

## Isis Pharmaceuticals Achieves Milestone In Amgen Antisense Drug Discovery Collaboration

August 14, 2002

CARLSBAD, Calif., Aug. 14 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it has achieved a research milestone in its drug discovery collaboration with Amgen (Nasdaq: AMGN). Isis has received a payment from Amgen for the accomplishment of this milestone. The milestone is related to research progress in the companies' three-year antisense drug discovery collaboration initiated in December 2001. The therapeutic area of the research agreement and specific financial terms of the payment were not disclosed.

"We are pleased to have made considerable progress in our antisense drug discovery collaboration with Amgen," said Brett P. Monia, Ph.D., Isis' Vice President of Antisense Drug Discovery. "We are optimistic that through the combination of Amgen's experience in discovering novel biopharmaceutical products and Isis' expertise in antisense technology, the prospects of new antisense drugs reaching the market in the coming years has been greatly enhanced."

Amgen and Isis are collaborating to discover and develop new antisense drugs utilizing Isis' proprietary second-generation chemistry, called 2'-O-methoxyethyl. Amgen has the right to develop and commercialize antisense drugs resulting from the collaboration. If drugs from the collaboration are successful, Isis will receive milestone payments upon key research, clinical and commercial achievements, as well as royalties on sales. In January 2002, Amgen and Isis expanded its antisense partnership into the functional genomics arena. Amgen gained access to Isis' antisense gene functionalization and target validation expertise and to specific patents within Isis' functional genomics suite of patents. As part of this intellectual property license, Amgen can use antisense inhibitors that use the Ribonuclease H (RNase H) mechanism of action for its in-house antisense-based functional genomics program.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has commercialized its first product, Vitravene® (fomivirsen), to treat CMV-induced retinitis in AIDS patients. In addition, Isis has 13 antisense products in its development pipeline, with two in late-stage development and six in Phase II human clinical trials. Affinitac™ (formerly called LY900003 and ISIS 3521), an inhibitor of PKC-alpha, is in Phase III trials for non-small cell lung cancer, and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is in Phase III human clinical trials for Crohn's disease. Isis has a broad patent estate, as the owner or exclusive licensee of more than 900 issued patents worldwide. Isis' GeneTrove™ division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services. Ibis Therapeutics™ is a division focused on the discovery of small molecule drugs that bind to RNA. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

This press release contains forward-looking statements concerning the collaboration between Isis Pharmaceuticals, Inc. and Amgen, the planned development activities and therapeutic potential for our products in our pipeline, and the potential value of the company's functional genomics and drug discovery technology platform. Any statement describing a goal, expectation, intention or belief of the company 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 financing such activities. Actual results could differ materially from those projected in this release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in the company's Annual Report on Form 10-K, for the year ended December 31, 2001, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

Affinitac™, a trademark of Eli Lilly and Company, is an investigational cancer compound being developed through an alliance between Lilly and Isis Pharmaceuticals, Inc. and marketed globally by Lilly.

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