

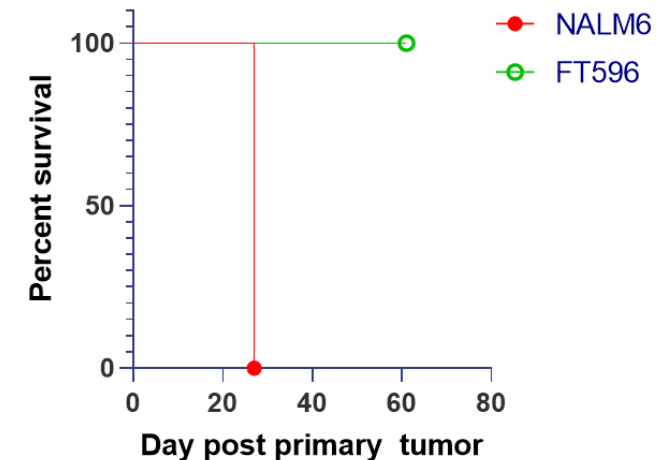
Leukemia xenograft NSG immunodeficient mouse model



Tumor Burden and Control



Survival Curve



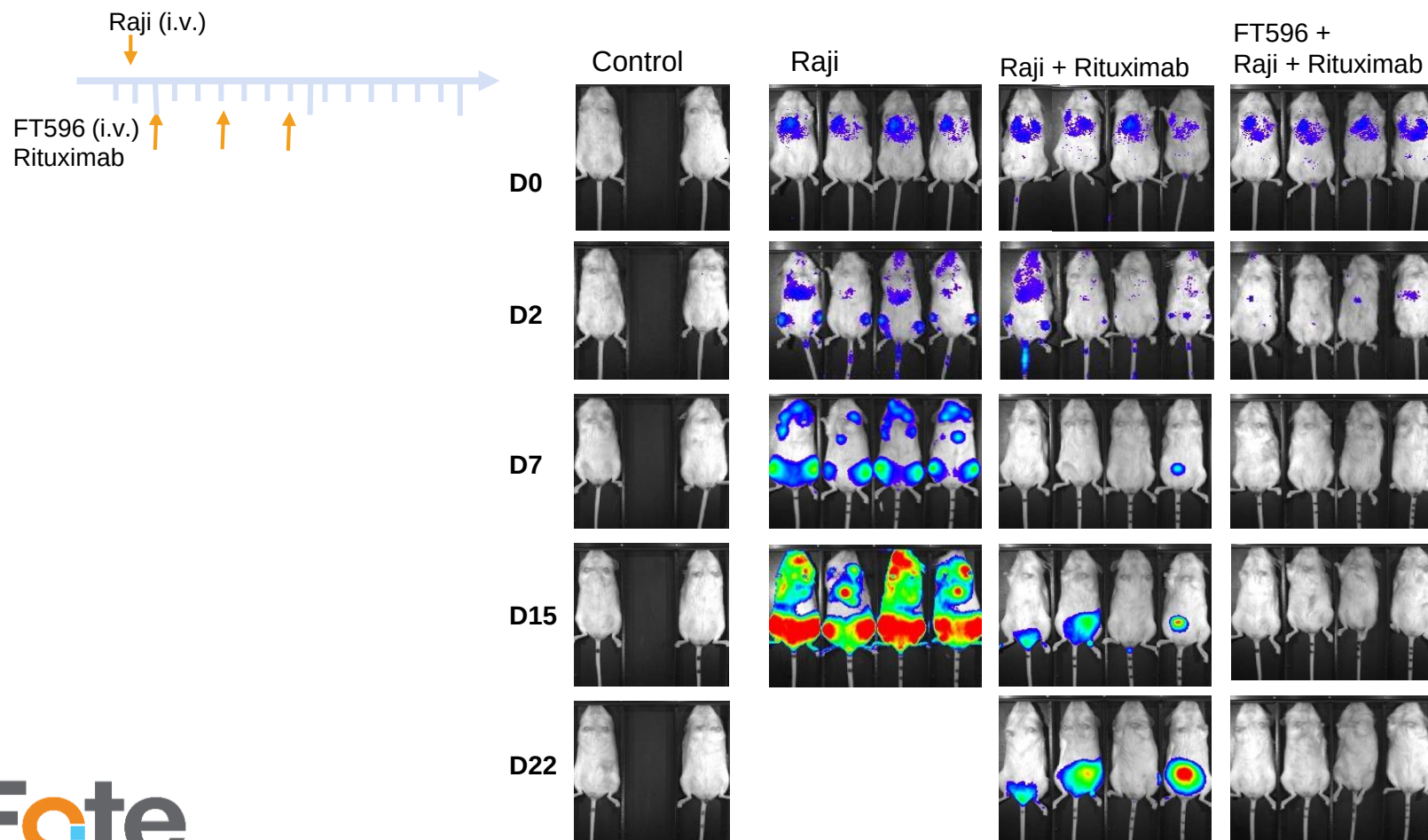
FT596 Combination Anti-tumor Activity *In Vivo*

Durable Anti-Leukemia and Anti-Lymphoma Activity in Various Xenograft Mouse Models

