# Preliminary Safety and Efficacy of PBCAR0191, an Allogeneic, Off-the-shelf CD19-targeting CAR-T Product, in Relapsed/Refractory (r/r) CD19+ NHL

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## INTRODUCTION

- Autologous CD19-directed CAR T products have demonstrated unprecedented efficacy in subjects with chemorefractory CD19+ NHL
- Manufacturing delays or failure remain important barriers to care, limiting utility for subjects with more rapidly growing disease and/or impaired T cell fitness.
- We have previously presented the safety and clinical activity of PBCAR0191 during dose escalation with standard lymphodepletion.
- We now present an update to safety, efficacy, and correlative assessments for the relapsed/ refractory (r/r) CD19+NHL subjects

## METHODS

- Subjects dosed prior to April 1, 2021 with either

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| **Dose Level 3** | 3 x $10^6$ cells/kg on Day 0 |

or

| | |
|---|---|
| **Dose level 4a** | 3 x $10^6$ cells/kg (D0) + 3 x $10^6$ cells/kg (D10)<br>• no additional LD between infusions<br>• no expansion observed with D10 infusion |

- Prior stem cell transplant and/or autologous CAR-T therapy were allowed.
- All subjects were lymphodepleted prior to administration of PBCAR0191 with either

| | |
|---|---|
| **Standard lymphodepletion (sLD)** | fludarabine 30 mg/m$^2$/day x 3 d + cyclophosphamide 500 mg/m$^2$/day x 3 d |

or

| | |
|---|---|
| **Enhanced lymphodepletion (eLD)** | fludarabine 30 mg/m$^2$/day x 4 d + cyclophosphamide 1000 mg/m$^2$/day x 3 d |

- Correlative laboratory samples were taken at baseline and while subjects remained on study for CAR T cell expansion, persistence, response to treatment and safety assessments.
- Data available as of April 9, 2021 is presented
  - 2 subjects have not completed 28-day evaluation period and are included in safety profile and cell expansion analysis, but non evaluable for treatment response assessment

PRECISION BIOSCIENCES

## RESULTS

### SUBJECTS ENROLLED WITH ADVANCED AND AGGRESSIVE DISEASE

- Over 85% of subjects had aggressive lymphomas
- 71% of subjects had 4+ courses of prior treatment
- Five subjects (30%) had prior autologous CD19 directed CAR T
- Over 70% of subjects with stage III/IV disease

**Table 1. Subject Demographics**

| | | sLD (n=6) | eLD (n=11) | Total (N=17) |
|---|---|---|---|---|
| **Age (y),** *median (min-max)* | | 56 (44-81) | 55 (34-64) | 55(34-81) |
| **Subtype,** *n (%)* | *Diffuse Large B-Cell* | 4 (67%) | 6(55%) | 10(59%) |
| | *CLL/Richter's Trans.* | 0 | 2(18%) | 2(12%) |
| | *Mantle Cell* | 1 (17%) | 0 | 1(6%) |
| | *Follicular Lymphoma* | 0 | 2(18%) | 2(12%) |
| | *High Grade B-cell* | 1 (17%) | 1(9%) | 2(12%) |
| **R/R,** *n (%)* | *Refractory* | 0 | 3 (27%) | 3(18%) |
| | *Relapsed* | 6 (100%) | 8 (73%) | 14(82%) |
| **Stage,** *n (%)* | *III/IV* | 4 (67%) | 8 (73%) | 12 (71%) |
| **Extranodal disease,** *n (%)* | | 3 (50%) | 5 (45%) | 8 (47%) |
| **Prior lines,** *n (%)* | *≥4+* | 3 (50%) | 9 (82%) | 12 (71%) |
| **Prior CAR T,** *n (%)* | | 2 (33%) | 3 (27%) | 5 (30%) |
| **Prior auto-SCT,** *n (%)* | | 0 | 4 (36%) | 4 (24%) |
| **Ki-67%[1],** *median (min-max)* | | 70 (30-95) | 60 (10-90)[2] | 60 (10-95) |
| **SPPD (cm$^2$),** *median (min-max)* | | 65.5 (2.8-289) | 23.7 (0-256)[5] | 32.1 (2.8-289) |

[1]A few subjects did not have information available; [2]n=8; [3]n=5; [4]n=6, [5]n=11, and one with non-measurable=0.

### SHORT TIME TO ACCESS PRODUCT

- Median time from eligibility assessment to treatment initiation was 1 day

### ADVERSE EVENTS OF SPECIAL INTEREST COMPARABLE LYMPHODEPLETION REGIMENS

- Most adverse events (AE) reported were mild
- Serious treatment related AEs were reported for 47% (8/17) of the subjects (17%, 1/6 in sLD and 64%, 7/11 in eLD regimen)
- 1 subject (6%) died of Febrile neutropenia on day 42 after treatment

**Table 2. PBCAR0191 Safety Profile[1]**

| | | sLD NHL (N=6) | eLD NHL (N=11) |
|---|---|---|---|
| **CRS** *(Cytokine Release Syndrome)* | *Grade 1 or Grade 2* | 3 (50%) | 5 (45%) |
| | *Grade 3 or higher* | 0 | 0 |
| **ICANS** *(Immune Effector Cell Neurotoxicity)* | *Grade 1 or Grade 2* | 2 (33%) | 2 (18%) |
| | *Grade 3 or higher* | 0 | 1 (9%) |
| **GvHD** *(Graft versus Host Disease)* | | 0 | 0 |
| **Infection** | *Grade 1 or Grade 2* | 0 | 0 |
| | *Grade 3 or higher*[2] | 0 | 2 (18%) |

