Preliminary Safety and Efficacy of PBCAR0191, an Allogeneic 'Off-the-Shelf' CD19-Directed CAR-T for Patients with Relapsed/Refractory (R/R) CD19+ B-ALL

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Disclosures

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Advisory Board /Honoraria

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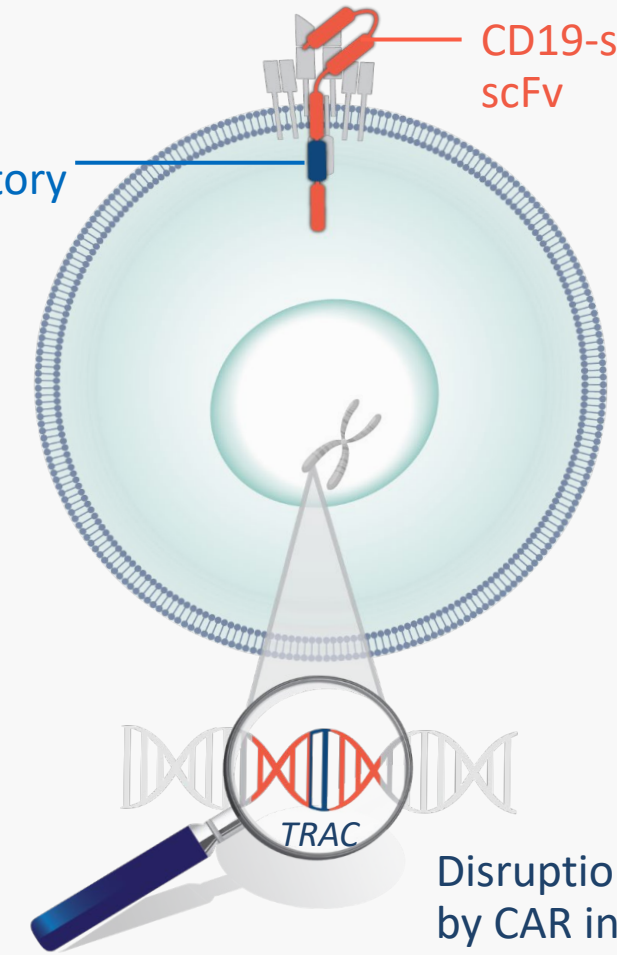
Background

- CD19-directed autologous CAR T products induce high response rates in adults with relapsed/refractory (R/R) B-ALL, yet many patients relapse within the first year
  - Cell manufacturing timelines and poor T-cell fitness may imperil efficacy, especially among those with proliferative disease
- This makes access to a donor-derived, readily available CAR T product of great interest in this patient population, particularly when considered as a transition to allo-hematopoietic cell transplant (HCT)
- We report preliminary safety, efficacy and CAR T pharmacokinetic data for subjects with R/R B-ALL dosed with at least 3×10^6 cells/kg of PBCAR0191, an allogeneic 'off-the-shelf' CD19-directed CAR T

Data presented for subjects with R/R B-ALL who received PBCAR0191 with a data cutoff of October 10, 2021 (N=15)

PBCAR0191: Allogeneic CAR T Cell Therapy



Disruption of TCR by CAR insertion into TRAC locus to prevent GvHD

- Allogeneic, CD19-directed cellular therapy derived from healthy donor cells
- Created with a **proprietary, single-step ARCUS gene editing process,** preserving an optimized proportion of naïve and effector memory cells while also minimizing translocations or off-target editing
- Mitigates graft-versus-host disease (GvHD) by knocking CAR directly into *TRAC* locus
- Improvements to PBCAR0191 expansion and persistence were investigated with modifications to standard lymphodepletion or increased PBCAR0191 doses

Subject Eligibility

Key Inclusion Criteria:

- Adults with CD19+ R/R B-ALL after **at least 2 prior lines** of therapy
- Prior allo-hematopoietic cell **transplant** (HCT) and/or **autologous CAR T** therapy was allowed

Among enrolled subjects

- Median prior lines of therapy was **5**, ranging between 2 and 12
- **Over 70%** of subjects had previously received 4 or more prior lines of therapy

Methods: Lymphodepletion and PBCAR0191 Dosing

PBCAR0191 Dose Levels

DL 3a/4	**Dose Level 3a** *OR* **Dose Level 4**	Day 0: 3×10^6 cells/kg Day 0: 3×10^6 cells/kg *plus* Day 10: 3×10^6 cells/kg
DL 4b	**Dose Level 4b**	Day 0: 500×10^6 flat dose

