

Isis Pharmaceuticals Enters First Asthma Drug Into Development

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Inhaled Second-Generation Antisense Drug Inhibits Interleukin A Receptor Alpha (IL4R-alpha)

CARLSBAD, Calif., April 27 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it has initiated development activities on its first drug for the treatment of asthma and related pulmonary diseases. The drug, ISIS 369645, is a second-generation antisense inhibitor of the alpha subunit of the interleukin 4 receptor, IL4R-alpha. Inhibiting the production of the IL4R-alpha inhibits the activity of two important cytokines in asthma, IL4 and IL13, that regulate inflammation, mucus overproduction and airway hyperresponsiveness.

"We are very excited about taking our first inhaled antisense drug into clinical trials. ISIS 369645 is the first drug from our relatively new lung-directed inflammation program to enter development and shows how rapidly antisense technology enables the screening, validation and prioritization of gene targets and pre-clinical profiling of potential drug candidates," said C. Frank Bennett, Ph.D., Isis' Vice President of Antisense Research. "ISIS 369645 is one of many compounds that demonstrate unique pharmacological profiles in human inflammatory and pulmonary epithelial cells. Inhaled antisense has the potential to provide highly specific, potent and effective therapies for the treatment of asthma and other chronic pulmonary inflammatory diseases with the convenience of weekly administration."

Isis has created a significant data portfolio to support ISIS 369645 as an attractive local treatment for asthma in pre-clinical studies. Isis has shown that a mouse-optimized antisense inhibitor of IL4R-alpha:

- * potently reduces IL4R-alpha: mRNA and protein levels;
- * reduces lung cytokine production and inflammation, and airway hyperresponsiveness in mouse models of asthma; and
- * when delivered by inhalation, rapidly distributes to the airways and achieves therapeutic drug concentrations in multiple cell types with little systemic exposure.

Isis 369645 is one of numerous drug candidates Isis is examining to target inflammatory diseases of the lung and the first to enter clinical development. The attractive profile of Isis' proprietary second-generation antisense drugs for aerosol delivery is an example of Isis' efforts to investigate and develop new methods of delivering antisense drugs that broadens the therapeutic utility of the technology.

ABOUT ISIS PHARMACEUTICALS, INC.

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 11 antisense products in development to treat metabolic, cardiovascular and inflammatory diseases, and cancer. Through its Ibis division, Isis is developing a system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,500 issued patents worldwide. Additional information about Isis is available at <http://www.isispharm.com>.

This press release includes forward-looking statements regarding antisense technology, the development and therapeutic potential of antisense drugs to specific inflammation targets, and the success of Isis' inflammation drug discovery programs. 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 discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, in developing and commercializing technology and systems used to identify infectious agents, and in the endeavor of building a business around such products and services. Our forward-looking statements also involve assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. As a result, you are cautioned not to rely on these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in Isis' Annual Report on Form 10-K for the year ended December 31, 2004, which is on file with the U.S. Securities and Exchange Commission (SEC), and available from the Company.

SOURCE Isis Pharmaceuticals, Inc.
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