Press Release

Preclinical Efficacy Data of Apogenix' HERA-CD40L Published in *Journal of Immunotherapy*

HERA-CD40L Induces T-Cell-Mediated Anti-Tumor Immune Response through Activation of Antigen-Presenting Cells

Heidelberg, Germany, October 11, 2018 – Apogenix, a biopharmaceutical company developing next generation immuno-oncology therapeutics, announced today that new data published in *Journal of Immunotherapy*[1] demonstrate the potent anti-tumor efficacy of Apogenix' HERA-CD40L. HERA-CD40L acts directly on cells of the innate immune system as well as on antigen-presenting cells, thereby promoting specific T cell-mediated anti-tumor immunity. In contrast to antibodies, HERA-CD40L does not depend on Fcγ receptor-mediated crosslinking for activity. As the first pure CD40 receptor agonist with a well-defined mechanism of action, HERA-CD40L is not restrained by dose-limiting toxicities observed with anti-CD40 antibodies.

The strong anti-tumor efficacy of HERA-CD40L was demonstrated in multiple *in vitro* and *in vivo* tumor models. A comprehensive *in vitro* analysis of the mechanism of action revealed that HERA-CD40L induced the development of pro-inflammatory antigen-presenting cells, including B cells, macrophages, and dendritic cells. Specifically, HERA-CD40L promoted a shift in the balance from tumor-promoting (M2-type) macrophages to anti-tumor (M1-type) macrophages. The potent antigen-specific activation of T cells by HERA-CD40L-treated macrophages led to an immune response specifically directed against the tumor. This is an important advantage over numerous other immunotherapeutic approaches that often cause serious side effects due to non-specific activation of the immune system.

HERA-CD40L is perfectly suitable for standard large-scale production processes. The mechanism of action of HERA-CD40L as a central mediator of T cell activation and co-stimulation predestines this molecule for combination with other therapeutic methods, such as radiotherapy or checkpoint inhibition.

"HERA-CD40L is a novel TNF superfamily receptor agonist based on our proprietary HERA-ligand technology platform that has demonstrated a strong anti-tumor efficacy in preclinical tumor models," said Harald Fricke, M.D., Chief Medical Officer of Apogenix. "CD40 is a key target because it has a unique role in initiating an antigen-specific immune response against tumors. We will continue to apply our HERA-ligand technology to address other TNF superfamily receptors that play a critical role in the anti-tumor immune response and evaluate the synergistic potential of these development candidates in combination with traditional cancer therapies as well as other immuno-oncology therapeutics."

[1] Merz C, Sykora J, Marschall V, Richards DM, Heinonen K, Redondo Müller M, Thiemann M, Schnyder T, Fricke H, Hill O, Gieffers C (2018). The Hexavalent CD40 Agonist HERA-CD40L Induces T-Cell-mediated Antitumor Immune Response Through Activation of Antigen-presenting Cells. J Immunother. 2018 Nov/Dec;41(9):385-398. doi: 10.1097/CJI.0000000000000246.

About Apogenix

Apogenix is a private company developing innovative immuno-oncology therapeutics for the treatment of cancer and other malignant diseases. The Heidelberg, Germany-based company has built a promising pipeline of immuno-oncology drug candidates that target 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. In 2017, asunercept received PRIME (PRIority MEdicines) designation by the European Medicines Agency (EMA) for the treatment of glioblastoma. Based on its proprietary technology platform for the construction of novel hexavalent TNF superfamily receptor agonists (HERA-ligands), Apogenix develops CD40, CD27, GITR, HVEM, 4-1BB, and OX40 receptor agonists for cancer immunotherapy.

In 2015, asunercept was exclusively licensed to CANbridge Life Sciences for the development and commercialization for the treatment of glioblastoma in China, Macao, Hong Kong, and Taiwan. CANbridge has received approval by the China Food and Drug Administration for a pivotal phase II/III trial with asunercept (CAN008) in glioblastoma in China. The HERA-TRAIL receptor agonist program was partnered with AbbVie in 2014. In 2017, AbbVie initiated a phase I trial with this HERA-TRAIL receptor agonist (ABBV-621) in patients suffering from solid tumors, non-Hodgkins´s lymphoma, or acute myeloid leukemia.

About HERA-Ligands

Apogenix has developed a proprietary technology platform for the construction of novel hexavalent 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 cross-linking. 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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