PRECISION BIOSCIENCES

2021 ASH: Allogeneic CAR T Pipeline Update

American Society of Hematology
December 11, 2021

Forward Looking Statements

This presentation (together with any other statements or information that we may make in connection herewith) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation (together with any other statements or information that we may make in connection herewith) that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the expected timing of clinical updates and interim updates related to PBCAR0191, PBCAR19B, PBCAR269A monotherapy and PBCAR269A in combination with nirogacestat, statements regarding our clinical development pipeline and the potential clinical benefit of our product candidates. In some cases, you can identify forward-looking statements by terms such as "aim," "anticipate," "believe," "could," "expect," "should," "plan," "intend," "estimate," "target," "mission," "goal," "may," "will," "would," "should," "could," "target," "potential," "project," "predict," "contemplate," "potential," or the negative thereof and similar words and expressions. Forward-looking statements are based on management's current expectations, beliefs and assumptions and on information currently available to us. Such statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to: our ability to become profitable; our ability to procure sufficient funding and requirements under our current debt instruments and effects of restrictions thereunder; risks associated with raising additional capital; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the success of our programs and product candidates in which we expend our resources; our limited ability or inability to assess the safety and efficacy of our product candidates; our dependence on our ARCUS technology; the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical or greenhouse studies and clinical or field trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, biotechnology and agricultural biotechnology fields; our or our collaborators' ability to identify, develop and commercialize product candidates; pending and potential liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators' development of product candidates; our or our collaborators' ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate; our or our collaborators' ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; potential manufacturing problems associated with the development or commercialization of any of our product candidates; our ability to obtain an adequate supply of T cells from qualified donors; our ability to achieve our anticipated operating efficiencies at our manufacturing facility; delays or difficulties in our and our collaborators' ability to enroll subjects; changes in interim "top-line" and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; the rate and degree of market acceptance of any of our product candidates; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events effects of the outbreak of COVID-19, or any pandemic, epidemic or outbreak of an infectious disease; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2021, as any such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC's website at www.sec.gov and the Investors page of our website under Events and Presentations at investor.precisionbiosciences.com.

All forward-looking statements speak only as of the date of this presentation and, except as required by applicable law, we have no obligation to update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

PRECISION BIOSCIENCES

Delivering on the Promise of Therapeutic Genome Editing

Ex vivo editing for Allogeneic CAR T immunotherapy
Gene edited, donor derived CAR T cells

ARCUS® Genome Editing

Derived from natural homing endonuclease for in vivo and ex vivo applications

***In Vivo* Editing for Genetic Diseases**
Potentially curative, one-time treatment

ARCUS: Advanced Genome Editing Platform for *in vivo* and *ex vivo* Editing

PRECISION

- Safety
- Specificity

&

VERSATILITY

- ARCUS is Easy to Deliver
- ARCUS Performs Complex Edits
  (Gene Insertion & Gene Repair)

CEO Takeaways from First 50 Days at Precision BioSciences

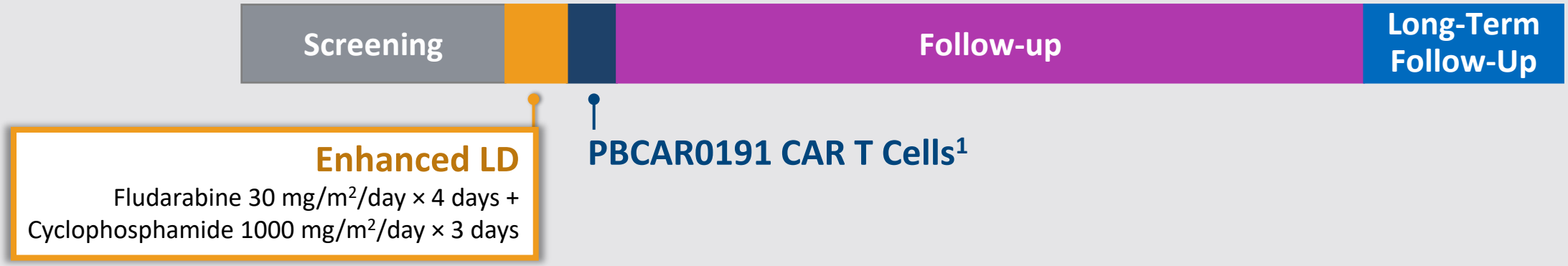
- Exceptional scientific team created ARCUS
- PBCAR0191 - potential First-in-Class allogeneic CAR T program
- PBCAR19B (stealth cell) - potential Best-in-Class CD19 targeting allogeneic CAR T
- Disciplined, data driven decisions
- *in vivo* gene editing pipeline is advancing with 3 planned IND/CTAs in next 3 years

Today's Topics

- Review of clinical data
  - PBCAR0191 with eLD - CD19
  - PBCAR269A - BCMA
- Allogeneic CAR T portfolio going forward
  - First-in-Class approach
  - Best-in-Class approach
- Expected 2022 CAR T program updates

First-in-Class: Allogeneic PBCAR0191 for Relapsed/Refractory B-Cell Malignancies

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



Objectives

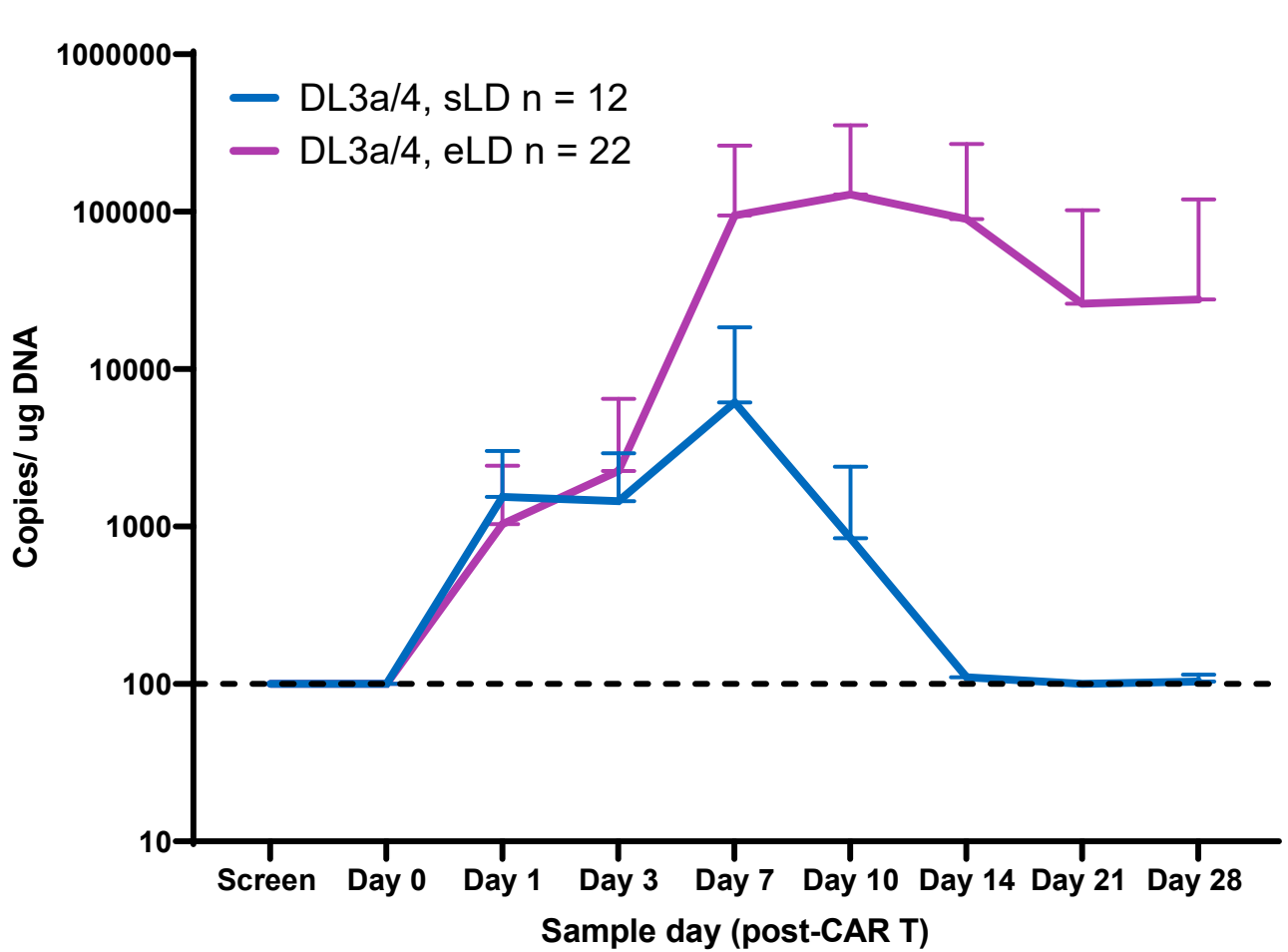
- Mitigate host immune rejection to improve PBCAR0191 expansion and persistence
- Increase frequency and durability of Complete Responses (CRs)
- Assess safety (e.g., Grade ≥3 CRS or ICANS)
- Evaluate activity in subjects with and without prior autologous CD19-directed CAR therapy