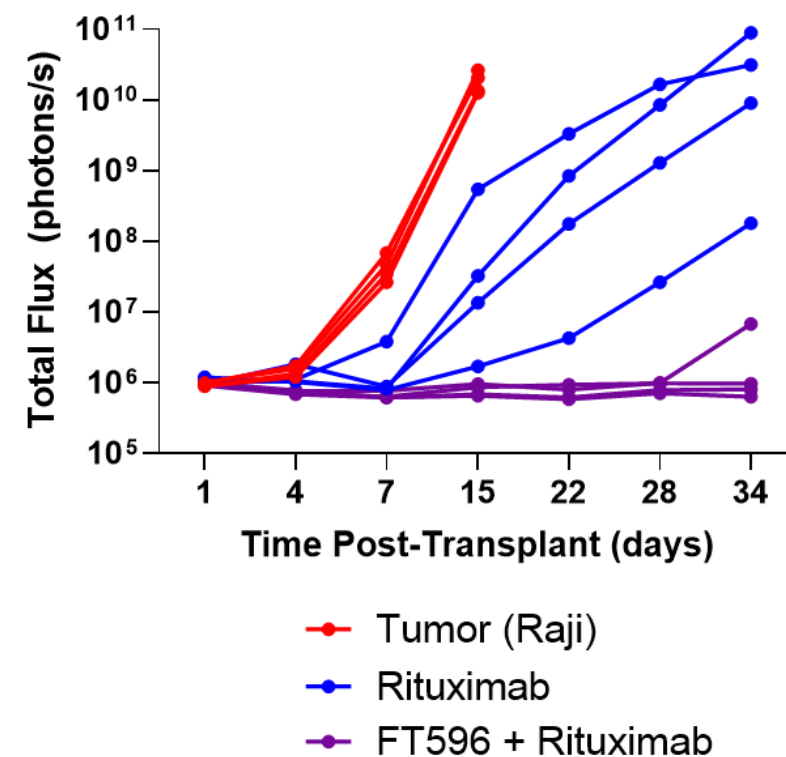


Combination

Lymphoma xenograft NSG immunodeficient mouse model



Tumor Burden and Control

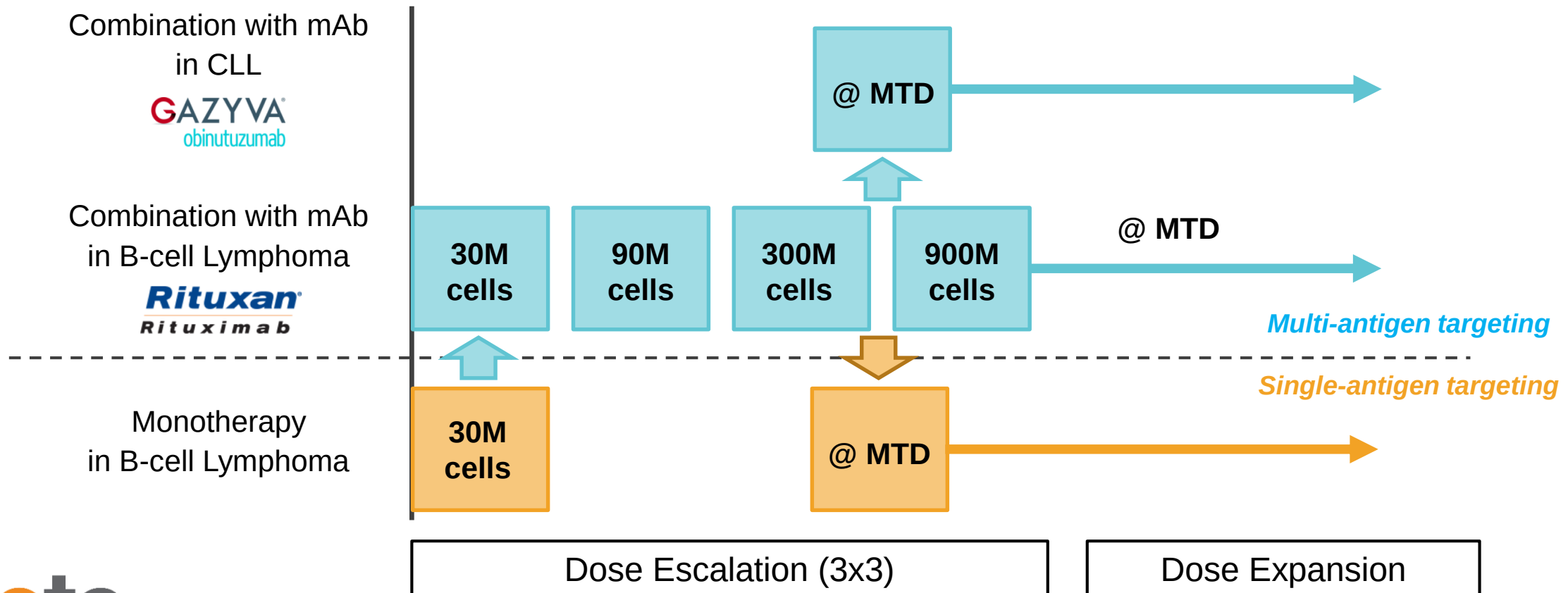


FT596 Universal, Off-the-Shelf Multi-antigen Targeted CAR NK Cell

Phase 1 Study Design in Relapsed / Refractory B-cell Lymphoma and CLL



Phase 1 Dose Escalation – Monotherapy and mAb Combination



FT596 Universal, Off-the-Shelf Multi-antigen Targeted CAR NK Cell

First Clinical Observations in Regimen A Monotherapy



Patient 1 (single dose of 30M FT596 cells as a monotherapy)

- Treated with 4+ lines of therapy for relapsed / refractory diffuse large B-cell lymphoma (DLBCL)
- Most recently had disease progression following CD19-targeting CAR T-cell therapy (axicabtagene ciloleucel)
- Day 29 protocol-defined response assessment showed progressive disease (PD)

Patient 2 (single dose of 30M FT596 cells as a monotherapy)

- Treated with 4+ lines of therapy for relapsed / refractory diffuse large B-cell lymphoma (DLBCL)
- Most recently refractory to experimental combo therapy comprised of expanded allogeneic NK cells, IL-2, and rituximab
- Day 29 protocol-defined response assessment showed partial response (PR)
 - >70% reduction in standardized uptake value (SUV) and >50% reduction in tumor size by PET-CT
 - Peak FT596 cell expansion detected at Day 8 (~1800 transgene copies / μ g DNA)
 - Seeking consent from FDA to re-treat with single-dose of 30M FT596 cells

No DLTs, no FT596-related SAEs, and no events of cytokine release syndrome, neurotoxicity, or graft-versus-host disease were reported by investigators in either patient

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

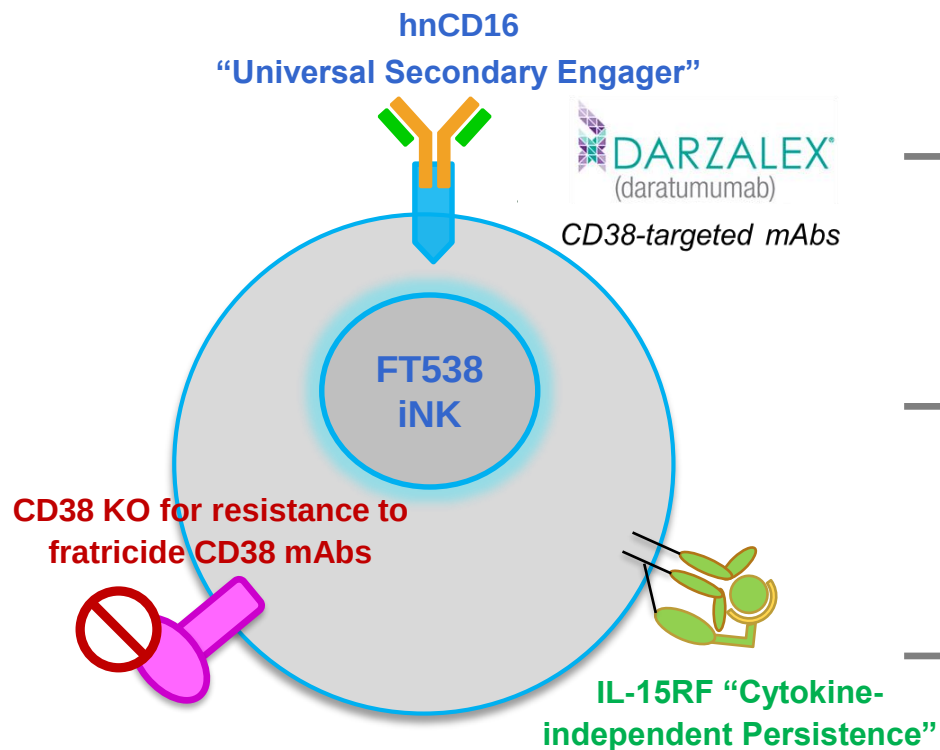
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+ IL-15 Receptor Fusion	<i>Enhance NK cell function</i>			✓	✓	✓
+ CAR Insertion	<i>Target tumor-associated antigen</i>			CD19		BCMA
+ CD38 Knock-out	<i>Resist CD38-mediated fratricide</i>				✓	✓
	Total # of Synthetic Elements	0	1	3	3	4

FT538 Off-the-Shelf hnCD16 CD38-KO NK Cell Product Candidate

Combination with anti-CD38 mAb for Multiple Myeloma



Overcome Endogenous NK Cell Deficiencies for Optimized ant-CD38 Activity in 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

