Press Release

Apogenix Presents Data on Novel Hexavalent TNF Receptor Agonists (HERA-Ligands) at the Upcoming Annual Meeting of the American Association for Cancer Research (AACR)

Agonists for GITR, CD27 and CD40 receptors in development for cancer immunotherapy exhibit significant in vitro- and in vivo activities

Heidelberg, Germany, March 20, 2017 – Apogenix, a biopharmaceutical company developing next-generation immuno-oncology therapeutics, announced today that comprehensive data on its novel HERA-ligands will be presented at the upcoming American Society for Cancer Research (AACR) Annual Meeting being held April 1-5 in Washington, D.C., USA. The results of immunomodulatory *in vitro* and *in vivo* studies on hexavalent GITR, CD27 and CD40 receptor agonists will be presented in one oral and two poster presentations.

The GITR receptor (GITR) plays an important role in initiating the immune response in the lymph nodes and in maintaining the immune response in the tumor tissue. The *in vitro* and *in vivo* properties of HERA-GITR-ligands were studied in primary immune cells and different mouse models. HERA-GITR-ligands demonstrated excellent *in vivo* stability. Their ability to enhance proliferation and activation of naïve $CD4^+$ and $CD8^+$ T cells and to induce memory formation render them attractive candidates for immunotherapeutic treatments of cancer.

CD27L is a potent co-stimulatory molecule that drives T cell activation and survival through binding to its receptor (CD27). This interaction can be exploited to improve an anti-tumor immune response. Binding of HERA-CD27-ligand to CD27 triggered a strong T cell expansion *in vitro* and *in viv*o. In two mouse tumor models treatment with HERA-CD27-ligand led to a dose-dependent inhibition of tumor growth and stimulated enhanced memory formation in both $CD4^+$ and $CD8^+$ T cells. With their potent immune cell-driven anti-tumor efficacy, HERA-CD27-ligands represent suitable candidates for further preclinical and clinical development for cancer therapy.

In the humoral immune system, the CD40 receptor plays a central role in the activation and maturation of B lymphocytes. HERA-CD40L could activate the CD40 signaling cascade in B cells and monocytes, thereby triggering direct cytolytic activation and proliferation of $CD4^+$ T cells as well as macrophage differentiation. Unlike bivalent CD40 antibodies or trivalent CD40L- based agonists, the hexavalent HERA-CD40L forms highly clustered signaling complexes with superior biological activity and without the need for Fc-receptor-mediated crosslinking. Our data demonstrate that HERA-CD40L is a novel candidate for cancer immunotherapy with exceptional features.

APOGENIX PRESENATIONS AT THE AACR

Title of the oral presentation: "Novel hexavalent GITR agonists stimulate T cells and enhance memory formation"
Abstract: # 4963**; Session**: MS.ET01.01 ("Novel Approaches for Experimental Therapeutics")
Session date and time: April 04, 2017, 03:00 - 05:00 p.m.
Presentation time: 03:05 - 03:20 p.m.
Room: Nr. 144, Level 1, Washington Convention Center
The abstract is available online at the AACR website and can be downloaded here.

Poster title: "HERA-CD40L: A novel hexavalent CD40 agonist with superior biological activity"
Abstract: #1688 / 7; **Poster Session 29**: "Adaptive Immunity to Cancer"
Date and time: April 03, 2017, 08:00 - 12:00 a.m.
The abstract is available online at the AACR website and can be downloaded here.

Poster title: "Hexavalent CD27 agonists show single agent anti-tumor activity and enhanced memory formation in mouse syngeneic tumor models"
Abstract: #4690 / 6; **Poster Session 30**: "Immunomodulatory Agents and Therapeutics"
Date and time: April 04, 2017, 01:00 - 05:00 p.m.
The abstract is available online at the AACR website and can be downloaded here.

About HERA-Ligands

Apogenix has developed a proprietary technology platform for the construction of novel hexavalent TNF superfamily receptor agonists (HERA-ligands). The specific molecular structure of these HERA-ligands induces a well-defined clustering of functional TNF receptors on the surface of target immune cells. By stimulating different TNF signaling pathways, HERA-ligands can increase the anti-tumor immune response. In contrast to agonistic antibodies, the 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 (ADCC) nor complement-dependent cytotoxicity (CDC) and exhibit a shorter half-life than antibodies. It is therefore expected that HERA-ligands will cause less side effects in clinical development. Apogenix utilizes its HERA-platform to develop GITR, CD40, CD27, 4-1BB, HVEM, and OX40 receptor agonists for cancer immunotherapy.

About Apogenix

Apogenix is a private company developing innovative immuno-oncology therapeutics for the treatment of cancer and other malignant diseases. The company has built a promising pipeline of immuno-oncology drug candidates that target different tumor necrosis factor superfamily (TNFSF)-dependent signaling pathways, thereby restoring the immune response against tumors. Since its inception in 2005, Apogenix has raised more than 100 million euros in financing rounds, public grants, as well as upfront and milestone payments from licensing agreements. The company is based in Heidelberg, Germany.

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