

Isis Initiates Broad Phase 2 Program of ISIS-EIF4ERx in Cancer

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Initial Studies Target Patients with Non-small Cell Lung Cancer and Prostate Cancer

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Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced the initiation of two Phase 2 studies of ISIS-EIF4ERx in patients with non-small cell lung cancer and prostate cancer. These studies are part of Isis' broad Phase 2 development program designed to evaluate ISIS-EIF4ERx in multiple types of cancer. ISIS-EIF4ERx targets eukaryotic initiation factor-4E (eIF-4E), a traditionally "undruggable" target that is thought to promote tumor growth and metastasis in many cancers.

"eIF-4E may represent a novel and broadly applicable target for cancers because it promotes cancer cell growth in many types of cancer," said Brett P. Monia, Ph.D., Vice President, Drug Discovery & Corporate Development at Isis. "In the Phase 1 study, ISIS-EIF4ERx reduced eIF-4E in tumors and was well tolerated at doses up to 1200 mg per week in patients with a variety of cancers. Initially, our Phase 2 program will evaluate ISIS-EIF4ERx in combination with first-line treatments in prostate cancer and non-small cell lung cancer. We plan to expand our Phase 2 program over time to evaluate ISIS-EIF4ERx in other cancers that over-express eIF-4E."

The first Phase 2 study is evaluating the safety and efficacy of ISIS-EIF4ERx in combination with carboplatin and paclitaxel in patients with non-small cell lung cancer. The second Phase 2 study is evaluating the safety and efficacy of ISIS-EIF4ERx in combination with docetaxel and prednisone in patients with castrate-resistant prostate cancer. Each randomized, controlled study will enroll approximately 100 patients. The endpoints for both studies include progression-free survival, response rates, overall survival, time to progression and the reduction of a variety of biomarkers.

"We are very encouraged by results obtained by our partners with our antisense anti-cancer drugs. We and our partners have shown that antisense drugs have unique effects in cancer without exacerbating the toxicity of chemotherapeutic agents. Our technology allows us to approach the many 'undruggable' targets that are of interest to treat cancer," continued Dr. Monia. "Data from these initial Phase 2 ISIS-EIF4ERx studies will also help inform future development decisions for patients with other types of cancer."

ABOUT ISIS-EIF4ERx

ISIS-EIF4ERx targets the gene that is responsible for the production of a protein, eIF-4E, which is over-expressed in a variety of cancers, including prostate, lung, ovarian, liver, breast, head and neck, bladder, colon, thyroid and lymphoma. eIF-4E facilitates the synthesis of tumor angiogenic factors, which are factors that facilitate the growth of new blood vessels to support the development and progression of tumors, growth factors and survival factors by selectively enhancing their translation. In preclinical studies, Isis and collaborators demonstrated marked anti-cancer activity in a broad range of animal models of cancer and provided the first in vivo evidence that tumor growth may be more susceptible to eIF-4E inhibition than growth of normal tissue. Eli Lilly and Company has certain rights to license ISIS-EIF4ERx.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 22 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic, and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alnylam Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis has designed and executed a patent strategy that has provided the Company with strong and extensive protection for Isis' drugs as well as all aspects of antisense drug discovery, development and manufacturing. Additional information about Isis is available at www.isispharm.com.

ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Isis Pharmaceuticals and the discovery and development of ISIS-EIF4ERx for the treatment of cancer. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2009 and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

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