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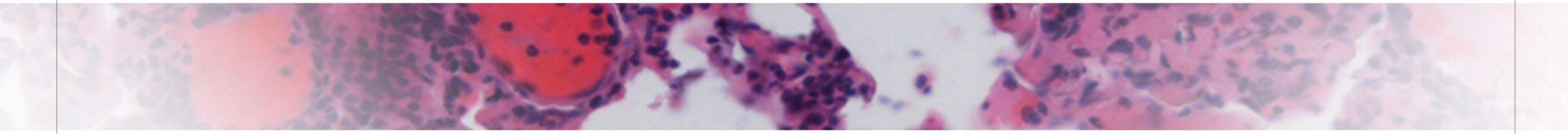

UNIVERSAL Updated Phase 1 Data Validates the Feasibility of Allogeneic Anti-BCMA ALLO-715 Therapy for Relapsed/Refractory Multiple Myeloma

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Presented by Sham Mailankody, MBBS

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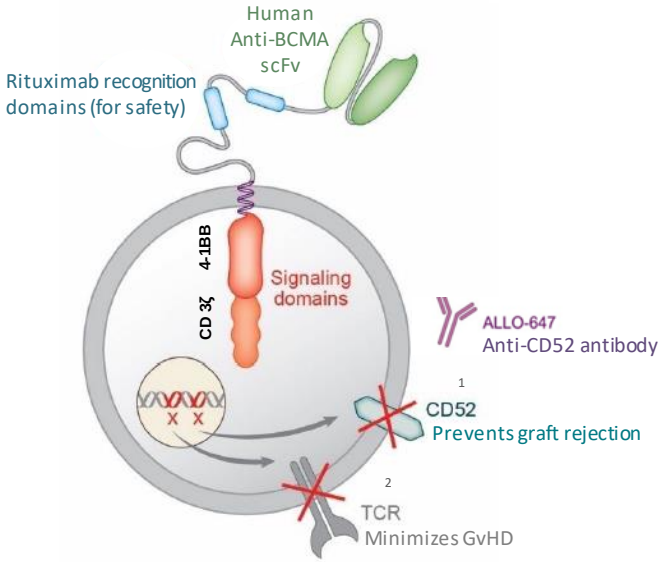
The First Allogeneic anti-BCMA CAR T Study for R/R Multiple Myeloma

- BCMA cell therapy has demonstrated unprecedented efficacy, but is not readily available to all patients
- Allogeneic chimeric antigen receptor (CAR) T cell therapy has the potential for all eligible patients to receive therapy on demand and supports re-dosing
- ALLO-715 (anti-BCMA) is an allogeneic CAR T cell product utilizing TALEN®* gene editing specifically designed to
  - Disrupt TCRα constant gene – to reduce the risk graft-versus-host disease (GvHD)
  - Edit CD52 gene – permits use of ALLO-647 (a humanized anti-CD5 mAb) to selectively deplete host T cells while protecting donor cel



*TALEN® gene editing is a technology pioneered and controlled by Cellectis.

1. TALEN-mediated CD52 KO allows selective lymphodepletion with ALLO-647
2. TALEN-mediated TRAC KO eliminates TCRα expression to minimize risk of GvHD

UNIVERSAL: First Allogeneic BCMA CAR T in Multiple Myeloma

Phase 1, Open-label, Multicenter Dose Escalation Study Enrolling in Fourteen US Centers

Key Eligibility Criteria

- Relapsed/refractory multiple myeloma
- ≥3 prior therapies including IMiD, proteasome inhibitor & anti-CD38
- Refractory to last prior therapy
- ECOG 0 or 1
- No donor-specific antibodies
- No prior systemic therapy within 2 weeks