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

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

PBCAR0191 Expansion by PCR

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



* All eligible subjects began LD within 1 day of eligibility determination

[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 3/4a (3 × 10^6 cells/kg Day 0 and Day 10)

Heavily Pre-Treated and Aggressive Lymphoma Population

	NHL (n=18)[2]	B-ALL (n=5)
Age (y), median (range)	57 (34-76)	50 (26-56)
Refractory to Prior Line of Therapy	6 (33%)	1 (20%)
Aggressive histology,[1] n (%)	14 (78%)	-
DLBCL	11 (61%)	-
CLL with Richter's	2 (11%)	-
High grade	1 (6%)	-
Number of prior treatments, median (range)	5 (2-15)	5 (4-12)
Prior CD19 directed CAR T, n (%)	5 (28%)	1 (20%)
Prior auto-HCT (NHL)/ allo-HCT (B-ALL), n (%)	7 (39%)	3 (60%)

[1] Four subjects with indolent disease: Three FL low grade and one CLL/SLL
[2] One death on study prior to Day 28 assessment

Predictable AESI Profile with Enhanced Lymphodepletion[1]

Data cutoff as of Nov 16, 2021

Number (%) of subjects experiencing events with max grade			NHL (n=18)[2]	B-ALL (n=5)
AE of special interest	**CRS**	*Grade 1 or Grade 2*	12 (67%)	4 (80%)
		Grade 3 or higher	0	0
	Time to onset (Days)	*Median (range)*	6.5 (3-19)	2.5 (0-7)
	ICANS	*Grade 1 or Grade 2*	4 (22%)	2 (40%)
		Grade 3 or higher	1 (6%)[3]	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*	2 (11%)	1 (20%)
		Grade 3 or higher [4]	8 (44%)	4 (80%)

[1] Enhanced LD (eLD) = Fludarabine 30 mg/m^2/day × 4 days + Cyclophosphamide 1000 mg/m^2/day × 3 days
[2] One subject non-evaluable for efficacy at Day 28 assessment due to death related to cardiac arrest after choking incident
[3] One grade 3 ICANS with resolution to ≤ Grade 2 in 72 hours
[4] One death among subjects in ongoing complete response deemed possibly related to treatment by investigator (as previously disclosed) and three deaths among subjects in ongoing complete response deemed unrelated to treatment by investigator

Best Response to PBCAR0191 with eLD Comparable Between Auto-CAR T Relapsed & Auto-CAR T Naïve Subjects

n (%)	All evaluable subjects (N=22)[1]	CAR T naïve (n=16)[2]	CAR T experienced (n=6)
Overall Response Rate (ORR) ≥Day 28	16 (73%)	10 (63%)	6 (100%)
Complete Response (CR) ≥Day 28	13 (59%)	9 (56%)	4 (66%)

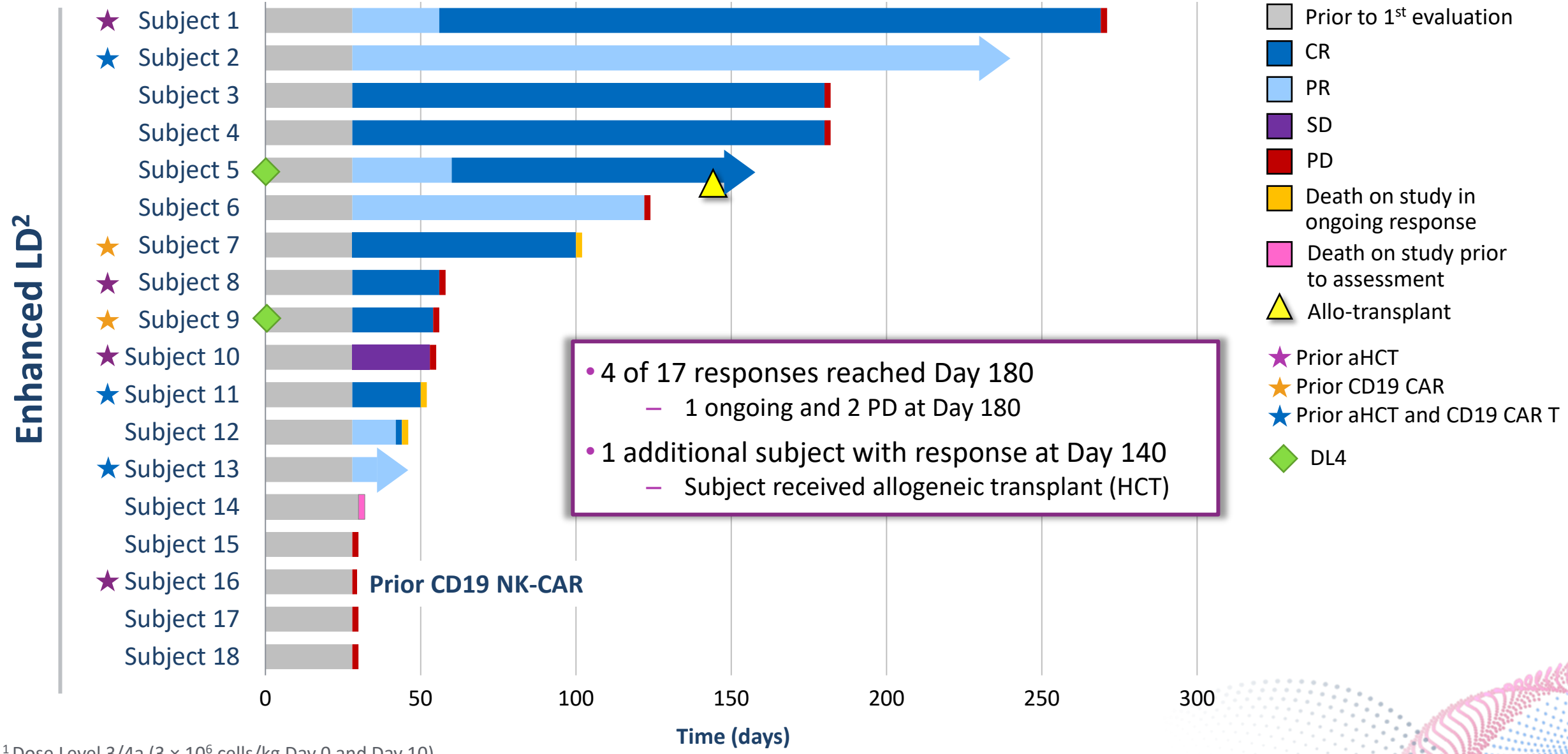
[1] One subject non-evaluable for efficacy at Day 28 assessment due to death related to cardiac arrest after choking incident
[2] One subject received CD19 NK-CAR therapy

