**CD4**

**NKT Cells**

**SRF114** activates tumor-infiltrating NK cells with greater potency than peripheral NK cells

Depletes intratumoral Tregs

**Background**

- Intratumoral T regulatory (Treg) cells support an immunosuppressive tumor microenvironment, and their increased frequency correlates with a poor prognosis.
- Chemokine receptor 9 (CCR9) is highly upregulated by intratumoral Treg cells compared with their peripheral counterparts and other T cell subsets.
- Anti-CCR8 antibodies have been shown to deplete intratumoral Tregs, reduce tumor growth, and synergize with anti PD-1 therapy in mouse cancer models.
- SRF114 is a fully human, afucosylated anti-CCR8 antibody designed to preferentially deplete intratumoral CCR8+ Treg cells.

**Results**

- SRF114-treated tumor samples and 55 dissociated primary tumor tissues from 12 different types of cancer.
- Tumor samples.
- CCR8 is preferentially expressed on tumor Treg cells.

**Representative CCR8 Count**

**Percent remaining of healthy PBMCs or dissociated primary tumor tissue (3 RCC, 1 CRC). Co-cultures 4-1BB expression.**

**Values of SRF114-based B7-H3 induction on myeloid cells from PBMC samples**

- Baseline association dissociation
- Fold change was calculated by doubling the PBMC sample EC50 by the tumor sample EC50

**Conclusions**

- **CCR8 is highly expressed on intratumoral T cells.**
- **SRF114 binds specifically to CCR8 and can potently induce ADCC and AADC activity.**
- **Low levels of CCR8 expression on peripheral T cell populations mediate activation of NK cells and monocytes by SRF114.**
- **Higher levels of CCR8 expression on tumor-infiltrating T cells trigger more potent activation of NK cells and myeloid cells by SRF114.**
- **MC8-implemented hCCR8 knock-in mice exhibit significant tumor growth reduction via preferential depletion of tumor-infiltrating T cells.**
- **IND filing for SRF114 planned for 2H 2022.**