

## Isis Pharmaceuticals to Make Early Payment of \$74 Million of 14% Senior Subordinated Debt

April 24, 2002

CARLSBAD, Calif., April 24 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), announced today that it plans to retire its 14% Senior Subordinated Notes. The total amount of this debt, including principle plus interest, is approximately \$74 million. The transaction will be effective May 1, 2002, contingent upon the successful completion of Isis' convertible debt offering, which was announced yesterday.

"The advance payment of these notes is financially beneficial to Isis. If we had continued paying principle plus interest through November 2007 according to the original schedule, we would have made quarterly cash interest payments totaling more than \$50 million," said B. Lynne Parshall, Isis' Executive Vice President and CFO.

Between 1997 and 1998, Isis obtained a total of \$40 million in private debt financing through the holder of the notes. The terms of the financing provided for a ten-year maturity on the debt, interest of 14% per annum and deferred interest payments for the first five years of the loan. After the first five years, interest would have been paid quarterly until the end of the loan. No principal repayments were required until the end of the loan. Because interest was deferred during the first five years, the principle balance would have been \$78 million on November 1, 2002.

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 Isis' plans regarding the retirement of its debt, the financial position of the company, 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.

Vitravene® is a registered trademark of Novartis AG. GeneTrove™ and Ibis Therapeutics™ are trademarks of Isis Pharmaceuticals, Inc. Affinitac™ is a trademark of Eli Lilly and Company.

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