Press Release

Publication in *Human Vaccines & Immunotherapeutics* Illustrates the Advantages of Hexavalent CD40 Agonists in Targeting CD40 in Immuno-Oncology

Heidelberg, Germany, September 19, 2019 – Apogenix, a biopharmaceutical company developing next generation immuno-oncology therapeutics, announced today that a new publication in *Human Vaccines & Immunotherapeutics* highlights the advantages of hexavalent CD40 agonists, such as HERA-CD40L, in the targeting of CD40 in immuno-oncology. Apogenix was invited to write this review paper of the various concepts for agonistic targeting of CD40 in immuno-oncology.

CD40 is expressed by antigen-presenting cells, endothelial cells, as well as numerous tumors. It is a key target in immuno-oncology because it has a fundamental role in initiating an antigen-specific immune response against tumors. The different strategies to induce CD40 signaling that were explored in the context of this review paper can be broadly grouped into agonistic antibody-based and CD40L-based approaches. There are currently seven antibodies and one CD40L-based hexavalent fusion protein in active clinical trials.

The review reveals that anti-CD40 antibodies do not achieve the appropriate clustering capacity required for effective signaling into the target cell because of their bivalent nature. They typically require Fcγ receptor-mediated crosslinking for biological activity, which often causes serious side effects due to non-specific activation of the immune system. Recent data with CD40 and other receptors of the tumor necrosis factor superfamily (TNFSF) have shown that hexavalent agonists overcome the limitations of antibody-based approaches. These hexavalent TNFSF agonists specifically bind to their cognate receptors on target cells and induce clustering of six receptor chains in a spatially well-defined manner. Importantly, the agonistic activity of the TNFSF ligands is independent of additional crosslinking via Fcγ receptors.

The full article titled “Concepts for agonistic targeting of CD40 in immuno-oncology” can be accessed here.

About Apogenix

Apogenix is a private company developing innovative immuno-oncology therapeutics for the treatment of solid tumors and hematological malignancies. The company’s pipeline of immuno-oncology drug candidates targets different tumor necrosis factor (TNF) superfamily-dependent signaling pathways, thereby restoring the immune response against tumors. Checkpoint inhibitor asunercept, the company’s lead immuno-oncology candidate, is in late-stage clinical development with PRIME (PRIority MEdicines) designation by the European

Medicines Agency for the treatment of glioblastoma. Based on its proprietary technology platform for the construction of novel TNF superfamily receptor agonists (HERA-ligands), Apogenix develops CD40, CD27, GITR, HVEM, and 4-1BB receptor agonists for cancer immunotherapy. The TRAIL receptor agonist program was outlicensed to AbbVie. AbbVie has initiated a phase I trial with TRAIL receptor agonist ABBV-621 in patients suffering from solid tumors, non-Hodgkins's lymphoma, or acute myeloid leukemia.

About Apogenix' TNF Superfamily Receptor Agonists (HERA-Ligands)

Apogenix has developed a proprietary technology platform for the construction of novel TNF superfamily receptor agonists (HERA-ligands). By stimulating different TNF signaling pathways, these HERA-ligands can increase the anti-tumor immune response. The specific molecular structure of Apogenix' HERA-ligands induces a well-defined clustering of functional TNF receptors on the surface of target immune cells. In contrast to agonistic antibodies, Apogenix' fusion proteins are pure agonists whose potent signaling capacity is independent of secondary Fcγ receptor-mediated crosslinking. In addition, HERA-ligands cause neither antibody-dependent cellular cytotoxicity nor complement-dependent cytotoxicity and exhibit a shorter half-life than antibodies. It is therefore expected that HERA-ligands will cause less side effects in clinical development.

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