PHE885, a Fully Human BCMA-Directed CAR-T Cell Therapy for Relapsed/Refractory Multiple Myeloma Manufactured in <2 Days Using the T-Charge™ Platform

**INTRODUCTION**

Chimeric antigen receptor (CAR) T-cell immunotherapy is a promising multiple myeloma (MM) treatment.

- MM is an incurable hematologic malignancy characterized by plasma cell proliferation, bone destruction, and hypercalcemia.

- The key to success in CAR-T cell immunotherapy is the development of a safe, efficient, and cost-effective manufacturing platform.

**METHODS**

- **Patient Eligibility**: Patients with MM with ≥2 prior lines of treatment, including BCMA-directed treatment.
- **Treatment**: PHE885 is a fully human BCMA-directed CAR-T cell therapy consisting of a solvency-cleavable single-chain variable fragment (scFv) targeting BCMA fused to CD3ζ and transmembrane domains, following CD19/CD20 co-engagement and CD3ζ transduction.
- **Manufacturing**: PHE885 is manufactured using the T-Charge™ platform, minimizing the in vitro culture time and reducing the manufacturing process to <2 days.

**RESULTS**

- **Baseline Characteristics of Patients**
  - All but one patient achieved a clinical response.
  - CR and very good partial response (VGPR) rates were observed at all dose levels.

- **Clinical Response to PHE885**
  - ORR of 93% (10/11) was observed at all dose levels.
  - 100% (3/3) of patients achieved CR with 100% (3/3) of patients achieving minimal residual disease (MRD) negativity.

- **Free sBCMA Concentration Over Time**
  - Serial in vivo measurements of free sBCMA in a dynamic model of tumor burdens, treatment dosing, and pharmacokinetic parameters were obtained.

**CONCLUSIONS**

- PHE885 showed a manageable safety profile and encouraging clinical activity in patients with MM at 0.001, 0.01, and 0.1% of normal, with no dose-limiting toxicities observed.
- Free sBCMA concentration over time demonstrated a potential for sustained efficacy.
- T-Charge™ process preserves T-cell clonality and functionality, potentially leading to better outcomes.

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- Tocilizumab is approved in the US for the treatment of rheumatoid arthritis and other autoimmune conditions, including systemic lupus erythematosus (SLE).