Note: DL's 3a & 4 combined due to lack of expansion upon 2nd infusion w/out LD in split dosing

Lymphodepletion Regimens

sLD	**Standard LD**	Fludarabine 30 mg/m^2/day × 3 days + Cyclophosphamide 500 mg/m^2/day × 3 days
eLD	**Enhanced LD**	Fludarabine 30 mg/m^2/day × 4 days + Cyclophosphamide 1000 mg/m^2/day × 3 days

Median time from screening completion to start of LD was 1 day

All eligible subjects received an infusion of PBCAR0191

Subject Characteristics

	DL3a/4[1] sLD[3] (n= 6)	DL3a/4[1] eLD[4] (n= 5)	DL4b[2] sLD (n=4)	Total (N=15)
Age (y), Median (min-max)	43 (27-49)	50 (26-56)	44 (22-66)	46 (22-66)
Male, n(%)	3 (50%)	3 (60%)	3 (75%)	9 (60%)
Pre-LD Baseline Marrow Blast %, Median (min-max)	47.5 (5-90)	25 (2-94)	49.5 (2-98)	45 (2-98)
Refractory to Last Line of Therapy, n(%)	2 (33%)	1 (20%)	2 (50%)	5 (33%)
Prior Lines of Therapy, median (min-max)	4.5 (2-7)	5 (4-12)	4.5 (3-10)	5 (2-12)
Prior 4+ Lines of Therapy, n(%)	4 (67%)	5 (100%)	2 (50%)	11 (73%)
Blinatumomab n(%)	4 (67%)	4 (80%)	4 (100%)	12 (80%)
Prior allo-HCT n(%)	3 (50%)	3 (60%)	0	6 (40%)
Prior CD19-directed CAR T, n(%)	0	1 (20%)	0	1 (7%)

[1]**Dose Level 3a/4** = 3×10^6 cells/kg Day 0 and Day 10
[2]**Dose Level 4b** = 500×10^6 cells flat dose;
[3]**Standard LD (sLD)** = Fludarabine 30 mg/m^2/day × 3 days + Cyclophosphamide 500 mg/m^2/day × 3 days;
[4]**Enhanced LD (eLD)** = Fludarabine 30 mg/m^2/day × 4 days + Cyclophosphamide 1000 mg/m^2/day × 3 days

AESI[1] Profile Across Dose Ranges and LD Approaches

Data cutoff of October 10, 2021

			DL3a/4[2] sLD[4] (n= 6)	DL3a/4[2] eLD[5] (n= 5)	DL4b[3] sLD (n=4)	Total (N=15)
AE of Special Interest	**CRS**	*Grade 1 or Grade 2*	3 (50%)	4 (80%)	3 (75%)	10 (67%)
		Grade 3 or higher	0	0	0	0
	Time to onset (Days)	*Median (range)*				1.5 (0-7)
	ICANS	*Grade 1 or Grade 2*	1 (17%)	2 (40%)	1 (25%)	4 (27%)
		Grade 3 or higher	0	0	1 (25%)	1 (7%)
	Time to onset (Days)	*Median (range)*				2 (1-11)
	GvHD		0	0	0	0
Other Notable AEs	**Neutropenia** (Grade ≥3) on ≥Day 28		0	2 (40%)	1 (25%)	3 (20%)
	Infection (Grade ≥3)		1 (17%)	4 (80%)	1 (25%)	6 (40%)

[1]**AESI-** AE of Special Interest;
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LD- and Dose-Dependent Changes in CAR T Expansion by PCR