High Response Rates to PBCAR0191 with eLD on Par with Autologous CAR T

n (%)	NHL (n=17)[1]	B-ALL (n=5)
Overall Response Rate (ORR) ≥Day 28	12 (71%)	4 (80%)
Complete Response (CR) ≥Day 28	9 (53%)	4 (80%)

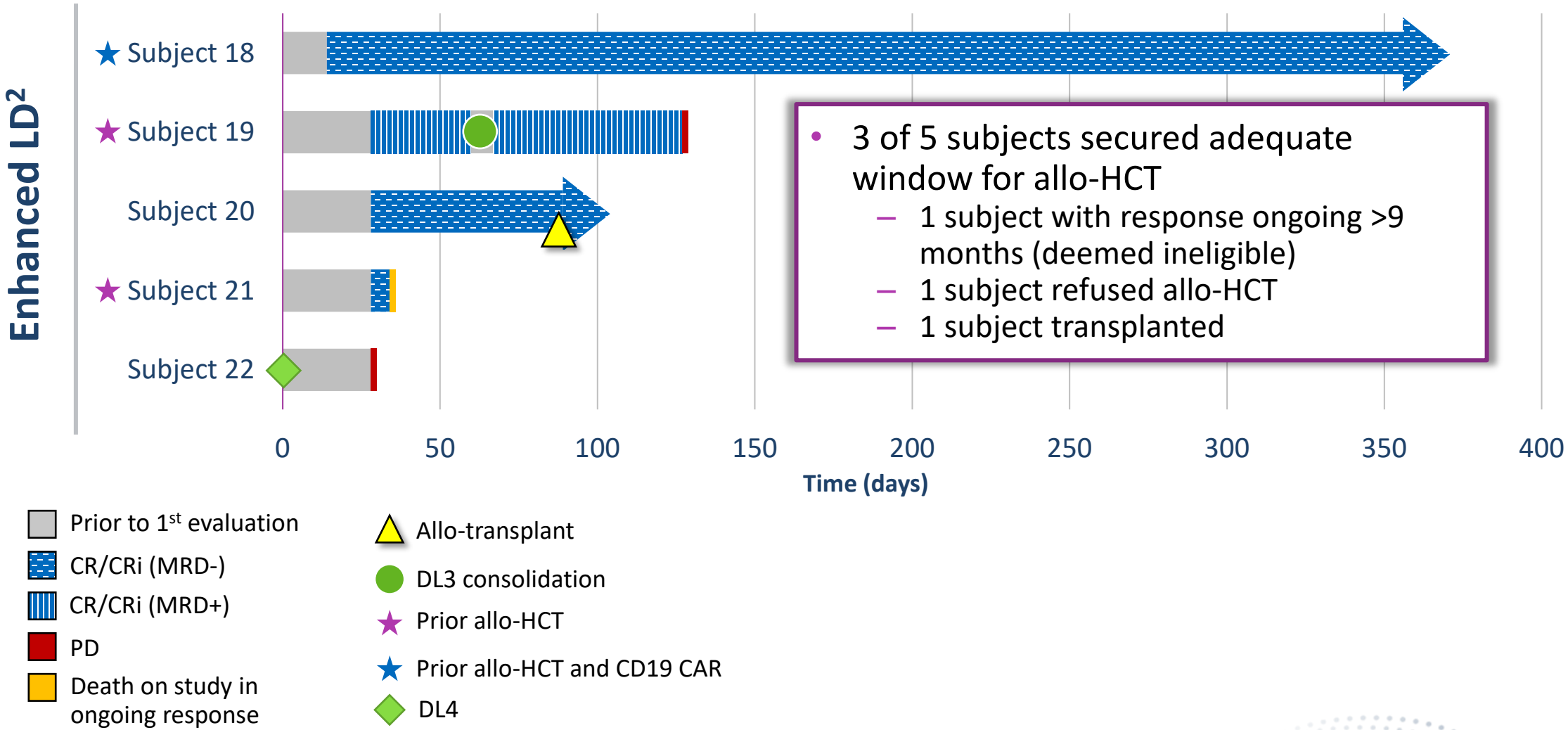
[1] One subject non-evaluable for efficacy at Day 28 assessment due to death related to cardiac arrest after choking incident

PBCAR0191[1] Response Duration by Subject in NHL



[1] Dose Level 3/4a (3×10^6 cells/kg Day 0 and Day 10)
[2] Enhanced LD (eLD) = Fludarabine 30 mg/m²/day × 4 days + Cyclophosphamide 1000 mg/m²/day × 3 days

PBCAR0191[1] Response Duration in B-ALL Subjects



- 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

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

PBCAR0191 with eLD Experience

- Enhanced LD mitigated PBCAR0191 rejection to **markedly improve peak cell expansion and persistence**
- **Predictable toxicity** without ≥ Grade 3 CRS, one Grade 3 self-limited ICANS. Prolonged cytopenias with ≥ Grade 3 infections required careful management
- In heavily pre-treated R/R subjects receiving eLD, **PBCAR0191 yielded ORR of 73%** and **CR rate of 59%** using a 3 x 10^6 cells/kg cell dose
- Overall and best **response rates** are **comparable to the auto-CAR T** experience in more heavily pre-treated patients
- **Durability** in this heavily treated population may be lower than auto-CAR T at current PBCAR0191 cell dose of 3 x 10^6 cells/kg
- All subjects dosed with PBCAR0191 began LD **within 1 day** of eligibility determination
- PBCAR0191 efficacy in **post-auto CAR T relapse** is a compelling signal to follow

Precision BioSciences Allogeneic CAR T Portfolio Going Forward: Our Focused Path to First-in-Class