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

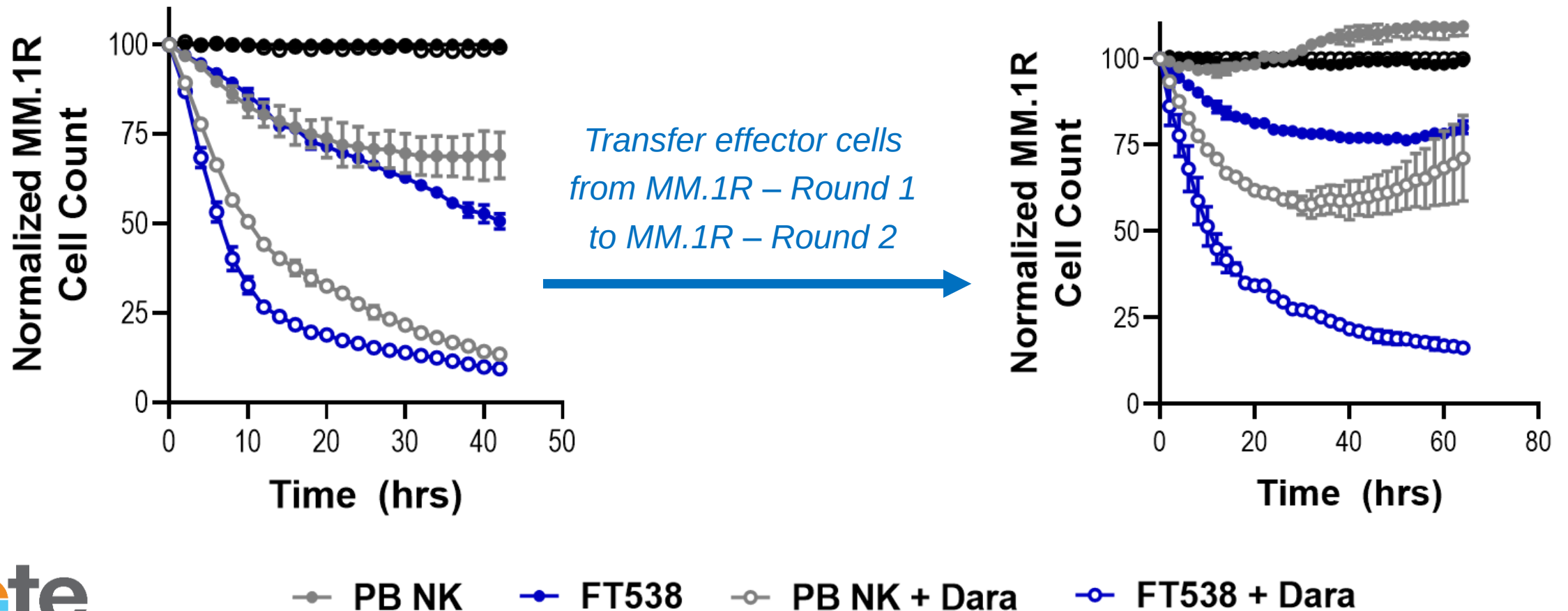
IL-15RF: Interleukin-15 receptor fusion, a potent cytokine complex that promotes survival, proliferation and trans-activation of NK cells and CD8 T cells

FT538 Off-the-Shelf hnCD16 CD38-KO NK Cell Product Candidate

Enhanced Cytotoxicity vs. PB NK Cells in a Serial Stimulation Cytotoxicity Assay

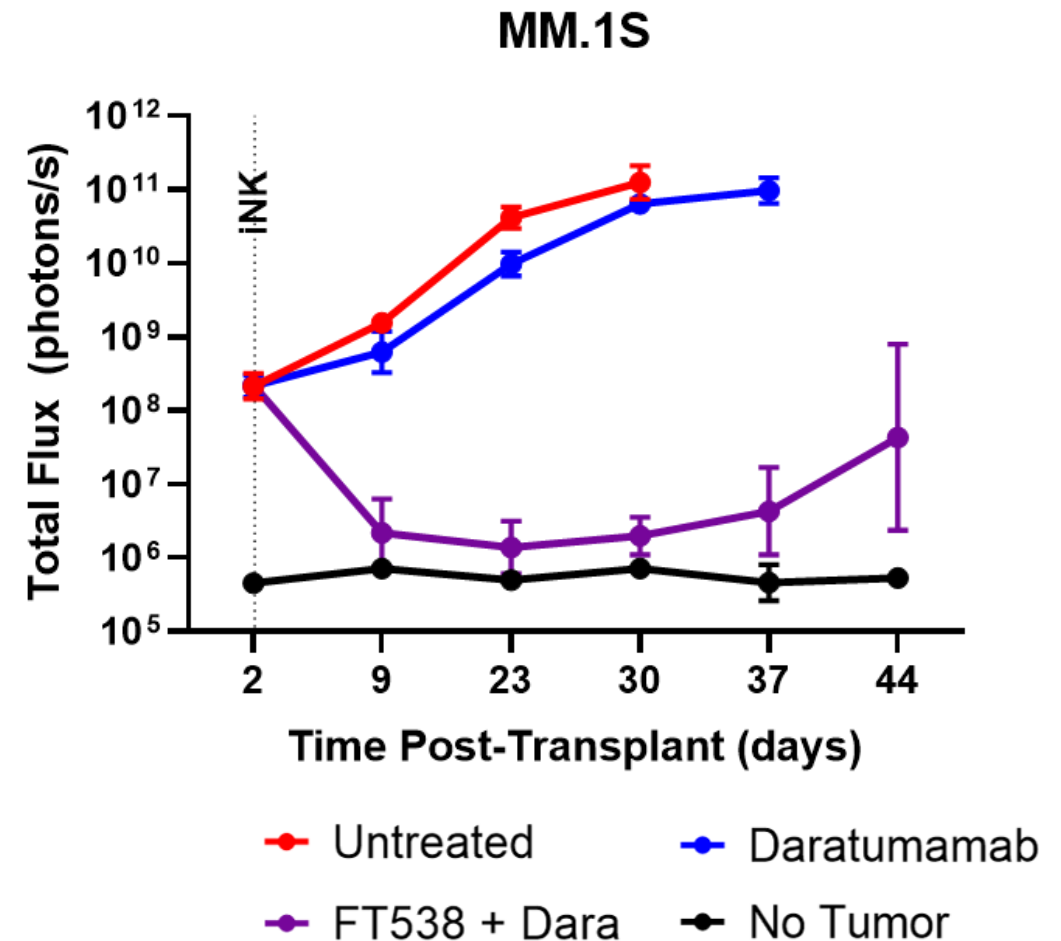
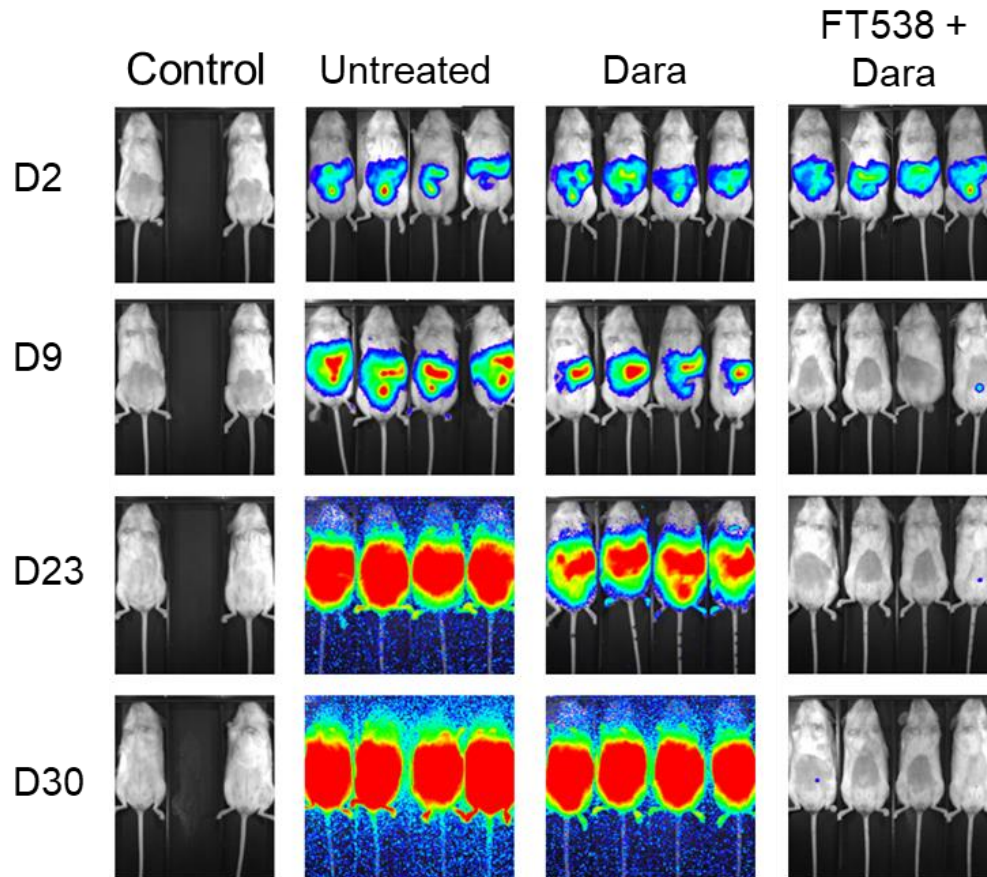