PBCAR0191 Expansion by PCR

Impact of *eLD in Same Dose*

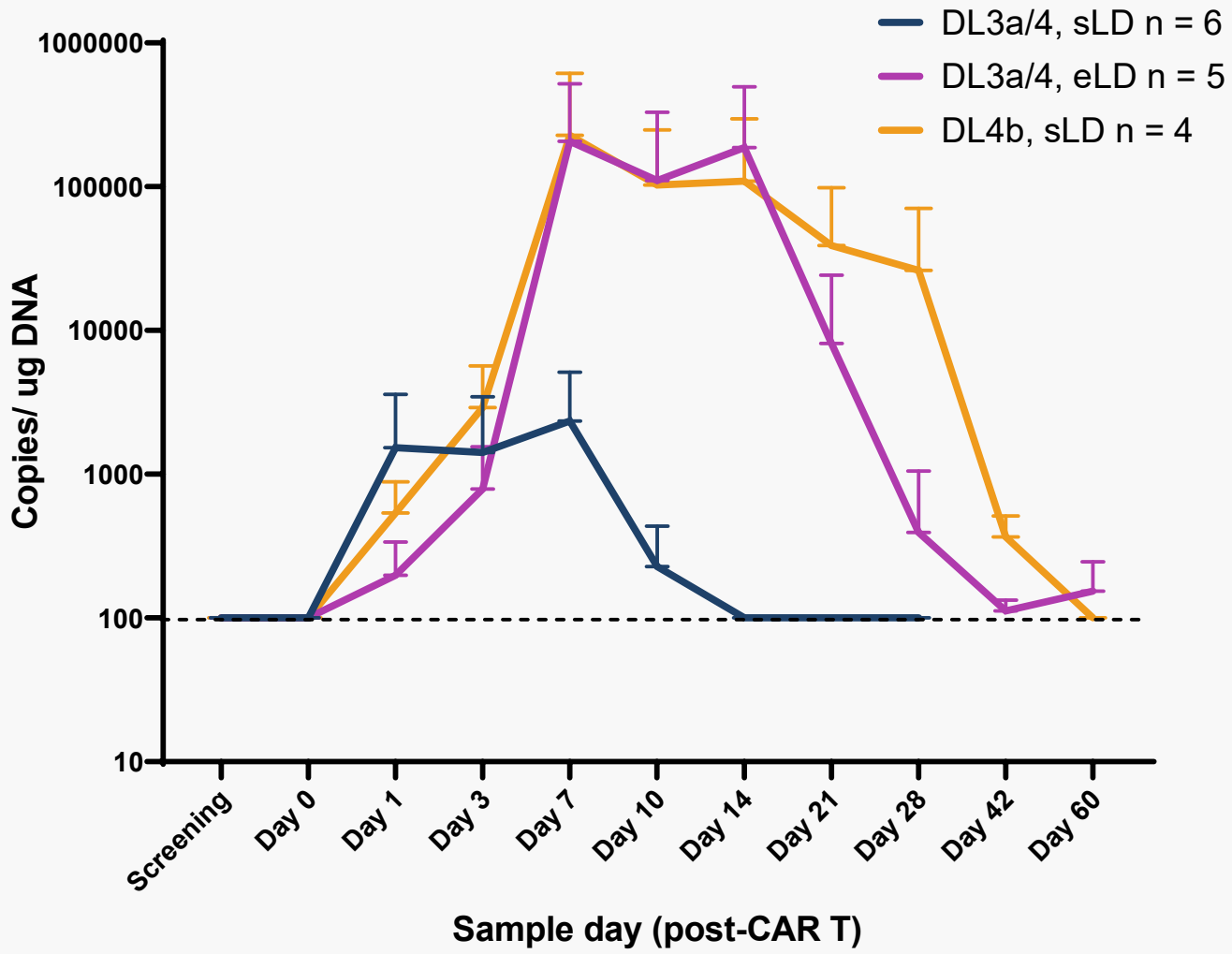
DL3a/4 sLD to **DL3a/4 eLD**

Mean Peak	~89X
Mean Area Under the Curve (AUC)	~127X

Impact of *Dose with Same LD*

DL3a/4 sLD to **DL4b sLD**

Mean Peak	~97X
Mean Area Under the Curve (AUC)	~123X



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High CR/CRi Rates in R/R B-ALL with either Higher PBCAR0191 Dose or Enhanced LD

n (%)	DL3a/4[1] sLD[3] (n=6)	DL3a/4[1] eLD[4] (n=5)	DL4b[2] sLD[3] (n=4)	Total (N=15)
CR/CRi at Day ≥28	2 (33%)	4 (80%)	3 (75%)	9 (60%)
MRD^{neg}	0 (0%)	3 (60%)	2 (50%)	5 (33%)
MRD^{pos}	2 (33%)	1 (20%)	1 (25%)	4 (27%)
Progressive Disease (PD) at Day ≥28	4 (66%)	1 (20%)	1 (25%)	6 (40%)

