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ISIS TO RECEIVE UP TO \$9.9 MILLION IN FUNDING TO DISCOVER AND DEVELOP AN ANTISENSE DRUG FOR HUNTINGTON'S DISEASE

CARLSBAD, Calif., October 26, 2007 – Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that CHDI, Inc. (CHDI), a non-profit foundation pursuing treatments for Huntington's Disease (HD), will provide up to \$9.9 million in funding to Isis for the discovery and development of an antisense drug for the treatment of HD, a fatal neurodegenerative disease. CHDI's funding builds upon an earlier successful collaboration between Isis and CHDI, in which CHDI provided Isis with funding for studies that demonstrated the feasibility of using antisense drugs to treat HD.

CHDI will provide Isis with up to \$9.9 million in funding over three years to identify and conduct IND-enabling studies on an antisense drug targeting the huntingtin gene. Mutations in the huntingtin gene are responsible for the production of the abnormal Huntingtin protein, which ultimately leads to onset and progression of the neurodegenerative disease. Upon completion of IND-enabling studies, Isis and CHDI will continue to collaborate to ensure that any resulting drugs will be broadly available to HD patients and Isis has the right to continue clinical development of those drugs arising from the collaboration.

"We are pleased to expand our relationship with CHDI to identify a potential new therapy for Huntington's Disease, a condition for which there are limited treatment options available. Through several collaborative efforts, we have been focusing on the use of antisense drugs to inhibit production of central nervous system targets including Huntingtin. With ISIS 333611, our drug targeting SOD1 for a hereditary form of ALS, we have demonstrated in rodents that direct delivery of an antisense drug to the spinal fluid via an implantable pump effectively reduces SOD1 RNA and protein. This partnership with CHDI complements our work in ALS, and should enable us to create additional antisense drugs for central nervous system targets," said C. Frank Bennett, Ph.D., Senior Vice President of Research at Isis Pharmaceuticals, Inc.

Under the previous research contract with CHDI, Isis scientists demonstrated a reduction in Huntingtin protein expression in both brain and peripheral tissues of normal mice using Isis' proprietary second-generation antisense oligonucleotides. In addition, the inhibition of normal Huntingtin expression was well tolerated. These positive results by Isis have led to this expansion of the collaborative efforts between Isis and CHDI to identify a drug development candidate for the treatment of HD.

ABOUT HUNTINGTON'S DISEASE (HD)

HD is a familial disease, passed from parent to child through a mutation in huntingtin gene that leads to the production of a variant of the Huntingtin protein. Inhibiting production of the Huntingtin protein is predicted to provide a therapeutic benefit in the treatment and/or prevention of HD. Each child of a HD parent has a 50-50 chance of inheriting the disease-inducing form of the huntingtin gene, which causes programmed degeneration of brain cells and results in emotional disturbance, loss of intellectual faculties and uncontrolled movements. Most people with HD develop the symptoms at midlife but in some people

onset occurs in infancy or old age. The average survival time after onset is approximately fifteen to twenty years. It is estimated that about one in every 10,000 persons has the disease-inducing form of the huntingin gene. At this time, there is no way to stop or reverse the course of HD.

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 18 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing drugs for a wide variety of diseases. Ibis Biosciences, Inc., Isis' wholly owned subsidiary, is developing and commercializing the Ibis T5000™ 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 over 1,500 issued patents worldwide, and Isis is a joint owner of Regulus Therapeutics, LLC, a company focused on the discovery, development and commercialization of microRNA therapeutics. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding Isis' plans for discovery and development of antisense drugs for Huntington's disease and other neurodegenerative disorders, and about its collaboration with CHDI. Any statement describing Isis' goals, expectations, financial or other projections, 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, 2006, and its quarterly report on Form 10-Q for the quarter ended June 30, 2007, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

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