Creating the Shift from Autologous to Allogeneic CAR T Therapy

CAR T and the Rise of Cellicon Valley

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CEO & Co-Founder
Allogene Therapeutics
May 2019

Allogene THERAPEUTICS

Disclosures

Executive/Board Member/Ownership Interest (Current and Previous)

- Allogene Therapeutics (President, Chief Executive Officer & Co-Founder)
- Kite Pharma (Former Executive Vice President of Research & Development/Chief Medical Officer)
- Kronos Bio (Scientific Advisory Board)
- A2 Biotherapeutics (Board Member)
- Peloton Biotherapeutics (Board Member)
- Vida Ventures (Venture Partner)

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To the extent statements contained in this Presentation are not descriptions of historical facts regarding Allogene Therapeutics, Inc. (“Allogene,” “we,” “us,” or “our”), they are forward-looking statements reflecting management’s current beliefs and expectations. Forward-looking statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry’s actual results, levels or activity, performance, or achievements to be materially different from those anticipated by such statements. You can identify forward-looking statements by words such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes. Forward-looking statements contained in this Presentation include, but are not limited to, statements regarding: (i) the success and timing of our product development activities and initiating clinical trials, (ii) the success and timing of our collaboration partner’s ongoing and planned clinical trials, (iii) our ability to obtain and maintain regulatory approval of any of our product candidates, (iv) our plans to research, discover and develop additional product candidates, including by leveraging next generation technologies and expanding into solid tumor indications, (v) our ability to establish manufacturing capabilities, and our and our collaboration partner’s ability to manufacture our product candidates and scale production, and (vi) our ability to meet the milestones set forth herein. Various factors may cause differences between Allogene’s expectations and actual results as discussed in greater detail in Allogene's filings with the Securities and Exchange Commission (SEC), including without limitation in its Form 10-Q for the period ended March 31, 2019 filed with the SEC.

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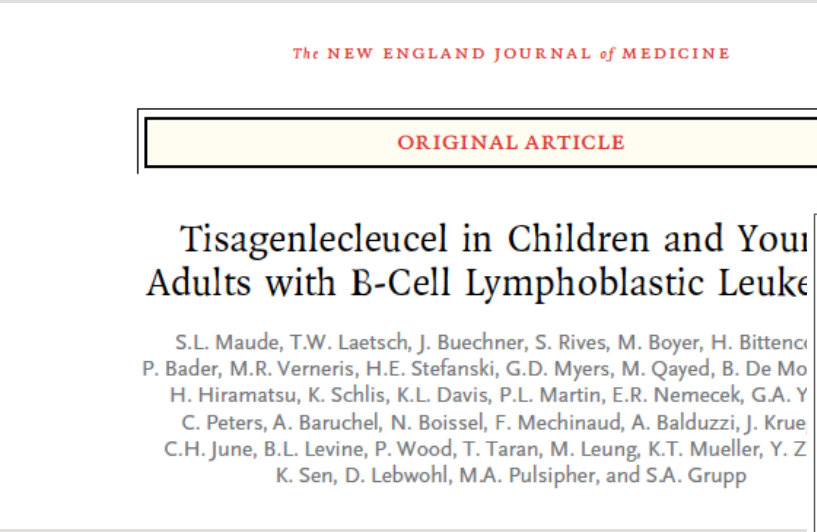
A Cancer Immunotherapy Journey to Engineered T-Cell Therapy

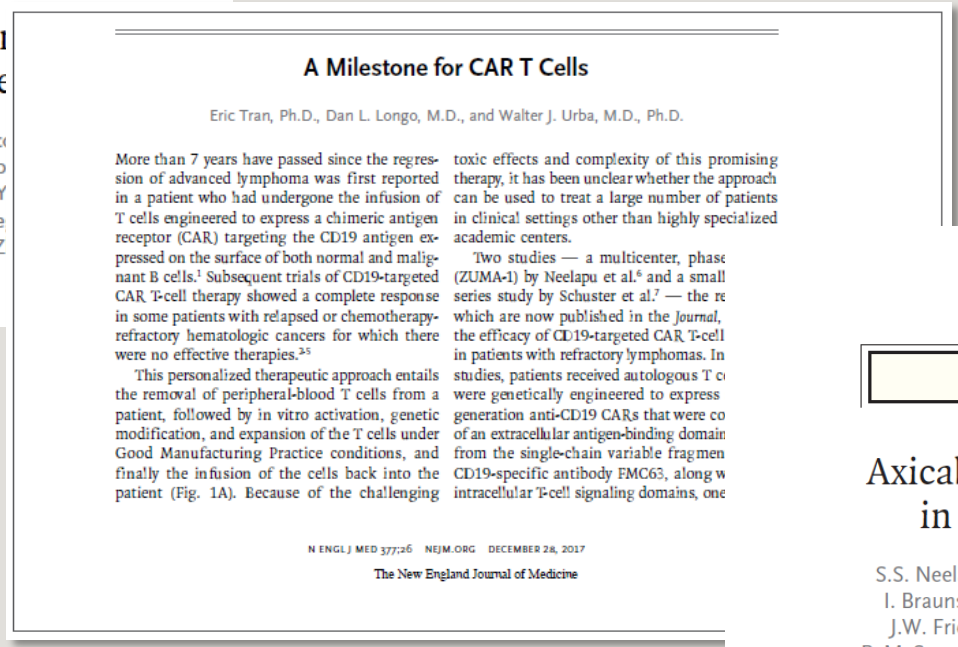

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tisagenlecleucel in Children and Youı
Adults with B-Cell Lymphoblastic Leuke

S.L. Maude, T.W. Laetsch, J. Buechner, S. Rives, M. Boyer, H. Bittenc
P. Bader, M.R. Verneris, H.E. Stefanski, G.D. Myers, M. Qayed, B. De Mo
H. Hiramatsu, K. Schlis, K.L. Davis, P.L. Martin, E.R. Nemecek, G.A. Y
C. Peters, A. Baruchel, N. Boissel, F. Mechinaud, A. Balduzzi, J. Krue
C.H. June, B.L. Levine, P. Wood, T. Taran, M. Leung, K.T. Mueller, Y. Z
K. Sen, D. Lebwohl, M.A. Pulsipher, and S.A. Grupp

08/30/2017
FDA approves Kymriah®


A Milestone for CAR T Cells

Eric Tran, Ph.D., Dan L. Longo, M.D., and Walter J. Urba, M.D., Ph.D.

More than 7 years have passed since the regression of advanced lymphoma was first reported in a patient who had undergone the infusion of T cells engineered to express a chimeric antigen receptor (CAR) targeting the CD19 antigen expressed on the surface of both normal and malignant B cells.[1] Subsequent trials of CD19-targeted CAR T-cell therapy showed a complete response in some patients with relapsed or chemotherapy-refractory hematologic cancers for which there were no effective therapies.[2-5]

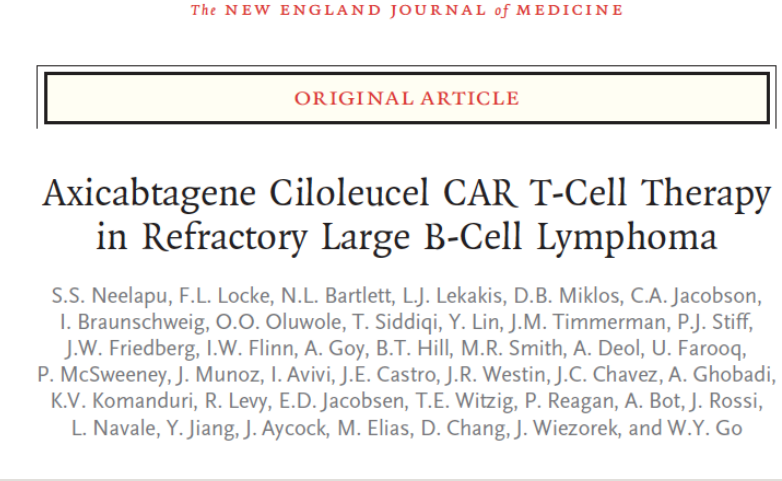
This personalized therapeutic approach entails the removal of peripheral-blood T cells from a patient, followed by in vitro activation, genetic modification, and expansion of the T cells under Good Manufacturing Practice conditions, and finally the infusion of the cells back into the patient (Fig. 1A). Because of the challenging toxic effects and complexity of this promising therapy, it has been unclear whether the approach can be used to treat a large number of patients in clinical settings other than highly specialized academic centers.

