**INTRODUCTION**

- B-cell maturation antigen (BCMA) is a clinically validated target in multiple myeloma (MM), with therapies targeting BCMA currently approved or in clinical development.
- Anti-BCMA chimeric antigen receptor T (CAR-T) cells have shown greatest results in early-phase clinical trials to date.
- However, duration of response is limited, and patients with rapidly progressing disease require a fast and reliable CAR-T cell manufacturing process.
- To improve existing BCMA CAR-Ts, two critical attributes of the CAR-T product were investigated:
  - The potency of the BCMA CAR construct, and
  - A rapid manufacturing process that would both preserve the stemness of T cells to ensure longer duration of response and provide timely access for patients with rapidly progressing, aggressive disease.
- Through extensive purifying and discriminating CAR-T functional assays to assess performance, we have identified a superior anti-BCMA CAR construct that when combined with an innovative T-Charge™ manufacturing platform produces a highly potent product.

**METHODS AND RESULTS**

**T-Charge™ Platform, an Innovative Manufacturing Platform**

**Preserves Naive/Tscm Cells in the Final Product**
- Naive (Tn) and stem-like memory T cells (Tscm) can expand into a more multifunctional pool of antigen-specific T cells in the patient.
- Extended T-cell culture periods in vitro deplete the CAR-T final product of Tn and Tscm populations that are associated with improved antitumor efficacy.
- Novartis’s novel T-Charge™ platform is an expansionless CAR-T manufacturing process that takes 2+ days to generate functional CAR-Ts.

**PHE885 is a Novel Autologous BCMA-Directed CAR-T Cell Therapy**
- PHE885 CAR contains:
  - An extracellular region composed of a fully human scFv domain, the lead clone identified via a serial screening process as described above.
  - A CD8 hinge and transmembrane region.
  - An intracellular 4-1BB/CD3ζ signaling domain.
- The lead scFv-carried by PHE885 demonstrates high specificity to human BCMA, by Retrogenix platform, using a commercial human plasma models.
- PHE885 is manufactured using the novel T-Charge™ platform.

**PHE885 retains Less Differentiated PHE885 Cells**

**PHE885 Exhibits Potent Anti-tumor Activity and Robust Cellular Expansion in a Preclinical MM Model**

**Disclosures**

- DB, XZ, BG, CPg, LMT, and LB report employment, hold stocks and patents in Novartis. MPO and KM report employment and hold stocks in Novartis. JL reports employment in Novartis, PB, and NB have current affiliation: Bristol Myers Squibb and former employment in the last 24 months with Novartis. LB has current affiliation: Ashenxena and former employment in the last 24 months with Novartis.

**References**