[1]2 subjects have not completed a 28- day safety evaluation period at the time of reporting; Number (%) of subjects experiencing events with Max Grade
[2] 1 subject had a Grade 3 sepsis related to a previously known septic joint; 1 subject had grade 3 sepsis – occurred prior to and resolved before cell administration

### ENHANCED LD INCREASES PEAK CAR T EXPANSION AND AUC, AND IS ASSOCIATED WITH DEEPER MORE DURABLE RESPONSES

- Peak PBCAR0191 Expansion increased 50X and AUC increased 40X using eLD compared to sLD

**Figure 1. CAR T Cell Expansion in sLD and eLD Populations (Peripheral blood)**

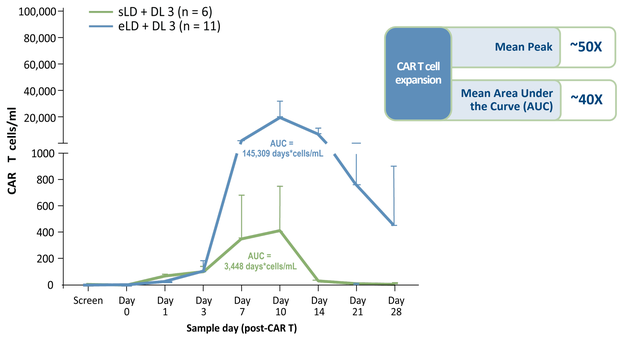



**Table 3. Treatment Response (evaluable subjects only)**

| | | sLD (n=6) | eLD (n=9) |
|---|---|---|---|
| **Objective Response Rate (ORR) at Day ≥28** | | 3 (50%) | 8 (89%) |
| **Best Response at Day ≥28** | *Complete Response (CR)* | 2 (33%) | 7 (78%) |
| | *Partial Response (PR)* | 1 (17%) | 1 (11%) |
| | *Progressive Disease (PD)* | 3 (50%) | 1 (11%) |

- Increased cell expansion with enhanced LD correlated with a 89% ORR (78% CR rate) in evaluable r/r NHL subjects
- Ongoing responses in 5 of 9 evaluable subjects
  - 80% of responses ongoing >2 months, 40% of responses ongoing >3 months

**Figure 2. Durability of Responses for PBCAR0191 in evaluable eLD r/r NHL Population**

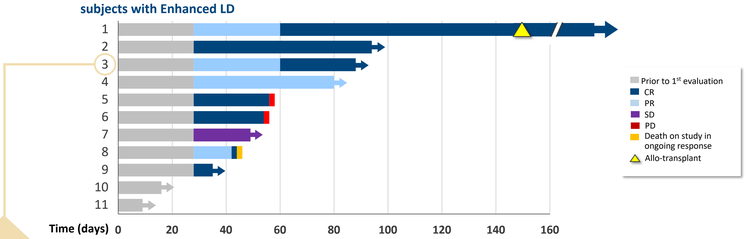
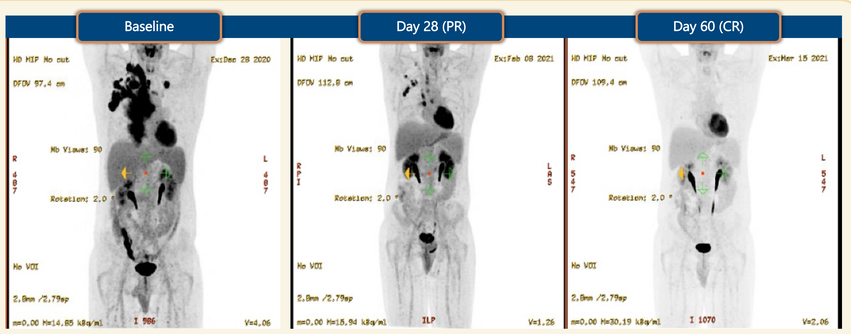



**Figure 3. Case Study: 34-Year-old Male with r/r Follicular Lymphoma**

| | |
|---|---|
| **Tumor Burden** | 83.8 cm$^2$ |
| **3 Previous Lines of Therapy** | 1) Bendamustine/Rituxan<br>2) Obinutuzumab/Cyclophosphamide/Doxorubicin/Vincristine<br>3) Auto-SCT |

- Partial Response recorded on Day 28
- Conversion to Complete Response recorded on Day 60
- Ongoing Complete response confirmed on Day 90




## CONCLUSIONS

- **Treatment with PBCAR0191 provided clinical benefit to a majority of treated r/r NHL subjects with an acceptable safety profile**
- **On-demand availability and absence of Graft versus Host Disease support potential off-the-shelf use of PBCAR0191**
- **Use of eLD mitigates early host rejection to markedly increase expansion and extend persistence of PBCAR0191 cells leading to higher Complete Response (CR) rates compared to sLD**
- **Limiting rejection demonstrates that PBCAR0191 cells are capable of effective killing, yet avoiding safety concerns associated with eLD would benefit a true off-the-shelf product**
- **Increasing the AUC by increasing peak expansion and/or prolonging persistence of allo-CAR T, without the need of enhanced lymphodepletion, may be addressed with the next generation of PBCAR**