Allogeneic CAR-T PBCAR0191 with Intensified Lymphodepletion is Highly Active in Subjects with Relapsed/Refractory B-Cell Malignancies

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Disclosures

Consulting and Education

- Amgen, Pfizer, Novartis, BMS/Celgene/Juno, Kite/Gilead, Precision BioSciences, Jazz, Acrotech, Beigene, Pharmacyclics, Adaptive, Century Therapeutics

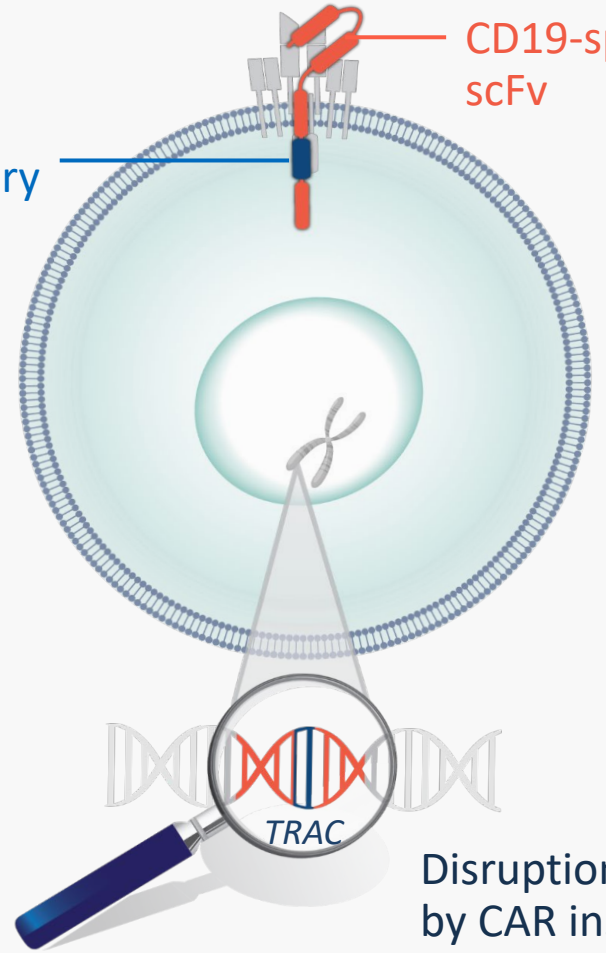
Grants and Investigator Initiated Trials

- Kite/Gilead, Jazz, Servier

Steering Committee

- PeproMene Bio

PBCAR0191: Allogeneic CAR T Cell Therapy



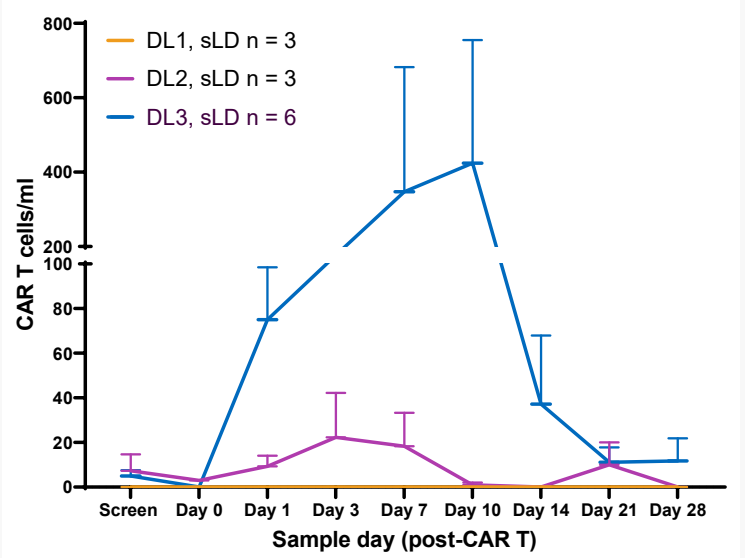
Disruption of TCR by CAR insertion into *TRAC* locus to prevent GvHD

