

Isis Pharmaceuticals and atugen AG Enter Patent License Agreement

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CARLSBAD, Calif., and BERLIN, Jan. 16 /PRNewswire-FirstCall/ -- atugen AG and the GeneTrove™ division of Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), announced today that they have entered into an intellectual property license agreement. Through the licensing of specific functional genomics patents from Isis, atugen supplements its existing intellectual property position by gaining rights to practice Isis' antisense-based functional genomics technology, and to use antisense for discovery and validation of targets and for small molecule drug discovery research in its in-house programs and for its customers. Specific financial details of the agreement were not disclosed.

"This new transaction with atugen is consistent with our business strategy to maximize the utilization of our intellectual property within the industry to create value for our shareholders. We believe the strength and depth of our patent position along with the number of agreements we have in place with pharmaceutical and biotechnology companies, such as atugen and others, is indicative of our leadership role in antisense-based functional genomics," said Richard K. Brown, Ph.D., Isis' Vice President and GeneTrove President.

"This agreement gives us access to Isis' antisense intellectual property, enhancing our patent portfolio and our ability to offer target validation services, including the elucidation of disease pathways to partners," said Thomas Christely, atugen's Chief Operating Officer. "Moreover, this agreement will support the increased demand for our service offerings, since atugen provides all major mRNA-based tools including antisense, ribozymes and siRNA, together with atugen's unique transfection reagents, for discovery and validation of targets and for small molecule drug discovery research."

atugen's intellectual property portfolio consists of an exclusive license from Ribozyme Pharmaceutical Inc. for 69 issued patents and more than 100 patent applications in the target discovery and validation field relating to ribozymes, antisense molecules, delivery vehicles and related technologies. This estate is complemented by atugen's own patent filings and several other licenses including a license to practice the RNA interference technology. atugen's current customers for target validation include Altana Pharma, AstraZeneca, Novo Nordisk, Oxford Glycosciences, Pfizer, Schering AG/Berlex Biosciences and University of California San Francisco amongst others.

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. This 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. GeneTrove also 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 Custom Target Validation services to Eli Lilly and Company, Celera Genomics, Abbott Laboratories, Amgen, Inc., Chiron Corporation, Merck & Co., Inc., Pharmacia Corporation, Johnson & Johnson, GlaxoSmithKline and Aventis.

atugen AG is a technology leader in disease pathway elucidation. Building on successful collaborations with a large number of pharmaceutical and biotechnology partnerships, atugen is positioned to take advantage of the industry's need to unravel the function of genes and to dissect signal transduction pathways. atugen has already proven the value of its technology and expertise by establishing a portfolio of validated targets and compounds inhibiting the PI 3-kinase pathway, which plays an important role in most cancer types, diabetes, wound healing and other indications. The company offers proprietary KnockDown™ technologies (GeneBlocs® antisense molecules, improved synthetic siRNA, vector expression systems for siRNA and ribozymes) and superior transfection reagents.

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- α , 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 press release contains forward-looking statements concerning Isis Pharmaceuticals' functional genomics division, GeneTrove, its product offerings and intellectual property, and the agreement between Isis Pharmaceuticals and atugen AG. 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.

GeneBlocs® and KnockDown™ are trademarks of atugen AG

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.

GeneTrove™ and Ibis Therapeutics™ are trademarks of Isis Pharmaceuticals, Inc.

Vitravene® is a registered trademark of Novartis AG.

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