Primary Endpoints

- Safety and tolerability

Secondary and Exploratory Endpoints

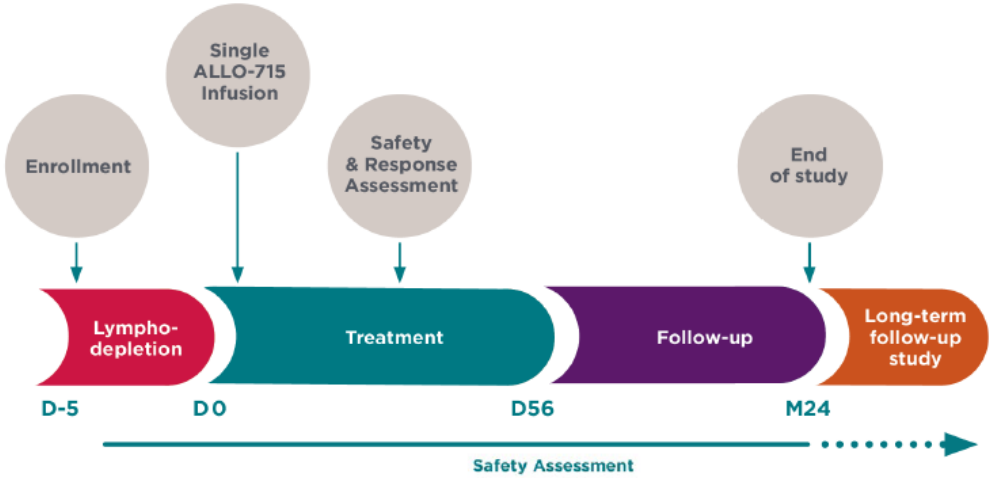
- Recommended ALLO-715 P2 dose and lymphodepletion (LD) regimen
- Anti-tumor activity (ORR, duration of response, PFS, and MRD)
- ALLO-715 cellular kinetics (blood levels of anti-BCMA CAR T cells)
- ALLO-647 pharmacokinetics (serum ALLO-647 concentrations)

Three Arms of the Study

- **Part A**:
  Dose Escalation of ALLO-715 with two different lymphodepletion regimens
- **Part B:**
  Evaluation of ALLO-715 in combination with nirogascestat
- **Part C:**
  Evaluation of consolidation dosing with ALLO-715

UNIVERSAL: First Allogeneic BCMA CAR T in Multiple Myeloma

Design for Part A*



ALLO-715 Dose Escalation: 40, 160, 320, 480 x 10^6 CAR$^+$ T cells	
Lymphodepletion Regimens (FCA**, CA†)	Doses
Fludarabine	30 mg/m^2/day x 3 days
Cyclophosphamide	300 mg/m^2/day x 3 days
ALLO-647	13 to 30 mg x 3 days

* Parts B (combination of ALLO-715 + nirogacestat) and C (consolidation regimen) are not reported here
** FCA conditioning with fludarabine, cyclophosphamide, and ALLO-647
† CA conditioning with cyclophosphamide and ALLO-647

Patient Flow

Median Time from Enrollment to Start of Treatment for All Patients: 5 Days

Part A Enrolled (N=48)

5 patients became ineligible due to organ failures from rapidly progressing disease

Part A Safety Population (N=43)

Part A Efficacy Population (N=43)

CAR+ T Cell Dose	Lymphodepletion Regimen			
	FCA39	FCA60	FCA90	CA39
40 x 10^6 Cells (DL1)	3	–	–	–
160 x 10^6 Cells (DL2)	4	–	–	3
320 x 10^6 Cells (DL3)	11	10	3	3
480 x 10^6 Cells (DL4)	3	3	–	–

*Overall median follow-up time = **4 Months***

- Patient flow includes patients enrolled in Part A of study
  - Part A was a single dose of ALLO-715 cells in dose escalation which was previously presented
  - Multiple LD regimens were evaluated at DL3 and DL4
- This presentation focuses on the results from the expansion of DL3

Heavily Pretreated Patients with Refractory Advanced-Stage Disease

Characteristics		Safety Population (N=43)
Age, median (range), years		64 (46, 77)
Gender, %	Male	63
	Female	37
ECOG PS, %	0	49
	1	51
ISS Stage III, %		19
High-risk cytogenetics*, %		37
Extramedullary disease, %		21
High tumor burden at screening†, %		33
Time since initial diagnosis, median (range), years		4.9 (0.9, 26.4)
Number of prior anti-myeloma regimens, median (range)		5 (3, 11)
Prior autologous SCT, %		91
Penta exposed/Penta-refractory, %		84/42

* High-risk cytogenetics is defined as del 17p, t(4;14), or t(14;16)
† High tumor burden considered when more than 50% plasma cells in bone marrow

- Patients had advanced disease
  - 19% of patients had ISS Stage III
  - 21% of patients had extramedullary disease
- Heavily pretreated patients in study
  - Median of 5 prior lines of therapy
  - All patients were refractory to last line
    - 91% were triple refractory and 42% were penta-refractory
- **No patient received bridging therapy**

ALLO-715 and ALLO-647 Demonstrated Manageable Safety Profile

TEAE of Interest* (N=43)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	All Grades
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cytokine Release Syndrome	13 (30)	10 (23)	1 (2)	0	0	24 (56)
Neurotoxicity†	4 (9)	2 (5)	0	0	0	6 (14)
Graft-versus-Host Disease	0	0	0	0	0	0
Infection‡	3 (7)	10 (23)	7 (16)	0	3 (7)	23 (54)
Infusion Reaction to ALLO-647	7 (16)	5 (12)	0	0	0	12 (28)