Two studies — a multicenter, phase (ZUMA-1) by Neelapu et al.[6] and a small series study by Schuster et al.[7] — the re which are now published in the *Journal*, the efficacy of CD19-targeted CAR T-cell in patients with refractory lymphomas. In studies, patients received autologous T c were genetically engineered to express generation anti-CD19 CARs that were co of an extracellular antigen-binding domain from the single-chain variable fragmen CD19-specific antibody FMC63, along w intracellular T-cell signaling domains, one

N ENGL J MED 377;26 NEJM.ORG DECEMBER 28, 2017

The New England Journal of Medicine

10/18/2017
FDA approves Yescarta®


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Axicabtagene Ciloleucel CAR T-Cell Therapy
in Refractory Large B-Cell Lymphoma

S.S. Neelapu, F.L. Locke, N.L. Bartlett, L.J. Lekakis, D.B. Miklos, C.A. Jacobson,
I. Braunschweig, O.O. Oluwole, T. Siddiqi, Y. Lin, J.M. Timmerman, P.J. Stiff,
J.W. Friedberg, I.W. Flinn, A. Goy, B.T. Hill, M.R. Smith, A. Deol, U. Farooq,
P. McSweeney, J. Munoz, I. Avivi, J.E. Castro, J.R. Westin, J.C. Chavez, A. Ghobadi,
K.V. Komanduri, R. Levy, E.D. Jacobsen, T.E. Witzig, P. Reagan, A. Bot, J. Rossi,
L. Navale, Y. Jiang, J. Aycock, M. Elias, D. Chang, J. Wiezorek, and W.Y. Go

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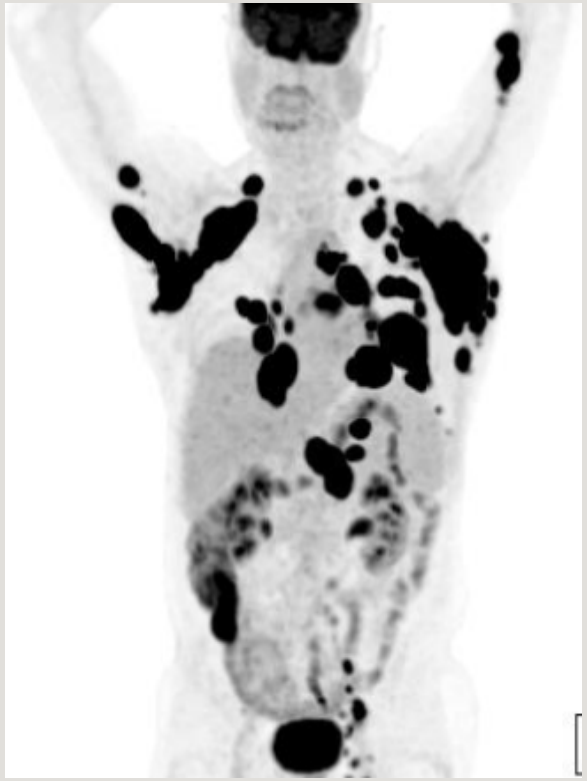
Autlogous CD19 CAR T Therapy in Relapsed and Refractory DLBCL

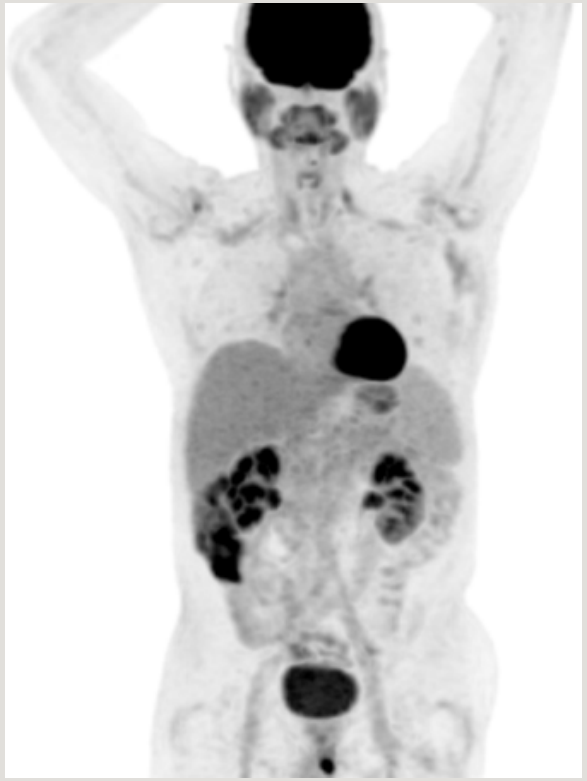
62-year-old man with refractory DLBCL

Prior Therapies

- R-CHOP
- R-GDP
- R-ICE
- R-Revlimid



Baseline



Day 90

Source: Kite Pharma

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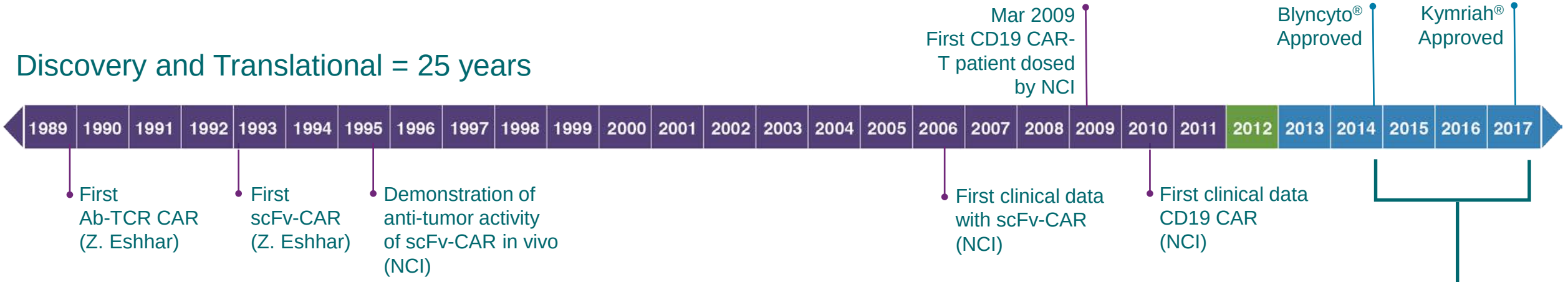
Engineered Cell Therapy: From Bench to Bedside

Discovery and Translational = 25 years



2014	2015		2016			2017			
Dec	Apr	Nov	Jul	Sep	Dec	Feb 28	Mar	Apr	Oct 18
IND Submitted	ZUMA-1 Ph1 Study: First Patient Enrolled	ZUMA-1 Ph2 Pivotal Study Opens	ZUMA-1 Pivotal Study Completes Enrollment	ZUMA-1 Pivotal Study Topline Interim Analysis	ZUMA-1 Pivotal Study Interim Analysis ASH Late Breaker	ZUMA-1 Pivotal Study Topline Primary Analysis	Completed BLA submission	ZUMA-1 Pivotal Study Primary Analysis at AACR	**Yescarta® Approved**

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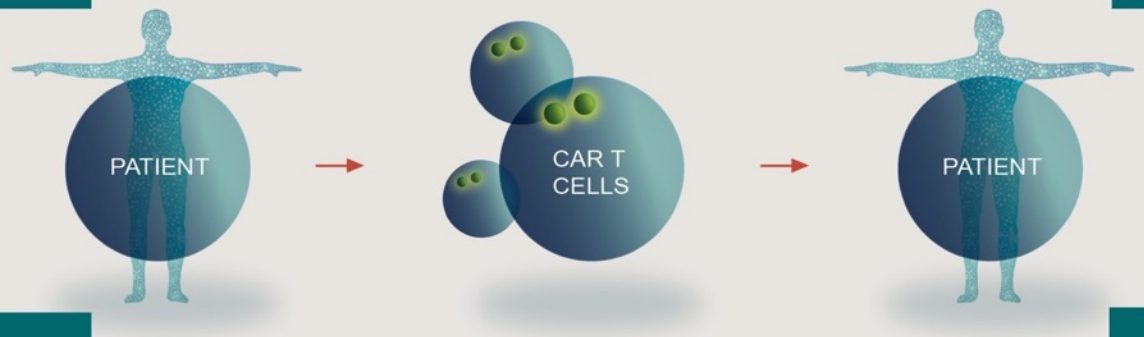
Autologous CAR T: Learning from the First Revolution

LENGTHY VEIN-TO-VEIN TIME

- Undesirable wait time in patients with poor prognosis
- Not all indicated patients may receive therapy

HIGH PRODUCTION COST

- Complicated logistics and inefficiency of scale
- Limited availability



VARIABLE POTENCY

- Compromised T cells in patients may affect product potency
- Such variability may cause unpredictable treatment outcome

MANUFACTURING FAILURES

- No ability to create inventory in individualized therapy
- Retreatment can be difficult due to limited patient starting material

