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December 7, 2010 5:00 AM EST

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ORLANDO, Fla., Dec 07, 2010 (BUSINESS WIRE) -- Researchers at Dana-Farber Cancer Institute in collaboration with MannKind Corporation (Nasdaq:MNKD) generated results confirming that targeting the unfolded protein response (UPR) through the XBP-1 pathway impacts the survival of myeloma cells, suggesting a novel therapeutic strategy in multiple myeloma. The new data generated on a MannKind tool compound were presented as a poster at the 52nd American Society of Hematology (ASH) Annual Meeting.

In myeloma, the UPR is not properly regulated, in part because an enzyme known as IRE-1a activates (through splicing) the XBP-1 gene that enhances molecular chaperone activity and protein degradation. The result is that tumor cells escape apoptosis, proliferate and/or become resistant to therapies that ordinarily induce cellular stress, such as chemotherapy, radiotherapy and certain drugs. Researchers believe that blocking the XBP-1 arm of the UPR will push cancer cells to apoptosis and leave normal cells healthy. The data presented at ASH confirm and expand results supporting the development of an IRE-1a inhibitor by MannKind for oncology indications.

Researchers from Dana-Farber Cancer Institute used MKC-3946, a tool compound, to demonstrate on-target inhibition of XBP-1 splicing in human myeloma cell lines. Results showed that the study compound:

- Inhibited XBP-1 splicing and XBP-1s protein in response to the antineoplastic agents bortezomib and the HSP90 inhibitor 17AAG;
- Contributed to cell death in combination with these agents and as a single agent with fresh bone marrow aspirates from myeloma patients;
- Inhibited proliferation of INA6 cells in combination with bortezomib and 17AAG even in the presence of IL-6 and bone marrow stromal cell supernatant.

"The next generation of biologically based therapies has 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, MD, director of the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute, Kraft Family Professor of Medicine at Harvard Medical School, and an author of the study. "Our findings show that targeting the XBP-1 pathway with an IRE-1a inhibitor is a novel therapeutic strategy in multiple myeloma that merits further evaluation in a clinical program."

"The collaboration with Dana Farber has been effective in generating valuable information on this novel target," said Peter Richardson, MRCP, Corporate Vice President and Chief Scientific Officer, MannKind Corporation. "These types of collaboration are important to the future of drug development especially in areas of unmet medical needs and first-in-class opportunities. We are pleased to have Ken Anderson - a recognized key opinion leader in the field of multiple myeloma - and his researchers as key collaborators on this project."

MannKind's IRE-1a inhibitor (MKC204) is currently undergoing the preclinical and nonclinical evaluation required to support an Investigational New Application (IND) with the U.S. Food and Drug Administration. In addition to multiple myeloma, MKC204 may have potential applications in other indications where the UPR pathway plays a key role, such as breast, brain, and pancreatic cancers; autoimmune diseases, such as rheumatoid arthritis and lupus; and neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) and specific metabolic disorders.

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer. The five-year relative survival rate for multiple myeloma is approximately 34 percent, one of the lowest of all cancers. In 2009, approximately 20,000 adults in the United States were diagnosed with multiple myeloma and approximately 11,000 people died 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 diabetes pipeline includes AFREZZA® and MKC253. MKC253 is currently in phase 1 clinical trials. In March 2009, MannKind submitted a NDA to the FDA requesting approval of AFREZZA for the treatment of adults with type 1 or type 2 diabetes for the control of hyperglycemia. In March 2010, MannKind received a Complete Response letter to this NDA from the FDA, requesting additional information. In July 2010, the FDA accepted MannKind's reply to the Complete Response letter and set a PDUFA action date of December 29, 2010. Other products in MannKind's pipeline include the cancer immunotherapy platform MKC1106, which is currently in phase 2 clinical trials. 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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