ALPN-102

Name: ALPN-102
Synonyms: CD28/ICOS antagonist
Indication: Cancer; colorectal cancer
Company: Alpine Immune Sciences

ALPN-202, a PD-L1/CTLA-4 dual antagonist with PD-L1 dependent CD28 costimulation

ALPN-202 is a novel molecule designed to block the inhibitory immune checkpoints PD-L1 and CTLA-4 while providing PD-L1 dependent T cell activation via the CD28 costimulatory pathway. It has previously been demonstrated to have efficacy in an MC38-based colorectal cancer model, superior to the FDA-approved PD-L1 inhibitor durvalumab. Today's poster correlates these findings with superior intratumoral immune cell infiltration and effector gene signatures, as well as favorable changes in T cell receptor profiles, consistent with ALPN-202's proposed multi-modal mechanism of action. "ALPN-202 is differentiated from currently approved checkpoint inhibitors by providing T cell costimulation in addition to dual checkpoint antagonism.

human clinical trials of ALPN-202 for the treatment of advanced malignancies in the fourth quarter of 2019." The preclinical study evaluated the anti-tumor responses of ALPN-202 compared with durvalumab in mice implanted with human PD-L1 transduced MC38 tumors. Results showed ALPN-202: Produced dose-dependent anti-tumor responses, including potent single-dose activity Induced a greater tumor inflammation gene signature than durvalumab Induced increased T cell infiltration and T cell-related effector gene signatures compared to durvalumab Promoted both increased T cell receptor clonality and richness, consistent with ALPN-202's multiple mechanisms of action NKp30/ICOSL vIgD-Fc program demonstrates tumor-localized costimulation In a second preclinical study, Alpine used its variant immunoglobin domain (vIgD) platform to engineer novel NKp30/ICOSL vIgD fusion proteins.

The resulting therapeutic is designed to agonize two T cell costimulatory receptors ICOS and CD28 only in the presence of B7-H6, a tumor antigen overexpressed in certain cancer types such as some forms of esophageal, kidney, rectal, and stomach cancers. Results showed the NKp30-ICOSL vIgD-Fc fusion proteins: Conferred potent T cell costimulation in vitro, with enhanced T cell proliferation and cytokine production only in response to B7-H6-expressing target cells. In contrast, ICOSL and NKp30 vIgDs alone in the absence of B7-H6 were not inflammatory. Demonstrated efficacy in a B7-H6-positive CT26 mouse colon cancer model, especially when administered in combination with a PD-1 inhibitor. The proteins were not effective on a B7-H6-negative parental CT26 tumors, demonstrating target specificity.