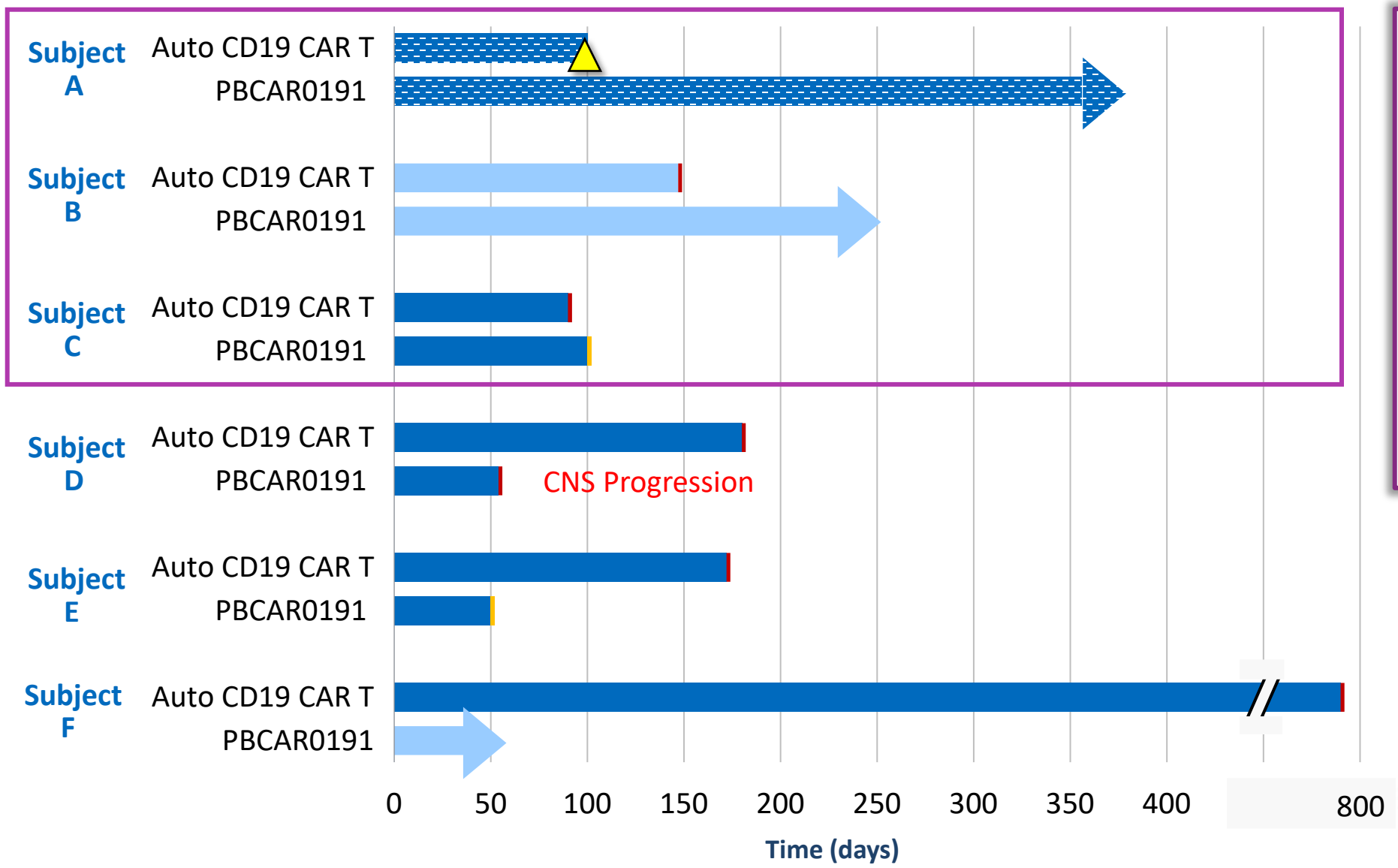
CD19-Directed Auto-CAR T Failure:

A Growing and Underserved Population with High Unmet Need

- **Auto-CAR T has changed the landscape** for 3rd line lymphoma patients and created an emerging group of patients with highest unmet need
- **~40%** of auto-CAR T treated patients **do not respond** AND **~60% of responders relapse**[1]
- **No FDA approved therapeutics** for patients who progress following auto-CAR T therapy; median overall survival of 3+ months[2]
- **Retreatment** with auto-CAR T is **not an effective option**
- As auto-CAR T moves to second line displacing auto transplant as standard of care, the number of **auto-CAR T patients who relapse will grow substantially** creating a vital opportunity for patients who may benefit from off-the shelf PBCAR0191

[1] Schuster SJ, et. al. N Engl J Med 2019;380:45-56.;
[2] Spiegel JY, et. al. Blood 2021; 137:1832.

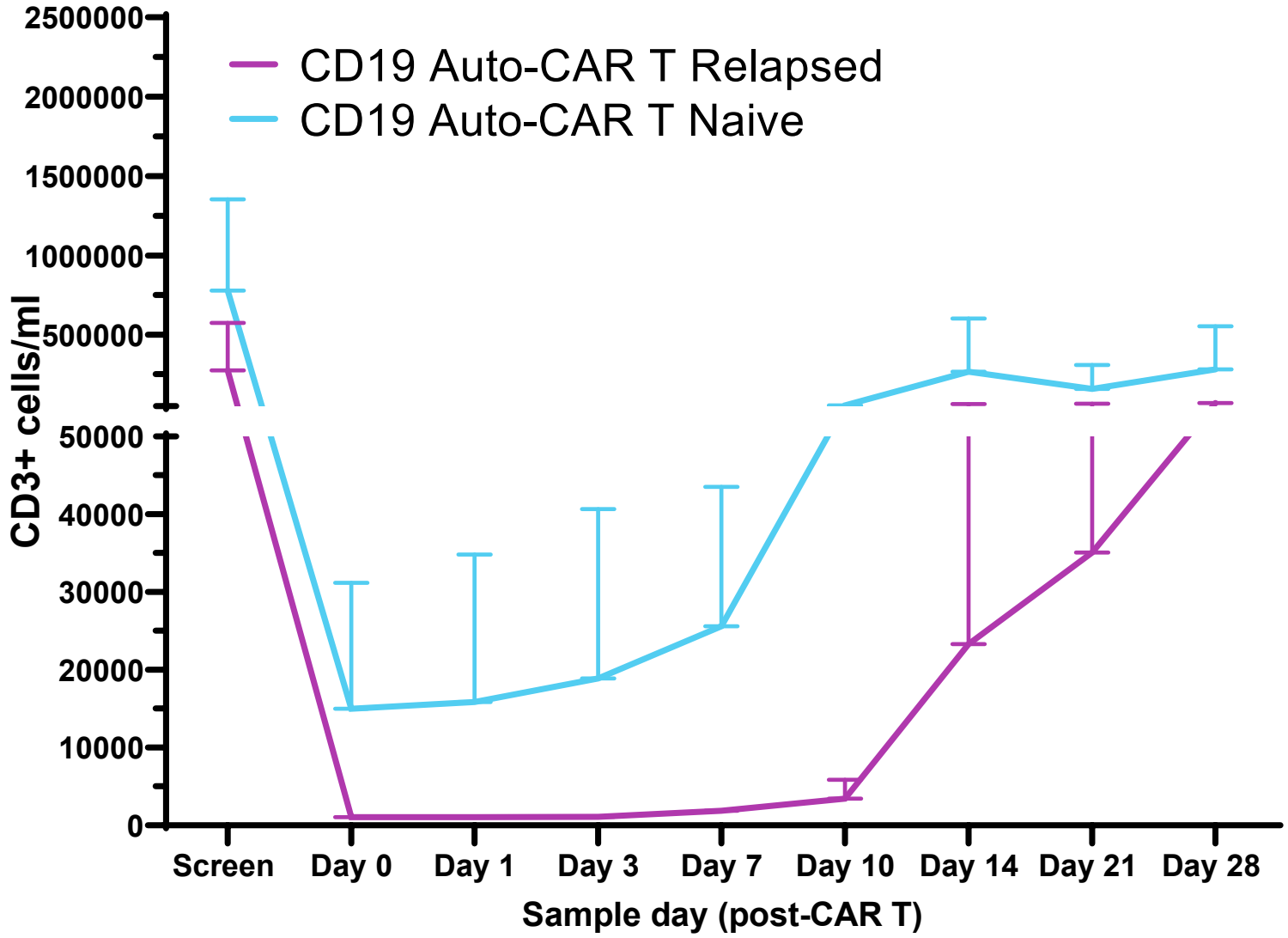
Depth & Duration of Response to PBCAR0191 in CD19 Auto-CAR T Relapsed Subjects



- 100% ORR in subjects who received prior auto-CAR T
- PBCAR0191 response duration exceeded original response to auto-CAR T in 3 of 5 evaluable 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

