

Isis Pharmaceuticals Broadens Micro-RNA Drug Discovery Program With Support From Singapore Economic Development Board

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Singapore EDB Contributes to Isis' SARS Drug Discovery Program

CARLSBAD, Calif. and SINGAPORE, Nov. 3 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc., (Nasdaq: ISIS) announced today that it is broadening two RNA-based drug discovery and development programs: micro-RNA drug discovery and antisense drug discovery targeting the coronavirus associated with Severe Acute Respiratory Syndrome (SARS). The work in both of these programs will be supported by the Singapore Economic Development Board (EDB)'s Biomedical Sciences Group.

Micro-RNA Research

Isis is expanding its micro-RNA program by establishing a Singapore-based research effort to discover and identify the function of micro-RNAs and to design and optimize antisense inhibitors and small molecule drugs to therapeutically attractive micro-RNA targets. New drug candidates emerging from this work will be based on Isis' proprietary antisense and Ibis technologies.

"Micro-RNAs are an exciting new area of biological exploration and we are pleased that Isis, the leader in developing RNA-focused drugs, will conduct ground-breaking research in Singapore," said Philip Yeo, Co-Chairman, Singapore EDB. "Singapore offers biomedical science companies such as Isis an efficient means of accessing scientific talent and funding. We are committed to becoming a world center for biomedical science research."

"Early data on micro-RNA targets suggest they hold significant promise as a new class of drug targets. Since micro-RNA molecules are short strands of RNA, by their very nature they are ideal targets for antisense drugs. The combination of our expertise in RNA and the additional support by the EDB in Singapore will enable us to exploit this opportunity more fully. We also intend with this program to further extend our leadership position and our intellectual property position in RNA-based drug discovery," said C. Frank Bennett, Ph.D., Isis' Vice President of Antisense Research.

SARS Antisense Drug Discovery

In June 2003, the Industrial and Technology Research Institute (ITRI) of Taiwan committed \$2 million to Isis to discover antisense drugs against SARS. Isis' Singapore operation will be responsible for determining the safety profile of a SARS antisense drug discovered by Isis' SARS program.

"We are making good progress in our SARS-focused antisense drug discovery program, which we initiated with support from Taiwan earlier this year," said Dr. Bennett. "The addition of support from Singapore EDB enhances our opportunity to address this potentially important public health threat."

About Micro-RNAs

Micro-RNAs represent an emerging class of new drug targets. Micro-RNA molecules are small non-coding RNA gene products that are found in all diverse multi-cellular organisms. Researchers estimate that there are approximately 250 micro-RNA molecules in humans. One known role of micro-RNAs is the regulation of translation of specific target genes, but very few micro-RNA target genes have been identified to date. Micro-RNA molecules are approximately 22 nucleotides in length, and are derived from larger segments of "precursor" RNA. Isis views both the precursor RNA and the micro-RNA as potential interaction sites for antisense drugs. Precursor RNAs, which have structure, may represent attractive sights for binding small molecule drugs discovered through Ibis Therapeutics mass-spectrometry based screening technology.

About SARS

Severe acute respiratory syndrome (SARS) is a respiratory illness that has recently been reported in Asia, North America, and Europe. According to the World Health Organization, approximately 8,098 probable cases and 774 deaths from SARS have been reported worldwide as of September 26, 2003. Scientists from multiple laboratories throughout the world have detected a previously unrecognized coronavirus (called SARS CoV) in patients with SARS. This novel coronavirus is believed to be the cause of SARS. SARS symptoms include fever, headache, an overall feeling of discomfort, body aches, and respiratory symptoms, which may be mild or may become severe and life threatening. The primary way that SARS appears to spread is by close person-to-person contact.

Isis responded to the SARS outbreak by initiating an aggressive antisense drug discovery program. The company has synthesized approximately 200 antisense inhibitors to regions of the coronavirus sequences that are unchanged, or conserved, across all known SARS related sequences.

About Antisense Technology

Antisense inhibitors (antisense drugs) work at the molecular level by binding to messenger RNA to interrupt the process by which disease-related proteins are produced. Antisense inhibitors can be used as functional genomics tools or as drugs. The effects of antisense gene inhibition help identify what a gene does in a biological process (gene functionalization) and help determine whether a specific gene is a good target for drug discovery (target validation). The same antisense inhibitor that is used as a functional genomics tool can be scaled up and studied as a drug candidate in animals and ultimately tested in man in clinical trials, making antisense drug discovery very rapid and efficient. Antisense drugs can be designed to treat a wide range of diseases. Due to their gene selectivity, they have the potential to be highly effective and less toxic than traditional small molecule drugs.

About SINGAPORE ECONOMIC DEVELOPMENT BOARD (EDB)

EDB's Biomedical Sciences Group is responsible for the development of the Biomedical Sciences cluster and works closely with other Singapore government agencies to develop Singapore's human, intellectual, and industrial capital for Biomedical Sciences. The Singapore Economic Development Board is the lead agency that plans and executes strategies to develop Singapore as a thriving global hub for business and investment. It enables multinational and Singapore-based companies to establish value-creating operations in both manufacturing and international tradeable services sectors. Additional information about EDB's Biomedical Sciences initiative is available at www.biomed-singapore.com

About Isis Pharmaceuticals, Inc.

Isis Pharmaceuticals, Inc., is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has successfully commercialized the world's first antisense product, and has 11 antisense products in development. In the company's GeneTrove™ program, Isis uses antisense technology as a tool to determine the function of genes and uses that information to direct the company's internal drug discovery research and that of its corporate partners. Through its Ibis Therapeutics™ program, Isis is developing a novel diagnostic tool to detect infectious organisms and is focused on the discovery of 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 1,300 issued patents worldwide. Additional information about Isis is available at www.isispharm.com

This press release contains forward-looking statements concerning Isis' drug discovery and development programs in the area of micro-RNAs and for the treatment of SARS. Any statement describing a goal, expectation, intention or belief of Isis 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 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 on Form 10-Q for the period ended June 30, 2003, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

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