- **Manageable safety profile with low-grade and reversible neurotoxicity and no GvHD**
  - 14% of patients with AEs of potential low-grade neurotoxicity
  - Low use of tocilizumab 23% and steroids 14%

- 20 (47%) patients with an SAE
- 30 (70%) patients experienced Gr3+ neutropenia
- 3 Gr5 infections; 2 previously reported and an additional one due to sepsis

* Number of patients with AE occurring from the start of study drug up to subsequent anti-cancer therapy. For patients reporting more than one AE within a preferred term, only one AE with the maximum grade is reported
† Analysis done using a broad SMQ of noninfectious encephalopathy/delirium with adjudication by clinical review
‡ All infections (bacterial, fungal, and viral) included

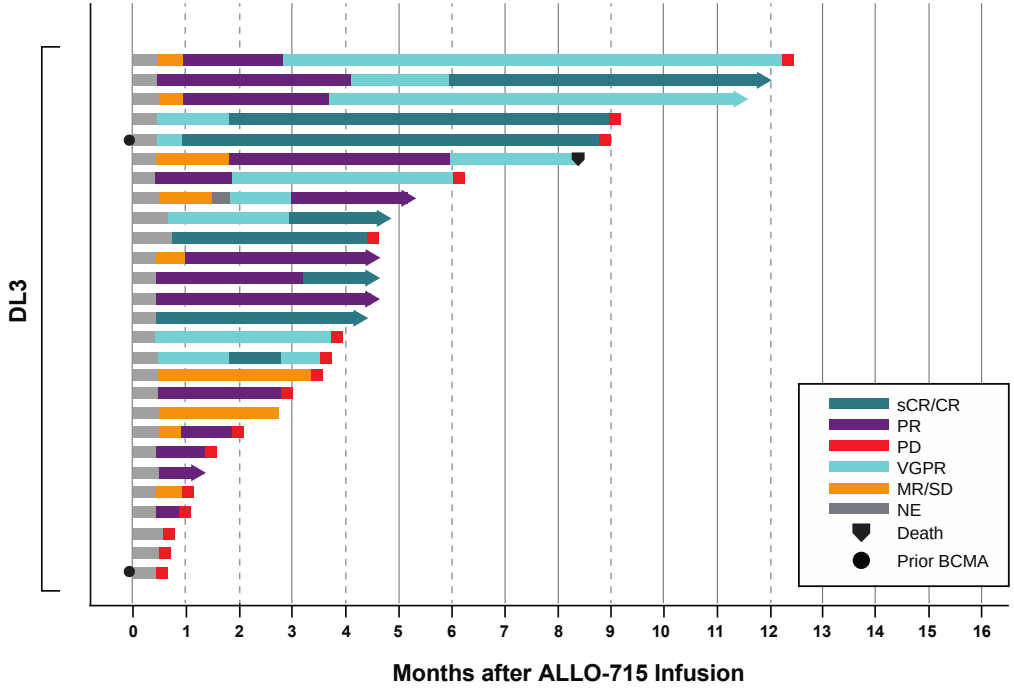
Encouraging Efficacy Seen with Additional Patients at DL3

Cell Dose & LD Regimen	DL3 (320M CAR+ T Cells)*				DL4 (480M CAR+ T Cells)	
	FCA39 N=11	FCA60 N=10	FCA90 N=3	FCA ALL N=24	FCA39 N=3	FCA60 N=3
ORR†, n (%) (95% CI)	**7 (64)** (31, 89)	**8 (80)** (44, 98)	**2 (67)** (9, 99)	**17 (71)** (49, 87)	**1 (33)** (0.8, 91)	**2 (67)** (9, 99)
VGPR+ Rate, n (%)	5 (46)	5 (50)	1 (33)	11 (46)	0	2 (67)
CR/sCR Rate, n (%)	3 (27)	3 (30)	0	6 (25)	0	0
mDOR, months (95% CI)	8.3 (3.4, 11.3)	NE (5.6, NE)	3.1 (2.4, 3.1)	8.3 (3.4, 11.3)	1.4 (NE, NE)	NE (1.5, NE)
Median follow-up, months (range)**	3.3 (0.5, 3.8)	3.8 (3.1, 11.2)	--	3.8 (0.5, 11.2)	--	7.4 (7.4, 7.4)

