Press Release

Excellent Preclinical Efficacy Data of Apogenix' HERA-GITRL Published in *Journal for ImmunoTherapy of Cancer*

HERA-GITRL Shows Strong Single-Agent Anti-Tumor Activity *in Vitro* and *in Vivo* and is Superior to Bivalent Clinical Benchmark Antibody

Heidelberg, Germany, July 23, 2019 – Apogenix, a biopharmaceutical company developing next generation immuno-oncology therapeutics, announced today that new data published in *Journal for ImmunoTherapy of Cancer*[1] demonstrate the potent anti-tumor efficacy of Apogenix' HERA-GITRL. HERA-GITRL is a hexavalent GITR receptor agonist that acts directly on immune cells, thereby enhancing their anti-tumor immunity. GITR is an especially important target for immunotherapy as GITR signaling provides co-stimulatory signals to boost T cell activation, differentiation, survival, and memory formation.

The strong single-agent anti-tumor activity of HERA-GITRL was demonstrated in two different cancer models. Treatment with HERA-GITRL resulted in dose-dependent tumor growth inhibition and increased T cell infiltration in the tumor. Further, it significantly boosted proliferation and differentiation of stimulated T cells while not producing any response in unstimulated T cells. In contrast to antibodies, HERA-GITRL does not depend on Fcγ receptor-mediated crosslinking for activity. In a direct *in vitro* comparison with a clinical benchmark anti-GITR antibody, only HERA-GITRL achieved full biological activity independent of additional crosslinking. Interestingly, while HERA-GITRL consistently increased T cell activity, the clinical benchmark anti-GITR antibody consistently reduced T cell activity.

In line with previously published findings with HERA-TRAIL, HERA-CD40L, and HERA-CD27L, the HERA-GITRL manuscript data show that optimal stimulation of tumor necrosis factor superfamily receptors can be achieved with the hexavalent structure of HERA-GITRL, which mimics the natural ligand. In contrast, bivalent compounds, such as antibodies, appear to be unsuitable for stimulating the TNF receptor superfamily due to fundamental structural and functional characteristics, including only two target-binding domains.

"We have developed HERA-GITRL, a potent GITR receptor agonist, to overcome the shortcomings of antibody-based approaches," said Thomas Hoeger, Ph.D., Chief Executive Officer of Apogenix. "While our HERA-ligands work well as stand-alone therapies, we are also assessing the synergies with traditional cancer therapies as well as other immuno-oncology therapeutics. HERA-GITRL and our other HERA-ligands have the ability to boost T cell priming and will therefore work well in combination with immune checkpoint inhibitors which depend on the presence of previously primed anti-tumor T cells. We look forward to advancing our HERA-ligands to the clinical stage."

[1] Richards DM, Marschall V, Billian-Frey K, Heinonen K, Merz C, Redondo Müller M, Sefrin JP, Schröder M, Sykora J, Fricke H, Hill O, Gieffers C and Thiemann M. (2019). HERA-GITRL activates T cells and promotes anti-tumor efficacy independent of FcγR-binding functionality. *J. Immunother. Cancer*. 7:191. doi: 10.1186/s40425-019-0671-4

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. CD95 ligand inhibitor asunercept, the company's lead candidate, is in late-stage clinical development with PRIME (PRIority MEdicines) designation by the European Medicines Agency for the treatment of glioblastoma. Asunercept is exclusively licensed to CANbridge Life Sciences under a development and commercialization license covering China, Macao, Hong Kong, and Taiwan. Based on Apogenix' proprietary technology platform for the construction of novel TNF superfamily receptor agonists (HERA-ligands), partner AbbVie 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. For additional information, please visit www.apogenix.com.

About 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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