

Press Release

Apogenix Announces Initiation of Clinical Development for ABBV-621 to Treat Solid and Hematologic Tumors by Partner AbbVie

ABBV-621 is a first-in-class, hexavalent Fc-fusion protein based on Apogenix' proprietary HERA technology platform and is acting as a potent TRAIL-receptor agonist

Heidelberg, Germany, April 11, 2017 – Apogenix AG, a biopharmaceutical company developing next-generation immuno-oncology therapeutics, announced today that a clinical phase I study with ABBV-621 has been initiated by its partner AbbVie. In this study, 92 patients suffering from solid tumors, non-Hodgkins' lymphoma (NHL) or acute myeloid leukemia (AML) will be recruited. The study ("*An Open-Label, Phase 1, First-In-Human Study of Safety and Tolerability of TRAIL Receptor Agonist ABBV-621 in Subjects With Previously Treated Solid Tumors and Hematologic Malignancies*"; Clinicaltrials.gov ID: NCT03082209) will be recruiting in the US, EU and Japan. The phase I objectives will be to establish the safety and tolerability of ABBV-621, as well as to understand its pharmacokinetic properties.

ABBV-621 is a novel, second-generation TRAIL-receptor agonist consisting of six receptor binding domains of TRAIL (TRAIL: TNF-related apoptosis inducing ligand), fused to the Fc-domain of a human IgG1 antibody. This novel protein was engineered by Apogenix employing its proprietary HERA technology platform (HERA: hexavalent receptor agonists; Gieffers et al., Mol. Cancer Ther. 2013, 2735-2747). The substance acts as a pure agonist by binding to TRAIL-receptors on tumor cells, thereby inducing their apoptosis (programmed cell death). ABBV-621 is designed to maximize receptor clustering but does not require Fc γ -receptor-mediated crosslinking for optimal efficacy. This has been deemed an activity-limiting step for competitor antibodies in the clinic. ABBV-621 induces dose-dependent apoptotic cell death at sub- to single-digit nanomolar potencies across a large panel of human hematologic and solid tumor cell lines *in vitro*. In tumor xenograft models, ABBV-621 exhibits potent antitumor activity *in vivo* as a monotherapy and in combination with targeted agents or chemotherapy using xenograft tumors derived from colorectal, lung, leukemia, and lymphoma cell lines. In toxicity studies, ABBV-621 was well tolerated with no adverse drug-related findings.

"We are excited to see our first HERA-ligand enter clinical development. The unique mechanism of action has the potential to induce apoptosis, thereby eliminating cancer cells, and offers a new treatment option in the fight against cancer," Thomas Hoeger, Ph.D., Chief Executive Officer of Apogenix, said. "We are looking forward to see first results of the recently initiated clinical study."

In summer 2014, AbbVie acquired the worldwide rights for all TRAIL-receptor agonists developed by Apogenix. AbbVie is responsible for preclinical and clinical development of these compounds.

About HERA

Apogenix has developed a proprietary technology platform for the construction of novel hexavalent TNF superfamily receptor agonists (HERA). The specific molecular structure of HERA 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 is utilizing its HERA technology platform to develop GITR, CD40, CD27, 4-1BB, HVEM, and OX40 receptor agonists for cancer immunotherapy. The TRAIL program was licensed to AbbVie in 2014.

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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