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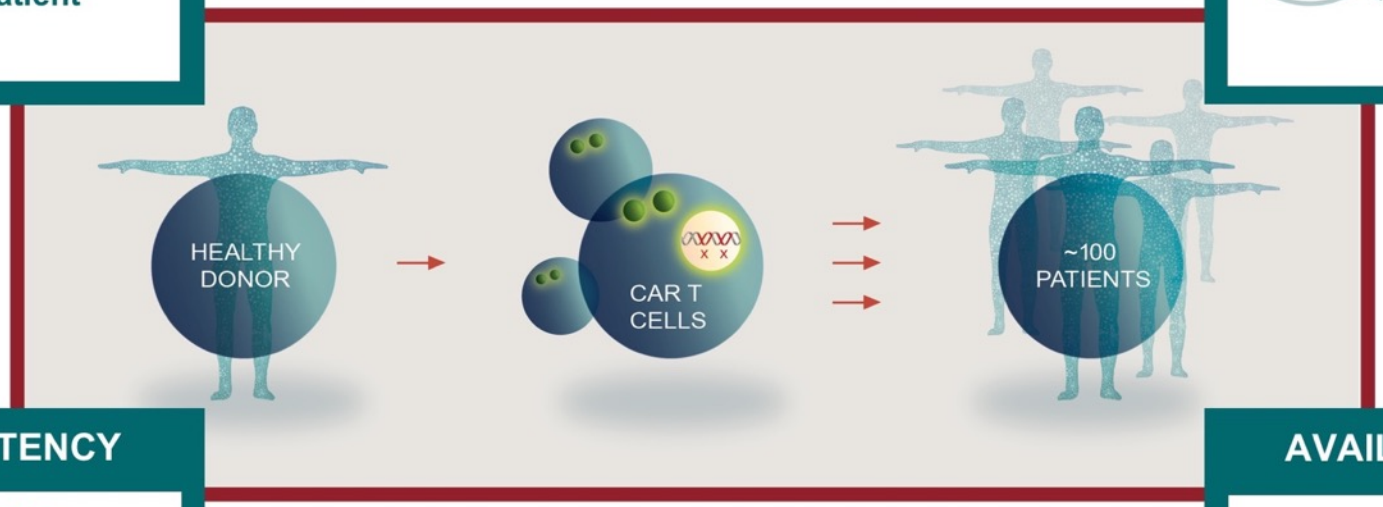
Allogeneic CAR T Therapy: The Next Potential Breakthrough

SPEED TO PATIENT

- Product delivery on demand from inventory
- Faster time to treatment may improve patient outcomes

EFFICIENCIES

- Potential to treat ~ 100 patients from a single manufacturing run
- Ability to scale production to further reduce cost



ENHANCED CELL POTENCY

- More uniform starting materials sourced from healthy donors
- Potential for more predictable safety and efficacy

AVAILABILITY AND ACCESS

- "Off-the-shelf" product enables creation of inventory
- Potential to treat all eligible patients
- Retreatment ease

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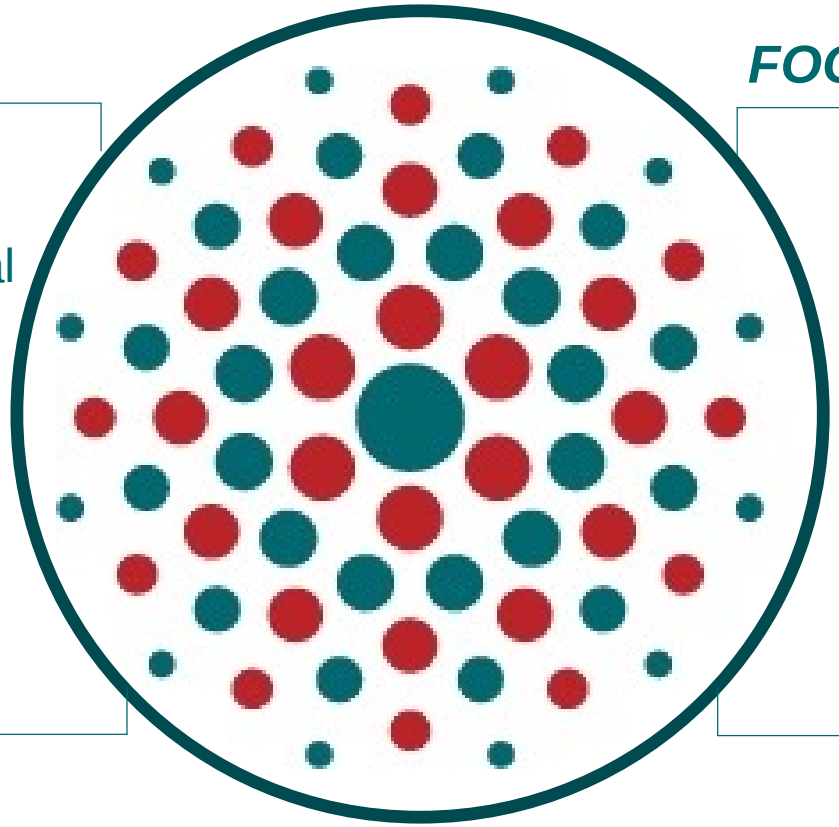
Allogene: Leading the Future of AlloCAR T™ Cell Therapy

UNIQUE EXPERIENCE

Deep understanding of CAR T manufacturing needs and notable success piloting a CAR T to approval

FOCUSED ALLOGENEIC PLATFORM

Technology platform focused 100% on bringing AlloCAR T therapy to patients



STRONG FOUNDATION

Strong balance sheet, expansive portfolio and knowledgeable team across all key functions

PATH TO APPROVAL

Experience in designing CAR T studies to potentially accelerate AlloCAR T™ development

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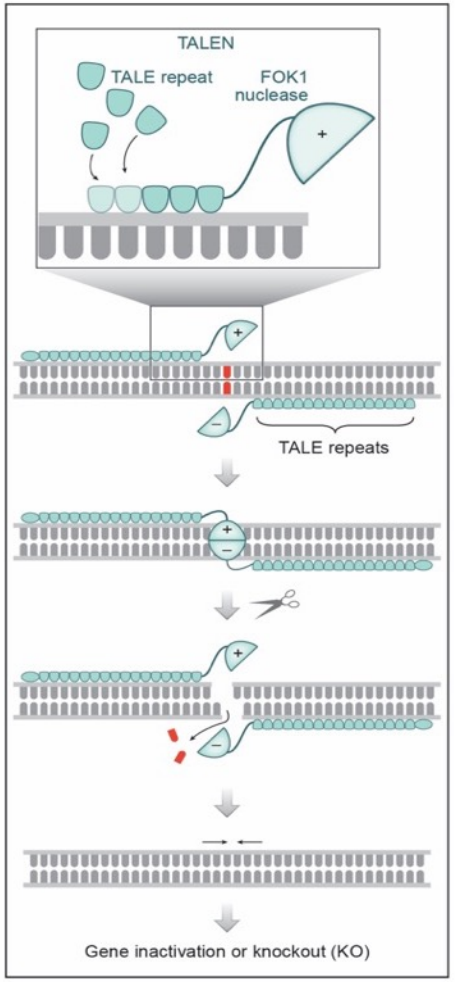
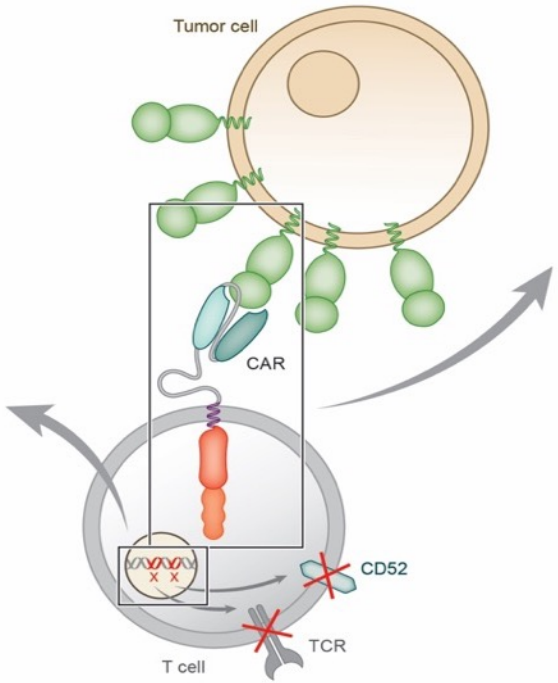
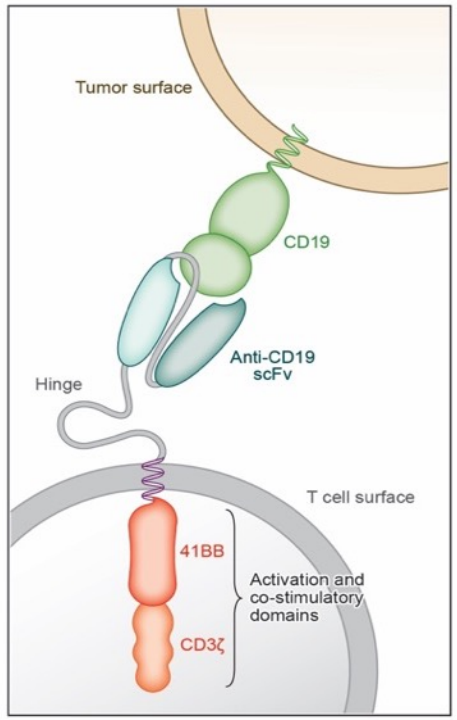
UCART19: The First AlloCAR T™ in Clinical Development



