Mipomersen Phase 3 Study in Patients with Heterozygous Familial Hypercholesterolemia Meets Primary Endpoint

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28 Percent LDL-C Reduction in High-Risk Patient Population

CAMBRIDGE, Mass. & CARLSBAD, Calif., Feb 10, 2010 (BUSINESS WIRE) -- Genzyme Corp. (NASDAQ: GENZ) and Isis Pharmaceuticals Inc. (NASDAQ: ISIS) today announced that the phase 3 study of mipomersen in patients with heterozygous familial hypercholesterolemia (heFH) met its primary endpoint with a highly statistically significant 28 percent reduction in LDL-cholesterol after 26 weeks of treatment, compared with an increase of 5 percent for placebo.

All of the 124 patients in the study had pre-existing coronary artery disease, were taking a maximally tolerated dose of a statin and in many cases additional lipid-lowering drugs. Patients’ average LDL-C at baseline was 150 mg/dL. Patients treated with mipomersen had an average LDL-C level of 104 mg/dL at the end of the study.

Forty-five percent of the mipomersen-treated patients achieved LDL-C levels of less than 100 mg/dL, a recognized treatment goal for high-risk patients. The reductions observed in the study were in addition to those achieved with the patients' existing therapeutic regimens.

"The average reduction in LDL-C of 28 percent in these high-risk, difficult-to-treat patients with severe inherited high cholesterol is very encouraging," said Evan A. Stein, M.D., Ph.D., Director of the Metabolic & Atherosclerosis Research Center, Cincinnati, Ohio, and an investigator on the study. "The nearly 50 mg/dL additional decrease in LDL-C when added to maximally tolerated statin therapy is above what we have seen with any other agent in this population, and the side effect profile of mipomersen continues to be acceptable."

The trial also met each of its three secondary endpoints with statistically significant reductions in apo-B, total cholesterol, and non-HDL-cholesterol. Study results are based on an intent-to-treat analysis (full analysis set). Data will be submitted for presentation at a future medical meeting.

"We are excited by these strong data in the second phase 3 trial of mipomersen," said Genzyme Chief Medical Officer Richard A. Moscicki, M.D. "This therapy has the potential to make a major difference in the lives of patients who are in great need of new treatment options. With these data, we remain on-track with our development plan for mipomersen."

There were no new areas of safety concerns identified in the trial. Of the 83 patients treated with mipomersen, 73 completed the study; nine of the discontinuations were related to adverse events. Consistent with previous studies evaluating mipomersen, the most commonly observed adverse events were injection site reactions and flu-like symptoms.

As in other mipomersen trials, elevations in liver transaminases were observed that were similar in magnitude and duration to those seen in other studies. None of these patients had changes in other laboratory tests to indicate hepatic dysfunction, and there were no Hy's Law cases.

"Mipomersen has again delivered positive results with this second phase 3 study, and continues to make progress toward the market," said Stanley Crooke, Chairman and Chief Executive Officer of Isis Pharmaceuticals. "Mipomersen represents the power of antisense technology and reflects our commitment to innovation and technological advancement to create potent and specific drugs to help people lead healthier and more hopeful lives."
The study was a randomized, double-blind, placebo-controlled trial that enrolled 124 heFH patients, aged 18 and older with LDL-C levels greater than 100 mg/dL. Patients were randomized 2:1 to receive a 200 mg dose of mipomersen or placebo weekly for 26 weeks. The trial was conducted at 26 sites in the United States and Canada.

Late-Stage Development Plan

Genzyme's initial U.S. and E.U. regulatory filings for mipomersen will seek marketing approval for the treatment of patients with homozygous FH (hoFH). The phase 3 study of mipomersen in hoFH met its primary endpoint with a 25 percent reduction in LDL-C, and results were presented at the annual American Heart Association meeting in November. In the first half of 2011, Genzyme expects to file for U.S. and E.U. approval of the treatment and to have made progress toward filing in other major international markets.

These two filings may also include patients with severe hypercholesterolemia. A phase 3 study of mipomersen in patients with severe hypercholesterolemia is fully enrolled with 58 patients and data are anticipated in mid-2010. The companies have also completed enrollment in a phase 3 trial involving 158 hypercholesterolemic patients at high risk for coronary heart disease, and data are anticipated in mid-2010.

