

Ascenta Therapeutics Presents New Clinical and Biological Data on AT-101 for the Treatment of Chronic Lymphocytic Leukemia

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Ascenta Therapeutics Inc., today announced new clinical and preclinical data on its Phase 2 compound, AT-101, at the 48th Annual Meeting of the American Society of Hematology in Orlando, Florida.

Data presented were from the Phase 2 clinical study of AT-101 in combination with Rituxan® for the treatment of relapsed or refractory chronic lymphocytic leukemia (CLL) and additional in vitro work done that sheds light on the effects of AT-101 on cell interactions in this chronic disease. Both studies were performed at the University of California at San Diego in the laboratory of Dr. Tom Kipps in La Jolla, California.

AT-101 is the only orally bioavailable pan-Bcl-2 inhibitor currently under clinical investigation. With inhibitory activity against Bcl-2 family proteins Bcl-2, Bcl-XL and Mcl-1, AT-101 acts to induce programmed cell death (apoptosis) of cancer cells which commonly rely on these anti-apoptotic proteins to survive.

Ascenta presented preliminary results on the effects of AT-101 in combination with Rituxan® on total lymphocyte count, lymphadenopathy and splenomegaly in 12 patients with relapsed or refractory CLL. Clinical responses were seen in 42% (5/12) of patients in the study, most of which showed improvement in at least two of the three disease compartments measured in the study. Four patients discontinued therapy due to treatment-related adverse events, including nausea and vomiting (2 patients), small bowel obstruction (1 patient) and diarrhea (1 patient). In no patients was any indication of myelosuppression observed.

"AT-101 continues to show significant effects in CLL patients when administered in combination with Rituxan®," said Dr. Jon T. Holmlund, Chief Medical Officer of Ascenta. "We are encouraged by these interim results and look forward to additional data on CLL patients undergoing treatment with AT-101, including high-risk patients. We plan additional enrollment using alternate AT-101 schedules in combination with Rituxan® in order to optimize efficacy and reduce GI toxicity of this important new medicine."

An additional study was undertaken in the Kipps lab to better understand the biological mechanisms underpinning the long term cell survival aspect of leukemic B cells in patients with the disease. In this study, non-neoplastic accessory cells called nurse-like cells (NLCs) were found to confer resistance to fludarabine-mediated apoptosis in leukemic B cells, mediated in part by upregulation of the key cell survival protein Mcl-1. Mcl-1 is a target for AT-101, and a member of the Bcl-2 family of anti-apoptotic proteins.

In the presence of AT-101, the fludarabine resistance seen in leukemic B cells cultured with NLCs is overcome, and these cells are instead driven to apoptosis.

"This study provides important insight into AT-101's effects on key cell-cell interactions involved in the pathobiology of CLL," said Dr. Holmlund. "The trophic microenvironment provided by NLCs in the bone marrow clearly plays a role in enhancing the longevity and defective apoptosis of leukemic B cells in CLL, and this cell-cell interaction appears to modulate the expression of Mcl-1, an important Bcl-2 family protein that has become implicated in a number of cancers that is targeted by AT-101. As clinical development of AT-101 continues to move forward, we are encouraged by experiments such as these which shed light on the activity of this important new molecule."

[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.