

## IND for Junshi Biosciences' FIH anti-BTLA antibody approved by FDA

Junshi Biosciences is pleased to announce that the world's first recombinant humanized anti-BTLA monoclonal antibody for injection (TAB004/JS004) specific to B- and T-lymphocyte attenuator (BTLA) independently developed by the company was recently officially approved by the U.S. Food and Drug Administration (FDA) for drug clinical trial, for the proposed indications of advanced unresectable or metastatic solid tumors, including patients refractory to prior immunotherapy.

**JS004 is world's first anti-BTLA monoclonal antibody for injection approved for clinical trials. It is also Junshi Biosciences' second self-developed product to obtain IND approval from FDA after toripalimab (anti-PD-1 antibody), which shows Junshi Biosciences' excellent drug discovery and development capabilities toward global market.**

**BTLA** is an immunoglobulin (Ig) receptor family member identified in 2003. It has a single IgV extracellular domain with sequence similarities with PD-1 and CTLA-4. BTLA is expressed on activated T and B lymphocytes, and subsets of DCs.

**HVEM**, a TNF receptor widely expressed in hematopoietic system, was identified as a counter receptor for BTLA in 2005. HVEM is expressed on T, B, NK, myeloid and dendritic cells, and a variety of tumor cells including NSCLC, melanoma, colorectal cancer and lymphomas. Tumor expression of HVEM has been associated with poor prognosis and immune escape.

BTLA contains two ITIM domains in its cytoplasmic region, which recruit SHP-1 and SHP-2 phosphatases upon receptor activation by mAb crosslinking or ligand engagement. BTLA-deficient mice are viable and fertile but show enhanced T cell activation in animal models of autoimmunity and inflammation, indicating an inhibitory function of BTLA to control T cell activation in vivo. Study of peripheral blood mononuclear cells (PBMC) from melanoma and NSCLC patients revealed that BTLA is expressed at high levels on tumor specific CTLs and inhibits T cell function upon engagement by tumor expressed HVEM, suggesting BTLA blockade might potentially improve T cell function and anti-tumor immunity. BTLA also coexpressed with PD-1 on tumor specific CTLs in melanoma and NSCLC patients.

Importantly, coblockade of BTLA and PD-1 pathways increased the frequency and effector cytokine production of melanoma specific CTLs, whereas either BTLA or PD-1 blockade alone had limited effect, suggesting BTLA pathway is a potential resistance mechanism for patients refractory to anti-PD-1 monotherapy.

In vitro and in vivo studies have shown TAB004 or JS004 can promote antigen specific T cell proliferation and effector function, reduce tumor burden and improve survival in human BTLA knock-in tumor models.

# News Release



The Company plans to initiate first-in-human (FIH) dose escalation study of TAB004 in advance solid tumors refractory to prior immunotherapy and explore combination use of TAB004 with toripalimab, its marketed anti-PD-1 antibody, in the dose expansion phase of the trial.

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