Isis Pharmaceuticals Initiates Phase 2 Study Of ISIS 301012 in Cardiovascular Disease

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Study Evaluates ISIS 301012 in Combination With Statins to Lower High Cholesterol

CARLSBAD, Calif., Nov. 7 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today it has initiated a Phase 2 study of ISIS 301012 in combination with a statin in patients with high cholesterol. The study is part of a broad Phase 2 development program of ISIS 301012, a second-generation antisense drug. ISIS 301012 selectively reduces apoB-100, a target critical to the synthesis and transport of the "bad" cholesterol involved in heart disease -- low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein (VLDL). Lowering cholesterol levels is a key component in the prevention and management of cardiovascular disease.

The Phase 2 study is designed to evaluate the safety and efficacy of ISIS 301012 in patients on stable simvastatin therapy, who are not achieving their cholesterol targets. In the study, patients will be dosed with either 30 mg, 100 mg or 200 mg of ISIS 301012 over a 5-week treatment period followed by an 8-week post-treatment evaluation period. In support of the Phase 2 combination study, Isis completed a drug-drug interaction study of ISIS 301012 administered with statins in healthy volunteers. This study supports the ability to dose ISIS 301012 in combination with statins without negative drug-drug interaction.

"Our comprehensive Phase 2 development program will allow us to examine the broad profile of ISIS 301012 as an add-on therapy to reduce cholesterol in patients who can not reach their therapeutic target or as an alternative for patients who can not tolerate currently available therapies," said Mark Wedel, MD, JD, Vice President of Clinical Research and Chief Medical Officer of Isis Pharmaceuticals. "In addition to our already initiated Phase 2 trials, we also plan to study ISIS 301012 in patients who have familial hypercholesterolemia or FH, a genetic disorder characterized by extremely high lipid levels."

"Our development plans for ISIS 301012 are to rapidly develop the drug for patients with high unmet medical need to provide further validation of the efficacy and utility for the drug," Dr. Wedel added. "Developing ISIS 301012 in patients with FH has the potential to provide an accelerated pathway to commercialization because of the unmet medical need in this desperate patient population. ISIS 301012 has the potential to lower cholesterol in patients with FH and, as a result, decrease cardiovascular risk and prolong lives. The currently initiated Phase 2 trials are designed to address the larger commercial market represented by the traditional population of patients with high cholesterol, who are still not reaching their targeted cholesterol levels. We believe that ISIS 301012 has the potential to help patients reach their targeted cholesterol levels and combat cardiovascular disease, the number one cause of death worldwide."

In addition to this Phase 2 combination trial, ISIS 301012 is also being studied in a Phase 2 single-agent trial designed to optimize dose and frequency of dosing and to further evaluate the safety and efficacy of the drug in patients with high cholesterol. In the study, patients are being dosed from 50 mg to 200 mg per week for three months followed by a six month post-treatment evaluation period. Additional Phase 2 trials are planned to study the effects of ISIS 301012 in patients with familial hypercholesterolemia (FH). FH is a genetic disorder characterized by extremely high lipid levels.

In 2005, Isis reported positive data from two Phase 1 studies of ISIS 301012, in which ISIS 301012 produced rapid, dose-dependent, and prolonged reductions of its target, apoB-100, with concomitant reductions in LDL-C, VLDL and total cholesterol levels in normal subjects with elevated cholesterol. In the first Phase 1 trial, reductions occurred after only one month of dosing (50 mg-400 mg), and lasted in some cases, more than 100 days. In the second Phase 1 study, normal subjects with elevated cholesterol levels also achieved significant reductions of apoB-100 and LDL-C after being treated with an average of 350 mg/week of ISIS 301012 for one month. The drug has been generally well tolerated.

ABOUT CHOLESTEROL AND CARDIOVASCULAR DISEASE

According to the American Heart Association, an estimated 106.9 million American adults have total blood cholesterol values of 200 mg/dL and higher, and of these about 37.7 million American adults have levels of 240 or above. In adults, total cholesterol levels of 240 mg/dL or higher are considered "high risk". Levels from 200 to 239 mg/dL are considered "borderline-high risk". Low-density lipoprotein, or LDL, known as the "bad" cholesterol, can clog arteries, increasing the risk of heart attack and stroke.

According to the World Health Organization (WHO), heart disease and stroke kill 17 million people a year, which is almost one-third of all deaths globally. By 2020, the WHO projects that heart disease and stroke will become the leading cause of both death and disability worldwide, with the number of fatalities projected to increase to over 20 million a year and by 2030 to over 24 million a year.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis Pharmaceuticals, Inc. 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 12 antisense drugs in development to treat metabolic, cardiovascular, ocular and inflammatory diseases, and cancer. In its Isis division, Isis is developing and commercializing the TIGER biosensor system, a revolutionary system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of approximately 1,500 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding the development, therapeutic potential and safety of ISIS 301012 to lower high cholesterol. Any statement describing Isis’ goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis’ goals. 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 products. 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, 2004, and its quarterly report on Form 10-Q for the quarter ended June 30, 2005, which are on file with the SEC. Copies of these and other documents are available from the Company.

SOURCE Isis Pharmaceuticals, Inc.
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