



Isis Pharmaceuticals Receives Another Important Antisense Patent

March 27, 2006

New U.S. Patent Strengthens Isis' Intellectual Property Estate and Exclusivity For Isis' Second-generation Drugs

CARLSBAD, Calif., March 27 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced the issuance of U.S. Patent 7,015,315 by the United States Patent and Trademark Office. This patent covers antisense drugs with modified sugars, frequently called "chimeric" oligonucleotides or "gapmers", including Isis' proprietary second-generation chemistry, generation 2.2 chemistry, and numerous other sugar-modified antisense compounds. This patent adds to Isis' several hundred U.S. patents that cover the chemistry and design of antisense compounds. Because this newly issued patent does not expire until March 2023, it significantly extends the duration of Isis' control over antisense drug chemistry and design, and most importantly, the patent life of Isis' second-generation antisense drugs. Isis and its partners currently have 12 second-generation antisense drugs in clinical development that are covered by the '315 U.S. Patent.

"Since our inception, we have focused on improving the properties of antisense drugs through medicinal chemistry," said B. Lynne Parshall, Executive Vice President and CFO of Isis Pharmaceuticals. "Our extensive patent portfolio is evidence that we aggressively protect our innovations and this patent is the most recent example. The '315 patent covers modifications to antisense oligonucleotides that provide improved drug properties. Most importantly, it provides another layer of patent protection for Isis' proprietary second-generation chemistry. This patent effectively extends the period of protection of our second-generation drugs, creating extremely valuable commercial opportunities."

As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of approximately 1,500 issued patents worldwide. Isis' extensive patent estate provides effective coverage of most oligonucleotide chemistries, the designs of antisense drugs, mechanisms by which antisense drugs work, specific drugs and gene targets, manufacturing and analytical methods and formulations.

ABOUT ISIS' SECOND-GENERATION CHEMISTRY

Second-generation antisense drugs that contain 2'-O-methoxyethyl or 2'MOE sugar modifications are composed of both RNA-like and DNA-like nucleotides while first-generation antisense drugs are entirely DNA-like. Because RNA hybridizes more tightly to RNA than to DNA, second-generation antisense drugs have a greater affinity for their RNA targets. In addition, the sugar modifications make these second-generation compounds more resistant to degradation and therefore, longer acting in the body. Second-generation antisense compounds have proven to be more potent and potentially safer than previous generations of antisense drugs, and have the potential to be less expensive and more convenient for patients, which significantly strengthens each drug's competitive profile.

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 13 antisense drugs in development to treat cardiovascular, metabolic, inflammatory and ocular 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 www.isispharm.com.

This press release contains forward-looking statements concerning Isis Pharmaceuticals and the potential of the Company's intellectual property position and drugs. 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, 2005, which is on file with the U.S. Securities and Exchange Commission (SEC) and available from the Company.

SOURCE: Isis Pharmaceuticals, Inc.

03/27/2006

CONTACT: Corporate Communications Navjot Rai of Isis Pharmaceuticals,
Inc., +1-760-603-2331

Web site: <http://www.isispharm.com>
(ISIS)