

# Isis Pharmaceuticals and GlaxoSmithKline Enter Into Target Validation Agreement

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CARLSBAD, Calif., Dec. 11 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that its GeneTrove™ division has entered into a target validation agreement with GlaxoSmithKline (NYSE: GSK). Through the collaboration, GlaxoSmithKline will functionalize and validate gene targets using Isis' proprietary antisense inhibitors and take a license to Isis' intellectual property for its internal antisense-based functional genomics program. Specific financial terms of the deal were not disclosed.

"This new partnership with GlaxoSmithKline is in alignment with our business plan for GeneTrove and recognizes Isis' leadership position in antisense intellectual property. Additionally, this partnership further promotes our goal of being the preferred provider of antisense technology and functional genomics expertise," said Richard K. Brown, Ph.D., Isis' Vice President and GeneTrove President. "GlaxoSmithKline already has a robust antisense program and we are pleased that GeneTrove continues to make great progress in maximizing the application of its technology and services within the pharmaceutical industry."

## Background information on GeneTrove

As a division of Isis, GeneTrove collaborates with pharmaceutical industry partners to meet critical and timely needs for target validation. 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 services to Eli Lilly and Company, Celera Genomics, Abbott Laboratories, Amgen, Inc., Chiron Corporation, Merck & Co., Inc., Pharmacia Corporation, Johnson & Johnson, and Aventis.

Isis' functional genomics patent suite is comprised of approximately 50 patents and applications. Central components of the patent suite are intellectual property surrounding RNase H and second generation antisense inhibitors designed to work through the RNase H mechanism of action. RNase H is the most common and potent mechanism of action employed by antisense when used as a functional genomics tool. The company's functional genomics suite of patents represents a subset of Isis' overall intellectual property estate of more than 1000 issued patents that Isis owns or exclusively licenses, covering RNA-based drug discovery and development.

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](http://www.isispharm.com).

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 GlaxoSmithKline. 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 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 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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