Creating the Shift from Autologous to Allogeneic CAR T Therapy

CAR T and the Rise of Cellicon Valley

David D. Chang, M.D., Ph.D.
CEO & Co-Founder
Allogene Therapeutics
May 2019
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.

Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. This Presentation shall not constitute an offer to sell or the solicitation of an offer to buy securities, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.
A Cancer Immunotherapy Journey to Engineered T-Cell Therapy

**Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia**


**08/30/2017**

FDA approves Kymriah®

**10/18/2017**

FDA approves Yescarta®

**A Milestone For CAR T Cells**

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

More than seven years have passed since the registration of a lymphoma cell 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. Since then, trials of CD19-targeted CAR T-cell therapy showed a complete response in some patients with relapsed or chemotherapy-refractory lymphocytic lymphoma for whom no effective therapies were available. 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 could be used to treat a large number of patients in clinical settings other than highly specialized academic centers.

Two studies — a multicenter phase 2/3 trial by Brudzynski et al. and a small series study by Schuster et al. — in which the efficacy of CD19-targeted CAR T cells in patients with relapsed lymphoma is studied, patients treated with CD19-targeted CAR T cells showed promising results. In one study, patients treated with CD19-targeted CAR T cells showed promising results. In another study, patients treated with CD19-targeted CAR T cells showed promising results.

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

62-year-old man with refractory DLBCL

Prior Therapies

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

Baseline

Day 90

Source: Kite Pharma
Engineered Cell Therapy: From Bench to Bedside

Discovery and Translational = 25 years

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1989</td>
<td>First Ab-TCR CAR (Z. Eshhar)</td>
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<tr>
<td>1990</td>
<td>First scFv-CAR (Z. Eshhar)</td>
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<tr>
<td>1991</td>
<td>Demonstration of anti-tumor activity of scFv-CAR in vivo (NCI)</td>
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<td>2016</td>
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<td>2017</td>
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</table>

- 2014: IND Submitted
- 2015: ZUMA-1 Ph1 Study: First Patient Enrolled
- 2015: ZUMA-1 Ph2 Pivotal Study Opens
- 2016: ZUMA-1 Pivotal Study Completes Enrollment
- 2016: ZUMA-1 Pivotal Study Topline Interim Analysis
- 2016: ZUMA-1 Pivotal Study Interim Analysis ASH Late Breaker
- 2017: ZUMA-1 Pivotal Study Topline Primary Analysis
- 2017: Completed BLA submission
- 2017: ZUMA-1 Pivotal Study Primary Analysis at AACR
- 2017: Yescarta® Approved
- 2017: Blyncyo® Approved
- 2017: Kymriah® Approved

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**2014**
- Dec: IND Submitted

**2015**
- Apr: ZUMA-1 Ph1 Study: First Patient Enrolled
- Nov: ZUMA-1 Ph2 Pivotal Study Opens

**2016**
- Jul: ZUMA-1 Pivotal Study Completes Enrollment
- Sep: ZUMA-1 Pivotal Study Topline Interim Analysis
- Dec: ZUMA-1 Pivotal Study Interim Analysis ASH Late Breaker

**2017**
- Feb 28: ZUMA-1 Pivotal Study Topline Primary Analysis
- Mar: Completed BLA submission
- Apr: ZUMA-1 Pivotal Study Primary Analysis at AACR
- Oct 18: 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
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

[Image of CAR T cell therapy process]
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
UCART19: The First AlloCAR T™ in Clinical Development

Gene editing
TALEN® Nuclease

TALEN® is a Cellectis gene editing technology
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)
Creating a Window of Persistence

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

Allogeneic CAR T cells lacking CD52 will not be eliminated by ALLO-647 (anti-CD52 mAb)
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/m² for adults; 150 mg/m² for pediatrics
Cyclophosphamide: 1500 mg/m² 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

### AEs related to UCART19

<table>
<thead>
<tr>
<th></th>
<th>G1 n (%)</th>
<th>G2 n (%)</th>
<th>G3 n (%)</th>
<th>G4 n (%)</th>
<th>G5 n (%)</th>
<th>All grades n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cytokine release syndrome</strong></td>
<td>4 (19.0)</td>
<td>12 (57.1)</td>
<td>2 (9.5)</td>
<td>1* (4.8)</td>
<td>-</td>
<td>19 (90.5)</td>
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<tr>
<td><strong>Neurotoxicity events</strong></td>
<td>7 (33.3)</td>
<td>1 (4.8)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>8 (38.1)</td>
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<tr>
<td><strong>Acute skin graft-versus-host disease</strong></td>
<td>2 (9.5)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 (9.5)</td>
</tr>
</tbody>
</table>