Gene editing
TALEN® Nuclease



Allogeneic
CAR T cell



CD19 CAR for
tumor recognition

TALEN® is a Cellectis gene editing technology

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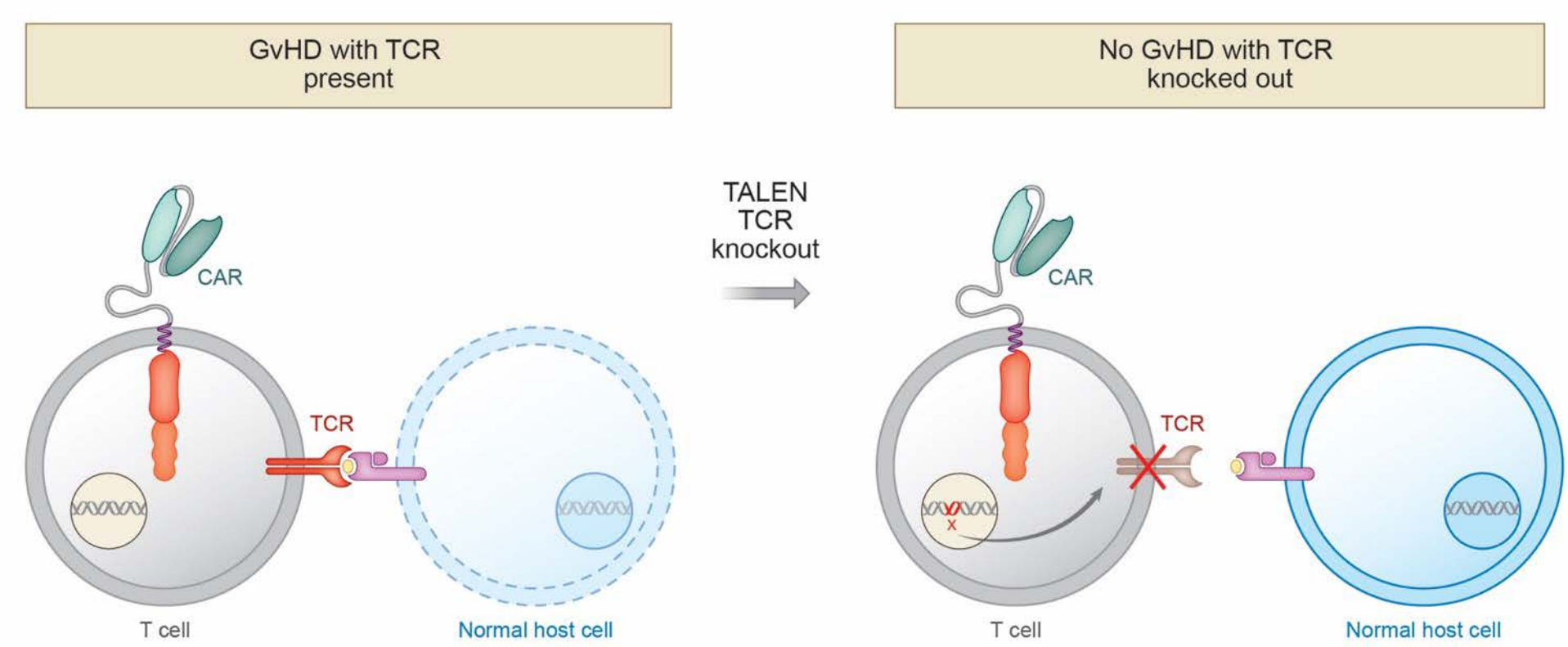
Controlling Graft-vs-Host Disease (GvHD) Reaction



- GvHD: a potentially serious complication where allogeneic cells (“the graft”) attack the patient’s healthy cells (“the host”)
- Risk of GvHD can be reduced by inactivating T cell receptors (TCR)
- Mild cases of Grade 1 acute GvHD reactions limited to skin observed with UCART19 in ongoing clinical studies (ASH 2018)

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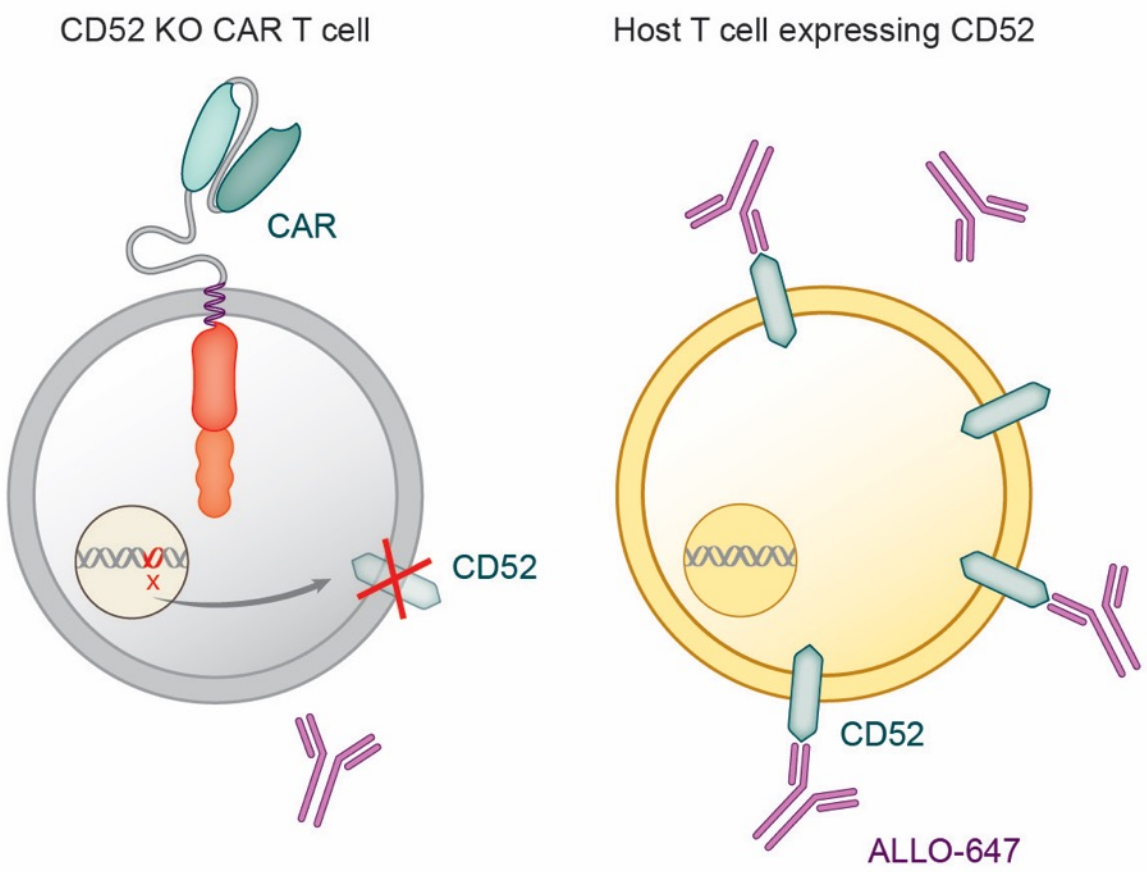
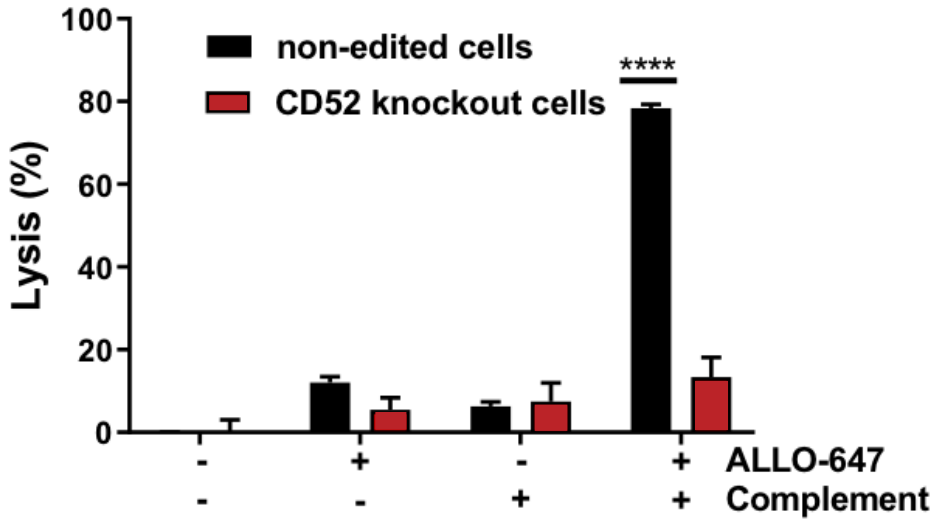
Creating a Window of Persistence



