

PRESS RELEASE



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Data from Two Mipomersen Phase 3 Trials Presented at ACC

- Study in Patients with Severe Familial Hypercholesterolemia Meets Primary Endpoint with 36 Percent LDL-C Reduction -

Paris, France - Cambridge, Massachusetts, and Carlsbad, California – April 5, 2011 – Genzyme (NASDAQ: GENZ), a subsidiary of sanofi-aventis Group (EURONEXT: SAN and NYSE: SNY), and Isis Pharmaceuticals Inc. (NASDAQ: ISIS) announced today that data from two phase 3 studies of mipomersen in patients who had high cholesterol levels while on lipid-lowering therapy were presented at the American College of Cardiology's 60th Annual Scientific Session.

In the study in patients with severe heterozygous familial hypercholesterolemia (heFH), mipomersen reduced LDL-C, the primary endpoint, by 36 percent compared with a 13 percent increase for placebo ($p < 0.001$). This study, which was presented today by Jean-Claude Tardif, M.D., of the Montreal Heart Institute, Montreal, Canada, also met each of its secondary endpoints. Frequently observed adverse events were injection site reactions, flu-like symptoms and elevations in liver transaminases, as seen in previous studies.

"We are excited about the potential of mipomersen to help these patients, who are in great need of new treatment options," said Paula Soteropoulos, Vice President and General Manager of Genzyme's cardiovascular business. *"We are committed to advancing our mipomersen development and commercialization plan to bring this uniquely targeted treatment to these patients, who are left behind by current treatments."*

This double-blind, placebo-controlled trial included 58 patients with severe heFH, who were already taking maximally tolerated lipid-lowering medications. Severe heFH patients were defined as those who had LDL-C levels ≥ 300 mg/dL or those who had LDL-C levels ≥ 200 mg/dL with coronary heart disease (CHD) or other forms of clinical atherosclerotic disease. Patients were randomized 2:1 to receive a self-administered 200 mg subcutaneous injection of mipomersen or placebo weekly for 26 weeks. This study was conducted at 26 sites in North America, Europe and South Africa.

Patients treated with mipomersen had an average LDL-C at baseline of 276 mg/dL. At the end of the trial, these patients had an average LDL-C level of 175 mg/dL, representing an average LDL-C reduction of 101 mg/dL (36 percent). The reductions observed in the study were in addition to those achieved with the patients' existing maximally tolerated lipid-lowering regimens.

Patients treated with mipomersen also experienced reductions in other atherogenic lipids, including: a 36 percent reduction in apolipoprotein B (apo-B) compared with an 11 percent increase for placebo; a 33 percent reduction in lipoprotein a (Lp(a)) compared with a 1 percent reduction for placebo; a 34 percent reduction in non-HDL-cholesterol compared with a 14 percent increase for placebo; and a 28 percent reduction in total cholesterol compared with an 11 percent increase for placebo (all $p < 0.001$). Study results are based on an intent-to-treat analysis (full analysis set).

Of the 39 patients treated with mipomersen, 27 completed treatment; of the 19 patients treated with placebo, 18 completed treatment. Eight of the discontinuations in the mipomersen group were reported as being related to adverse events, the nature of which was generally similar to previous studies. The placebo discontinuation was reported as being related to an adverse event. The most common adverse events were injection site reactions (90 percent mipomersen; 32 percent placebo) and flu-like symptoms (46 percent mipomersen; 21 percent placebo.) There was one death in the study due to acute coronary syndrome in a patient treated with mipomersen.

Elevations in liver transaminases (ALTs) in patients treated with mipomersen were observed that were generally similar in character with those seen in other studies. In this study, 15 percent of mipomersen patients had persistent ALT elevations above 3X ULN (three times the upper limit of normal) during the treatment period. Persistent is defined as consecutive elevations at least one week apart. No patients had changes in laboratory tests indicative of clinically significant hepatic dysfunction, and there were no Hy's Law cases. In general, increases in ALT levels appeared to be associated with rapid and larger drops in LDL-C.

"There remains a significant unmet medical need for new lipid-lowering therapies for patients such as those included in this study," said Mary McGowan, M.D., of the Concord Hospital Cholesterol Treatment Center, Concord, N.H. *"These are patients who are on maximally tolerated doses of currently available treatments, and still very far from appropriate target goals, leaving them at high risk of cardiovascular events. These patients have a need for additional lipid lowering, which mipomersen could potentially provide."*

Results of a Phase 3 study of mipomersen in patients with high cholesterol at high risk for CHD were also presented in a poster at ACC. In this study, mipomersen reduced LDL-C, the primary endpoint, by 37 percent compared with a 5 percent reduction for placebo ($p < 0.001$). The study, which was presented by William Cromwell, M.D., of the Presbyterian Cardiovascular Institute, Charlotte, N.C., also met each of its secondary endpoints.

