

## Press Release

### **New Publication Underlines Huge Potential of Apogenix' Compounds to Efficiently Eliminate Human Cancer Stem Cells**

Heidelberg, October 10, 2007 - 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 advisors Prof Giorgio Stassi, M.D., and Matilde Todaro, M.D., in this month's *Cell Stem Cell* (October 2007).

The data demonstrate that human cancer stem cells can be eliminated with high efficacy by combining chemotherapeutic drugs with compounds blocking the so-called IL-4 signaling pathway. Cancer stem cells are thought to be responsible for the development of metastases, which may re-appear years after the removal of a primary tumor and subsequent chemotherapy. Apogenix develops a promising portfolio of IL-4 blockers to address this mechanism and expects to initiate first clinical trials by 2010.

Stassi and co-workers had already shown in previous publications that both cancer cells and cancer stem cells produce the cytokines IL-4 and IL-10 to increase the production of anti-apoptotic proteins. "We have now demonstrated that cancer stem cells also use this mechanism to protect themselves from dying by apoptosis. Thus, chemotherapeutic drugs that would otherwise cause the death of these cells lose their efficacy," said Dr Giorgio Stassi, Professor at the Department of Surgical and Oncological Sciences, of the University of Palermo, Italy, and lead author of the study. "In addition, we have shown that treatments with antagonists blocking the IL-4 receptor or with antibodies neutralizing IL-4 strongly enhance the anti-tumor efficacy of standard chemotherapeutic drugs. These findings hold great potential, especially for increasing long-term survival of cancer patients."

"The publication is the culmination of more than five years of ground-breaking research performed by Giorgio Stassi, Matilde Todaro and co-workers," said Dr Thomas Höger, CEO/CFO of Apogenix. "Now our goal is to demonstrate the efficacy of our compounds in clinical studies. This could be the first therapeutic approach to not only combat primary tumors but also to reduce the risk of relapses and development of metastases."

Apogenix develops several compounds blocking IL-4 signaling. APG201 is an IL-4 receptor antagonist interfering with IL-4 receptors, while APG232 is an antibody directed at IL-4. It intercepts IL-4 to prevent interaction with the receptor. Both approaches have already delivered promising research and pre-clinical data. As an example, *in vivo* and *in vitro* data have shown that both compounds combined with chemotherapy can efficiently reduce tumor growth induced by cancer and cancer stem cells. Their mechanism of action, a so-called "two-hit attack", is simple but highly effective: First, Apogenix' drug candidates normalize the expression of anti-apoptotic proteins through IL-4 blockade, so that cancer cells regain sensitivity to apoptosis. Consequently, apoptosis can be induced by standard chemotherapy.

The Company owns extensive IP rights covering the use of apoptosis restoring compounds in combination with chemotherapy and/or radiation for the treatment of cancer.

### **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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