Allogeneic CAR T cells lacking CD52 will not be eliminated by ALLO-647 (anti-CD52 mAb)

Anti-CD52 mAb (ALLO-647) intended to reduce the likelihood of the patient's immune system from rejecting AlloCAR T™ cells



BCMA CAR T cells knocked out for CD52 are resistant to ALLO-647 in a complement-dependent cytotoxicity assay

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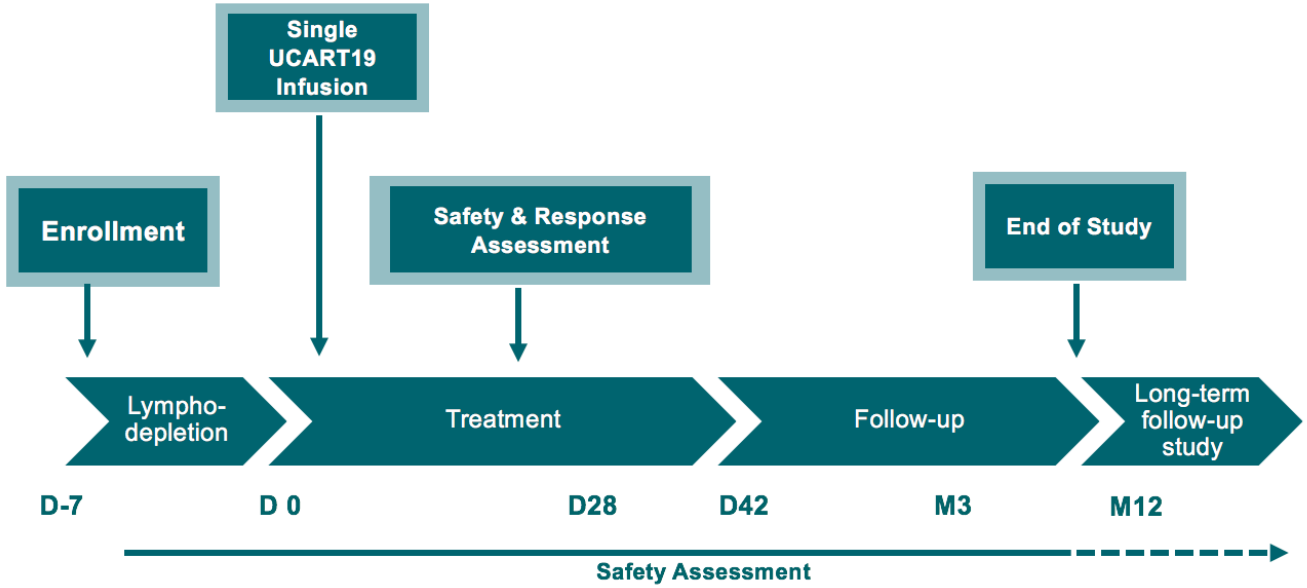
UCART19 PALL & CALM Studies Targeting CD19 R/R ALL

UCART19 ALL Pediatric (PALL) and Adults (CALM) Study Overview
Servier Sponsored

- Eligible patients with CD19+ B-ALL and:
  - Morphological or MRD+
  - Failed previous treatment options
- Objectives:
  - Primary: Safety and tolerability
  - Secondary: Anti-leukemic activity
  - Exploratory: UCART19 expansion and persistence
- PALL ongoing:
  - ✓ n= 7 treated with 2 x 10^7 total cells
- CALM dose escalation ongoing:
  - ✓ n= 6 treated at DL1 (6 x 10^6 total cells)
  - ✓ n= 6 treated at DL2 (6 to 8 x 10^7 total cells)
  - → DL3 (1.8 to 2.4 x 10^8 total cells) ongoing



- Fludarabine: 90 mg/m^2 for adults; 150 mg/m^2 for pediatrics
- Cyclophosphamide: 1500 mg/m^2 for adults; 120mg/kg for pediatrics
- Anti-CD52 mAb: 1 mg/kg both adults and pediatrics

PALL/CALM ASH 2018

UCART19: Manageable AE Profile in Phase 1 Studies

N=21	G1 n (%)	G2 n (%)	G3 n (%)	G4 n (%)	G5 n (%)	All grades n (%)
AEs related to UCART19						
Cytokine release syndrome	4 (19.0)	12 (57.1)	2 (9.5)	1* (4.8)	-	19 (90.5)
Neurotoxicity events	7 (33.3)	1 (4.8)	-	-	-	8 (38.1)
Acute skin graft-versus-host disease **	2 (9.5)	-	-	-	-	2 (9.5)
AEs related to lymphodepletion and/or UCART19						
Viral infections †	1 (4.8)	2 (9.5)	4 (19.0)	1 (4.8)	-	8 (38.1)
Prolonged cytopenia***	-	-	-	6 ‡ (28.5)	-	6 (28.5)
Neutropenic sepsis				1 (4.8)	1* (4.8)	2 (9.5)
Febrile neutropenia/ septic shock					1 (4.8)	1 (4.8)
Pulmonary hemorrhage					1‡ (4.8)	1 (4.8)

ASH 2018

n: number of patients with at least one AE by worst grade
* 1 DLT at DL1 related to UCART19: G4 CRS associated with G5 neutropenic sepsis (death at D15 post-infusion)
** GvHD confirmed by biopsy in 1 out of 2 cases
******* Persistent Grade 4 neutropenia and/or thombocytopenia beyond Day 42 post UCART19 infusion, except if >5% bone marrow blasts
‡ 1 DLT at DL2 related both to UCART19 and LD: G4 prolonged cytopenia associated with infection and pulmonary hemorrhage (death at D82 post-infusion)
† Viral infections: CMV, ADV, BK virus, metapneumovirus

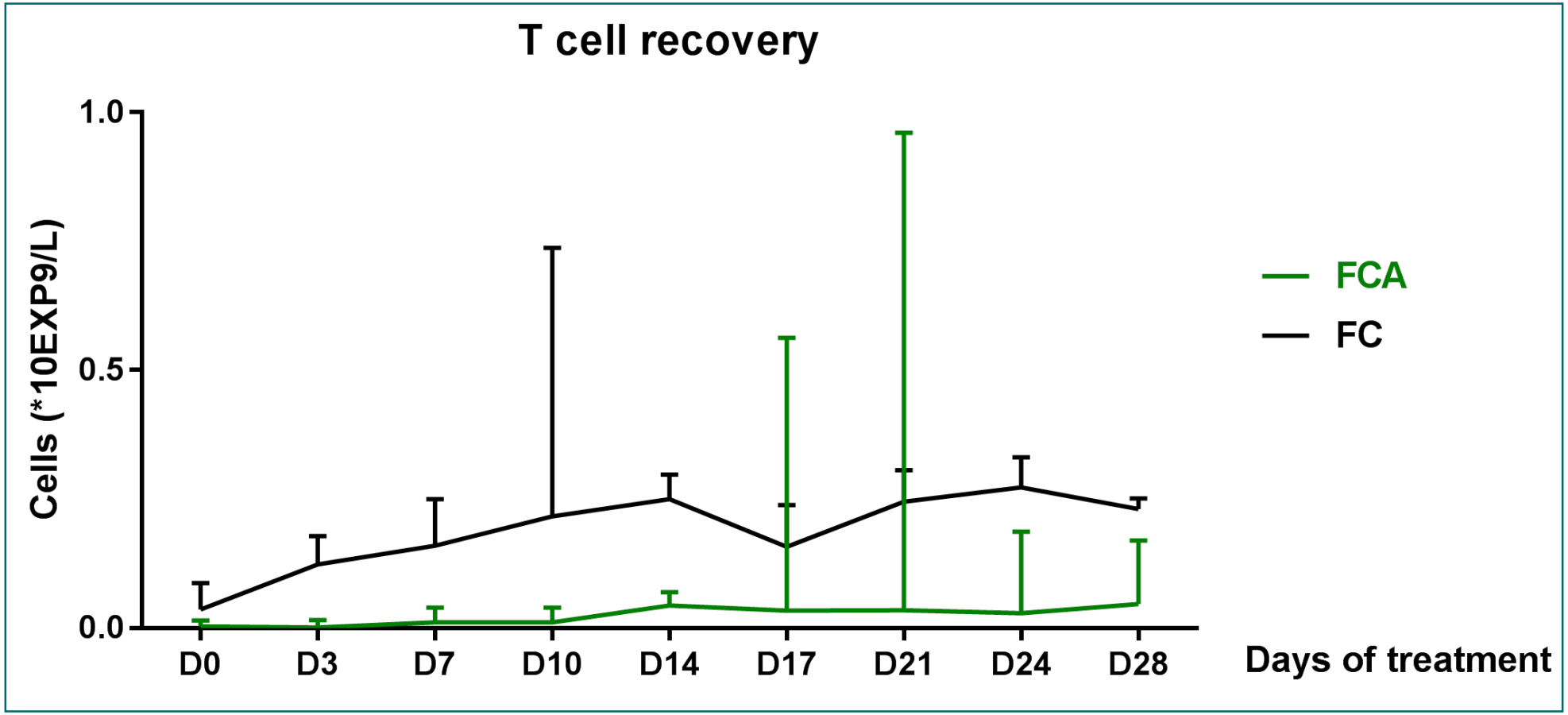
UCART19: 82% CR/CRi with FCA Lymphodepletion Regimen

