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May 31, 2012 4:00 AM EDT

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VALENCIA, Calif.--(BUSINESS WIRE)--May. 31, 2012-- Results published in *Blood*, the official journal of the American Society of Hematology, confirm that inhibition of the IRE1α-XBP1 pathway impacts the survival of myeloma cells, suggesting a promising therapeutic option in multiple myeloma. The pre-clinical study, conducted by researchers at Dana-Farber Cancer Institute in collaboration with MannKind Corporation (Nasdaq: MNKD), confirm that blocking the XBP1 arm of the unfolded protein response with MannKind's novel, first-in-class IRE1α RNase domain inhibitor, MKC-3946, alone or in combination with bortezomib or 17AAG, inhibited growth in multiple myeloma cells, while leaving normal cells intact.

"Results from this research study demonstrate that biologically based therapies have great potential to advance the treatment of multiple myeloma and extend the lives of patients with this devastating and deadly disease," said Kenneth C. Anderson, M.D., director of the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute, Kraft Family Professor of Medicine at Harvard Medical School, and corresponding author of the study. "Our findings show that targeting the XBP1 pathway with a selective IRE1α inhibitor, in this case the small molecule inhibitor MKC-3946, is a promising therapeutic strategy, providing the preclinical basis for future trials evaluating the clinical efficacy of this approach to improve patient outcomes in multiple myeloma."

In healthy individuals, a key signaling process, known as the unfolded protein response, regulates protein folding and facilitates cellular homeostasis. In patients with multiple myeloma, this process is not properly regulated, in part because the IRE1α enzyme activates the XBP1 gene, allowing myeloma cells to escape cell death, grow and/or become resistant to chemotherapy, radiotherapy and certain cancer drugs. Researchers believe that by restoring normal cell regulation and function, myeloma tumor cells no longer continue to multiply, and become more susceptible to common oncology treatments.

Findings from this pre-clinical study show that MKC-3946 inhibited the IRE1α-XBP1 pathway of myeloma cells, successfully blocking XBP1 splicing. Results also showed that the study compound:

- Enhanced cytotoxicity induced by the oncology agents bortezomib or 17AAG, even in the presence of bone marrow stromal cells or exogenous IL-6;
- Contributed to cell death in combination with these agents and as a single agent with fresh bone marrow aspirates from myeloma patients;
- Inhibited growth of multiple myeloma cells in vivo alone and in combination with these agents

MannKind's IRE-1α inhibitor MKC-3946 is part of a drug discovery program (MKC204) targeting the key biochemical signaling pathway of unfolded protein response that may play a role in a number of diseases. Through this program, MannKind has identified and optimized several IRE-1α inhibitors as potential investigational agents. In addition to multiple myeloma, IRE-1α inhibitors may have potential applications in other indications where this pathway plays a key role, such as breast, brain and pancreatic cancers as well as autoimmune diseases, neurodegenerative diseases and certain metabolic disorders.

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer with a five-year relative survival rate of approximately 41 percent, one of the lowest of all cancers. In 2012, an estimated 21,700 adults in the United States will be diagnosed with multiple myeloma and approximately 10,710 people will die from the disease.

About MannKind Corporation

MannKind Corporation (Nasdaq:MNKD) focuses on the discovery, development and commercialization of therapeutic products for patients with diseases such as diabetes and cancer. Its lead product candidate, AFREZZAR, is in late stage clinical investigation for the treatment of adults with type 1 or type 2 diabetes for the control of hyperglycemia. MannKind maintains a website at www.mannkindcorp.com to which MannKind regularly posts copies of its press releases as well as additional information about MannKind. Interested persons can subscribe on the MannKind website to e-mail alerts that are sent automatically when MannKind issues press releases, files its reports with the Securities and Exchange Commission or posts certain other information to the website.

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