Overcome Endogenous NK Cell Deficiencies for Optimized ant-CD38 Activity in Myeloma



FT538 Off-the-Shelf hnCD16 CD38-KO NK Cell Product Candidate

Enhanced ADCC in Combination with anti-CD38 mAb In Vivo



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
Multi-faceted Innate Immunity		✓	✓	✓	✓	✓
+ High-Affinity, Non-cleavable CD16	<i>Augment mAb therapy</i>		✓	✓	✓	✓
+ IL-15 Receptor Fusion	<i>Enhance NK cell function</i>			✓	✓	✓
+ CAR Insertion	<i>Target tumor-associated antigen</i>			CD19		BCMA
+ CD38 Knock-out	<i>Resist CD38-mediated fratricide</i>				✓	✓
	Total # of Synthetic Elements	0	1	3	3	4

Building New Product Candidates from Master Engineered iPSC Lines

Leveraging FT538 Backbone for Best-in-Class Multi-antigen Targeting Strategy in Myeloma



Molecular Therapy

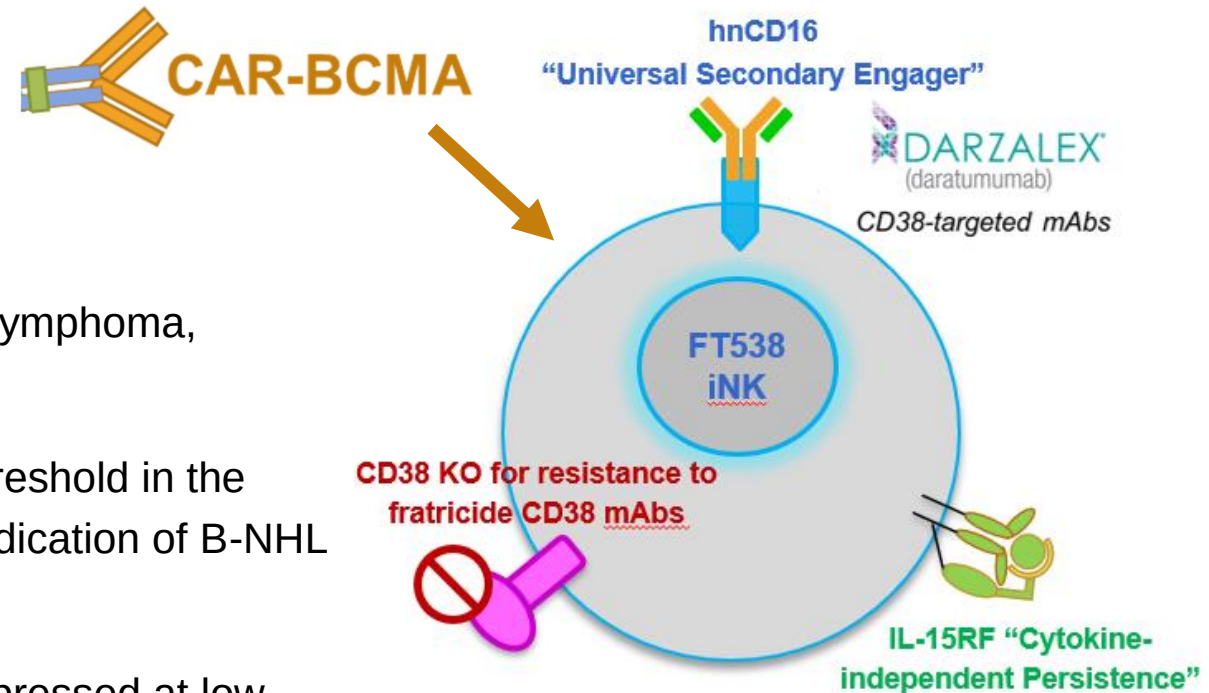
Original Article



CAR T Cells with Enhanced Sensitivity to B Cell Maturation Antigen for the Targeting of B Cell Non-Hodgkin's Lymphoma and Multiple Myeloma

Julia Bluhm,¹ Elisa Kieback,¹ Stephen F. Marino,² Felix Oden,¹ Jörg Westermann,³ Markus Chmielewski,⁴ Hinrich Abken,⁴ Wolfgang Uckert,¹ Uta E. Höpken,¹ and Armin Rehm¹