Trial	Patients Enrolled & Treated	CR/CRi with FCA	CR/CRi with FC only	CR/CRi Overall
PALL	7	100% (6/6)	0% (0/1)	86% (6/7)
CALM	14	73% (8/11)	0% (0/3)	57% (8/14)
Pooled	21	82% (14/17)	0% (0/4)	67% (14/21)

ASH 2018 ; FCA: Fludarabine, cyclophosphamide & alemtuzumab (anti-CD52 mAb); FC: Fludarabine & cyclophosphamide

- UCART19 expansion observed in 15/17 patients with FCA and 0/4 patients with FC only
- Allogene will use its Proprietary anti-CD52 mAb (ALLO-647) for AlloCAR T™ Programs

Anti-CD52 Antibody May Lead to Deeper Immune Suppression



FCA- Fludarabine,Cyclophosphamide, Anti-CD52 mAb
FC- Fludarabine,Cyclophosphamide

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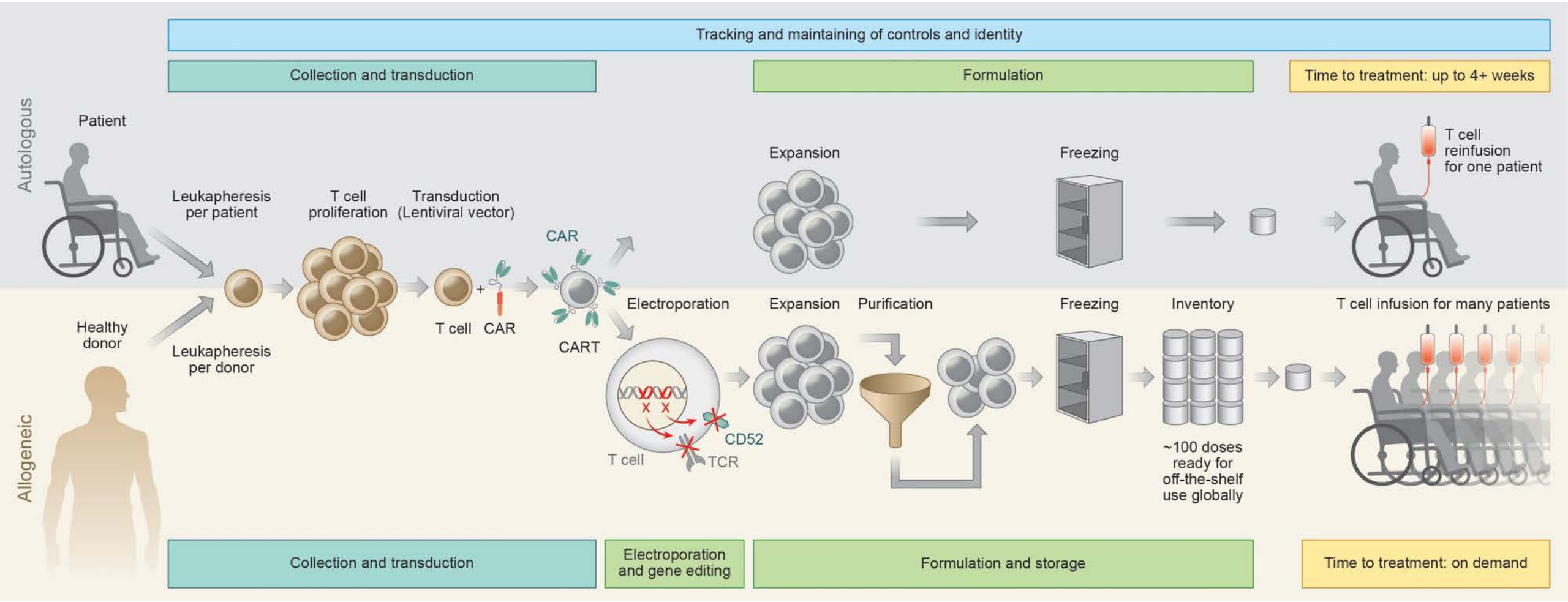
AlloCAR T™ Cells Will Be Available On Demand



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Current Manufacturing Capabilities & Planned Expansion

Current South San Francisco Facility

- Manufacturing process development & optimization
- Analytic methods for in-process characterization & improvement
- Quality Assurance and Quality Control support

Planned East Bay Area Facility (Newark, CA)

- 118,000 sq./ft facility planned
- In-house manufacturing capability build underway:
  - GMP manufacturing for clinical supply
  - Potential commercial launch upon approval

Current CMO Support

- Dedicated purpose built GMP suite
- Clinical supply manufacturing, formulation & release

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Deep AlloCAR T™ Pipeline Targeting Vast Array of Tumor Types

CATEGORY	PROGRAM	PRE-CLINICAL	PHASE 1	PHASE 2/3[1]
Hematological Malignancies	UCART19 (CD19/ALL)[2] (Servier Sponsored)			
	ALLO-501 (CD19/NHL)[2]			
	ALLO-715 (BCMA/MM)			
	ALLO-819 (FLT3/AML)			
	CD70 (Hematological Malignancies)			
Solid Tumors	CD70 (RCC)			
	DLL3 (SCLC)			
Lymphodepletion Agent	ALLO-647 (Anti-CD52 mAb)[3]			

[1] *Phase 3 may not be required if Phase 2 is registrational*
[2] *Servier holds ex-US commercial rights*
[3] *ALLO-647 intended to enable expansion and persistence of allogeneic CAR T product candidates*

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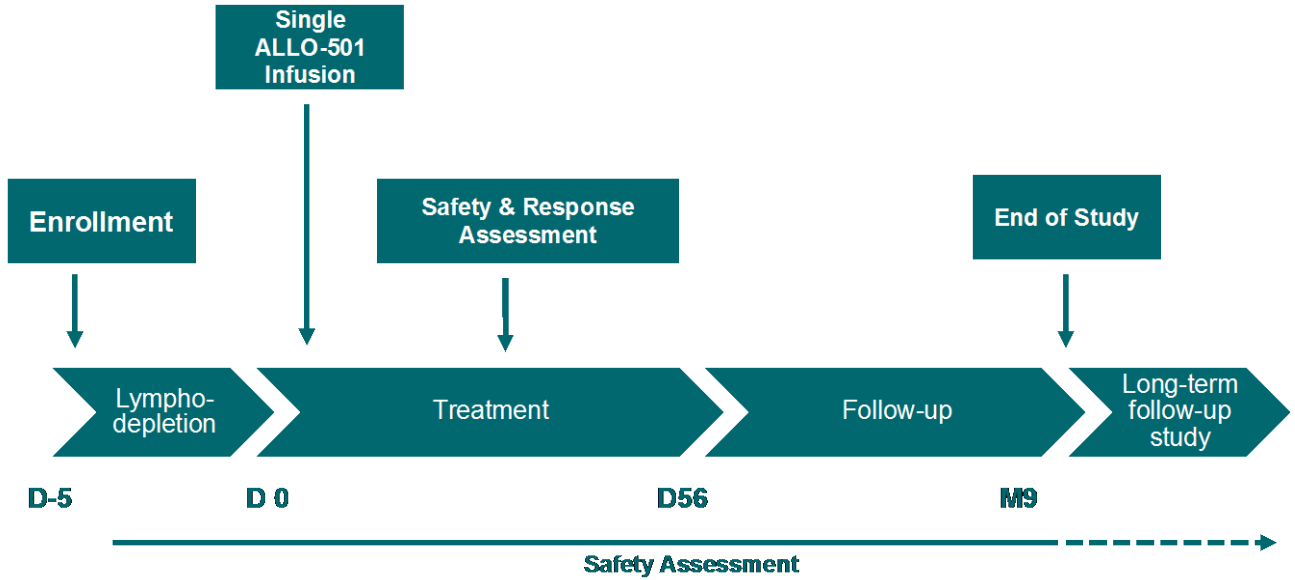
ALLO-501 ALPHA Study Targeting CD19 in R/R NHL