- 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

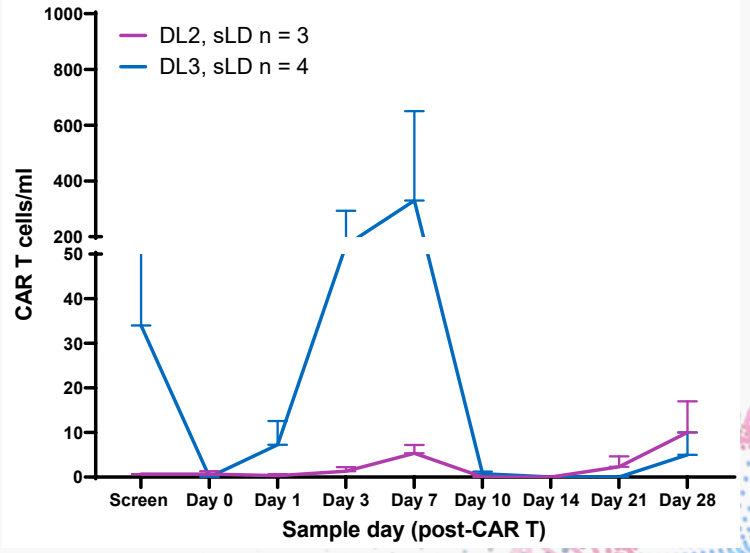
Findings from Standard Lymphodepletion

- No limiting toxicity in subjects receiving Dose Level (DL) 1-3 using standard lymphodepletion[1] (sLD)
  - No Grade 3 or greater immune effector cell-associated neurotoxicity (ICANs) or cytokine release syndrome (CRS)
  - No evidence of graft versus host disease (GvHD)
- Dose-dependent increase in PBCAR0191 expansion with modest peak and rapid attrition attributed to PBCAR0191 cell rejection
  - Clear evidence of dose-dependent PBCAR0191 activity, however with limited durability
- Data suggests an intensified lymphodepletion regimen might improve cell expansion and persistence

NHL



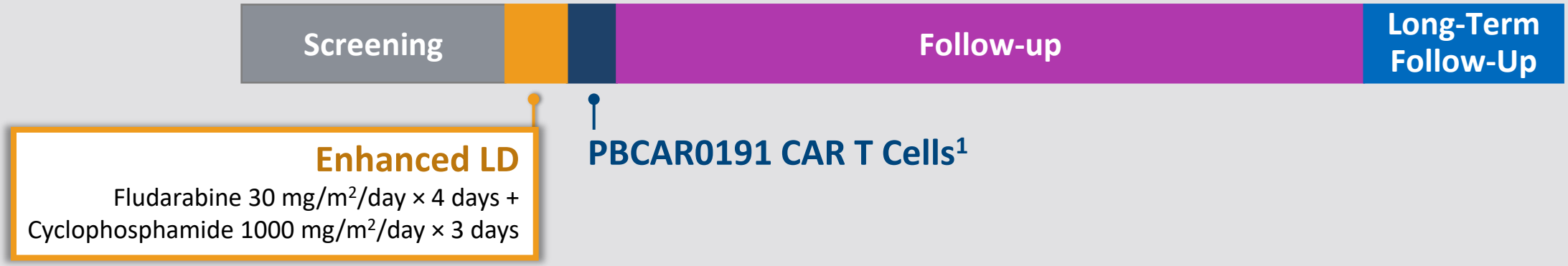
B-ALL



[1]**Standard LD (sLD)** = Fludarabine 30 mg/m2/day × 3 days + Cyclophosphamide 500 mg/m2/day × 3 days

