

Isis Gains Full Ownership of Orasense(TM) and HepaSense(TM) Subsidiaries and Eliminates Future Royalty Payments to Elan

June 9, 2004

Agreement Terminates Preferred Stock Dividend Accretion and Minimizes Dilution

CARLSBAD, Calif., June 9 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it has entered into an agreement with a subsidiary of Elan Corporation, plc, to acquire Elan's minority interest in Orasense and HepaSense, joint ventures arising out of prior collaborations between Isis and Elan. Through this acquisition, Isis has eliminated all future royalties to Elan related to the oral delivery platform developed within the Orasense collaboration and to ISIS 14803, Isis' antisense drug for the treatment of the hepatitis C virus, which is currently in Phase 2 clinical trials and was the focus of the HepaSense collaboration. As previously announced, Elan's participation in these collaborations concluded in January 2003 and November 2002, respectively.

In addition to eliminating all future royalty payments to Elan, the agreement allows Elan to transfer its shares of Isis Series B Preferred Stock to a third party. Upon transfer, the preferred stock will immediately convert to 1,055,502 shares of Isis common stock, eliminating the 5 percent in-kind dividend, thereby reducing future dilution of approximately 86,000 shares of Isis' common stock. Further, Elan has agreed to surrender its warrant to purchase 14,881 shares of Isis common stock to Isis for cancellation.

"We are extremely pleased to have completed this transaction as it allows us to recognize the full financial potential of our oral delivery platform and our proprietary drug to treat hepatitis C. In addition, it simplifies our capital structure and eliminates dividend accretion of approximately \$1.2 million between now and maturity in 2006 as a result of the early conversion of the Series B Preferred Stock," said B. Lynne Parshall, J.D., Executive Vice President and Chief Financial Officer of Isis. "This is the latest achievement in our ongoing efforts to further strengthen our financial position and streamline our balance sheet. As a result of these efforts over the past two years, we have retired more than \$125 million in high interest debt, eliminated a significant amount in future interest payments and reduced total potential dilution of our common stock by 2.2 million shares."

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and for its partners. The company has successfully commercialized the world's first antisense drug and has 11 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,300 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding our business, our financial position, the therapeutic and commercial potential of our technologies and products in development and the benefit we expect to receive from the transaction described herein. Any statement describing our goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology and systems used to identify infectious agents, in discovering and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this press 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 Isis' Annual Report on Form 10-K for the year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended March 31, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

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