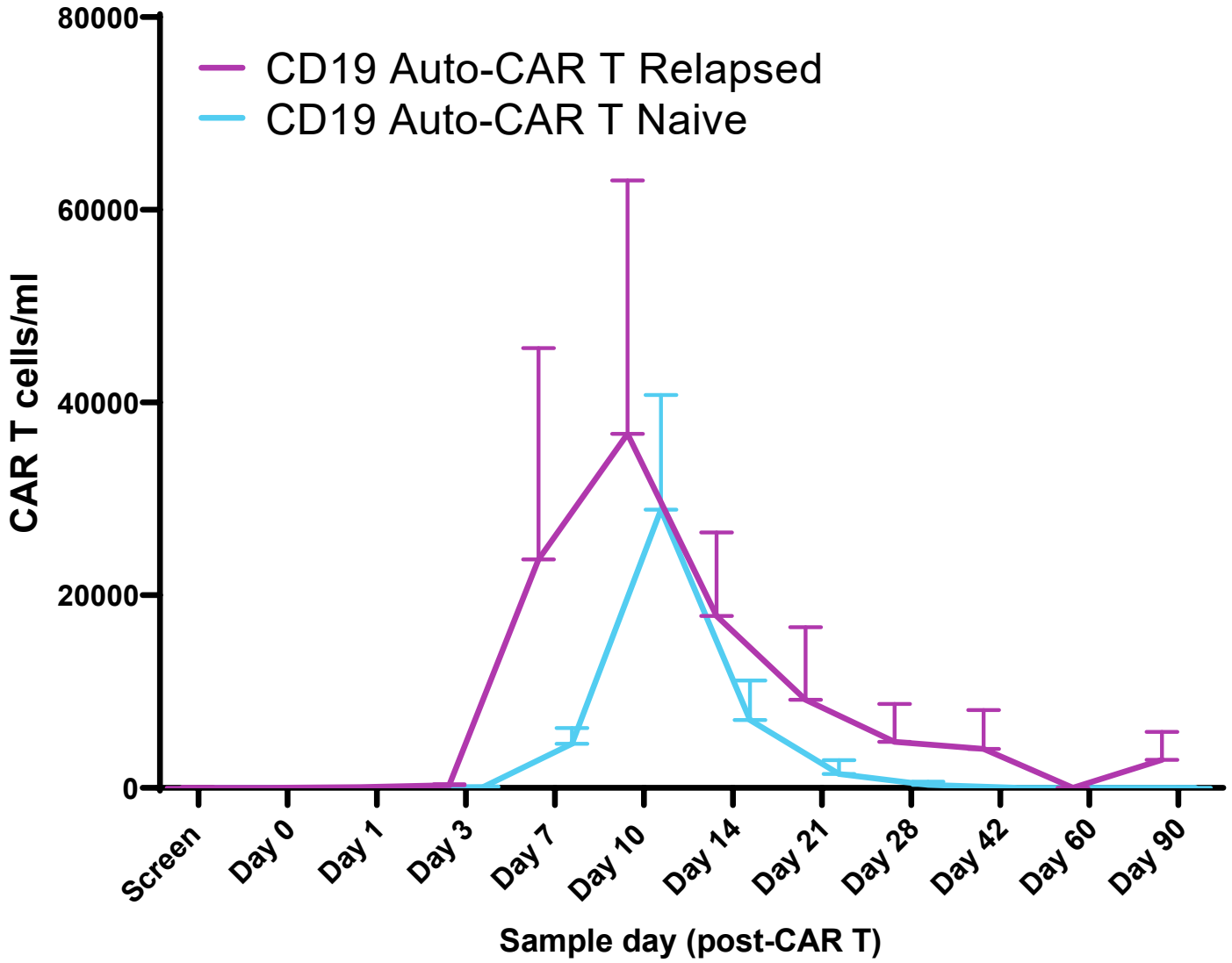
Auto-CAR T Relapsed Subjects Have Deeper Nadir & Delayed CD3 Cell Recovery that May Delay Allo-CAR T Rejection



- Lymphoma treatment reduces early-lineage T cells necessary for auto-CAR T cell expansion[1]
- Poor functional attributes of CAR T effectors is a key determinant of relapse from CD19-directed auto-CAR T[2]

[1]Das RK, et. al. Blood Adv 2020; 4: 4653
[2]Maude SL, et. al. N Engl J Med 2014; 371:1507–17

PBCAR0191 with eLD: Earlier Expansion, Higher Peak & Prolonged Persistence in Relapsed Auto-CAR T Setting



PBCAR0191 Expansion by Flow

- CD19 auto-CAR T relapsed subjects have 3.2x higher PBCAR0191 AUC vs. CD19 auto-CAR T naïve subjects
- Results consistent with impaired allo-CAR T rejection

Evidence for PBCAR0191 + eLD in Auto CAR T Relapsed

PBCAR0191 + eLD may offer effective salvage for relapsed auto-CAR T patients whose progression results from sub-optimal product fitness

- PBCAR0191 CAR T cells from healthy donor using single gene edit optimizes expansion & cytotoxicity
- Impaired immune integrity reduces PBCAR0191 rejection, increases peak cell expansion & persistence

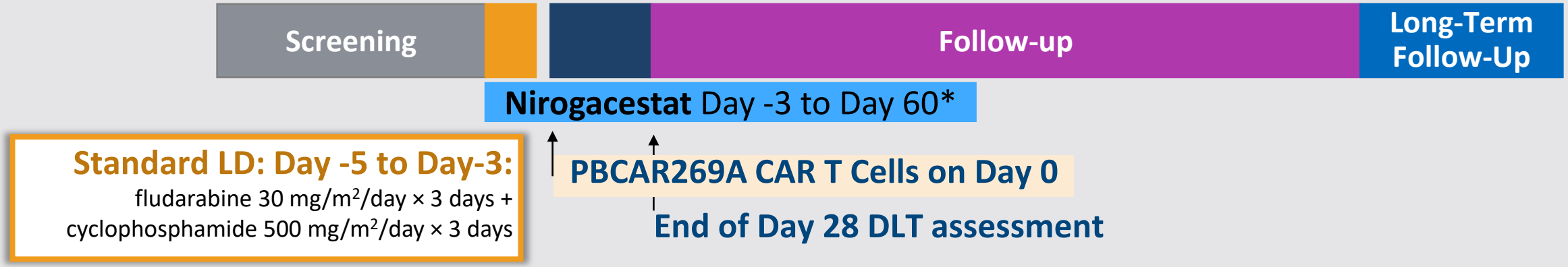
All six subjects who progressed following CD19 auto-CAR T therapy responded to PBCAR0191 following eLD with 66% CR rate

- Duration of response exceeded auto-CAR T response in 3 of 5 evaluable subjects
- B-ALL subject remains in MRD negative CR >1 year after relapse from 2 prior allo-HCTs and CD19 auto-CAR T prior treatment

*** Next Steps for Precision: Further investigate CD19 auto-CAR T relapsed lymphoma subjects to validate activity and safety in this growing population with high unmet need**

Study Update on PBCAR269A - BCMA

PBCAR269A with or without Nirogacestat[1] in R/R Multiple Myeloma



Objectives

- Identify maximum tolerated dose based on dose-limiting toxicities
- Evaluate the clinical activity and safety profile of PBCAR269A with or without nirogacestat