DL1 $0.3x10^6$ cells/ kg
DL2 $1.0x10^6$ cells/ kg
DL3 $3.0x10^6$ cells/ kg

PBCAR0191 with Enhanced Lymphodepletion in R/R CD19+ B-Cell Malignancies



Objectives

- Mitigate host immune rejection to improve PBCAR0191 expansion and persistence
- Increase frequency and durability of Complete Responses (CRs)
- Assess safety (e.g., Grade ≥3 CRS or ICANS)
- Evaluate activity in subjects with and without prior autologous CD19-directed CAR therapy

[1]PBCAR0191 Dosed at Dose level 3a (3×10^6 cells/kg Day 0) or Dose level 4 (3×10^6 cells/kg Day 0 plus 3×10^6 cells/kg Day 10; DL's 3a & 4 combined due to lack of expansion upon 2nd infusion w/out LD in split dosing

Subject Characteristics:
Predominance of Advanced and Aggressive Disease

	NHL (n=17)	B-ALL (n=5)
Age (y), median (range)	59 (34-76)	50 (26-56)
Refractory to LLT	6 (35%)	1 (20%)
Aggressive histology,[1] n (%)	13 (77%)	-
DLBCL	10 (59%)	-
CLL with Richter's	2 (12%)	-
High grade	1 (6%)	-
Number of prior treatments, median (range)	5 (2-15)	5 (4-12)
Prior CD19directed CAR T, n (%)	4 (24%)	1 (20%)
Prior auto-HCT (NHL)/ allo-HCT (B-ALL), n (%)	6 (35%)	3 (60%)

[1] 4 subjects with indolent disease: 3 FL low grade and 1 CLL/SLL

AESI[1] Profile with Enhanced Lymphodepletion

Data cutoff as of October 10, 2021

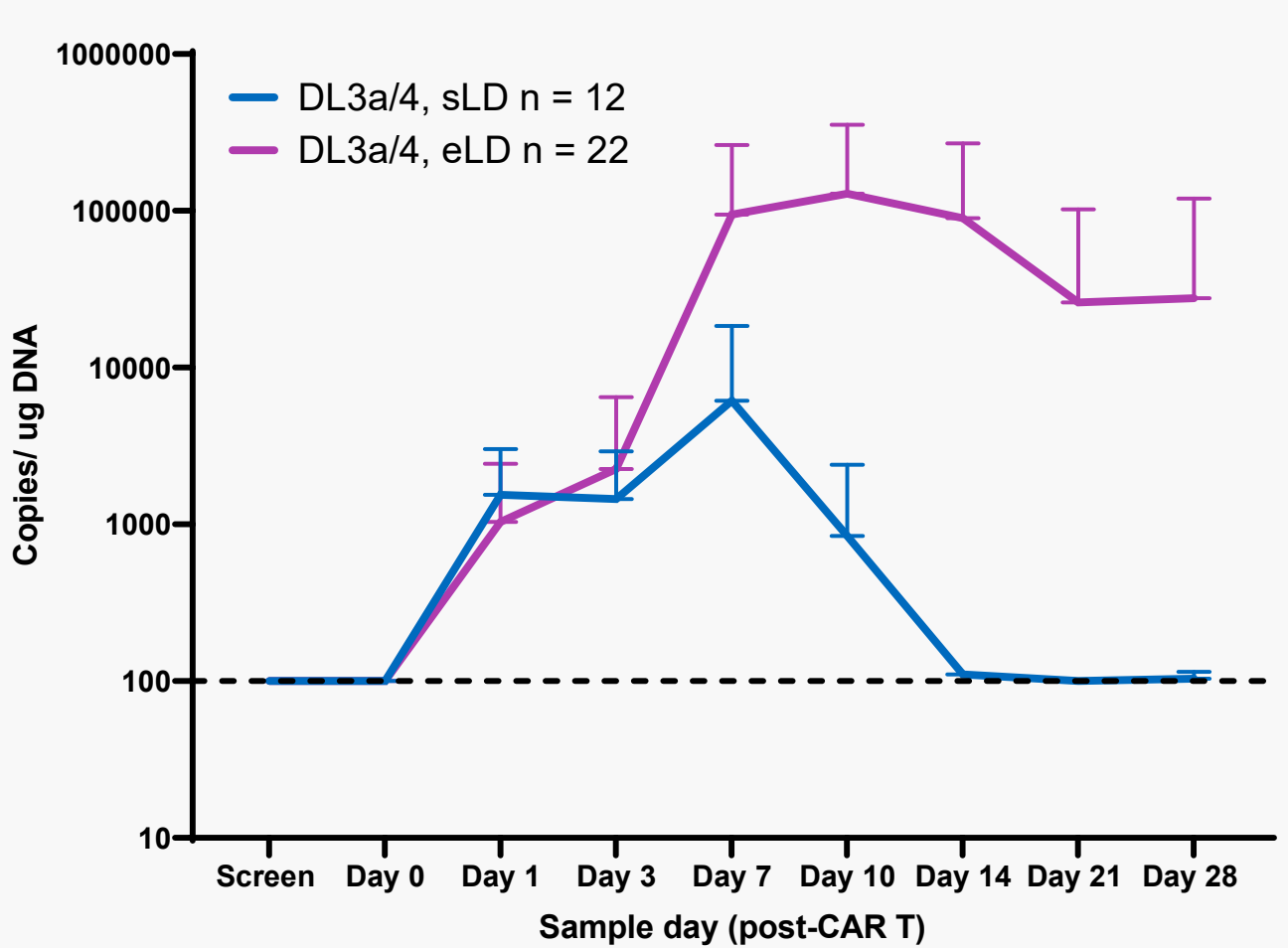
Number (%) of subjects experiencing events with max grade			NHL (n=17)	B-ALL (n=5)
AE of special interest	**CRS**	*Grade 1 or Grade 2*	11 (65%)	4 (80%)
		Grade 3 or higher	0	0
	Time to onset (Days)	*Median (range)*	7 (3-19)	2.5 (0-7)
	ICANS	*Grade 1 or Grade 2*	4 (24%)	2 (40%)
		Grade 3 or higher	1 (6%)	0
	Time to onset (Days)	*Median (range)*	6 (1-13)	3.5 (2-5)
	GvHD		0	0
Other notable AEs	**Infection**	*Grade 1 or Grade 2*	3 (18%)	1 (20%)
		Grade 3 or higher	7 (41%)	4 (80%)

