ISIS 301012 Reduces Atherosclerotic Plaques in Animal Models

April 27, 2006

Data Confirms That ISIS 301012 Has Potential to Benefit Patients With Cardiovascular Disease

CARLSBAD, Calif., April 27, 2006 /PRNewswire-FirstCall via COMTEX News Network/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced results of a study showing that ISIS 301012 reduced atherosclerotic plaques, apoB-100, and circulating inflammatory cytokines in an animal model of atherosclerosis. These data support a growing body of evidence demonstrating that ISIS 301012 has the potential to treat patients with coronary artery disease. Isis recently reported in a Phase 2 trial that ISIS 301012 produced rapid, dose-dependent and prolonged reductions of its target, apoB-100, with concomitant reductions in low density lipoprotein (LDL or "bad" cholesterol), very low density lipoprotein (VLDL), total cholesterol and triglyceride levels in patients with high cholesterol. ISIS 301012 is a second-generation antisense drug that inhibits the expression of apoB-100, a protein critical to the formation and transport of the "bad" cholesterol particles involved in heart disease -- LDL and VLDL. Rosanne Crooke, Ph.D., Director of Cardiovascular Research of Isis Pharmaceuticals, presented these data at the Arteriosclerosis, Thrombosis and Vascular Biology (ATVB) meeting in Denver, Colorado.

ISIS 301012 was administered to mice that were bred to contain no LDL receptor. These transgenic mice also expressed human apoB-100. In this transgenic model, mice develop extensive atherosclerotic plaques. A 14-week treatment with ISIS 301012 produced a dose-dependent reduction in apoB-100 levels, with concomitant decreases in aortic plaque volume. At 50 mg/kg/wk, ISIS 301012 treatment reduced the levels of apoB-100 by 69%