Isis Pharmaceuticals Earns $10 Million Milestone Payment from AstraZeneca For ISIS-AR Rx to Treat Prostate Cancer

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CARLSBAD, Calif., June 3, 2013 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that AstraZeneca has added a second development candidate, ISIS-ARRx, to its collaboration with Isis. Isis earned a $10 million milestone payment associated with this decision. ISIS-ARRx is an antisense drug designed to treat patients with prostate cancer by inhibiting the production of the androgen receptor (AR). AstraZeneca is planning to develop ISIS-ARRx broadly to treat patients under a variety of settings during the course of prostate cancer treatment, including both as a single agent and in combination therapy.

"Our collaboration with AstraZeneca has started very well. Within six months, we have broadened the clinical development of ISIS-STAT3Rx to include patients with advanced lymphoma and liver cancer and have advanced a second drug, ISIS-ARRx, in our collaboration. AR is a well-validated target in prostate cancer, and our antisense approach may allow us to avoid the limitations of other therapeutic approaches that others have tried to inhibit this target," said B. Lynne Parshall , chief operating officer at Isis. "AstraZeneca's extensive experience in successfully developing and commercializing drugs to treat hormone-related cancers, like prostate cancer, is a significant advantage for program success. We look forward to working closely with AstraZeneca as we design and implement the development program for ISIS-ARRx to treat patients with prostate cancer."

ISIS-ARRx, also referred to as AZD5312 and previously referred to as ISIS-AZ1Rx, is an antisense drug designed to inhibit the production of AR for the treatment of patients with prostate cancer. Prostate cancer is the second leading cause of cancer deaths in American men, with approximately 30,000 deaths each year in the United States. Prostate cancer growth, proliferation and progression are all androgen-dependent, and AR function is involved in disease progression at all stages of prostate cancer. For patients diagnosed with metastatic prostate cancer, current treatments largely involve opposing the action of androgens by blocking the androgen receptor or removing circulating androgens. Although androgen deprivation therapy approaches are initially effective in delaying disease progression in patients with metastatic prostate cancer, over time the course of the disease will progress in many of these patients. Resistance to current therapies is frequent and can occur through a variety of mechanisms including the activation of AR signaling in tumor cells through the amplification, over expression and mutation of the AR gene. Because ISIS-ARRx can inhibit the production of all known forms of AR, including variants of the AR gene, this drug has the potential to be an effective treatment for all stages of prostate cancer, including prostate cancer patients who are resistant to current therapies.

"We are pleased to be working with AstraZeneca to expand our efforts in developing antisense drugs to treat prostate cancer. The role of AR in prostate cancer is well understood as are many of the mechanisms that lead to resistance to current AR-targeted therapies. Treatments that interfere with androgen signaling have been shown to provide initial therapeutic benefit in patients with prostate cancer, but unfortunately, many of these patients develop resistance to such treatments, and their disease progresses. An AR-targeted strategy that avoids the emergence of resistance has the potential to provide significant therapeutic benefit to cancer patients at all stages of their disease," said Brett Monia , Ph.D., senior vice president antisense drug discovery at Isis. "In our preclinical studies, we have observed impressive inhibition of AR production under various settings, including conditions involving AR production and expression of alternative forms of AR including mutant AR. Furthermore, we have observed anti-tumor activity in animal models of prostate cancer, including a model resistant to enzalutamide, a small molecule AR antagonist often used in patients with castration-resistant prostate cancer. Because of its antisense mechanism of action, ISIS-ARRx has the potential to be effective in patients with prostate cancer regardless of the type of mutation they may have in their AR gene, further broadening the potential applicability of ISIS-ARRx in various stages of disease."

In 2012, Isis entered into a collaboration with AstraZeneca to discover and develop antisense drugs to treat cancer. The collaboration combines AstraZeneca's experience and expertise in developing anti-cancer agents with Isis' antisense technology platform to broaden Isis' cancer franchise. With the selection of ISIS-ARRx, Isis has earned $35 million in upfront and milestone payments from AstraZeneca and is eligible to earn additional milestone payments as the drug progresses in development as well as royalties on sales if ISIS-ARRx is successfully commercialized.

Conference Call

At 2:00 p.m. Eastern Time today, June 3, 2013, Isis will conduct a live webcast conference call to discuss recent highlights from its cancer franchise, including the addition of ISIS-ARRx to its cancer franchise and data from the Phase 1 study of ISIS-

STAT3Rx being presented today at the American Society of Clinical Oncology. Interested parties may listen to the call by dialing 866-652-5200, or access the webcast at www.isispharm.com. A webcast replay will be available for a limited time at the same address.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its leadership position in antisense technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 28 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO™, in the United States for the treatment of patients with HoFH. Genzyme is also pursuing marketing approval of KYNAMRO in other markets. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at www.isispharm.com.

ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Isis' strategic alliance with AstraZeneca and the discovery, development, activity, therapeutic and commercial potential and safety of ISIS-ARRx. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of KYNAMRO, 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, 2012, 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.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

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