Isis Pharmaceuticals and Rosetta Genomics Announce Joint Research Collaboration to Develop Micro-RNA Related Therapies for the Treatment of Liver Cancer

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Research Published in Cell Metabolism Demonstrates Therapeutic Potential of MicroRNA as a Drug Target Using Antisense

CARLSBAD, Calif. and REHOVOT, Israel, Feb 22, 2006 /PRNewswire via COMTEX News Network/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) and Rosetta Genomics Ltd., a privately held biopharmaceutical company that is developing microRNA-based diagnostic and therapeutic products, today announced a joint research collaboration to discover and develop antisense drugs that regulate microRNAs (miRNAs) for the treatment of the most prevalent type of liver cancer, hepatocellular carcinoma (HCC). The collaboration will bring together the complementary expertise of both companies in miRNA and leverage Rosetta's database of novel miRNA genes and Isis' expertise in oligonucleotide chemistry and antisense drug discovery and development.

MicroRNAs are naturally expressed small RNAs that play a critical role in many essential cellular functions in the body, including protein production, cell differentiation and cell death; abnormalities in miRNA function may play a role in human disease. Antisense drugs bind to complementary RNA sequences, such as miRNAs, inhibiting the function of miRNAs. Research recently conducted by Isis has shown that antisense inhibition is a powerful technique to regulate the function of miRNAs, which are naturally expressed small RNAs believed to play a central role in the progression of many forms of cancer and other serious illnesses.

"We believe miRNAs are most easily accessible using antisense technologies and look forward to working with Rosetta Genomics to discover antisense drugs targeted to miRNAs for the treatment of liver cancer," said C. Frank Bennett, Ph.D., Senior Vice President, Antisense Research at Isis. "Our recently published research demonstrates pharmacological activity in vivo using well validated antisense chemistry to inhibit miRNAs. We believe our collaborative efforts with Rosetta Genomics will enable both companies to take advantage of miRNAs as potential new drug targets for the treatment of a range of diseases, including liver cancer."

Isis recently published new research in the February 2006 issue of Cell Metabolism demonstrating that antisense inhibition is a powerful technique in regulating the function of miRNAs in the liver. To determine the role of miR-122 in the adult liver, Isis scientists inhibited miR-122 with an antisense oligonucleotide in mice. The antisense inhibition of miR-122 in normal and high fat-fed mice resulted in a significant improvement in numerous metabolic and cardiovascular risk factors as evidenced by reduced plasma cholesterol levels, increased hepatic fatty-acid oxidation, decreased hepatic fatty-acid and cholesterol synthesis rates and reduced fat in the liver (steatosis). These results implicate miR-122 as a key regulator of cholesterol and fatty-acid metabolism in the adult liver and suggest that miR-122 may be an attractive therapeutic target for cardiovascular and metabolic diseases.

"MiRNAs appear to regulate at least one-third of all gene expression and represent a new class of drug targets for the pharmaceutical industry," said Amir Avniel, President of Rosetta Genomics. "We are pleased to join forces with Isis and view antisense as the optimal platform for inhibiting miRNA function. Given the prevalence of HCC and the limited treatment options for patients with hepatocellular carcinoma, we are especially eager to begin working with Isis to discover and develop potential new treatment options for patients around the world."

ABOUT MicroRNA (miRNA)

MiRNA molecules are a recently discovered class of small RNA molecules that occur naturally within all mammalian cells and are critical in cell function in humans, animals, and plants. There are at least 330 confirmed miRNA genes in the human genome and there are many other predicted miRNAs remain yet to be confirmed. MiRNAs are believed to regulate at least one-third of genes in the human genome and are also likely play significant roles in the manifestation of many disease states, including cancer and many metabolic and infectious diseases.

ABOUT HEPATOCELLULAR CARCINOMA

Hepatocellular carcinoma is the most common primary cancer of the liver. Worldwide, hepatocellular carcinoma (HCC) is the third most common cause of cancer deaths in men and the seventh most common in women, according to the National Cancer Institute. A recent study published in the New England Journal of Medicine found that 95% of people with liver cancer die within five-years of diagnosis.

ABOUT ROSETTA GENOMICS

Rosetta Genomics Ltd., a private biopharmaceutical company with operations in the United States and Israel, is a world leader in the development of microRNA-based therapeutic and diagnostic agents. The company has developed a large and growing database of novel microRNA genes identified via its proprietary chip technology and computational algorithms. The company has filed several patents related to its novel microRNAs. Rosetta's current development endeavors include unique classes of microRNA agents with potential applications in the diagnosis and treatment of a wide range of diseases. For more information, please visit Rosetta Genomics at: http://www.rosettagenomics.com

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 11 antisense drugs in development to treat metabolic, cardiovascular, ocular and inflammatory diseases, and cancer. In its Ibis division, Isis is developing and commercializing the TIGER biosensor system, a revolutionary system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of approximately 1,500 issued patents worldwide. Additional information about Isis is available at http://www.isispharm.com.

This press release includes forward-looking statements regarding the research collaboration agreement between Isis and Rosetta Genomics to discover and develop antisense drugs that regulate miRNAs for the treatment of hepatocellular carcinoma. Any statement describing Isis' 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' goals. 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 in the endeavor of building a business around such products. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2004, and its quarterly report on Form 10-Q for the quarter ended September 30, 2005, which are on file with the SEC. Copies of these and other documents are available from the Company.

SOURCE Rosetta Genomics Ltd.

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