Objective

• PBCAR0191 is an off-the-shelf allogeneic CD19-targeted chimeric antigen receptor (CAR) T cell that consists of an engineered CAR T cell product and an adenovirus-based transduction vector that delivers the CAR construct.

• The goal is to achieve and maintain tumor control and reduce the possibility of graft-versus-host disease (GVHD) and other chronic complications. The treatment plan involves PBMC expansion and CAR T cell generation.

Methods

• Phase 1/2 trial-Standard 4-dose regimen

  - Base dose level 1 (DL1): 2 x 10^6/kg on days 1, 2, 3 & 4
  - Base dose level 2 (DL2): 5 x 10^6/kg on days 1, 2, 3 & 4
  - Base dose level 3 (DL3): 1 x 10^7/kg on days 1, 2, 3 & 4

• The primary objective is to demonstrate safety and tolerability of PBCAR0191 administered with and without lymphodepletion. A phase 2a clinical study has shown:

  - Objective evidence of cell-mediated anti-tumor effect has been observed in NHL/DL1.
  - Lymphodepletion, that a clinical study has shown:

    - CAR T cell expansion and persistence using standard criteria, and further evaluation of AEs and adverse events of special interest, Hypertension, Hyperglycemia, Neutropenia, Neutrophil decrease, Platelet count decreased, Febrile neutropenia, Platelet count decreased, Neutropenia, Neutrophil decrease, Platelet count decreased.

• Secondary Endpoint:

  - Response to last therapy
  - Best Response

• Dose dependent demonstration of mechanism of action

  - qPCR performed on DNA extracted from isolated PBMC. Note: extremely low PBMC isolation in 6-NHL-DL2, 7-

  - Larger patient numbers required for true correlation

• Case Studies:

  - Case Study 1: Patient 3-NHL-DL1
  - Case Study 2: Patient 4-NHL-DL2

Results

• Non-Hodgkin Lymphoma Subset Baseline Characteristics, Prior Treatments, Prognostic Indicators, and Outcomes

  | Survival Category | # Patients | Prognostic Indicator | CR Rate | PR Rate | MRD/NR/NR | # Patients
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<td>Complete Response</td>
<td>0/3</td>
<td>1 (100%)</td>
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<td>0/2 (0%)</td>
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• Acute Lymphoblastic Leukemia Subset Baseline Characteristics, Prior Treatments, Prognostic Indicators, and Outcomes

  | Survival Category | # Patients | Prognostic Indicator | CR Rate | PR Rate | MRD/NR/NR | # Patients
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Conclusions

• First-in-human study of PBCAR0191: adverse event profile is acceptable and may compare favorably with approved autologous products (Table 4, 7)

• Much information is gained from this study

• No Maximum Tolerated Dose has yet been identified

• No dose level 6 observed in NHL/DL2, 4 (NHL), 9 (B-ALL), or 6 (ALL) cohorts

• Objective evidence of cell-mediated anti-tumor effect has been observed in NHL/DL1.

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• Patient with relapsed/refractory B cell ALL

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• Case Study 1: Patient 3-NHL-DL1

  - Case Study 1: Patient 3-NHL-DL1

• Case Study 2: Patient 4-NHL-DL2

  - Case Study 2: Patient 4-NHL-DL2

• Case Study 3: Patient 5-NHL-DL3

  - Case Study 3: Patient 5-NHL-DL3