This double-blind, placebo-controlled trial included 158 patients with hypercholesterolemia (LDL-C \geq 100 mg/dL) and at high risk of developing CHD who were taking a maximally tolerated dose of a statin. Patients were randomized 2:1 to receive a self-administered 200 mg subcutaneous injection of mipomersen or placebo weekly for 26 weeks.

Patients treated with mipomersen had an average LDL-C at baseline of 123 mg/dL. At the end of the study, these patients had an average LDL-C level of 75 mg/dL, representing an average LDL-C reduction of 48 mg/dL (37 percent). Half of the mipomersen-treated patients achieved LDL-C levels of less than 70 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 maximally tolerated statin regimens. Patients treated with mipomersen also experienced statistically significant reductions in apo-B, Lp(a), non-HDL-cholesterol and total cholesterol. Study results are based on an intent-to-treat analysis (full analysis set).

Of the 105 patients treated with mipomersen, 60 completed treatment; of the 53 patients treated with placebo, 44 completed treatment. Twenty-six of the discontinuations in the mipomersen group were reported as being related to adverse events, the nature of which was generally similar to previous studies. Two of the discontinuations in the placebo group were reported as being related to adverse events. The most common adverse events were injection site reactions and flu-like symptoms. There was one death during the on-treatment study period due to acute myocardial infarction in a patient treated with placebo. During the post-treatment follow-up period, one patient died due to liver failure, acetaminophen toxicity, pneumonia and myocardial infarction 149 days after receiving the last dose of mipomersen treatment.

Elevations in ALTs in patients treated with mipomersen were observed that were generally similar in character with those seen in other studies. In this study, 10 percent of patients had persistent ALT elevations above 3X ULN during the treatment period. Persistent is defined as consecutive elevations at least one week apart. As measured by MRI, mipomersen-treated patients had a moderate increase in liver fat from baseline compared with placebo-treated patients. In general, increases in liver transaminases and liver fat appeared to be associated with the greatest reductions of LDL-C, and in the six-month follow-up period after treatment was discontinued, returned toward baseline along with all lipids, including LDL-C, apo-B and Lp(a).

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.

Genzyme and Isis have completed the four Phase 3 studies that are planned to be included in the initial U.S. and EU filings for marketing approval of mipomersen. As previously reported, the Phase 3 study of mipomersen in homozygous (ho) FH patients met its primary endpoint with 25 percent LDL-C reduction, and the Phase 3 study in heFH patients met its primary endpoint with a 28 percent LDL-C reduction.

Genzyme expects to file for EU marketing approval of mipomersen for the treatment of patients with hoFH and severe heFH in the first half of this year. Genzyme also expects to file for U.S. approval for the hoFH indication in the second half of this year.

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 24 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 has designed and executed a patent strategy that has provided the Company with strong and extensive protection for Isis' drugs and technology. Additional information about Isis is available at www.isispharm.com.

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 its founding in 1981, the company has introduced breakthrough treatments across several areas of medicine that have provided new hope for patients. Today, approximately 10,000 Genzyme employees serve patients in nearly 100 countries.

Genzyme's products are focused on rare inherited disorders, kidney disease, orthopaedics, cancer, transplant, and immune disease. The company'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 is part of the sanofi-aventis Group.

About sanofi-aventis

Sanofi-aventis, a leading global pharmaceutical company, discovers, develops and distributes therapeutic solutions to improve the lives of everyone. Sanofi-aventis is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

Isis Forward Looking Statements

This press release includes forward-looking statements regarding Isis' collaboration with Genzyme Corporation, its financial and business development activities, and the development, activity, therapeutic and commercial 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 drugs. 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, 2010, which is on file with the SEC. Copies of this 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.

Genzyme Forward Looking Statements

This press release contains forward-looking statements regarding Genzyme's business plans and strategies regarding mipomersen including, without limitation, statements about its potential uses, the expected timing of regulatory filings in the U.S. and E.U. and the studies that are expected to form the basis of the regulatory filings. 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: that regulatory authorities determine additional clinical studies of mipomersen are needed to support a 2011 filing; that Genzyme is unable to reach agreement with regulatory authorities regarding additional clinical studies; that Genzyme is unable to continue to support its clinical and other development efforts related to mipomersen; that regulatory authorities determine mipomersen's safety profile does not support approval for treatment of any or all of the targeted population; 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-K for the period ended December 31, 2010. Genzyme cautions investors not to place undue 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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Sanofi-aventis Forward Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although sanofi-aventis' management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of sanofi-aventis, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the

FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such products candidates, the absence of guarantee that the products candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, the Group's ability to benefit from external growth opportunities as well as those discussed or identified in the public filings with the SEC and the AMF made by sanofi-aventis, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in sanofi-aventis' annual report on Form 20-F for the year ended December 31, 2010. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.