

Ascenta Therapeutics Novel MDM2-p53 Inhibitors Demonstrate Preclinical Single Agent Efficacy in Multiple Tumor Models

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Ascenta Therapeutics Inc., a privately-held clinical stage biopharmaceutical company today announced the presentation of promising preclinical data from their MDM2-p53 inhibitor development program at the 2006 American Association of Cancer Research (AACR) Annual Meeting held in Washington, D.C.

The invention of compounds that inhibit protein-protein interactions is critical to the development of new drugs for the treatment of cancer that modulate intracellular signaling pathways such as those involved in apoptosis. However, researchers have long considered the development of such compounds to be extremely difficult compared to those developed using traditional receptor-ligand based drug design approaches.

MI-147, designed and developed in the laboratory of Dr. Shaomeng Wang, Co-Director of the Molecular Therapeutics Program at the University of Michigan Comprehensive Cancer Center, is exactly such a compound. A potent, highly selective small molecule inhibitor of the MDM2-p53 interaction, MI-147 is representative of a new class of molecules being developed by Ascenta for the treatment of the approximately 50% of human cancers that express the wild-type p53 protein.

In the AACR poster abstract presented at this meeting, Ascenta and University of Michigan researchers describe extensive *in vitro* and *in vivo* evaluation of this new class (as exemplified by MI-147) of drug-like, ultra-potent, non-peptidic small-molecule inhibitors of the MDM2-p53 interaction. In addition to being a single digit nanomolar inhibitor of the MDM2-p53 interaction, MI-147 shows excellent oral bioavailability and pharmacokinetics *in vivo* and is highly selective in inducing apoptosis in a range of cancer cell lines versus normal cells. When given orally as a single agent, MI-147 demonstrated excellent antitumor activity *in vivo* in multiple animal models of human cancer with no or minimal toxicity.

"We are extremely excited with this new class of anticancer agents that have demonstrated both strong *in vivo* antitumor activity and significant druglike properties in our preclinical evaluations," said Dajun Yang, MD, PhD Ascenta Vice President of Research and General Manager, Ascenta Shanghai. "The combination of deep, highly productive scientific innovation in Dr. Wang's group coupled with the extensive preclinical and clinical drug development expertise we have at Ascenta has proven highly successful in rapidly advancing our pipeline forward, and the development of MI-147 is representative of a number of Ascenta drug candidates targeting multiple classes of critical molecular targets in the apoptosis pathway."

Founded in 2003, Ascenta is a privately-held biopharmaceutical company that discovers and develops targeted new medicines for the treatment of cancer. The company has offices in San Diego, California and a preclinical research facility in Shanghai, China. Its technology is focused on discovering molecules that hit vulnerable targets in endogenous apoptosis pathways and shut down cell growth and proliferation in cancer cells. Ascenta's broad pipeline of compounds is licensed from both the National Institutes of Health and the laboratory of Dr. Shaomeng Wang at the University of Michigan.