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ISIS PHARMACEUTICALS LICENSES ANTI-HIV DRUG TO IMQUEST PHARMACEUTICALS

*ImQuest Plans to Develop ISIS 5320 as a Topical Microbicide Therapy to Prevent the
Sexual Transmission of HIV*

Frederick, MD, and Carlsbad, Calif., USA, April 19, 2006 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) and ImQuest Pharmaceuticals Inc. announced today that Isis has granted an exclusive worldwide license to ImQuest for the development and commercialization of ISIS 5320, a compound that has been shown *in vitro* and *in vivo* to be a potent and specific inhibitor of HIV, the virus that causes AIDS. ImQuest plans to develop ISIS 5320 as a topical microbicide therapy to prevent the sexual transmission of HIV throughout the world, but especially in developing countries.

ISIS 5320, a phosphorothioate oligonucleotide, specifically and potently inhibits the attachment of HIV to target cells by interfering with the interaction of the HIV receptor gp120 with CD4 on target cells. The safety of ISIS 5320 has been demonstrated in human clinical trials as a therapeutic treatment for systemic HIV infection and thus ImQuest projects that the time to develop the agent as a microbicide will be significantly shortened, allowing the microbicide to enter human clinical trials in early 2007. ImQuest is also exploring the use of ISIS 5320 in combination with other microbicide products in their drug portfolio. ImQuest expects to file a new Investigational New Drug Application (IND) with the FDA in the fourth quarter of 2006.

“ImQuest Pharmaceuticals and ImQuest BioSciences have significant experience with the preclinical and clinical development of topical microbicides to inhibit the sexual transmission of HIV,” states Dr. Robert W. Buckheit, Jr., President and Chief Scientific Officer at ImQuest Pharmaceuticals. “Our Company is dedicated to playing a major role in the humanitarian global effort to develop an effective female controlled preventive therapy that will result in decreased incidence of HIV transmission, especially in developing countries of Africa and Southeast Asia. ISIS 5320 is one of a series of novel microbicides that we believe will provide significant therapeutic options for women when used as a single-agent or in combination with other drugs.”

“Licensing ISIS 5320 to ImQuest will allow us to benefit from ImQuest’s expertise and highly focused research efforts in anti-HIV therapeutics, while ImQuest will benefit from our experience in oligonucleotide drug development and access to our intellectual property,” said C. Frank Bennett, Ph.D., Senior Vice President, Research at Isis Pharmaceuticals. “This transaction with ImQuest is yet another example of our successful satellite company strategy, where we gain from a partner’s knowledge in concentrated research programs and we grant our partner access to our expertise in RNA-based drug development and access to our proprietary chemistries and leading patent estate. Through these relationships, we are expanding the reach and potential of our discoveries in RNA-based therapeutics and participating in the success of multiple companies and products.”

As part of the agreement, ImQuest Pharmaceuticals will have sole responsibility for clinical development and commercialization of the drug and will pay Isis royalties on product sales.

ABOUT ISIS 5320

ISIS 5320 is a phosphorothioate oligonucleotide that acts by a novel non-antisense mechanism to prevent viral replication. ISIS 5320 forms a stable tetrameric structure which directly interacts with the gp120 protein envelope glycoprotein of HIV and prevents the critical interaction of gp120 with the CD4 receptor on human target cells. In order for HIV to infect human cells, the virus must attach to the human cells via the binding of gp120 to CD4, initiating events leading to the fusion of the viral and cellular membranes and introduction of the infectious virus into the cell. ISIS 5320 specifically interacts with the V3 loop of gp120, a highly conserved and essential region involved in virus attachment and fusion. The positively charged nature of the V3 loop is believed to be essential for mediation of fusion between the two negatively charged cell membranes. ISIS 5320 is negatively charged and its binding to the V3 loop effectively prevents virus-to-cell and cell-to-cell transmission.

ABOUT HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Acquired Immunodeficiency Syndrome (AIDS) was first reported in the United States in 1981 and has since become a major worldwide epidemic. AIDS is caused by the Human Immunodeficiency Virus (HIV). By killing or damaging cells of the body's immune system, HIV progressively destroys the body's ability to fight infections and certain cancers. People diagnosed with AIDS may get life-threatening diseases called opportunistic infections, which are caused by microbes such as viruses or bacteria that usually do not make healthy people sick.

According to the latest report from The Joint United Nations Programme on HIV/AIDS (UNAIDS) in 2005, over 25 million people have died since the first case of AIDS was identified in 1981 and the number of people living with HIV worldwide continues to expand—from 35 million in 2001 to an estimated 40 million in 2005. In 2005, an estimated 3.8 million human deaths were attributed to AIDS worldwide. The rate of HIV infection and AIDS related deaths is projected to increase over the course of the next decade with rapid expansion in Asia, Africa, and Eastern Europe. The epidemic is not limited to underdeveloped and low to middle income countries as the rate of HIV-infection has also risen in the United States and Western Europe.

ABOUT IMQUEST PHARMACEUTICALS, INC.

ImQuest Pharmaceuticals, Inc. is a leading developer of novel therapeutic agents for the treatment of infectious diseases, cancer and inflammation. Founded in 2005, ImQuest's mission is to develop novel therapeutic agents which target under-explored disease pathways, develop molecules with highly unique properties that enhance drug potency, and develop highly potent topical microbicides for the inhibition of sexually transmitted disease. ImQuest's lead candidates for HIV therapy, microbicide treatment and cancer are in late preclinical development. It is expected that the company will initiate clinical testing on three infectious disease treatments and two cancer therapies in 2007. More information about ImQuest BioSciences and ImQuest Pharmaceuticals can be found at the company's websites at www.imquest.com and www.imquestpharma.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 15 drugs in development to treat cardiovascular, metabolic, inflammatory and ocular diseases, and cancer. In its Isis 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 includes forward-looking statements regarding Isis Pharmaceuticals and ImQuest's licensing agreement and the development, therapeutic potential and safety of ISIS 5320 as a topical microbicide therapy to prevent the sexual transmission of HIV. 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.

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