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For Immediate Release

ISIS PHARMACEUTICALS ANNOUNCES ADOPTION OF SECURITIES TRADING PLAN UNDER SEC RULE 10b5-1

Carlsbad, CA – April 2, 2002 – Isis Pharmaceuticals (NASDAQ: ISIS) announced today that it has implemented a stock trading program for Isis Board of Directors, corporate executive officers and other insiders, under Rule 10b5-1 of the Securities and Exchange Act of 1934. When there is no material non-public information available, Rule 10b5-1 allows corporate insiders to establish plans that permit prearranged future sales of his or her securities.

“We have adopted a plan under Rule 10b5-1 that allows Isis insiders to ‘pre-program’ stock option or stock sales in a manner that is completely independent of inside information,” said B. Lynne Parshall, Isis’ Executive Vice President and Chief Financial Officer. “As in many publicly-traded corporations, stock options are a key component of Isis’ executive compensation. We are fortunate to have retained a strong and highly committed management team, many of whom have been with the company for 10 years or more. Several Isis insiders have 10-year-old options that they have chosen not to exercise and that begin to expire this year. These insiders may be compelled to sell shares in order to avoid losing the value these options hold. Such sales will be pre-programmed to be made independent of company news. The securities trading plan we’ve adopted will facilitate such sales in an orderly fashion.”

Under the Isis trading plan, corporate insiders prepare a written plan to sell shares on a prearranged basis over a set period of time. An independent broker then executes the pre-planned trades, according to the plan’s instructions, without regard to any subsequent non-public information the individual might receive. Once the insider’s plan is in place, he or she cannot influence the broker’s trading activities of Isis stock. Additionally, Isis insiders that participate in the plan are only allowed to sell stock through the plan.

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 products in its development pipeline, with two in late-stage development and six in Phase II human clinical trials. LY900003 (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 nearly 900 issued patents worldwide. Isis' GeneTrove™ division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services. Isis 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.

This press release contains forward-looking statements concerning Isis Pharmaceuticals, its business activities and the planned sale of stock by its Board of Directors and Company officers. 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, the reader is 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 10K, for the period 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.

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