Bellicum Pharmaceuticals

**GoTCR™**: Inducible MyD88/CD40 (iMC) Enhances Proliferation and Survival of Tumor-Specific TCR-Modified T Cells, Increasing Anti-Tumor Efficacy

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1Cancer immunotherapy using T cells engineered to express tumor antigen-associated TCRs has shown clinical promise; however, durable responses have been limited by poor T cell expansion and persistence in vivo.

2Additionally, MHC class I downregulation on tumor cells diminishes T cell recognition, leading to reduced therapeutic efficacy.

3Inducible MyD88/CD40 ("iMC") is a rimiducid (AP1903)-dependent costimulatory molecule that enhances DC activation1 and T cell proliferation and survival. It can be added to CARs ("GoCARs") and TCRs ("Go-TCRs").

4PRAME (PReferentially expressed Antigen in MElanoma) is a cancer testis antigen (CTA) that is overexpressed in a number of cancers, including melanoma, sarcoma, AML, CML, neuroblastoma, breast, lung, head and neck cancers, but not in normal tissues.

5Bob1 is also known as OCA-B, OBFI or POU2AF1 is a B cell-specific transcriptional co-activator that is highly expressed in CD19+B cells, ALL, CLL, MCL and multiple myeloma (MM).

6Herein, we investigate the feasibility and potential benefits of "GoPRAME" and "GoBob1" TCRs that incorporate iMC costimulation.

**Results**

Specific recognition of SLL peptide-pulsed APCs

(A) Retroviral vectors expressing B01 TCR, goPRAME-TCR and iMC/surface marker; (B-D) PRAME-TCR recognition of SLL peptide-pulsed T2 cells synergizes with rimiducid-dependent iMC signals for maximal IL-2, IFN-γ and IL-6 secretion.

**Summary**

- Rimiducid-driven activation of iMC provides potent costimulatory signals to transduced T cells, which synergize with signals from exogenous PRAME-specific or Bob1-specific TCRs, leading to enhanced T cell proliferation/survival and improved anti-tumor efficacy both in vitro and in vivo.

- iMC activation upregulates HLA class I levels on tumor targets, potentially improving cytotoxicity by genetically modified and existing T cells.