ALLO-501 and ALLO-647 Phase 1 Study Overview (Allogene-Sponsored)

- Initiated 1H 2019
- Eligible patients with relapsed/refractory large B-cell lymphoma or follicular lymphoma and:
  - Failed at least two prior lines of therapy
  - No prior anti-CD19 therapy
  - Absence of pre-existing donor (product)-specific anti-HLA antibodies
- Objectives:
  - Primary: Safety, tolerability and recommended P2 doses for ALLO-501 and ALLO-647
  - Secondary: Anti-tumor activity, ALLO-501 cellular kinetics, ALLO-647 PK, immunogenicity and host lymphocyte reconstitution
- Dose-escalation of ALLO-501: 40 to 360 x 10^6 CAR+ cells in 3+3 design
- Up to 24 patients

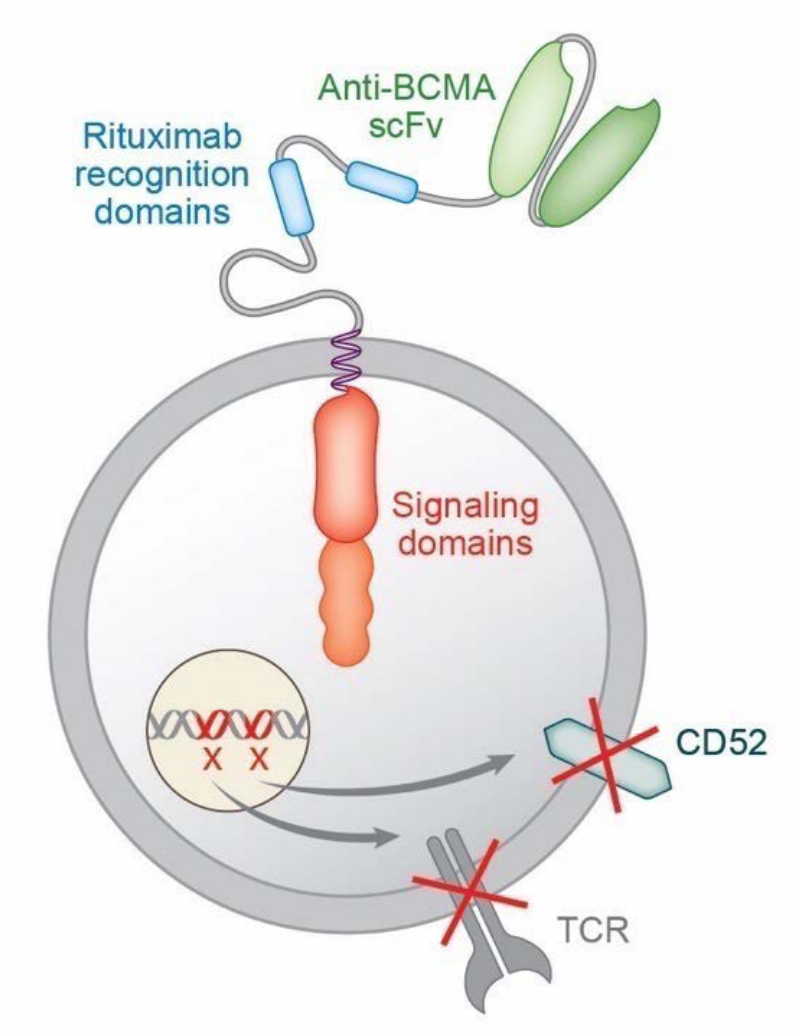


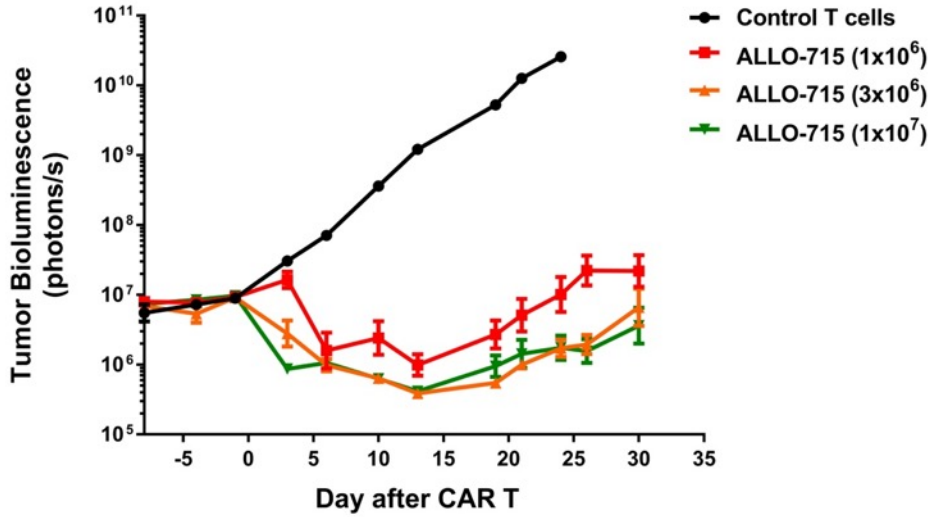
Treatment:
- Starting cell dose: 40 X 10^6 CAR+ cells

Lymphodepletion:
- ALLO-647: 13 mg/d x 3 days
- Fludarabine: 30 mg/m^2/d x 3 days
- Cyclophosphamide: 300 mg/m^2/d x 3 days

Servier holds ex-US rights to ALLO-501

ALLO-715: BCMA AlloCAR T™ for Multiple Myeloma (MM)





ALLO-715 showed activity *in vitro* against myeloma cell lines and *in vivo* in xenograft models

- IND Submitted 1H 2019
- Phase 1 clinical trial initiation expected in 2019
  - Open label, multi-center, dose escalation study in r/r MM
- Pre-clinical study published in *Molecular Therapy* validates the potential for an AlloCAR T to treat MM

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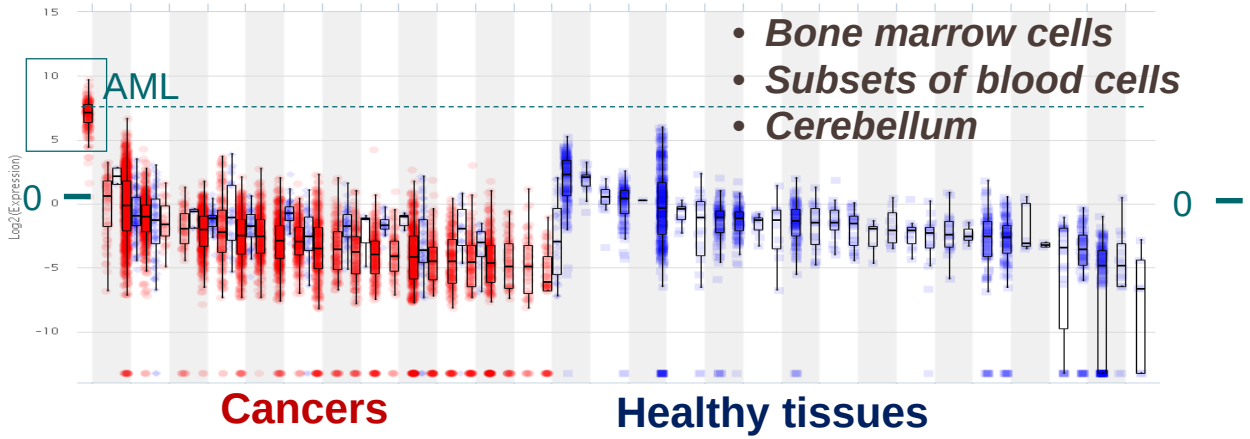
ALLO-819: FLT3 CAR T for Acute Myeloid Leukemia (AML)