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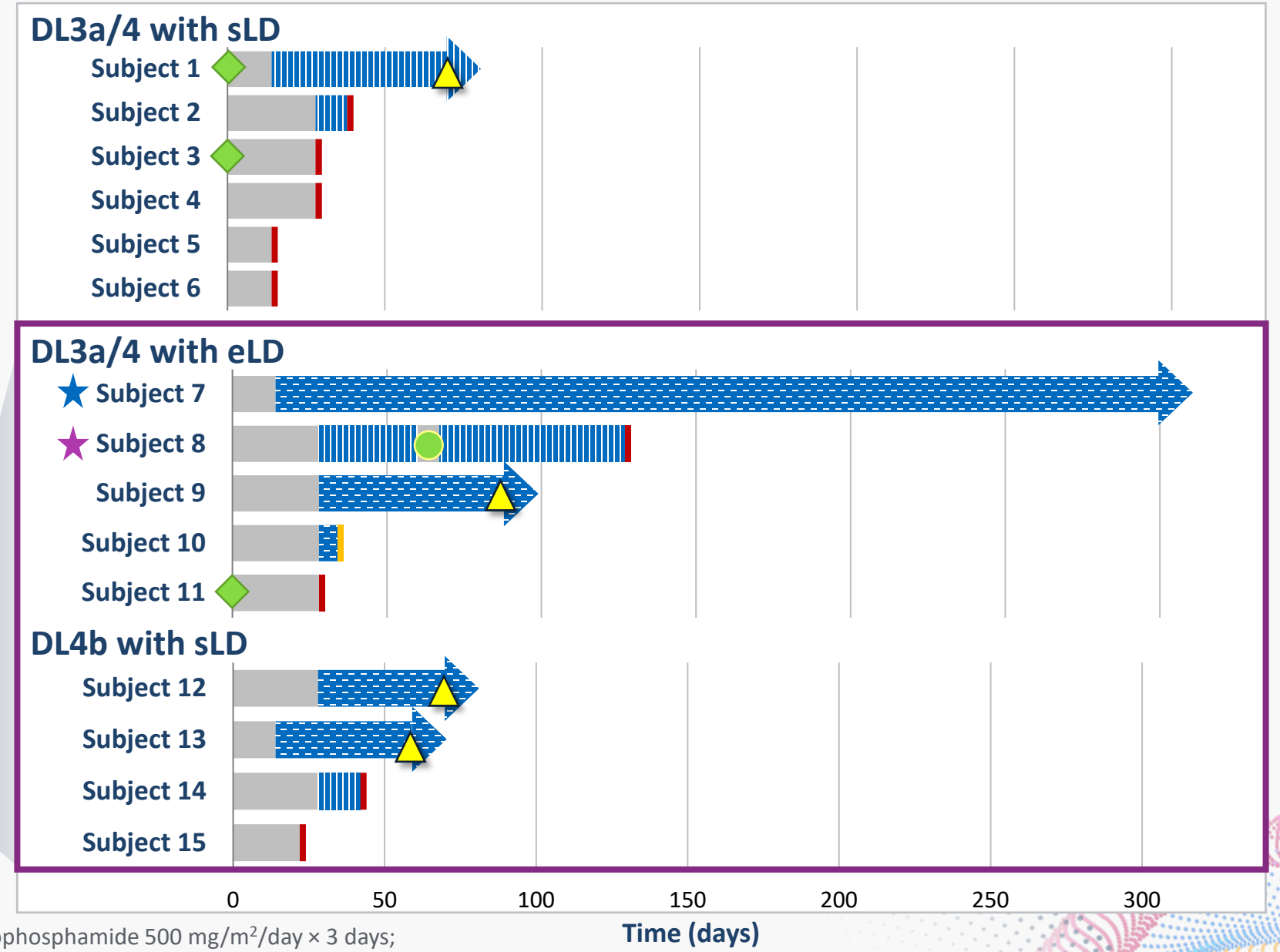
Durability of Response for PBCAR0191 in R/R B-ALL

- Prior to 1st evaluation
- CR/CRi (MRD-)
- CR/CRi (MRD+)
- PD
- Death on study in ongoing response
- Allo-HCT
- DL3 consolidation
- DL4
- Transplant ineligible
- Eligible for transplant post-consolidation; refused then progressed



At DL3a/4 eLD or DL4b sLD:

- 1 subject with ongoing response >9 months
- 5 of 9 subjects in eLD or DL4b secured adequate window for allo-HCT with 3 proceeding to transplant

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ClinicalTrials.gov identifier: NCT03666000

Conclusions

- PBCAR0191 demonstrated a manageable safety profile
- PBCAR0191 dose level & enhanced LD markedly increased peak cell expansion and persistence in heavily pre-treated subjects with a median of 5 prior lines of therapy
- PBCAR0191 yielded a 78% complete remission rate with either enhanced LD or a higher PBCAR0191 dose
- Immediate availability of PBCAR0191 was evident compared to autologous CAR T
  - Median time from screening completion to start of LD was 1 day
  - All eligible subjects received an infusion of PBCAR0191
- Readily accessible highly active CD19-directed allogeneic CAR T may provide a bridge for R/R B-ALL patients with high unmet need

Thank you