[1] **AESI-Adverse Events of Special Interest**
[2] **Enhanced LD (eLD)** = Fludarabine 30 mg/m^2/day × 4 days + Cyclophosphamide 1000 mg/m^2/day × 3 days

eLD[1] Markedly Increased PBCAR0191 Peak Expansion vs. sLD[2]

PBCAR0191 Expansion by PCR

Mean Peak	~21X
Mean Area Under the Curve (AUC)	~47X



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

High Response rates to PBCAR0191 with eLD at ≥Day 28

n (%)	**NHL** (n=16)[1]	**B-ALL** (n=5)
Overall Response Rate (ORR)	11 (69%)	4 (80%)
Complete Response (CR)	9 (56%)	4 (80%)

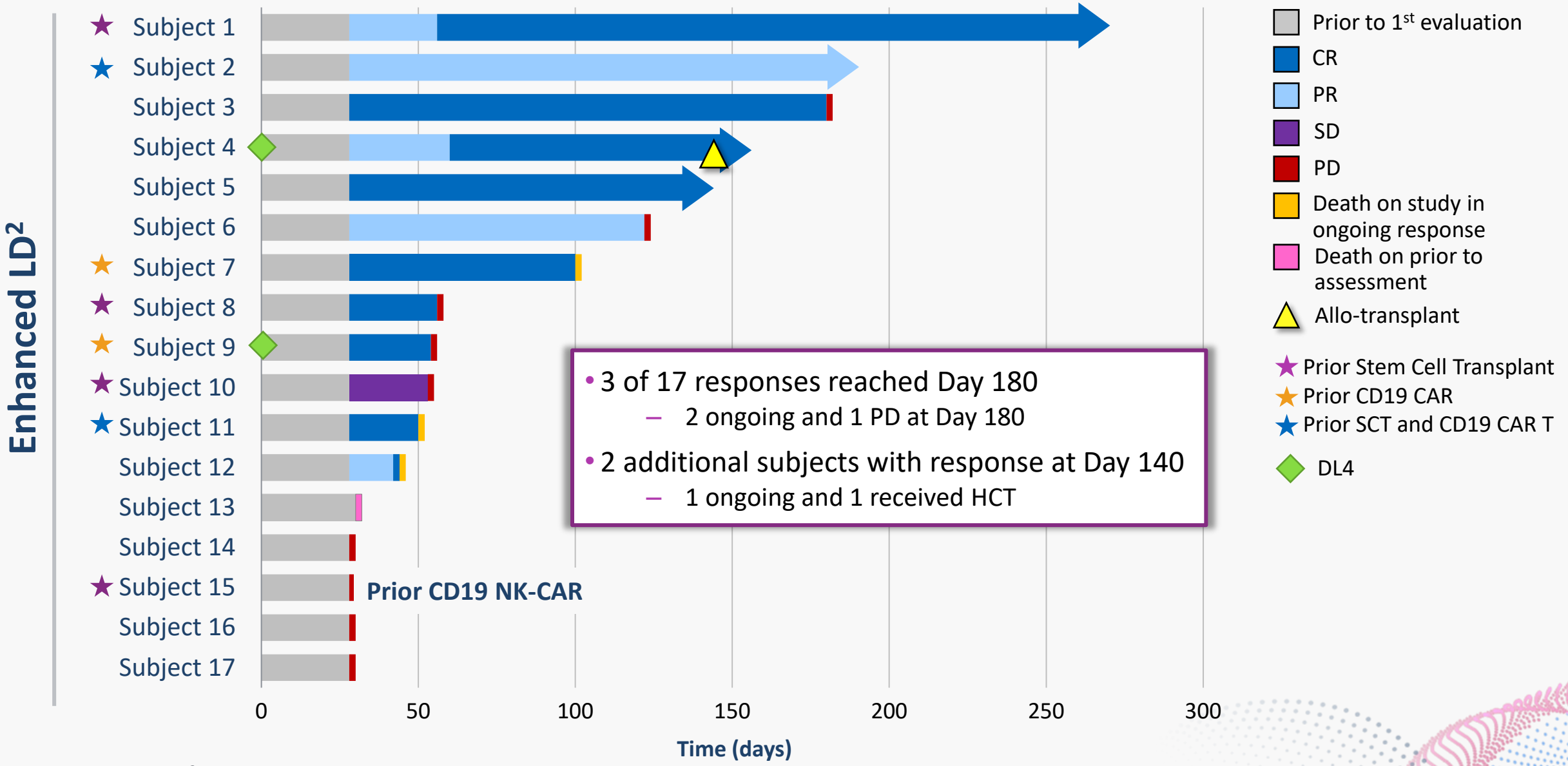
[1]One death on study prior to Day 28 assessment

Best Response to PBCAR0191 at Day ≥28 According to Prior Auto-CAR T Cell Therapy

n (%)	**All evaluable subjects** (N=21)[1]	**CAR T naïve** (n=16)[2]	**CAR T experienced** (n=5)
Overall Response Rate (ORR)	15 (71%)	10 (63%)	5 (100%)
Complete Response (CR)	13 (62%)	9 (56%)	4 (80%)

[1]One death on study prior to Day 28 assessment
[2]One subject received CD19 NK-CAR therapy

