



## Isis Pharmaceuticals to Receive \$24 Million for a Portion of Its Macugen(R) Royalty Rights

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### Isis Retains Significant Portion of Royalty Stream on Macugen Sales

CARLSBAD, Calif., Dec. 21 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it has sold a portion of its royalty rights in Macugen® (pegaptanib sodium injection) to Drug Royalty USA, Inc. (DRC) in exchange for aggregate payments of \$24 million over the next three years. Under the terms of the agreement, Isis and DRC will share the royalty rights on Macugen through 2009. After 2009, Isis retains all royalties to Macugen.

In 2001, Eyetech Pharmaceuticals, Inc., the company developing Macugen, licensed from Isis specific patents necessary to develop, manufacture and commercialize Macugen. Under the license agreement, Isis receives royalties on sales of Macugen and milestones upon the approval of Macugen for new therapeutic indications. Macugen is approved for the treatment of wet age-related macular degeneration and is being investigated in clinical trials for diabetic macular edema.

Under the agreement, through 2009 DRC will receive royalties on the first \$500 million of annual sales of Macugen. Isis and DRC will each receive 50 percent of royalties on annual sales between \$500 million and \$1 billion. Isis retains 90 percent of all royalties on annual sales in excess of \$1 billion and 100 percent of all royalties after 2009.

Isis has retained all milestones payable to Isis by Eyetech under the license agreement. Isis has earned \$6 million in milestones to date from Eyetech in relation to the development of Macugen. Earlier this week, Isis earned a \$3 million milestone payment associated with the marketing clearance of Macugen by the U.S. Food and Drug Administration (FDA) for wet AMD. Also in 2004, Isis earned a \$1 million milestone payment from Eyetech associated with Eyetech's filing of a New Drug Application (NDA) for Macugen for wet AMD.

"We are very pleased to have completed this transaction with DRC. It allows us to accelerate a portion of the value we anticipate from our Macugen royalty and use the \$24 million to accelerate the development of our exciting pipeline of antisense drugs," said B. Lynne Parshall, Executive Vice President and Chief Financial Officer of Isis. "The transaction is structured to provide a near-term cash flow while retaining a substantial portion of the Macugen royalty going forward. We are excited about this drug and its prospects, and look forward to benefiting from its commercial success. The transaction with DRC not only allows us to accelerate cash from a portion of our Macugen royalty but also allows us to mitigate some of the risks associated with the timing and magnitude of commercial success of a new product."

"The DRC transaction is yet another example of the value Isis is realizing from our broad intellectual property position. Our significant oligonucleotide chemistry program and patents arising out of it should continue to provide significant licensing opportunities in the future," continued Ms. Parshall.

Isis has taken advantage of its work in RNA-based drug discovery and development to build the industry's leading intellectual property position in this field. While Isis continues to patent its inventions, the company actively leverages its intellectual property rights and seeks licensing partners.

### About Wet AMD and Macugen

Age-related macular degeneration (AMD) is the leading cause of severe vision loss in Americans age 65 years and over. The "wet" form of macular degeneration accounts for about 10 percent of all AMD cases. Macugen is a pegylated anti-vascular endothelial growth factor (VEGF) aptamer (an oligonucleotide) which binds to and thus inhibits the activity of VEGF. VEGF is a protein that plays a critical role in angiogenesis (the formation of new blood vessels) and increased permeability (leakage from blood vessels), two of the primary pathological processes responsible for the vision loss associated with wet AMD.

### About Isis Pharmaceuticals

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and for its partners. The company has successfully commercialized the world's first antisense drug and has 10 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases, and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,400 issued patents worldwide. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

### About Drug Royalty USA, Inc.

Drug Royalty USA, Inc. is a wholly owned subsidiary of Drug Royalty Corporation Inc., a leading specialty finance company providing royalty based financing to the life sciences industry. Since its founding in 1992, Drug Royalty has completed over 25 transactions to acquire a portfolio of royalty interests in pharmaceutical products and medical device technologies. Drug Royalty's business model is to monetize royalties on commercialized intellectual property owned by inventors, research and academic institutions, pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. For more information on the advantages of royalty financing, please visit the Drug Royalty web site at [www.drugroyalty.com](http://www.drugroyalty.com) or contact [info@drugroyalty.com](mailto:info@drugroyalty.com).

This press release includes forward-looking statements concerning Isis Pharmaceuticals and the potential of the company's intellectual property position and potential future payments to the company related to the success of Macugen. Any statement describing our goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology and in discovering and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such products. Actual results could differ materially from those discussed in this press 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 Isis' Annual Report on Form 10-K for the year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended September 30, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

Macugen® is a registered trademark of Eyetech Pharmaceuticals, Inc.

Ibis Therapeutics® is a registered trademark of Isis Pharmaceuticals, Inc.

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