Press Release

Apogenix' new CD40 agonist HERA-CD40L significantly reduces tumor growth in prostate cancer model

- **Preclinical data published in *Frontiers in Immunology*, a leading peer-reviewed journal**
- **Induction of pro-inflammatory state through functional switch from pro-tumor macrophages (TAMs) to anti-tumor macrophages**
- **Combination with radiotherapy provides significant benefit in prostate cancer models refractory to anti-PD-1 treatment**

Heidelberg, Germany, June 01, 2023 – Apogenix, a biopharmaceutical company developing next generation immunotherapeutics, announced today that new preclinical data were published in the leading peer-reviewed journal *Frontiers in Immunology*[1]. In the studies, Apogenix, in collaboration with the group from Professor Tim Illidge at the University of Manchester, UK, demonstrated the therapeutic benefits of the hexavalent CD40 agonist HERA-CD40L in models of prostate cancer refractory to anti-PD-1 therapies, both as monotherapy and in combination with radiotherapy.

Importantly, HERA-CD40L was able to significantly reduce tumor growth through a threefold mechanism of action: it increased intratumoral T-cell concentration; modulated the tumor microenvironment (TME) towards a pro-inflammatory state; and reversed the macrophage balance from pro-tumor macrophages (tumor-associated macrophages; TAMs) to anti-tumor macrophages.

Thomas Hoeger, PhD, CEO of Apogenix, said*: "Immune checkpoint inhibitors have revolutionized cancer treatment, however, the overall response rate for all cancer types in patients is still below twenty percent. New immunotherapeutic strategies are required and with this next-generation HERA-ligand we investigated a potentially viable treatment option – as a monotherapy and in combination with radiotherapy – to improve cancer treatment outcomes."*

The full article titled: "*The CD40 agonist HERA-CD40L results in enhanced activation of antigen presenting cells, promoting an anti-tumor effect alone and in combination with radiotherapy*" can be accessed here.

HERA-CD40L is a novel molecule from Apogenix' platform of hexavalent Tumor Necrosis Factor Receptor Superfamily (TNFRSF) agonists. CD40L is a key regulator of the immune system. The CD40-CD40L

[1] https://doi.org/10.3389/fimmu.2023.1160116

immune axis is primarily linked to B cells and is important for sustained antibody production, antibody class switching, and the production of memory B cells. Due to its characteristic of bridging the transition from innate immunity to the initiation of adaptive immunity, CD40 represents a very attractive target for drug development.

About Apogenix

Apogenix is a private company developing innovative immunotherapeutics for the treatment of cancer and viral infections, such as COVID-19. The company's pipeline of immunotherapy drug candidates targets different tumor necrosis factor receptor (TNFR) superfamily-dependent signaling pathways in order to restore the anti-tumor immune response in cancer patients and reduce lymphopenia and inflammatory cell death in patients with viral infections. Checkpoint inhibitor asunercept, the company's lead immunotherapy candidate, is in late-stage clinical development for COVID-19 and glioblastoma 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, Apogenix develops CD40 and GITR receptor agonists for cancer immunotherapy. The TRAIL receptor agonist program was out licensed to AbbVie and is currently in clinical phase I trials.

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

Apogenix has developed a proprietary technology platform for the construction of novel TNF receptor superfamily agonists (HERA-ligands). By stimulating different TNFR 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 favorable shorter half-life than antibodies. It is therefore expected that HERA-ligands will cause less side effects in clinical development.

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