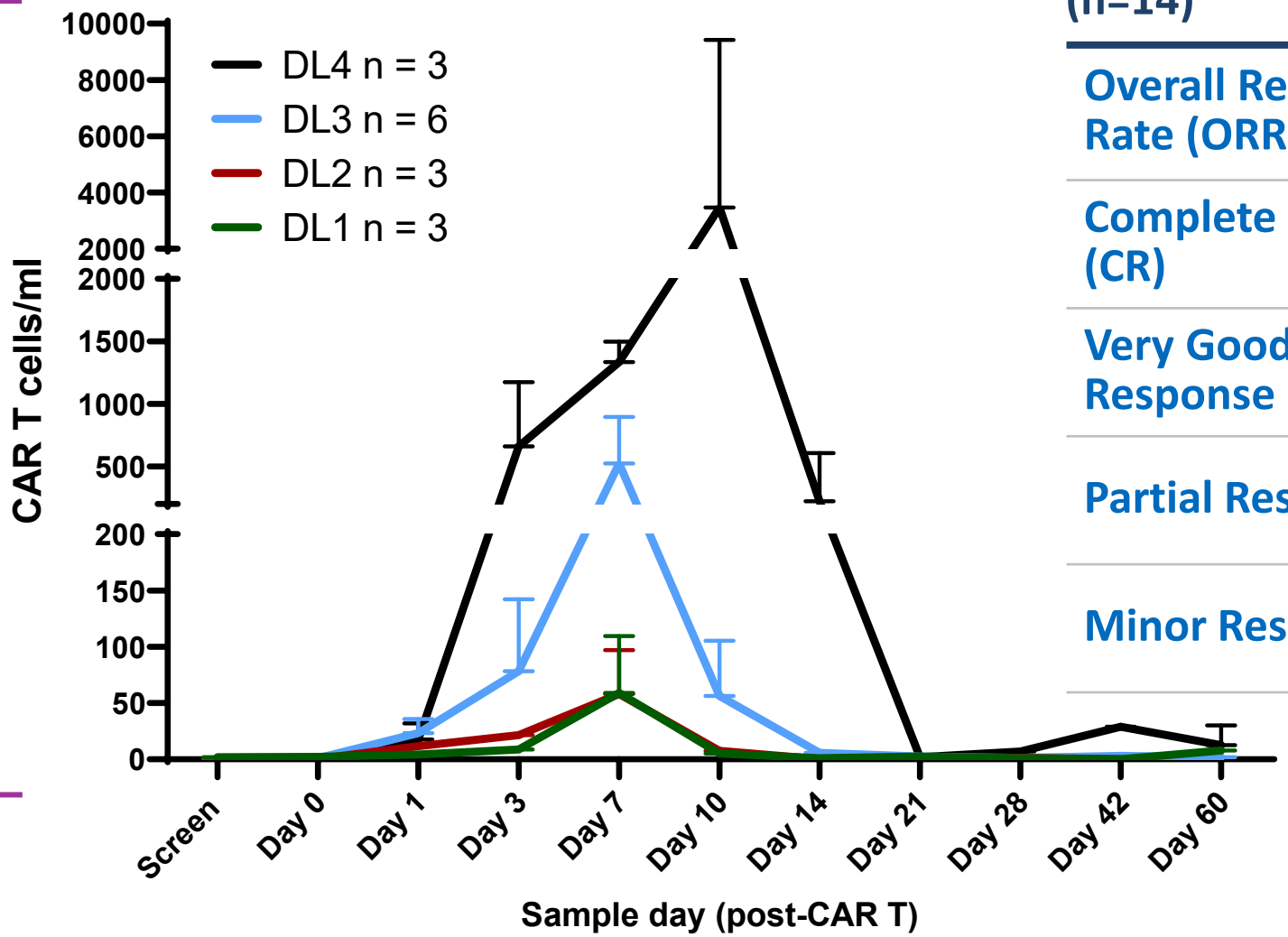
Design: 3+3

- *Cohort A: dose escalation of PBCAR269A alone* → **Cohort B: dose escalation of PBCAR269A with GSI:*
  - Dose level 1: 0.6×10^6 cells/kg
  - Dose level 2: 2.0×10^6 cells/kg
  - Dose level 3: 6.0×10^6 cells/kg
  - Dose level 4: 960×10^6 cells flat dose
  - Dose level 2: 2.0×10^6 cells/kg
  - Dose level 3: 6.0×10^6 cells/kg
  - Dose level 4: 960×10^6 cells flat dose

[1] Gamma secretase inhibitor provided by SpringWorks THERAPEUTICS

Dose-dependent Increase in CAR T Expansion with PBCAR269A Monotherapy

PBCAR269A Expansion by Flow



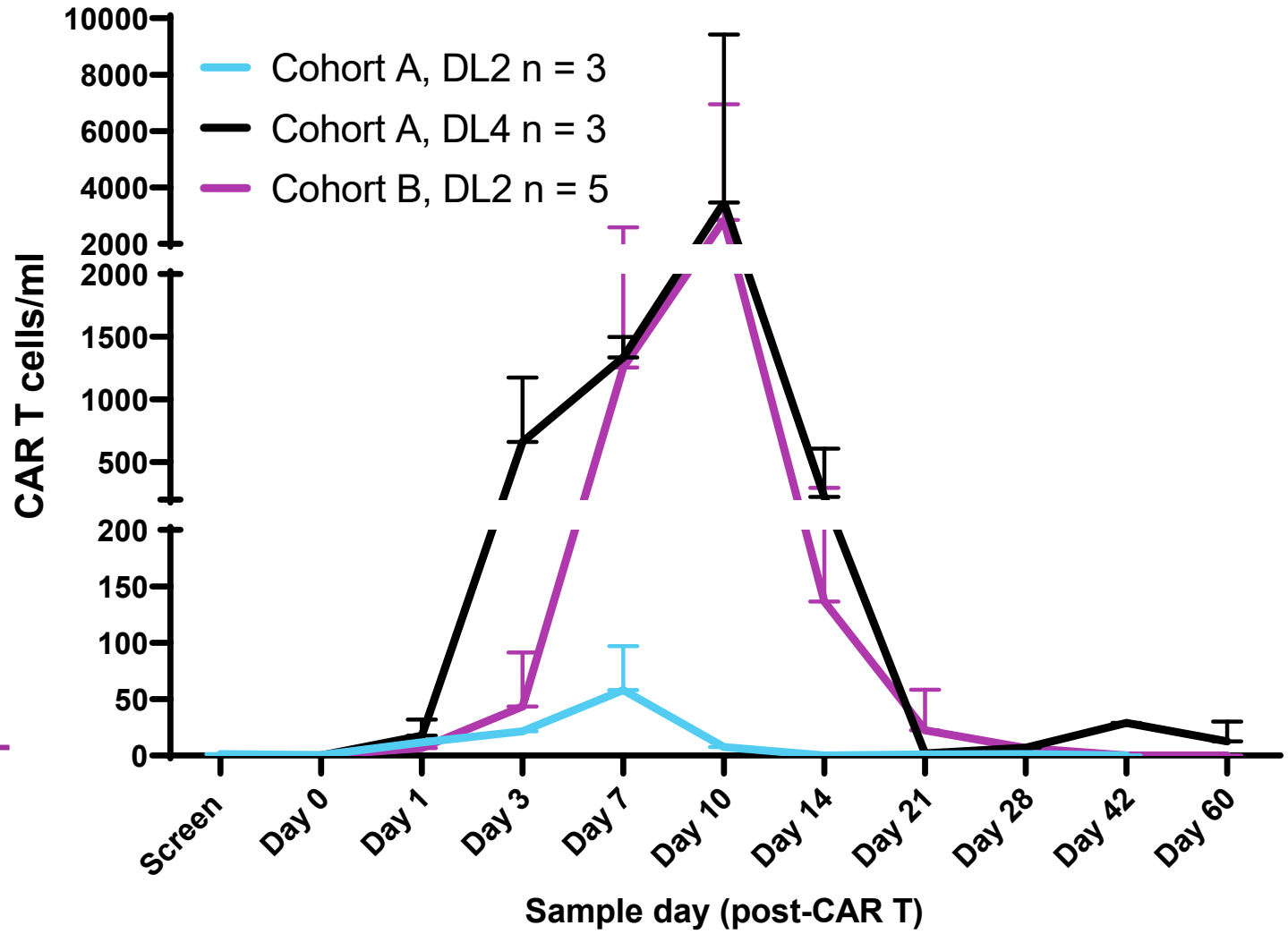
Response to PBCAR269A at ≥Day 28 (n=14)

