

Isis Pharmaceuticals And Amgen Enter Into Target Validation And Patent License Agreement

January 3, 2002

CARLSBAD, CA, January 3, 2002 - Isis Pharmaceuticals, Inc. (NASDAQ: ISIP) announced today that its GeneTrove™ division has entered into a functional genomics alliance with Amgen (NASDAQ: AMGN). Under the terms of the agreement, Amgen gains access to Isis' antisense gene functionalization and target validation expertise and to specific patents within Isis' functional genomics suite of patents. As part of this intellectual property license, Amgen can use the Ribonuclease H (RNase H) mechanism of action for its in-house antisense-based functional genomics program. This new agreement extends Isis' antisense research efforts with Amgen. Recently, the companies announced the initiation of a three-year antisense drug discovery collaboration. Specific financial terms of the deals were not disclosed.

"GeneTrove is delighted to add Amgen to a growing list of companies that are working with us on gene functionalization and target validation activities and utilizing Isis' expertise to enhance their own programs," said Richard K. Brown, Ph.D., Isis' Vice President and President of GeneTrove. "This alliance is the second such arrangement the division has announced within the last month, and we believe these new transactions demonstrate the industry's increasing recognition of the benefits of Isis' antisense expertise and technology."

As a division of Isis, GeneTrove provides three major product offerings to the pharmaceutical and biotechnology industry: 1) custom target validation collaborations, 2) the Human Gene Function database, introduced in 2001, and 3) an intellectual property licensing program. The division's offerings are designed to meet critical and timely needs of the pharmaceutical industry, and to help partners make strategic drug target selections for drug discovery. In GeneTrove's custom target validation collaborations, the division aids corporate partners in identifying the role of a specific gene (gene functionalization) and whether a specific gene is a good target for drug discovery (target validation). GeneTrove currently provides these services to Eli Lilly and Company, Celera Genomics, Abbott Laboratories, Johnson & Johnson, Aventis and Chiron Corporation.

Isis' functional genomics patent suite is comprised of approximately 50 patents and applications. A central component of the patent suite is intellectual property surrounding RNase H. RNase H is a naturally occurring cellular enzyme that cleaves the RNA portion of a RNA/DNA duplex, such as that formed when an antisense inhibitor binds to RNA. Isis owns intellectual property that broadly covers the use of RNA/DNA oligonucleotides, or antisense inhibitors, in gene functionalization and target validation. These patents include: chemistries; antisense inhibitor designs called "motifs;" methods of use of antisense inhibitors; and mechanisms of action by which antisense inhibitors activate any RNase H used for functional genomics screening activities in cells. The company's functional genomics suite of patents represents a subset of Isis' overall intellectual property estate of nearly 900 issued patents that Isis owns or exclusively licenses, covering RNA-based drug discovery and development.

Isis expects GeneTrove's Human Gene Function database to be the first database product to contain information on the selective inhibition of up to 10,000 human genes. By providing the most comprehensive biological view of the human genome to date, the database will allow partners to rapidly prioritize genomic information to identify and discover new drug targets, expediting drug discovery and development programs.

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 seven in Phase II human clinical trials. 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 and access to an extensive gene function database. Ibis Therapeutics™ is a division focused on the discovery of small molecule drugs that bind to RNA.

This press release contains forward-looking statements concerning Isis Pharmaceuticals' functional genomics division, GeneTrove, its product offerings and intellectual property, and the collaboration between Isis Pharmaceuticals and Amgen. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of conducting gene functionalization and target validation activities, in launching new products and services for or with collaborators, and in 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 Quarterly Report on Form 10Q, for the period ended September 30, 2001, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

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