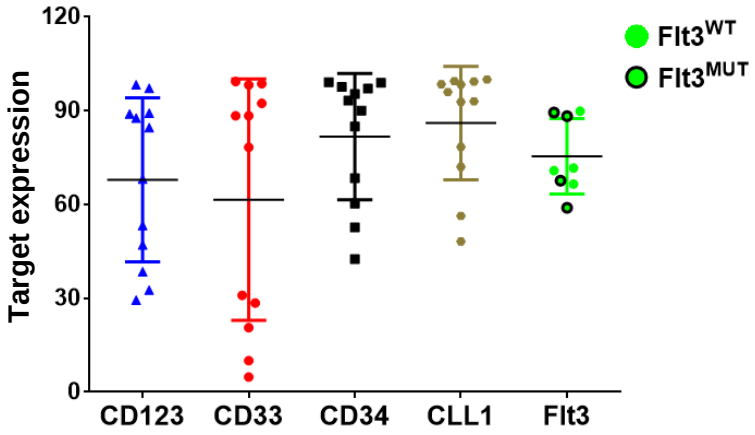
AML is a high unmet medical need with limited treatment options

- Cancer of hematopoietic progenitor cells most common in adults
- Lower survival rate of all hematological malignancies (5-year OS < 28%)
- Majority of patients relapse, novel therapies are urgently needed

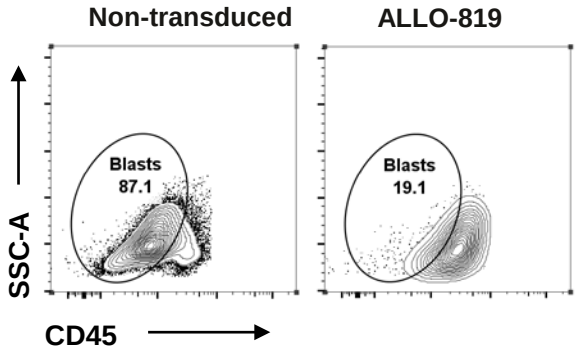
FLT3 - Most Favorable RNA Expression Profile of 4 Most Commonly Investigated AML Targets but May Have Some Normal Tissue Liabilities

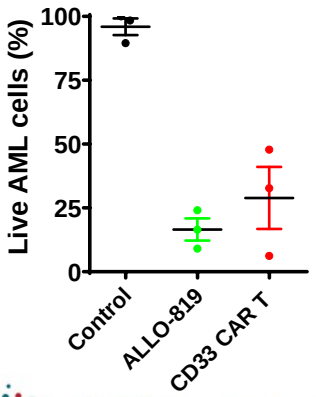


FLT3 is Present on a High Proportion of Primary AML Samples



ALLO-819 Depletes Primary AML Blasts *Ex Vivo*





- Primary AML cells vs. TCR KO CAR Ts, 1:1 (E:T); 48-h killing assay

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CD70 for Renal Cell Carcinoma (RCC)

CD70 is the ligand for the co-stimulatory receptor CD27

- Normal CD70 expression is limited to activated lymphocytes and APCs

CD70 expression[1]:

- RCC tumor samples (80-100%)
- AML (96%)
- DLBCL (71%), MM (63%), CLL (50%),
- GBM (35%)

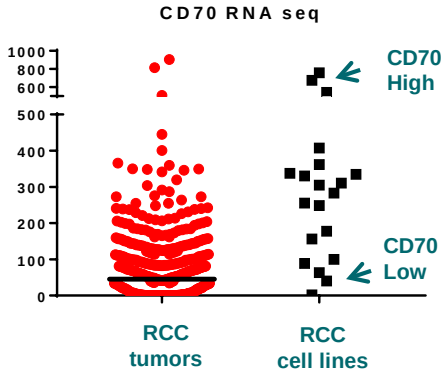
Lead CARs chosen from several Abs targeting different regions of the protein

- Candidates screened to show long-lived activity in low-expressing cell lines similar to disease level expression

Pre-clinical data presented at AACR 2019; candidate to be selected for IND-enabling studies

CD70 Expression High in RCC and Low in Normal Tissues

CD70-Low Cell Line Models Match Median Expression in Tumors



[1] Expert Opin Ther Targets. 2008 Mar; 12(3): 341–351. doi: 10.1517/14728222.12.3.341

Allogene THERAPEUTICS

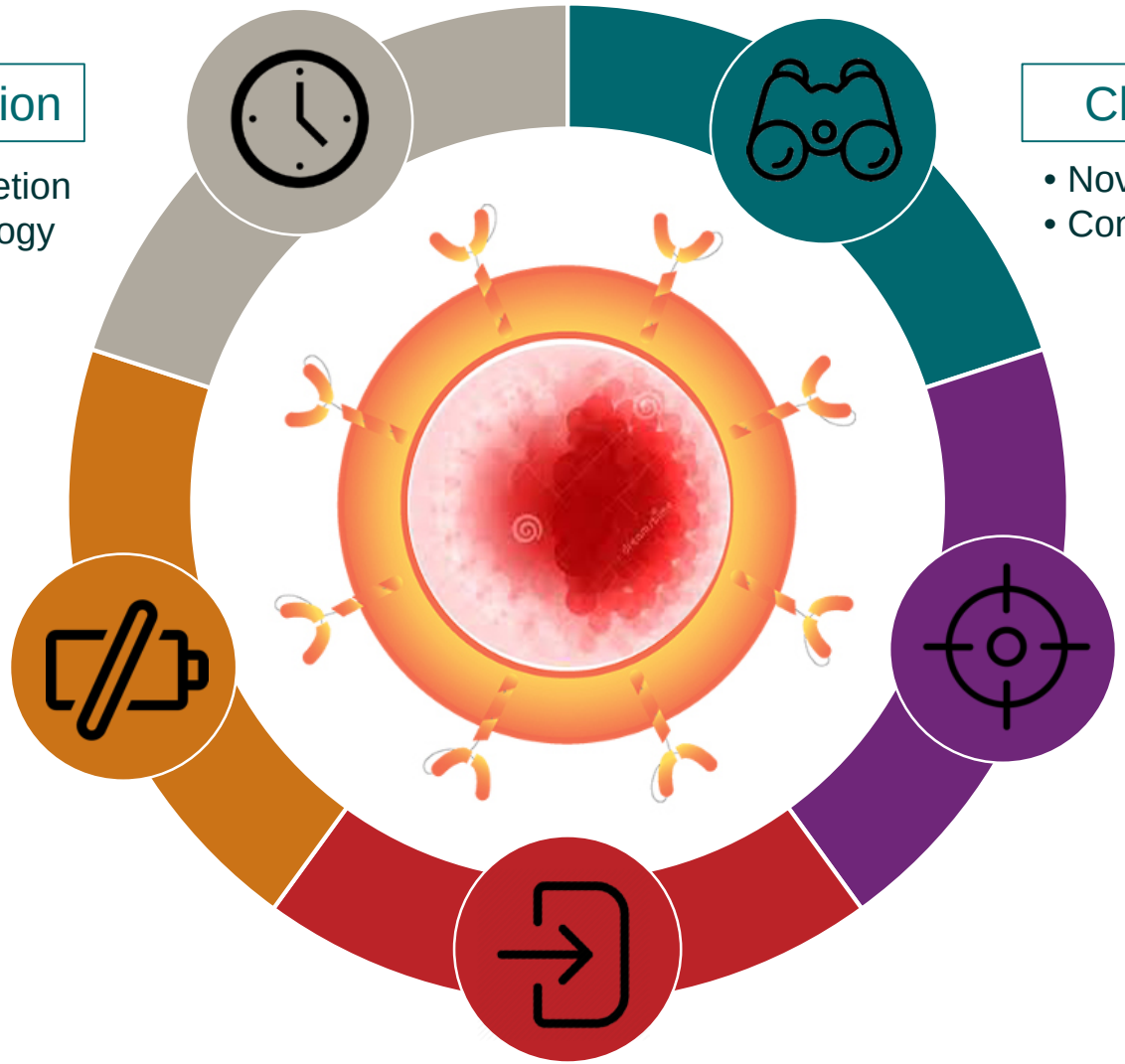
Engineering a Future for AlloCAR T™ in Solid Tumors

Control Rejection

- Novel lymphodepletion
- “Cloaking” technology

Clean Targets

- Novel targets
- Controlled activation of CAR T



Overcoming Exhaustion in TME

- Switch receptors
- Localized cytokine effects

Targeting Tumor Heterogeneity

- Multivalent CARs
- Bystander killing

Trafficking T cells to Tumor

- Locoregional delivery
- Manipulating chemokine receptor

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