

Ascenta Therapeutics Presents New Preclinical Data on Mdm2 Inhibitor Portfolio Compound MI-63

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Ascenta Therapeutics Inc., today announced new preclinical data on its MDM2 inhibitor compound MI-63 at the 48th Annual Meeting of the American Society of Hematology in Orlando, Florida.

Ascenta scientists in collaboration with scientists from the MD Anderson Cancer Center in Houston, Texas and the Mayo Clinic in Rochester, Minnesota presented preclinical data on Ascenta's MDM2 inhibitor program compound activity against both acute myeloid leukemia (AML) and multiple myeloma (MM) cells *in vitro*.

Experiments done at the MD Anderson Cancer Center demonstrated p53-dependent apoptosis could be triggered in AML cells with Ascenta MDM2 inhibitor MI-63. In contrast, both p53-null and p53 knockdown AML cell lines were both resistant to MI-63. In addition to inducing increased levels of p53 in wild-type AML cells, MI-63 decreased levels of MDM4, an MDM2 homolog which also regulates p53 protein expression.

Consistent with a model in which p53 modulation increases BH3-mediated sensitization to apoptosis, MI-63 exhibited potent synergy with Ascenta's pan-Bcl-2 inhibitor AT-101. Taken together, these results support preclinical evaluation of MI-63 alone and in combination with pan-Bcl-2 inhibitor AT-101 for the treatment of AML.

MI-63 was also shown to have robust significant *in vitro* activity against several different MM cell lines, including those lines resistant to conventional chemotherapeutic agents such as melphalan, doxorubicin and dexamethasone. In work performed in the laboratory of Dr. Shaji Kumar at the Mayo Clinic in Rochester, Minnesota, MI-63 exhibited apoptotic effects against MM cells in culture, even those cultured in the presence of stromal cells, VEGF, or IL-6, all of which mimic the trophic marrow microenvironment.

"In addition to Ascenta's Phase 2 pan-Bcl-2 inhibitor, AT-101, our robust preclinical pipeline of pro-apoptotic compounds shows considerable promise for the treatment of several different cancers, including many hematological malignancies," said Ascenta Vice President of Research Dajun Yang, MD, PhD. "Our ability to rapidly advance preclinical leads towards clinical candidates is a direct outcome of our unique business model, which leverages both our subsidiary in Shanghai, China and our direct relationships with top-tier clinical investigators across the United States. We look forward to bringing additional compounds to the clinic in 2007, and advancing our Phase 2 program forward for our lead clinical compound AT-101 next year, as well."

[Link to poster 1](#)

[Link to poster 2](#)

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.