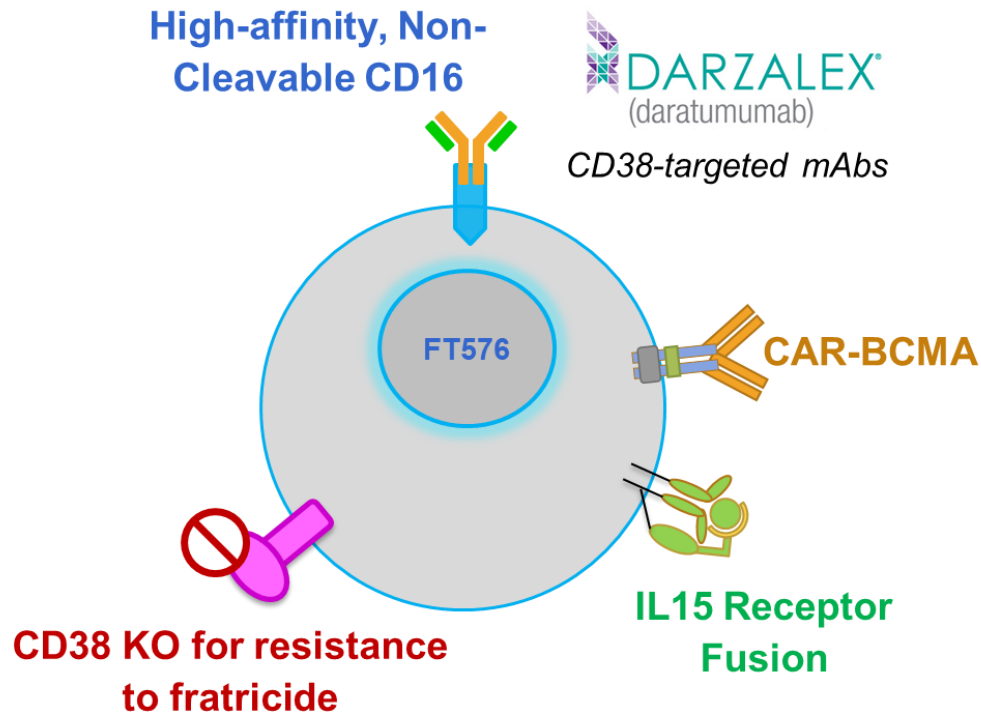
- ✓ Validated CAR BCMA in diffuse large B cell lymphoma, follicular lymphoma, mantle cell lymphoma, and chronic lymphocytic leukemia
- ✓ BCMA CAR T cells triggered target cell lysis with an activation threshold in the range of 100 BCMA molecules, which allowed for an efficient eradication of B-NHL cells in vitro and in vivo
- ✓ Potential novel therapeutic option for patients where BCMA is expressed at low abundance or where anti-CD19 immunotherapies have failed due to antigen loss



FT576 Off-the-Shelf Multi-Targeted CAR-BCMA NK Cell Product Candidate

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

CAR NK Cell Product Engineered with Four Anti-tumor Modalities



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; shown to improve NK cell fitness and potency through optimization of metabolic signaling



iPSC-derived CAR T-Cell Franchise

Off-the-Shelf CAR T-Cell Cancer Immunotherapy

Memorial Sloan Kettering Collaboration



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

LETTERS

Generation of tumor-targeted human T lymphocytes from induced pluripotent stem cells for cancer therapy

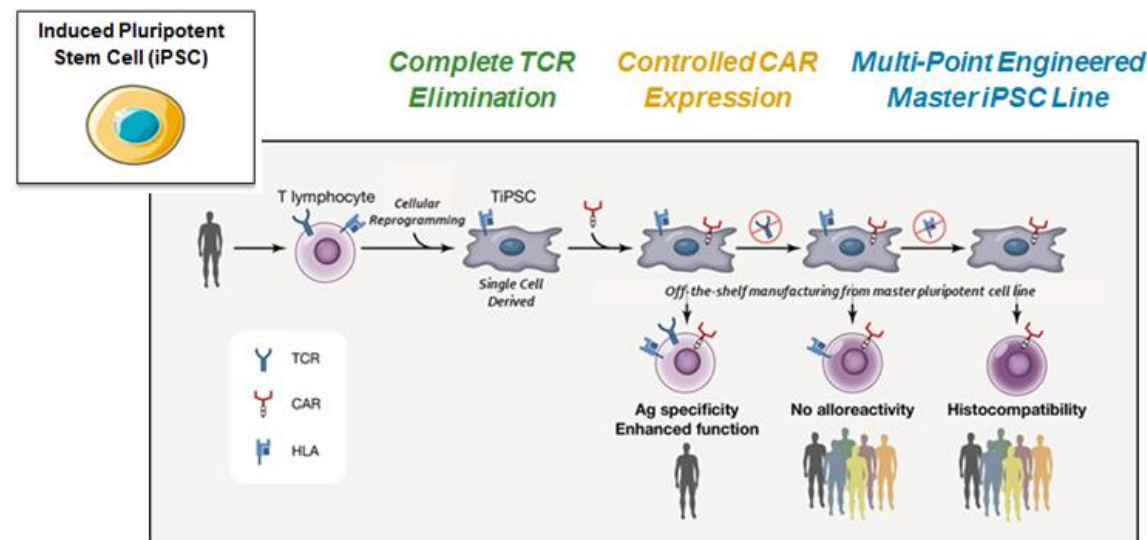
nature
biotechnology

Cell Stem Cell
Perspective

New Cell Sources for T Cell Engineering and Adoptive Immunotherapy



“Engineering therapeutic attributes into pluripotent cell lines is a breakthrough approach to renewably generate potent T-cell immunotherapies. This unique approach offers the prospect for off-the-shelf delivery of T-cell therapies with enhanced safety and therapeutic potential at the scale necessary to serve significant numbers of patients.”