- In the FCA 320M CAR+ cell dose group, 17 patients **(71%) achieved an overall response rate (ORR)**
  - 11 (46%) were VGPR+, of those 6 (25%) were CR/sCR

* Three patients treated with 320M CAR+ cells and the CA LD regimen are not included above. Two of those responded with one pt achieving a CR
† Clinical response evaluation was based on IMWG response criteria, Kumar et al, 2016
** Median follow-up is for censored pts

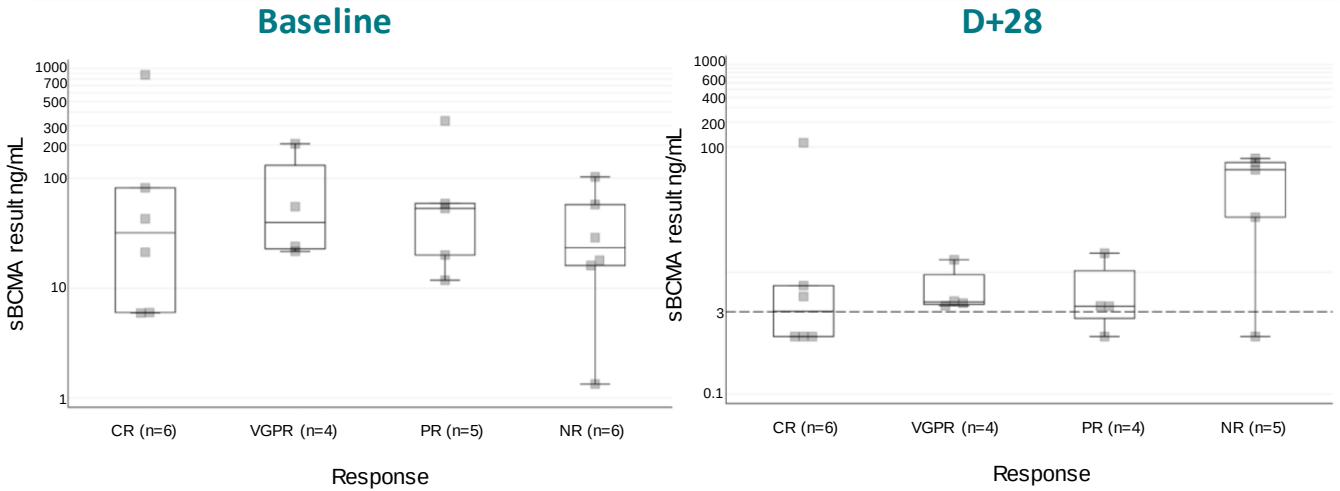
320M CAR T+ Cell Dose Achieves Durable Responses



- **Median time to response was 16 days**
- In the expansion of DL3 FCA, 9 pts with an initial response remain in response with median duration of response of 8.3 months
  - Of those with a confirmed response of VGPR+, **92% were MRD negative**
  - MRD negativity is associated with a durable response and period of progression-free survival

Reduced sBCMA on D28 Associated with Clinical Response

sBCMA by Response



- Baseline sBCMA levels were comparable across all treated patients
- sBCMA levels were 10x lower in responders compared to non responders
- sBCMA suppression is associated with responses

D0 sBCMA equals Baseline/Screen levels
Data shown include subjects in FCA39 and FCA60 cohorts

Summary

- ALLO-715 UNIVERSAL Trial is the first allogeneic anti-BCMA CAR T study to demonstrate safety and substantial efficacy in MM
- “Off-the-shelf” AlloCAR Ts have potential to addresses significant unmet need in patients with rapidly progressive disease
  - No bridging therapy required
  - Median time from enrollment to start of therapy of 5 days
  - 90% enrolled patients received treatment
- ALLO-715 with ALLO-647 is well tolerated with low-grade CRS, low-grade reversible neurotoxicity, no GvHD, and manageable safety
- 71% ORR and 46% VGPR+ with 320M cell dose and FCA comparable to approved autologous CAR T therapy
  - 92% VGPR+ responses were MRD negative
  - 8.3 months median durability of response
- ALLO-715 consolidation with two doses and ALLO-715 in combination with nirogacestat are also being evaluated; Next generation anti-BCMA TurboCAR (ALLO-605) currently in Phase 1 development

THANK YOU

To patients, their families and caregivers,
clinical trial investigators, and sites

ALLO-715 (BCMA) utilizes TALEN® gene-editing technology pioneered and owned by Cellectis. Allogene has an exclusive license to the Cellectis technology for allogeneic products directed at this target and holds all global development and commercial rights for this investigational candidate.

Disclosure

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