AB154 is a humanized antibody that blocks human TIGIT (CD395) receptor immunoreceptor with IgG1 and Fc domain(s), an inhibitory receptor expressed on natural killer (NK) cells, T cell, CD8 T cells and regulatory T (Treg) cells. Preclinical data identified AB154 as a monotherapy with the potential to synergize with other ICBs (e.g., PD-1/PD-L1) to greatly extend the reach of the ICB therapeutic landscape. Preclinical data revealed in vitro and in vivo biological advantage of PD-1 and TIGIT co-blockade. AB154 demonstrated high affinity to TIGIT and selectivity for TIGIT on NK cells compared to other targets, including PD-L1 and PD-L2.}

**Methods**

**Gene Expression:** Expression of TIGIT, PD-1 (PD-L1), and CD226 on isolated tumor types were derived from TCGA and the Cancer Genome Atlas (TCGA).

- **Immunohistochemistry (IHC):** Anti-TIGIT antibody (Cal) was used in cryo-FREE human tissues. Samples were deparaffinized according to standard methods and heat-induced epitope retrieval was performed under optimal antigen retrieval. Rabbit anti-TIGIT and rabbit anti-CD45 were used for detection.

- **ADCC Assay:** AB154 was assessed against NK cell lines (K562 and L929 cells) with NK cell lysis detected using Chromium release assay. Depletion of TIGIT receptors blocked the ADCC activity of AB154.

- **Enhanced Effector Function Results in NK-Mediated Killing of Activated TIGIT-CD8+ T Cells:** Enhanced effector function results in NK-mediated killing of activated TIGIT-CD8+ T cells.

**Conclusion**

TIGIT and PD-1 are highly expressed in human tumors and monocytes and are comparably affected by dosage of AB154. AB154 demonstrated high affinity to TIGIT and CD8 T cells with NK cell lysis detected using Chromium release assay. Depletion of TIGIT receptors blocked the ADCC activity of AB154.

**Safety and Tolerability of AB154**

- **AB154 Post-Dose Monitoring:** After first dose of AB154, no grade 3-4 side effects were observed.
- **AB154+AB122 (240 mg)**: No dose-limiting toxicities were observed.

**AB154 Clinical Trials:**

- **Monotherapy (Phase 1):** Phase 1 dose-escalation study is underway to evaluate AB154 as a monotherapy and in combination with AB154 as a post (PD)-CD8+ in subjects with advanced solid tumors. Primary objectives are to determine the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and safety profile of AB154 in combination with AB154.

- **Combination (Phase 1):** Phase 1 dose-escalation study is underway to evaluate AB154 in combination with other ICBs (e.g., PD-1, PD-L1) in subjects with advanced solid tumors. Primary objectives are to determine the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and safety profile of AB154 in combination with other ICBs.

**AB154 Clinical Trials (Continued):**

- **Monotherapy (Phase 2):** Phase 2 dose-escalation study is underway to evaluate AB154 as a monotherapy and in combination with AB154 as a post (PD)-CD8+ in subjects with advanced solid tumors. Primary objectives are to determine the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and safety profile of AB154 in combination with other ICBs.

- **Combination (Phase 2):** Phase 2 dose-escalation study is underway to evaluate AB154 in combination with other ICBs (e.g., PD-1, PD-L1) in subjects with advanced solid tumors. Primary objectives are to determine the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and safety profile of AB154 in combination with other ICBs.

**AB154 Clinical Trials (Continued):**

- **Monotherapy (Phase 3):** Phase 3 dose-escalation study is underway to evaluate AB154 as a monotherapy and in combination with AB154 as a post (PD)-CD8+ in subjects with advanced solid tumors. Primary objectives are to determine the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and safety profile of AB154 in combination with other ICBs.

- **Combination (Phase 3):** Phase 3 dose-escalation study is underway to evaluate AB154 in combination with other ICBs (e.g., PD-1, PD-L1) in subjects with advanced solid tumors. Primary objectives are to determine the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and safety profile of AB154 in combination with other ICBs.