Manufacture of an Allogeneic CAR-T Stem Cell Memory Product Candidate for Multiple Myeloma, P-BCMA-ALLO1, Is Robust, Reproducible and Highly Scalable

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ABSTRACT

Chimeric antigen Receptor (CAR) T cell therapy has generated unprecedented efficacy in the treatment of multiple hematologic malignancies. For relapsed/refractory Multiple Myeloma (MM), autologous CAR-T products directed against the B cell maturation antigen (BCMA), such as Poseida’s P-BCMA-101, have demonstrated significant efficacy. P-BCMA-101 is comprised of a high-purity engineered T cell memory product candidate, resulting in a product that is much safer and potentially more durable than other autologous BCMA allogeneic products currently being developed. P-BCMA-101 is produced using a multi-step platform manufacturing process including transduction of donor T cells with a high-purity engineered anti-BCMA CAR-T vector, followed by ex vivo expansion, T cell dose selection, and final product release. P-BCMA-101 has shown highly desirable clinical characteristics, including: high purity, robust manufacturing, and ease of manufacturing.

METHODS & RESULTS

Overview of P-BCMA-ALLO1 Manufacturing Process

Phenotype of P-BCMA-ALLO1 Product

Fig. 1. Cas-CLOVER™ Gene Editing System - The Best of Both Worlds

A) The Cas-CLOVER™ gene editing system combines the strengths of CRISPR/Cas and TALEN/锌指核酸酶 assembly systems, and efficiently edits in residing T cells. B) The site-specific Cas-CLOVER™ gene editing system consists of a donor gDNA guide-susceptible editing activity, into a pair of gRNAs allowing for more of design in vivo as well as multiplexing ability from CRISPR/Cas-based systems. By the same time editing activity is contingent on homology of the gDNA donor first (1:1). When in vivo endonuclease activity is present, the ability to edit at any desired gDNA donor site is instantaneous. C) Efficiency of Cas-CLOVER™ gene editing system in T cells. Open editing, efficient deletion of furin expression via CRISPR/Cas and ZFN was detected in the frequency of 81-92%.

Fig. 2. Cas-CLOVER™ editing in the TCR and BCL11A loci does not show off-target editing activity by NGS. A) Cas-CLOVER™ was used to edit residing T cells. Using BCL11A a sequence targeting a BCL11A susceptible dimer of gRNAs was used. No NGS detected the presence of off-target editing activity in the TCR or BCL11A genes indicating a high degree of specificity.

Fig. 3. A Booster Molecule Increases Yield of P-BCMA-ALLO1

A) Booster molecule with CAR and T cell phenotype increases the yield of P-BCMA-ALLO1 cells. B) Booster Molecule increases the yield of P-BCMA-ALLO1 cells. C) Booster Molecule increases the yield of P-BCMA-ALLO1 cells. D) Booster Molecule increases the yield of P-BCMA-ALLO1 cells.

Fig. 4. P-BCMA-ALLO1 Defines Tumor and MM Targeting Potential in vivo


Fig. 5. P-BCMA-ALLO1 Does Not Mediate an Allogeneic Response

A) P-BCMA-ALLO1 does not elicit any detectable immune response in vivo. B) P-BCMA-ALLO1 does not elicit any detectable immune response in vivo. C) P-BCMA-ALLO1 does not elicit any detectable immune response in vivo.

CONCLUSIONS

- Highly desirable T-cell rich phenotype and potentiative proliferative
- Allogeneic CAR-T equivalent or better than unedited healthy donor CAR-T in vivo and in vitro
- Robust non-viral manufacturing process compatible with majority of healthy donors & ability to generate hundreds of doses per manufacturing run
- Superior safety due to TCR phenotypic, novel off-target gene editing, and safety switch
- Results support rapid advancement of P-BCMA-ALLO1 into the clinic for treatment of MM