Characterization of CHS-1000, a Humanized Anti-ILT4 Monoclonal Antibody for Reprogramming Suppressive Myeloid Cells in Solid Tumors

Narendran Rajasekaran, Xiaoguang Wang, Scott Klakamp, Sruthi Ravindranathan, Suzanna Tatariewicz, Julia Du, Brian Nguyen, Kate Widmann, Nessa Hawkins, Daniel J. Chin, Theresa LaVallee, Varun N. Kapoor

Coheresa Biosciences, Redwood City, CA

**Background**

- Myeloid cell-mediated immunosuppression in the tumor microenvironment (TME) contributes to tumor immune evasion and PD-1 resistance.
- ILT4 (ILT4B2) is an immunoreceptor tyrosine-based inhibitory motif (ITIM)-containing receptor that is widely expressed in myeloid cells in the TME.
- Interaction of ILT4 with its primary ligands, HLA-A and HLA-G, promotes development of tolerogenic dendritic cells (DCs), immunosuppressive M2 macrophages, and inhibits pro-inflammatory cytokine production.

**Objective**

- Characterization of CHS-1000, a humanized anti-ILT4 monoclonal antibody (mAb) that potentially and specifically targets ILT4 and blocks its interaction with HLA-A and HLA-G.

**Results**

- CHS-1000 promotes reprogramming of suppressive M2 macrophages to potent inflammatory M1 phenotype and enhances activation of DCs and T cells.
- Combination of CHS-1000 with therapeutic anti-PD-L1 (PD-L1 inhibitor) or other immunotherapeutics holds promise for improved antitumor therapies.

**Conclusion**

- CHS-1000 demonstrates potential for enhanced anti-tumor activity and clinical benefit in multiple solid tumors.

**Figures**

- CHS-1000 Mechanism of Action
- CHS-1000 Lacks Effector Functions
- CHS-1000 PK Profile Is Similar to Bevacizumab (g01) in a Human FcRn Transgenic Mouse Model
- CHS-1000 Binds Selectively to Human Granulocytes, Monocytes, and DCs
- CHS-1000 Treats Leads to Activation of Human Dendritic Cells
- CHS-1000 Treatment Leads to Activation of Human Dendritic Cells
- CHS-1000 Binds to Human myeloid cells and enhances activation of DCs and T cells
- CHS-1000 treatment results in T cell activation in a mixed lymphocyte reaction assay