PBCAR0191 DL3a/4[1] NHL: Response Duration



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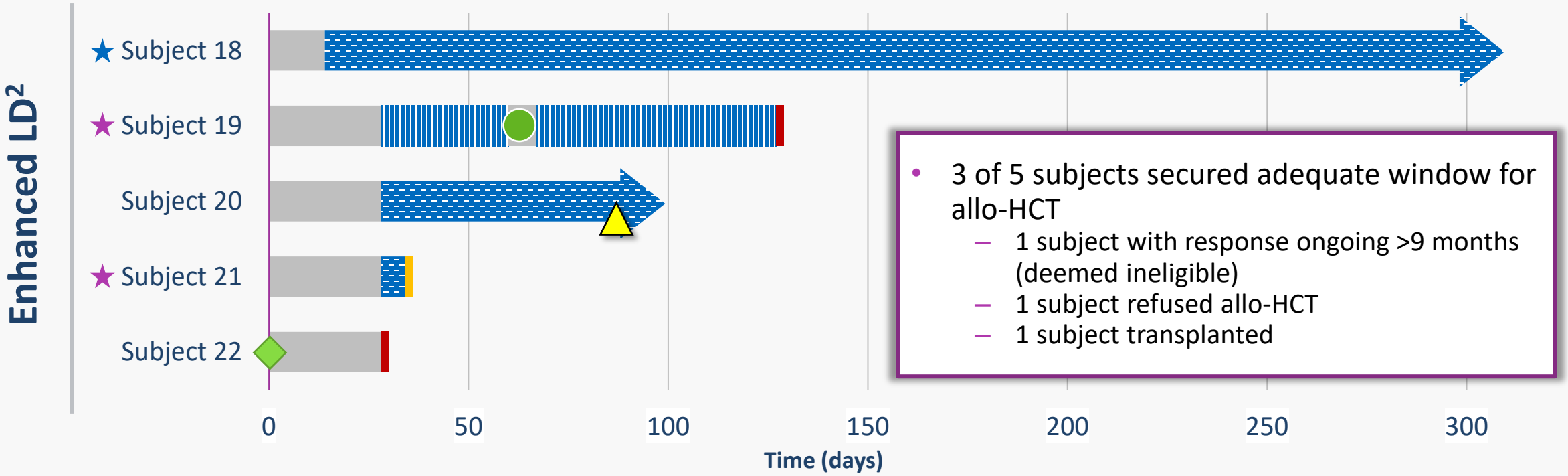
PBCAR0191 DL3a/4[1] B-ALL: Response Duration



- 3 of 5 subjects secured adequate window for allo-HCT
  - 1 subject with response ongoing >9 months (deemed ineligible)
  - 1 subject refused allo-HCT
  - 1 subject transplanted