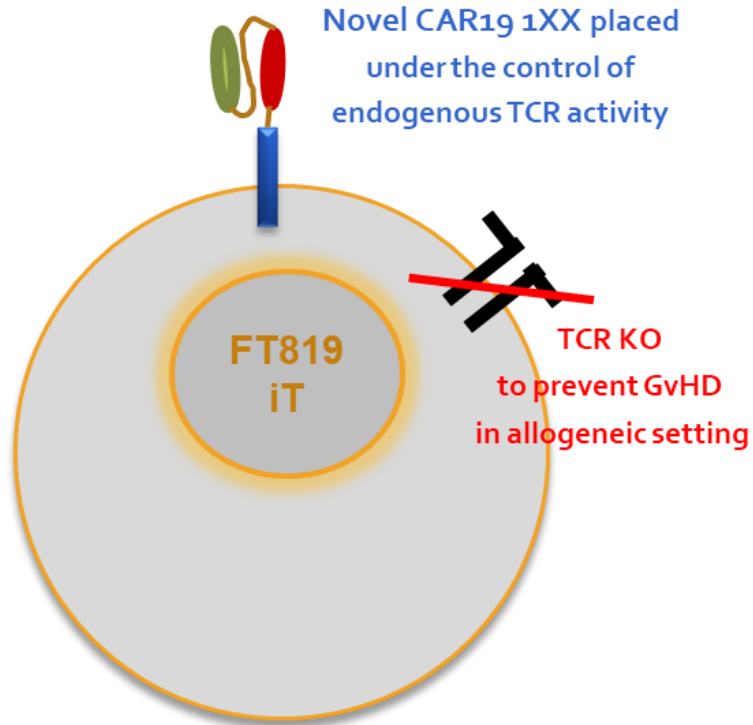


Adapted from: Themeli, Riviere & Sadelain, *Cell Stem Cells*, 2015

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



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



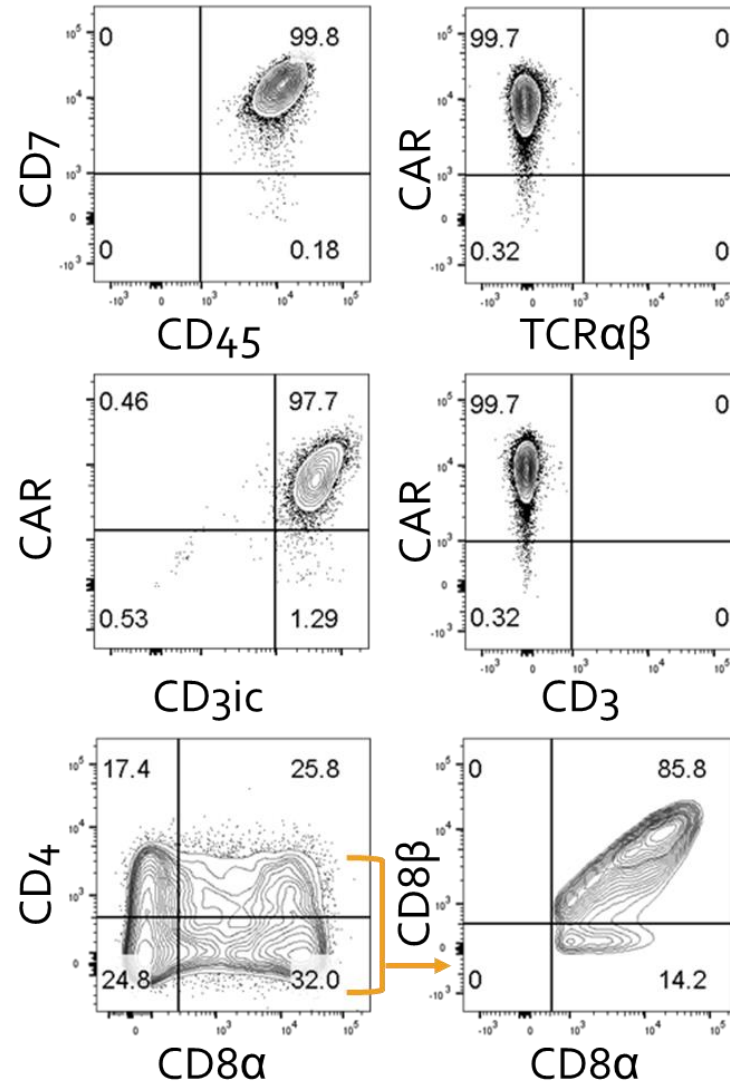
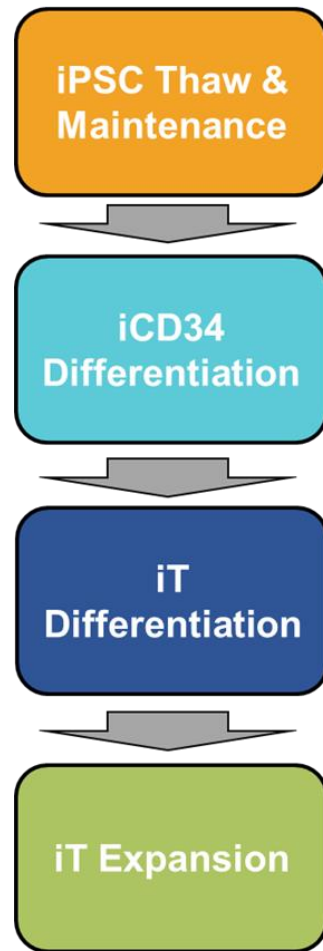
1XX CAR19: Novel chimeric antigen receptor consisting of CD28 costimulatory domain and modified CD3z signaling domain for optimal effector cell persistence and anti-tumor potency

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

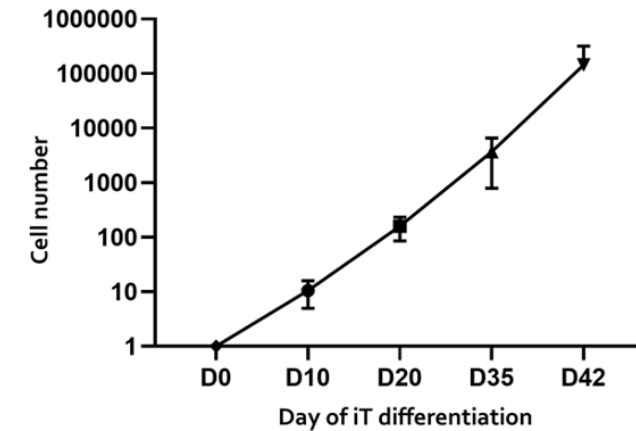
TCR-KO: Bi-allelic disruption of TRAC at the clonal level for complete removal of TCR expression and the elimination for the possibility of GvHD in allogeneic setting

