

Isis Pharmaceuticals Reports Clinical Development Goals

February 9, 2006

Key Data Milestones for Cholesterol and Diabetes Drugs Expected This Year

CARLSBAD, Calif., Feb. 9 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), today announced its clinical development goals. Financial guidance and results for 2005 will be reported on March 9, 2006.

"In 2006, we expect results from key clinical trials on our two most important assets, ISIS 301012 and ISIS 113715," said Mark Wedel, M.D., J.D., Senior Vice President of Development and Chief Medical Officer at Isis Pharmaceuticals. "The data on these two drugs will allow us to more fully understand their potential profile and guide our strategy for the future development path of our entire pipeline."

Isis' Clinical Development Programs and Goals

ISIS 301012 (Targeting apoB-100 for the treatment of high cholesterol)

In Phase 1 trials, ISIS 301012 produced impressive, dose-dependent, statistically significant, long-lasting reductions in apoB-100, LDL-C, VLDL, total cholesterol and triglycerides.

Studies in patients with high cholesterol

- * Report single agent Phase 2 data (2Q06)
- Demonstrate safety and activity as a single agent after 3 months of treatment

- Define dose and schedule for longer term studies

* Report Phase 2 combination studies (4Q06)

- Demonstrate safety and activity in combination with statins

- Define minimal effective dose and schedule as a combination agent

* Report Phase 1 drug-drug interaction studies (1H06)

* Initiate longer-term Phase 2 studies (4Q06/1Q07)

* Continue to define profile upsides

Studies in patients with familial hypercholesterolemia (FH)

* Advance toward early commercialization in the 2008/2009 timeframe

- Demonstrate preliminary activity and safety in FH and define dose to support registration trials (4Q06)

ISIS 113715 (Targeting PTP1-B for the treatment of type 2 diabetes)

In an ongoing Phase 2 monotherapy trial, ISIS 113715 improved glucose control in patients with type 2 diabetes, did not cause hypoglycemia and was well tolerated. Data in animals further support a unique profile of ISIS 113715 in combination with oral anti-diabetic drugs.

* Report single agent Phase 2 data in patients with type 2 diabetes (at the American Diabetes Association meeting in June)

- Report final results demonstrating safety and activity after 6 weeks treatment

- Report initial results demonstrating safety and activity after 12 weeks treatment

* Initiate mechanistic study in patients with type 2 diabetes (2Q06)

* Initiate combination trials with other anti-diabetic agents (2Q06)

Alicaforsen enema (Targeting ICAM-1 for the treatment of ulcerative colitis)

In five Phase 2 trials, alicaforsen enema, a first-generation antisense drug, was safe and effective and produced prolonged effects in patients with ulcerative colitis.

* Partner and prepare to initiate a Phase 3 program (2H06)

Partner Pipeline

Milestones projected for our partnered drugs:

OncoGenex

OGX-011 (Targeting Clusterin for the treatment of breast, prostate and lung cancers)

* Advance four Phase 2 clinical trials

* Report Phase 1 data in NSCLC (2Q06)

Eli Lilly

LY2181308 (Targeting Survivin for the treatment of cancer)

* Initiate Phase 2 clinical trials (4Q06)

LY2275796 (Targeting eIF-4E for the treatment of cancer)

* Progress Phase 1 clinical trials in patients with cancer

Antisense Therapeutics Limited

ATL-1102 (Targeting VLA4 for the treatment of Multiple Sclerosis)

* Progress Phase 2 studies in patients with Multiple Sclerosis

iCo Therapeutics

iCo 007 (Targeting c-raf kinase for the treatment of eye diseases)

* Initiate Phase 1 clinical trials (4Q06/1Q07)

Isis will conduct a live webcast conference call to discuss this press release on Friday, February 10 at 8:30am Eastern time. To participate over the Internet go to <http://www.videonewswire.com/event.asp?id=32301> or <http://www.isispharm.com/>. A replay of the webcast will be available at these addresses for a limited time.

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 12 antisense drugs in development to treat metabolic, cardiovascular, ocular and inflammatory 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 includes forward-looking statements regarding Isis Pharmaceuticals' clinical development goals and the therapeutic and commercial potential of the Company's products in development. 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, 2004, and its quarterly report on Form 10-Q for the quarter ended September 30, 2005, which are on file with the SEC. Copies of these and other documents are available from the Company.

SOURCE Isis Pharmaceuticals, Inc.

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