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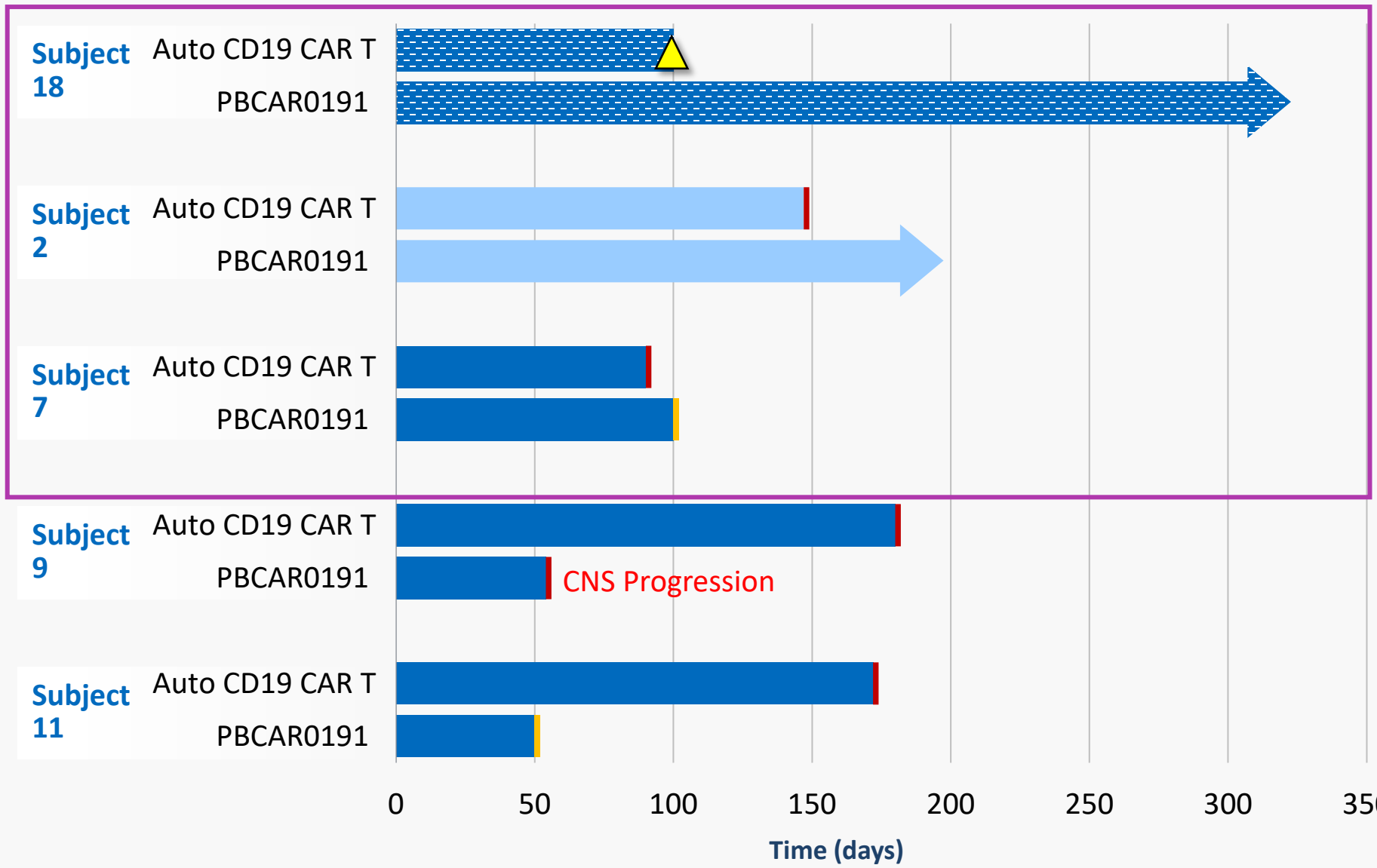
CD19 Auto-CAR T vs. PBCAR0191 Responses



- 100% ORR in subjects who received prior auto-CAR T
- PBCAR0191 response duration exceeded original response to auto-CAR T in 3 of 5 subjects
- B-ALL subject in MRD^{neg} CR at >9 months after relapse from 2 prior allogeneic HCTs and CD19 auto-CAR T

CR/CRi (MRD-)
CR
PR
PD
Death on study in ongoing response
Allo-transplant

Conclusions

- Enhanced LD mitigated PBCAR0191 rejection to markedly improve peak cell expansion and persistence with predictable toxicity
- In 21 heavily pre-treated R/R subjects, with five prior lines, a single infusion of PBCAR0191 following enhanced LD yielded an ORR of 71% and CR rate of 62% at 3 x 10^6 cells/kg
  - All eligible subjects were dosed with PBCAR0191
  - Overall and CR rate comparable to auto-CAR T recipients
  - Durability in this heavily treated population may be lower than auto-CAR T at current PBCAR0191 dose
- Among five subjects who progressed following CD19 auto-CAR T therapy (4 NHL, 1 ALL):
  - 100% ORR
  - Response duration exceeded original response to auto-CAR T in 3 of 5 subjects
  - B-ALL subject in MRD^{neg} CR >9 months after relapse from 2 prior allo-HCT transplants and CD19 auto-CAR T prior treatment
- Continue to explore signal in additional CD19 auto-CAR T experienced subjects to further define activity in this growing population with high unmet need

Thank you