Overall Response Rate (ORR)[1]	4 (29%)
Complete Response (CR)	0
Very Good Partial Response (VGPR)	1 (7%)
Partial Response (PR)	3 (21%)
Minor Response	2 (14%)

[1] ORR=CR+VGPR+PR

Nirogacestat[1] Profoundly Increases PBCAR269A CAR T Expansion at Dose Level 2 Versus Monotherapy

PBCAR269A Expansion by Flow



[1] Gamma secretase inhibitor provided by SpringWorks THERAPEUTICS

Summary of PBCAR269A in Multiple Myeloma

Monotherapy (n=14)

- Dose-dependent increase in peak expansion
- No grade ≥ 3 CRS or ICANS
- One subject achieved deep response (VGPR[1]) with monotherapy at dose level 4
- Monotherapy has favorable safety profile however, activity is below high threshold autologous CAR T
- Therefore, we **will focus on PBCAR269A in combination with nirogacestat (GSI)**

Combination therapy with GSI is ongoing (n=5)

- DL2 enrolling with greater expansion observed
- Continue investigation of the PBCAR269A in combination with GSI; **data expected mid-2022**

PBCAR269B/BCMA stealth

- Await maturity of data with PBCAR269A in combination with GSI prior to IND

[1] VGPR = Very Good Partial Response

Best-in-Class: Allogeneic PBCAR T Cell Products for Subjects with Relapsed/Refractory B-Cell Malignancies

Best in Class Allogeneic CAR T Attributes

Objective

- **Single dose**
- ARCUS **single-gene edit** minimizing translocation safety concerns
- Therapeutic index **as good as or better than** approved auto-CAR T product profiles

Challenge

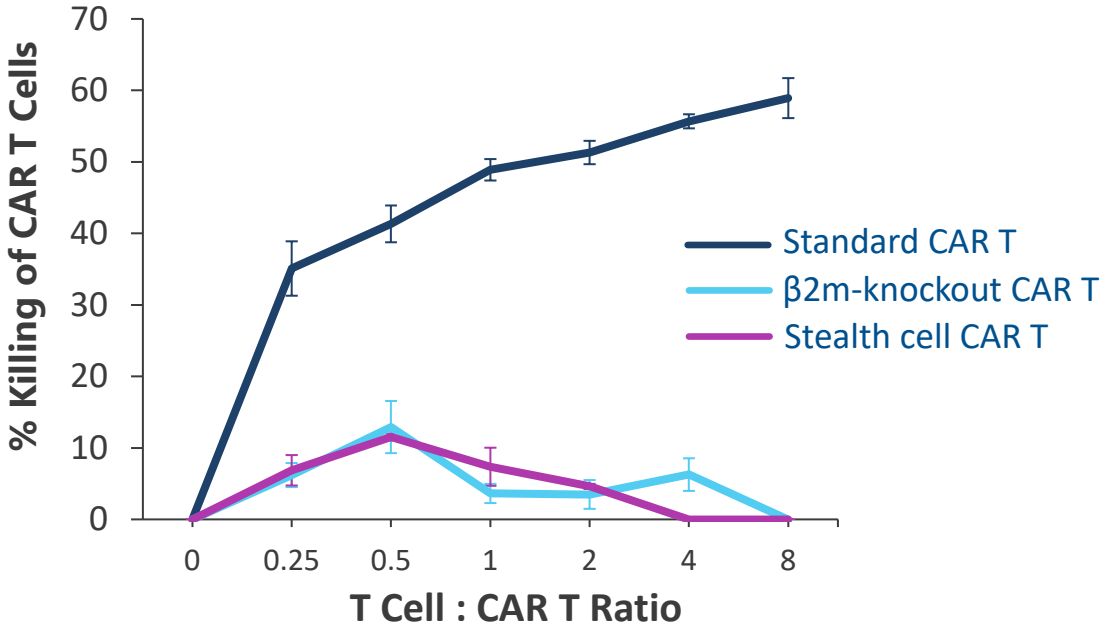
- **Overcome rejection** of allogeneic CAR T cells by patient immune system

Second-Generation "Stealth Cell" CAR T Platform

- The Stealth Cell vector incorporates an anti-β2m shRNA and an HLA-E transgene
- Stealth Cell CAR Ts resist rejection by T cells & NK cells in mixed-lymphocyte reactions

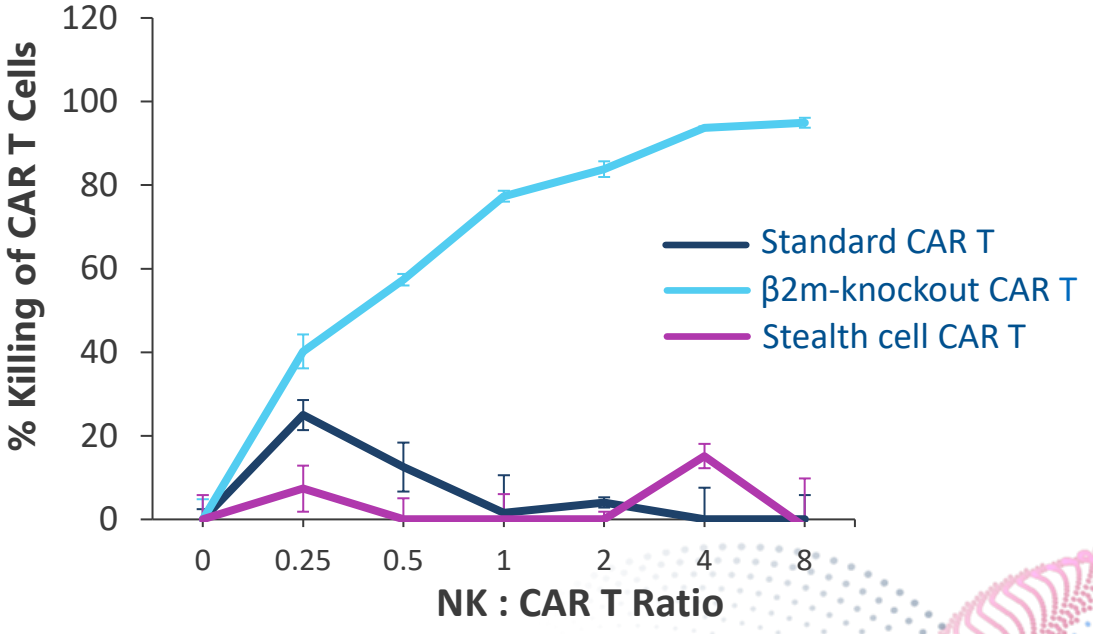
Rejection by T cells

(n=4 mismatched donors)