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

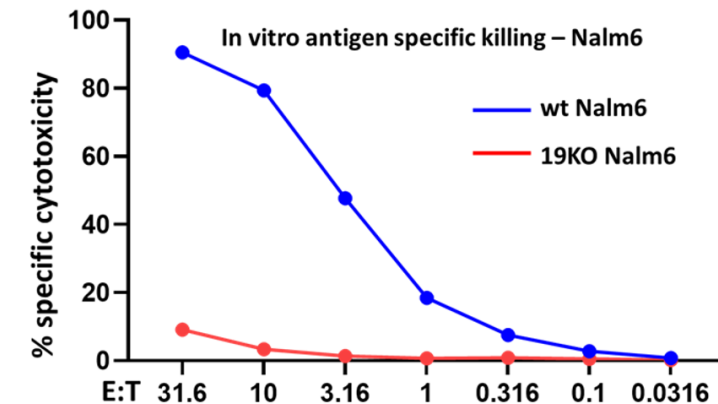
Phenotype, Proliferation and Potency



Expansion

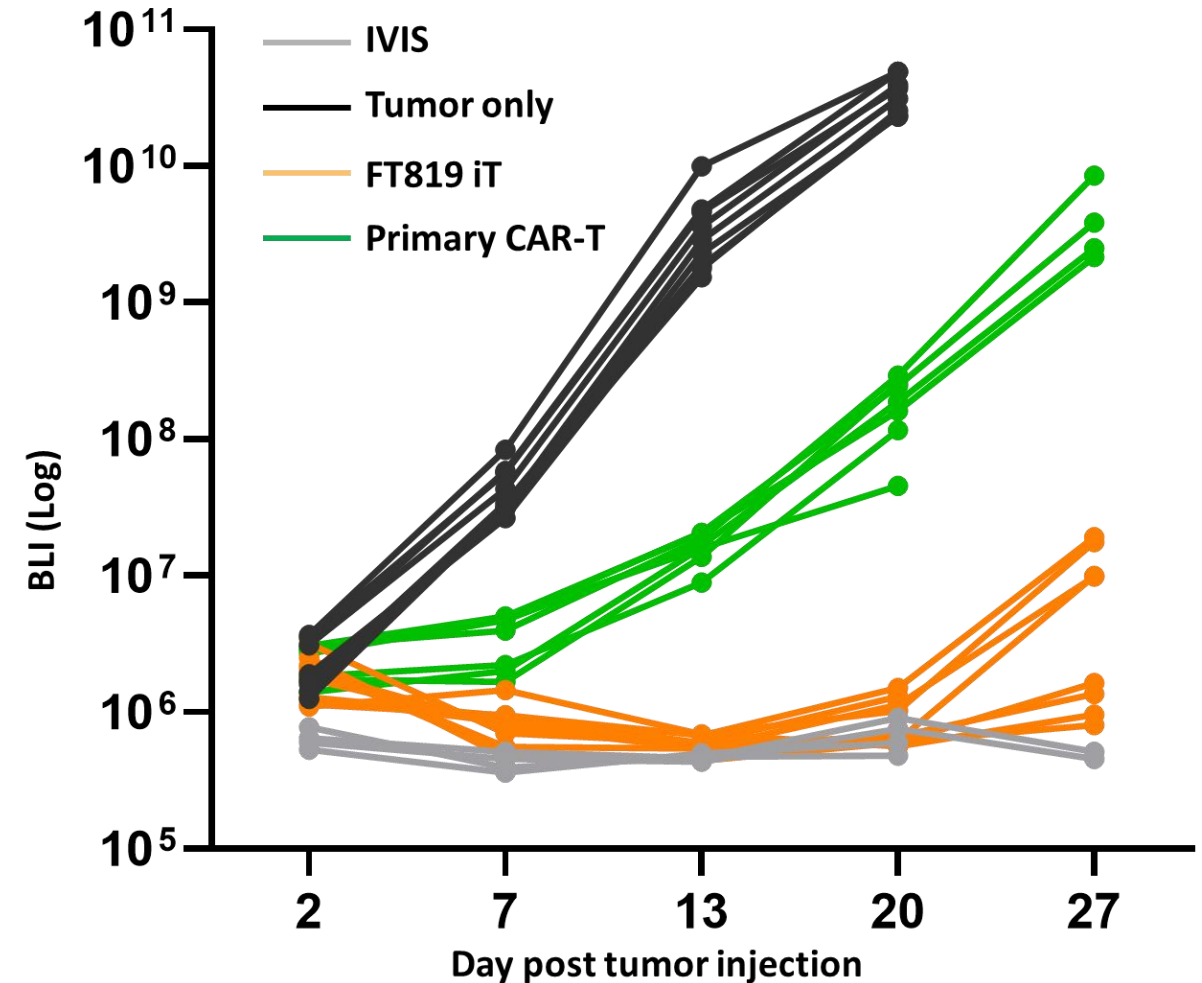
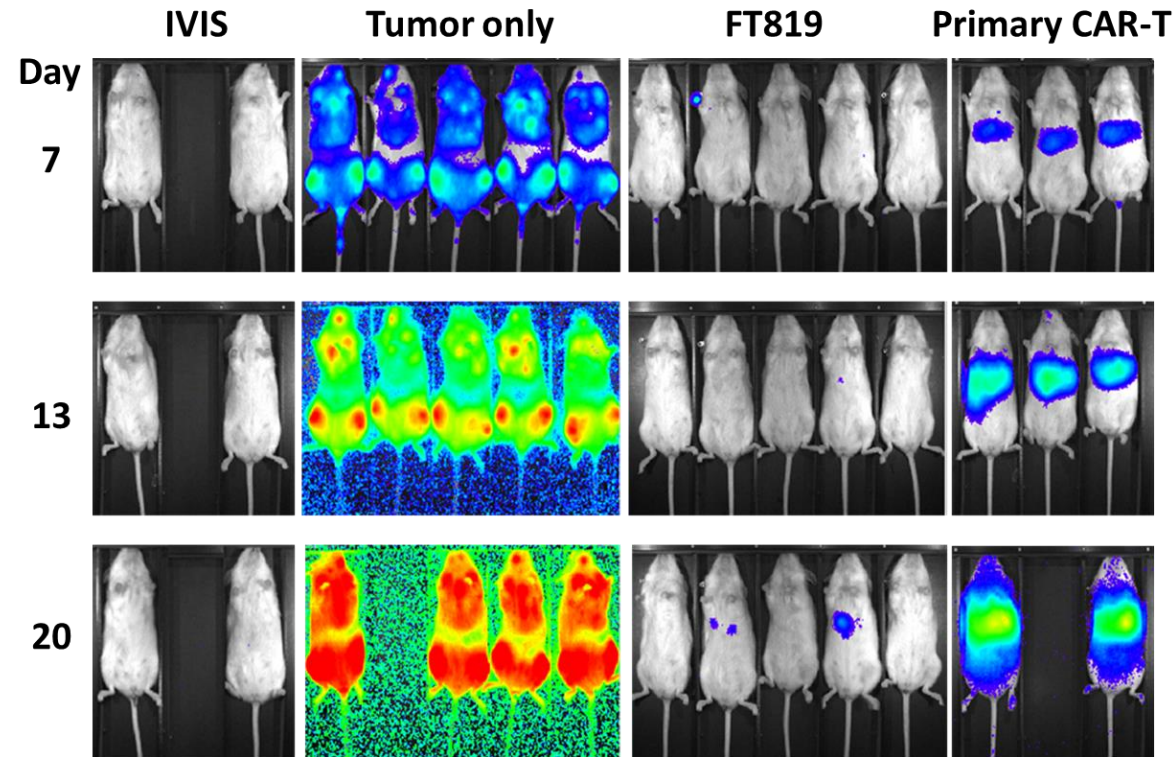


Potency & Specificity



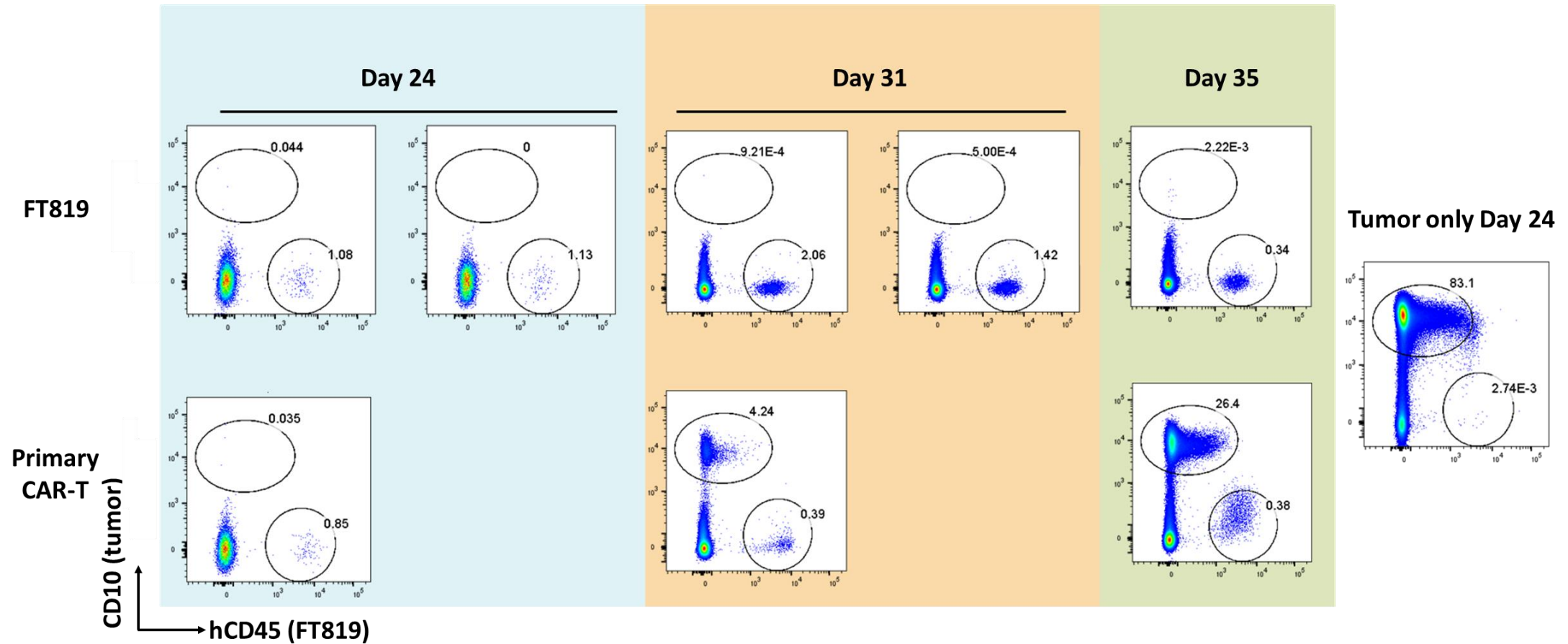
FT819 Enhanced Tumor Control vs. Primary CAR T Cells