About Mipomersen

Mipomersen is a first-in-class apo-B synthesis inhibitor currently in late-stage development. It is intended to reduce LDL-C by preventing the formation of atherogenic lipids. It acts by decreasing the production of apo-B, which provides the structural core for all atherogenic lipids, including LDL-C, which carry cholesterol through the bloodstream.

About Familial Hypercholesterolemia

FH is a genetic disorder that results in elevated LDL cholesterol levels. FH patients are unable to properly metabolize LDL-C due to dysfunctional LDL receptors, which are responsible for clearing LDL from plasma. These patients experience a markedly increased risk of premature cardiovascular disease (CVD) and CVD-related death.

There are two forms of FH: homozygous (hoFH), where a defective gene is inherited from both parents, or heterozygous (heFH), where a defective gene is inherited from only one parent so that some LDL receptor function is preserved. HoFH is a very rare condition estimated to affect approximately one in a million people worldwide. HeFH is a more common form of the disorder, with a prevalence of approximately one in 500.

About Genzyme

One of the world's leading biotechnology companies, Genzyme is dedicated to making a major positive impact on the lives of people with serious diseases. Since 1981, the company has grown from a small start-up to a diversified enterprise with more than 12,000 employees in locations spanning the globe and 2009 revenues of approximately $4.5 billion.

With many established products and services helping patients in approximately 100 countries, Genzyme is a leader in the effort to develop and apply the most advanced technologies in the life sciences. The company's products and services are focused on rare inherited disorders, kidney disease, orthopaedics, cancer, transplant and immune disease, and diagnostic testing. Genzyme's commitment to innovation continues today with a substantial development program focused on these fields, as well as cardiovascular disease, neurodegenerative diseases, and other areas of unmet medical need.

Genzyme's press releases and other company information are available at http://www.genzyme.com and by calling Genzyme's investor information line at 1-800-905-4369 within the United States or 1-678-999-4572 outside the United States.
About Isis

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 22 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic, and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alnylam Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,600 issued patents worldwide. Additional information about Isis is available at [http://www.isispharm.com](http://www.isispharm.com).

Genzyme Safe Harbor Statement

This press release contains forward-looking statements regarding Genzyme's future business plans and strategies including, without limitation, statements about the presentation of the data from the phase 3 clinical study of mipomersen in patients with heterozygous familial hypercholesterolemia; the expected timing of the mipomersen development plan and regulatory filings; and the potential uses and benefits of mipomersen. These statements are subject to risks and uncertainties that could cause actual results to differ materially from those forecasted. These risks and uncertainties include, among others: the actual timing of the completion of the analysis of the clinical study results; Genzyme's ability to accurately understand and predict the outcome and impact of its clinical studies related to mipomersen; Genzyme's ability to continue to support its clinical and other development efforts related to mipomersen; the actual efficacy and safety of mipomersen; the outcome of discussions with regulatory authorities regarding clinical studies of mipomersen; and the risks and uncertainties described in Genzyme's SEC reports filed under the Securities Exchange Act of 1934, including the factors discussed under the caption "Risk Factors" in Genzyme's Annual Report on Form 10-Q for the period ended September 30, 2009. Genzyme cautions investors not to place substantial reliance on the forward-looking statements contained in this press release. These statements speak only as of the date of this press release and Genzyme undertakes no obligation to update or revise the statements.

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Isis Safe Harbor Statement

This press release includes forward-looking statements regarding Isis' collaboration with Genzyme Corporation, its financial and business development activities, and the development, activity, therapeutic potential and safety of mipomersen in treating patients with high cholesterol. 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. 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, 2008, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

Isis Pharmaceuticals is a registered trademark of Isis Pharmaceuticals, Inc. Regulus Therapeutics is a trademark of Regulus Therapeutics Inc.
Conference Call Information
At 8:30 a.m. Eastern Time today, Isis will conduct a live webcast conference call to discuss the results of the phase 3 mipomersen study in heFH patients. Interested parties may listen to the call by dialing 866-831-6272 and refer to passcode "ISIS 2010," or access the webcast at http://www.isispharm.com. A webcast replay will be available for a limited time at the same address.

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