

Isis Receives 1,000th Patent

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Company Achieves Major Innovation Milestone in RNA-based
Drug Discovery and Development

CARLSBAD, Calif., Sept. 18 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced the issuance of its 1,000th patent. The issued patent, U.S. Patent No. 6,448,079, covers antisense compounds targeted to genes encoding p38 mitogen activated protein kinases (p38 MAP kinases). p38 MAP kinases regulate many biological processes related to inflammatory diseases and cancer. Antisense drugs that target p38 MAP kinases may be useful for treating disorders related to these conditions. This patent also represents the company's 200th gene-related patent.

"The receipt of our 1,000th patent marks a significant milestone in Isis' history and is symbolic of the innovative spirit of the company and our shareholders," said Stanley T. Crooke, M.D., Ph.D., Isis' Chairman and CEO. "For 13 years, we have worked diligently to create new drug discovery technologies based on RNA and build an intellectual property estate that supports Isis' leadership position. Intellectual property is a key asset to the company. We believe the ownership of technology that could create a new category of drugs in the pharmaceutical industry will generate great value for our shareholders. We will continue to actively exploit our inventions to return value to our shareholders."

In addition to the 1,000th patent, nine additional Isis' patents have also issued. Four of these are gene-related patents, U.S. Patent Nos. 6,448,080; 6,448,081; 6,451,538; and 6,451,602. Four of these patents are chemistry patents, U.S. Patent Nos. 6,447,998; 6,448,373; 6,451,968; and 6,451,991. The remaining patent, U.S. Patent No. 6,451,524, covers a method of identifying target nucleic acid sequences.

Isis controls a broad intellectual property estate of more than 1,000 patents covering the use of antisense technology in all steps of drug discovery. The comprehensive patent portfolio addresses the use of antisense inhibitors as drugs, including chemistries, antisense inhibitor designs called "motifs," methods of use of antisense inhibitors, mechanisms of action by which antisense inhibitors inactivate an RNA target and improved methods for manufacturing antisense oligonucleotides. Isis' patent estate also covers the use of antisense inhibitors as tools for gene functionalization and target validation.

p38 MAP kinases are a family of proteins, which play an important role in signal transduction in response to cytokines and growth factors. Specific responses elicited by p38 MAP kinases include inflammation conditions such as rheumatoid arthritis and apoptosis (programmed cell death).

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™, 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 trials for Crohn's disease. Isis has a broad patent estate as the owner or exclusive licensee of more than 1,000 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 press release contains forward-looking statements concerning Isis Pharmaceuticals and the potential of the company's intellectual property position. 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 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.

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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Web site: <http://www.isispharm.com>

CONTACT: Kristina Peterson of Isis Pharmaceuticals, Inc., +1-760-603-2521