Disseminated Xenograft Model of Lymphoblastic Leukemia



FT819 Persistence in Bone Marrow vs. Primary CAR T Cells

Disseminated Xenograft Model of Lymphoblastic Leukemia

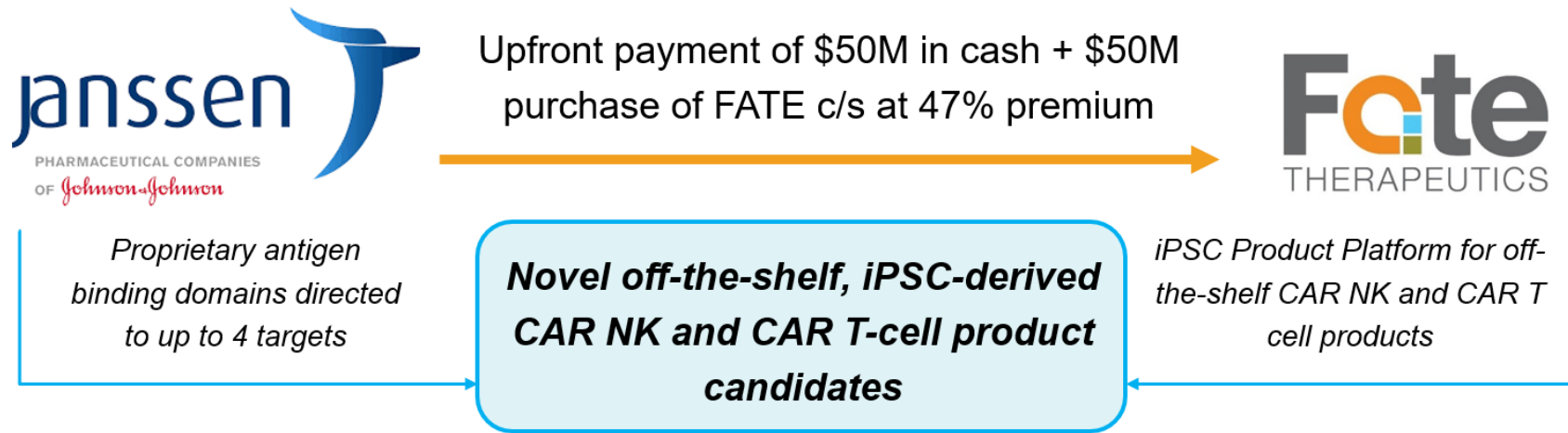




Partnerships

Janssen Cancer Immunotherapy Collaboration

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



- FATE to incorporate Janssen proprietary antigen binding domains into iPSC-derived CAR NK- and CAR T-cells
 - Up to 4 antigen targets, including targets expressed on hematologic malignancies and solid tumors
- FATE to preclinically develop product candidates to IND submission
 - Janssen to pay for all collaboration costs
- Janssen to conduct global clinical development and commercialization
 - FATE retains a right to opt-in to 50-50 commercialization arrangement in U.S.
 - FATE primarily responsible for clinical and commercial manufacture
- FATE eligible to receive up to \$3.0BN in milestones (\$1.8BN in dev / reg; \$1.2BN in commercial) plus double-digit royalties on commercial sales



ONO Pharmaceutical Cancer Immunotherapy Collaboration

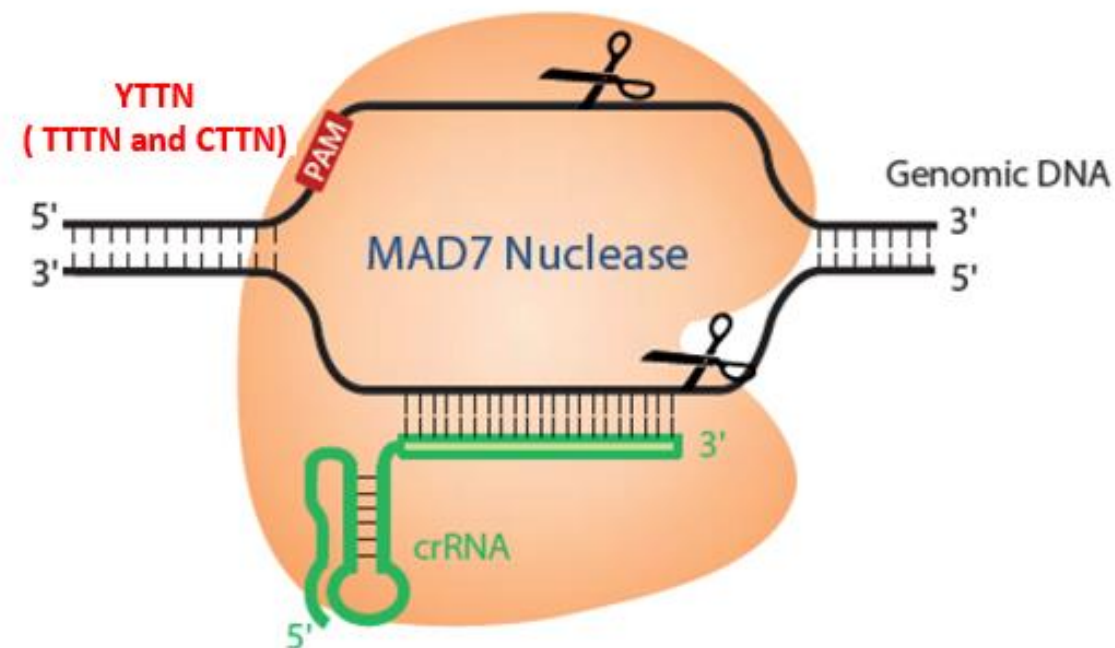
Off-the-shelf, iPSC-derived CAR T-Cell Collaboration



	Product 1 CAR T-cell targeting Antigen “ND”	Product 2 CAR T-cell targeting Antigen “ND”
Tumor Type	Lymphoblastic leukemia	Solid tumor
Antigen Binding Domain	FATE to contribute	ONO to contribute novel TAA binder
Preclinical Funding	Up to \$70M, including \$10M upfront plus \$20M in committed research funding and up to an additional \$40M in contingent fees	
FATE Rights	Worldwide excluding Asia	Opt-in to 50-50 clinical development and commercialization in the U.S. and Europe
Post-Option Economics	Up to \$285M in clinical development, regulatory and sales milestones plus royalties	Up to \$895M in clinical development, regulatory and sales milestones plus royalties

ND = Not publicly disclosed

- Patent-protected, RNA-guided, Class 2 Type V CRISPR nuclease isolated from *Eubacterium rectale*
- Improved features over commonly-used CRISPR-Cas9 nucleases:
 - More versatile PAM recognition domain
 - Smaller size of nuclease facilitates transfection efficiency
 - Differentiated cleavage kinetics with potential for fewer off-target edits
- MAD7 validated in FATE iPSC Product Platform
 - Efficient cleavage efficiency demonstrated in CD38, TRAC and safe harbor loci



FATE secured license to make and use MAD7 for research, development and commercialization of iPSC-derived cell products

