Press Release

Publication in *Cancer Cell* Supports Therapeutic Potential of APG101 in Glioblastoma

New indication for lead compound of Apogenix

Heidelberg, March 10, 2008 - Apogenix GmbH, a biopharmaceutical company developing novel protein therapeutics based on the targeted modulation of apoptosis (programmed cell death), today announced the publication of new research findings of its scientific advisor, Dr Ana Martin-Villalba, in this month's *Cancer Cell* (March 2008).

The publication reveals a novel mechanism by which isolated tumor cells invade healthy brain tissue during the development and growth of Glioblastoma multiforme (GBM), the most common and aggressive type of primary brain tumors. This mechanism involves the so-called death system CD95/CD95L, which - when triggered - normally induces controlled cell death (apoptosis). Dr Martin-Villalba and her co-workers were able to demonstrate that, contrary to widely held beliefs, glioblastoma tumor cells take advantage of the CD95/CD95L system to increase their capacity to infiltrate healthy tissue. As a result, inhibition and not induction of this system should be considered as a therapy for GBM.

"We found that glioblastoma cells induce the expression of so-called CD95 ligands in surrounding healthy tissue," said Martin-Villalba, lead author of the study and scientific advisor of Apogenix. "This ligand in turn activates CD95, a death receptor on the surface of the tumor cells. However, instead of inducing apoptosis, triggering of CD95 on glioblastoma cells leads to the induction of enzymes that, among others, facilitate the invasion of tumor cells in surrounding tissue. We have already shown in animal models that a neutralization of CD95 activity dramatically reduces the number of infiltrating GBM cells."

"The development of treatment strategies in GBM has not led to a notably improved survival of patients in the last three decades," added Dr Thomas Höger, CEO of Apogenix. "The findings of Dr Martin-Villalba open new perspectives for treatment options for GBM patients using our lead drug candidate APG101."

APG101, a human, soluble fusion protein combining the extracellular domain of the CD95-receptor and the Fc-portion of IgG, blocks the CD95/CD95L system by binding to the ligand. At present, Apogenix is developing the compound for the prevention of "acute Graft-versus-Host Disease" (aGvHD). For this indication, Apogenix has been granted orphan drug status by the European Commission in 2006 and plans to initiate clinical phase I studies in the first half of 2008.

"Infiltration of tumor cells into the surrounding brain is regarded to be responsible for the refractory nature of GBM to treatment. We have already shown in animal models that APG101 successfully blocks the invasive behavior of GBM cells. Apogenix is now looking to advance APG101 into clinical trials and to explore the drug's potential benefit for patients," said Dr Harald Fricke, CMO of Apogenix.

The study published in *Cancer Cell* was conducted by Dr Martin-Villalba of the German Cancer Research Center (DKFZ) and co-workers of the DKFZ, as well as the Universities of Heidelberg and Mannheim, and Apogenix.

About Glioblastoma multiforme (GBM)
Glioblastoma multiforme accounts for about 50% of all primary brain tumor cases and 20% of all intracranial tumors. Current treatment options include surgery, chemotherapy, and radiotherapy. However, none of these strategies is curative as GBM is characterized by a diffuse, infiltrative growth pattern so that it is usually impossible to surgically remove the tumor, and is highly resistant to chemo- and radiotherapy. Median survival time from the time of diagnosis without any treatment is three months, and even if treatment is initiated, only one in twenty glioblastoma patients survives for more than three years. Long-term disease-free survival is unlikely, as the tumor will often reappear, usually within centimeters of the original site.

About APG101
APG101 is a human, soluble fusion protein combining the extracellular domain of the CD95-receptor and the Fc-portion of IgG. It prevents the initiation of controlled cell death ("apoptosis") by binding to the CD95 ligand expressed on effector cells so that it cannot trigger the so-called death receptor CD95.

There is experimental evidence for the theory that blockade of CD95L plays an important role in the pathophysiology of diseases characterized by an excess of apoptosis, such as myocardial infarction, acute "Graft-versus-Host Disease" (aGvHD), sepsis, and stroke.

APG101 has already demonstrated a dose-dependent effect in animal models of the above mentioned diseases and is in development for the prevention of aGvHD.

APG101 is covered by four different patent families claiming the composition of matter as well as its use for different indications.

About Apogenix
Apogenix is a biopharmaceutical company developing novel protein therapeutics based on the targeted modulation of apoptosis (programmed cell death). Apoptosis is a natural and highly controlled mechanism to clear the body of old, damaged or abnormally transformed cells. In many disease indications, this process has become out of balance causing either an uncontrolled removal of healthy cells and tissue (e. g. acute Graft-versus-Host Disease, stroke and spinal cord injuries) or a lack of removal of damaged and abnormal cells (e.g. in case of tumors). Apogenix is a spin-out from the German Cancer Research Center (DKFZ), and is based in Heidelberg, Germany. In 2005, the company has received 15 million Euro in a Series A round from the family of the renowned biotech investor and SAP co-founder Dietmar Hopp.

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