Isis Pharmaceuticals Statement Regarding UBS Warburg Report

December 6, 2002

Isis and Lilly Remain Blinded to Affinitak™ Phase III Clinical Trial

CARLSBAD, Calif., Dec. 6 /PRNewswire-FirstCall/ -- In response to a research note published today by a UBS Warburg analyst, which downgraded the company's stock based on anecdotal information obtained from clinical investigators, Isis Pharmaceuticals, Inc., (Nasdaq: ISIS) issues the following statement regarding the status of the 600-patient Phase III clinical trial of Affinitak in combination with chemotherapy in patients with non-small cell lung cancer:

-- The Phase III clinical trial remains blinded to both companies.
   No clinical investigator nor company representative has access to all
   the data. Further, no analysis of any kind has been initiated.

-- The Phase III study design prevents insights.
   The study and data management systems have been designed to make it
   impossible for any clinical investigator to have sufficient information
   to draw any inference about the trial. In fact, the trial design
   prevents any single site from enrolling more than 5% of the
   total number of patients. Therefore, no clinical investigator could
   have sufficient experience to draw any conclusions about
   the performance of Affinitak.

-- The trial database is secure.
   The database is maintained at Isis only. All Isis employees are
   blinded. No one at the company has sufficient access to unblind the
   data. We have confirmed that there has been no breach of security.
   We further confirm that no one at Isis or Lilly has unblinded
   information about this trial.

-- The analysis and new drug application (NDA) plans have been finalized.
   Isis and Lilly have just completed important meetings that finalized
   the analysis plan for this trial, and the strategy for compiling a NDA
   should the results be sufficiently positive to support a single study
   filing. The companies plan to conduct the analysis of the Phase III
   data in March 2003. Based on detailed planning, the March timeframe
   has been adopted to support the maturation of the study and to coincide
   with the preparation of the CMC, or manufacturing section, of the NDA.

-- Isis and Lilly remain enthusiastic about the potential for Affinitak in
   cancer.
   The Lilly Phase III trial of Affinitak in combination with
   Gemzar/cisplatin in patients with non-small cell lung cancer continues
   to enroll well. Additional Phase II trials of Affinitak are in
   progress and the work necessary to support a single study NDA is well
   underway.

Isis will conduct a live webcast conference call to discuss this statement today, Friday, December 6 at 5:30 p.m. Eastern time. To participate over the Internet go to www.isispharm.com . A replay of the webcast will be available at this address for up to 30 days.

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 (formivirsen), 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. Affinitak (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 1000 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 .

This statement contains forward-looking statements about the potential of the investigational compound Affinitak in the treatment of non-small cell lung cancer. 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 and quarterly report on Form 10-Q for the periods ended December 31, 2001 and September 30, 2002, respectively, which are on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

Affinitak, 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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Vitravene is a registered trademark of Novartis AG.

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