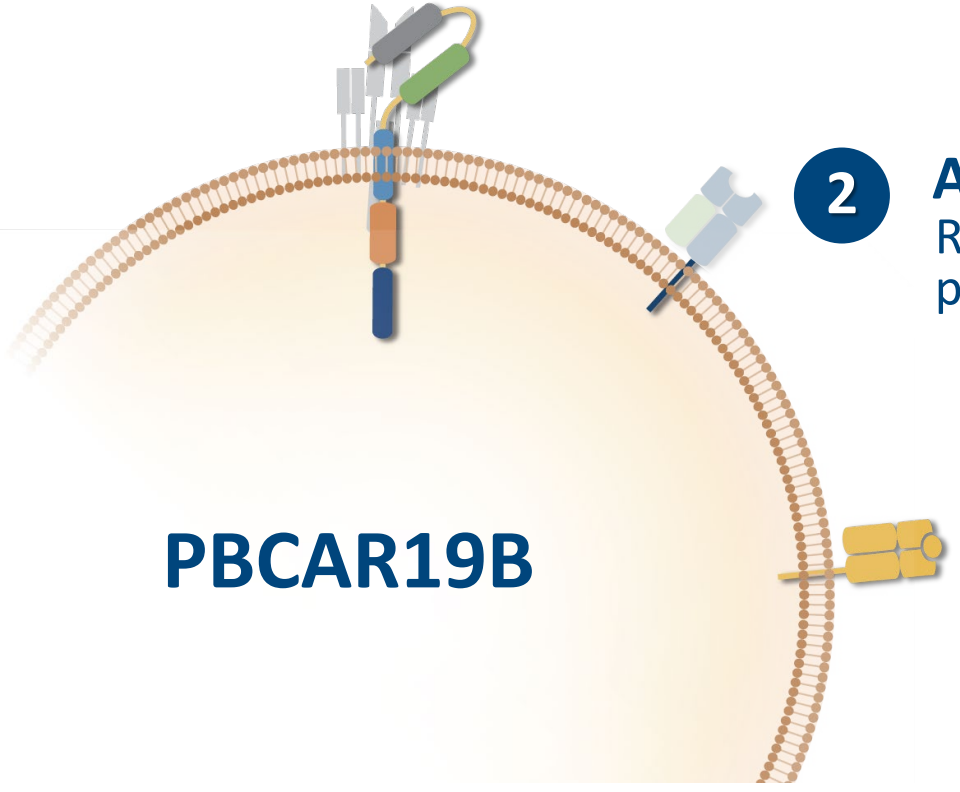
Rejection by NK cells

(n=3 mismatched donors, strong activation protocol)



PBCAR19B is an Anti-CD19 Stealth Cell CAR T

***Accomplished with a single-step gene edit to minimize risk of chromosome abnormalities**



1 **Anti-CD19 CAR**
TCR is knocked-out to prevent GvHD

2 **Anti-beta-2 microglobulin (β2m) shRNA**
Reduces MHC I expression to
prevent rejection by T cells

3 **HLA-E transgene**
Prevents rejection by NK cells

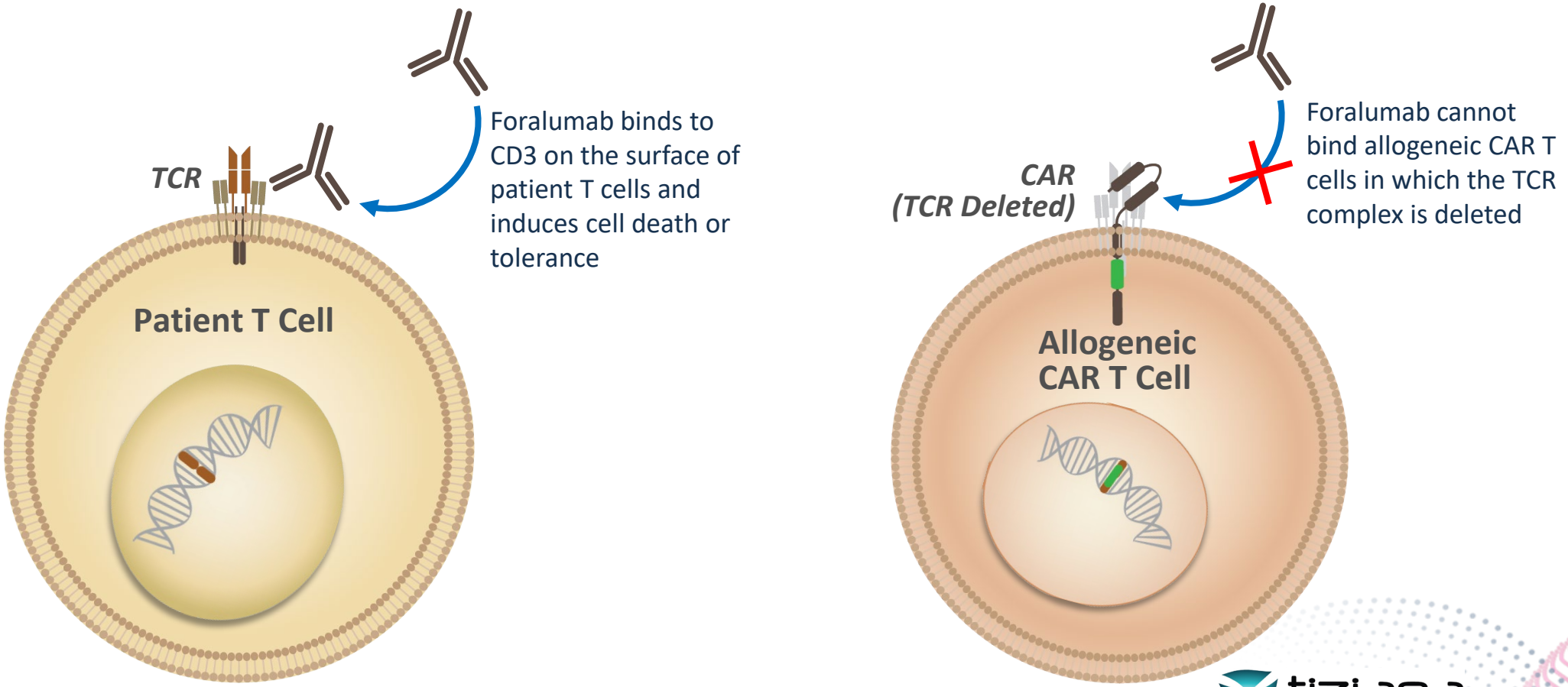
PBCAR19B Stealth Cell Progress in Clinic

- Phase 1 study initiated June 30, 2021
- Subjects receive increasing flat dose levels (2.7×10^8 - 8.1×10^8 CAR T cells) plus standard lymphodepletion[1]
- First three patients dosed at dose level 1
- Currently enrolling at multiple sites
- Expect initial clinical updates mid-year 2022

[1] Fludarabine 30 mg/m2/day x 3 days plus Cyclophosphamide 500 mg/m2/day x 3 days

Foralumab[1] is an Anti-CD3 Antibody for Selective Depletion of Patient T Cells

- Including foralumab in the lymphodepletion regimen may prevent CAR T cell rejection by eliminating the anti-CAR T response



[1] Exclusive license agreement with Tiziana to evaluate foralumab with allogeneic CAR T candidates for cancer treatment

Combination with Foralumab to Prevent CAR T Cell Rejection

- Including foralumab in the LD regimen may **prevent CAR T cell rejection** by eliminating the anti-CAR T response
- Foralumab may induce tolerance in host T-cells via CD3 internalization and homeostatic recovery to **maximize CAR T persistence**
- **PBCAR T cells are resistant to foralumab** because they are engineered to remove CD3 from the cell surface
- Foralumab has more **specific action & shorter duration of effect** than an anti-CD52 mAb, potentially maximizing persistence without long-term immune suppression
- Foralumab **can be used in combination with any PBCAR therapy**. We will investigate foralumab first in combination with an anti-CD19 CAR T

Precision BioSciences Focused Execution of Allogeneic CAR T Pipeline

First in Class approach:

- PBCAR0191 with eLD:
  - **Focus enrollment on CD19 auto-CAR T relapsed B-cell lymphoma subjects**
  - **Next data in mid-2022**

Best in Class approaches:

- **NHL:** PBCAR19B stealth cell clinical trial enrolling Dose Level 1 – **update in mid-2022**
- **Multiple Myeloma:** PBCAR269A combination with nirogacestat – **update in mid-2022**
- **Early stage:** Develop combination with foralumab to directly target CD3+ T cells involved in rejection – **update IND in 2022 to enable combination use**

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December 11, 2021