



Isis Earns \$5 Million Milestone Payment From Ortho-McNeil, Inc. for Initiation of Phase 1 Study of ISIS 325568

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ISIS 325568 is an Antisense Drug Targeting Glucagon Receptor for Treatment of Type 2 Diabetes

CARLSBAD, Calif., Oct 02, 2007 /PRNewswire-FirstCall via COMTEX News Network/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today it has earned \$5 million from Ortho-McNeil, Inc. (OMI), a Johnson & Johnson company, for achieving the first development milestone of initializing the Phase 1 clinical trial of ISIS 325568.

The collaboration between Isis and OMI, announced on September 13, 2007, includes the licensing of two second-generation antisense drugs, ISIS 325568 and ISIS 377131, both of which represent novel approaches for the treatment of metabolic disease. ISIS 325568 was designed to selectively inhibit the production of glucagon receptor and has demonstrated improved glucose control in animal models of Type 2 diabetes.

"We are pleased to have achieved this milestone so early in our collaboration with Ortho-McNeil, Inc.," said Jeffrey Jonas, M.D., Executive Vice President, Isis Pharmaceuticals. "OMI will be providing all funding for this study, while Isis will be managing the study through to completion before handing all additional development responsibilities over to our partner."

ABOUT GLUCAGON RECEPTOR (GCGR), TARGET OF ISIS 325568

Glucagon is a hormone that opposes the action of insulin and stimulates the liver to produce glucose. In Type 2 diabetes, unopposed action of glucagon can lead to increased blood glucose levels. Reducing the expression of liver GCGR using antisense inhibitors, and thereby reducing excessive liver glucose production, is expected to lower blood glucose levels and help control Type 2 diabetes. In preclinical studies, antisense inhibitors of GCGR led to improved glucose control and reduced levels of blood triglycerides without producing hypoglycemia. In addition, treatment with ISIS 325568 led to an increase in circulating glucagon-like peptide, or GLP-1, which is a hormone that helps to preserve pancreatic function, thereby enhancing insulin secretion.

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 17 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing drugs for a wide variety of diseases. Ibis Biosciences, Inc., Isis' wholly owned subsidiary, is developing and commercializing the Ibis T5000(TM) 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 over 1,500 issued patents worldwide. Additional information about Isis is available at <http://www.isispharm.com>.

This press release includes forward-looking statements regarding Isis' collaboration with Ortho-McNeil, Inc., the discovery and development of drugs for diabetes and metabolic diseases, and the therapeutic potential of ISIS 325568 for Type 2 diabetes. 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, 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, 2006, and its quarterly report on Form 10-Q for the quarter ended June 30, 2007, 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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