### AEs related to lymphodepletion and/or UCART19

<table>
<thead>
<tr>
<th></th>
<th>G1 n (%)</th>
<th>G2 n (%)</th>
<th>G3 n (%)</th>
<th>G4 n (%)</th>
<th>G5 n (%)</th>
<th>All grades n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viral infections</strong> †</td>
<td>1 (4.8)</td>
<td>2 (9.5)</td>
<td>4 (19.0)</td>
<td>1 (4.8)</td>
<td>-</td>
<td>8 (38.1)</td>
</tr>
<tr>
<td><strong>Prolonged cytopenia</strong>*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6 ‡ (28.5)</td>
<td>-</td>
<td>6 (28.5)</td>
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<tr>
<td><strong>Neutropenic sepsis</strong></td>
<td>1 (4.8)</td>
<td>1* (4.8)</td>
<td>2 (9.5)</td>
<td></td>
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<tr>
<td><strong>Febrile neutropenia/ septic shock</strong></td>
<td>1 (4.8)</td>
<td>1 (4.8)</td>
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<tr>
<td><strong>Pulmonary hemorrhage</strong></td>
<td>1‡ (4.8)</td>
<td>1 (4.8)</td>
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</table>

**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 thrombocytopenia 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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patients Enrolled &amp; Treated</th>
<th>CR/CRi with FCA</th>
<th>CR/CRi with FC only</th>
<th>CR/CRi Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>PALL</td>
<td>7</td>
<td>100% (6/6)</td>
<td>0% (0/1)</td>
<td>86% (6/7)</td>
</tr>
<tr>
<td>CALM</td>
<td>14</td>
<td>73% (8/11)</td>
<td>0% (0/3)</td>
<td>57% (8/14)</td>
</tr>
<tr>
<td>Pooled</td>
<td>21</td>
<td>82% (14/17)</td>
<td>0% (0/4)</td>
<td>67% (14/21)</td>
</tr>
</tbody>
</table>

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

**T cell recovery**

Cells (*×10^9 EXP/L*)

- **FCA** (Fludarabine, Cyclophosphamide, Anti-CD52 mAb)
- **FC** (Fludarabine, Cyclophosphamide)

Days of treatment:
- D0
- D3
- D7
- D10
- D14
- D17
- D21
- D24
- D28

FCA- Fludarabine, Cyclophosphamide, Anti-CD52 mAb
FC- Fludarabine, Cyclophosphamide
AlloCAR T™ Cells Will Be Available On Demand
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
# Deep AlloCAR T™ Pipeline Targeting Vast Array of Tumor Types

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>PROGRAM</th>
<th>PRE-CLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2/3&lt;sup&gt;1&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Hematological Malignancies</td>
<td>UCART19 (CD19/ALL)&lt;sup&gt;2&lt;/sup&gt; (Servier Sponsored)</td>
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<tr>
<td></td>
<td>ALLO-501 (CD19/NHL)&lt;sup&gt;2&lt;/sup&gt;</td>
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<td>ALLO-715 (BCMA/MM)</td>
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<td>ALLO-819 (FLT3/AML)</td>
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<td></td>
<td>CD70 (Hematological Malignancies)</td>
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<tr>
<td>Solid Tumors</td>
<td>CD70 (RCC)</td>
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<td></td>
<td>DLL3 (SCLC)</td>
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<tr>
<td>Lymphodepletion Agent</td>
<td>ALLO-647 (Anti-CD52 mAb)&lt;sup&gt;3&lt;/sup&gt;</td>
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<sup>1</sup> Phase 3 may not be required if Phase 2 is registrational  
<sup>2</sup> Servier holds ex-US commercial rights  
<sup>3</sup> ALLO-647 intended to enable expansion and persistence of allogeneic CAR T product candidates
ALLO-501 ALPHA Study Targeting CD19 in R/R NHL

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
**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

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**FLT3 is Present on a High Proportion of Primary AML Samples**

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

- Bone marrow cells
- Subsets of blood cells
- Cerebellum

**ALLO-819 Depletes Primary AML Blasts Ex Vivo**

- Primary AML cells vs. TCR KO CAR Ts, 1:1 (E:T); 48-h killing assay
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 expression¹:
• 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

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

Locoregional delivery
- Manipulating chemokine receptor

 Trafficking T cells to Tumor

• Novel targets
• Controlled activation of CAR T