



Mipomersen Data Presented at European Atherosclerosis Society Congress

- Phase 3 Studies Highlight Investigational Drug's Potential in Lowering Lp(a) and Reducing Necessity for Lipid-Apheresis -

Paris, France, and Carlsbad, California – June 28, 2011 – Genzyme, a Sanofi company (EURONEXT: SAN and NYSE: SNY), and Isis Pharmaceuticals Inc. (NASDAQ: ISIS) announced today that two additional analyses from phase 3 studies of mipomersen were presented at the 79th European Atherosclerosis Society (EAS) Congress.

In a presentation entitled *“Mipomersen, A First-in-Class ApoB Synthesis Inhibitor, Lowers Lp(a) in Patients with Heterozygous Familial Hypercholesterolemia (HeFH) and High Baseline Lp(a): Results from two Phase 3 studies,”* Elisabeth Steinhagen-Thiessen, M.D., of the Lipid Ambulatory Clinic, University of Berlin, Germany, focused on the effects of mipomersen on elevated Lp(a) levels.

Lp(a) is an independent risk factor for heart disease and cardiovascular events. Elevated Lp(a) levels are recognized to have a strong genetic component and are particularly common in people with familial hypercholesterolemia (FH). The EAS consensus panel recommended screening and treatment for elevated Lp(a) in 2010, and the U.S.-based National Lipid Association's expert panel on FH published guidance this year noting that having elevated Lp(a) levels places FH patients at very high cardiovascular risk.

Data from two randomized, placebo-controlled phase 3 trials in patients with HeFH showed that mipomersen reduced Lp(a), LDL-C, and other measures of atherogenic lipoproteins when added to existing lipid-lowering therapy. One study included 124 HeFH patients with CAD, and the other included 58 severe HeFH patients. All of the patients were already taking a maximally tolerated dose of a statin, as well as additional lipid-lowering drugs in most cases. Both trials met all of their primary, secondary and tertiary endpoints. In these trials, mipomersen decreased LDL-C by 28 and 36 percent compared with increases of 5 and 13 percent for placebo, respectively (both $p < 0.001$), meeting primary endpoints in both studies.

In addition to evaluating percent reduction in LDL-C as their primary endpoints, both trials also evaluated percent reduction in Lp(a) as tertiary endpoints. Most patients in the two trials (71 and 62 percent) had elevated Lp(a) levels > 20 mg/dl at baseline. Mipomersen decreased Lp(a) by a median 21 and 39 percent, compared with zero and five percent for the placebo groups (both $p < 0.001$). Mipomersen lowered Lp(a) by ≥ 50 percent in 22 percent of mipomersen patients across both studies. The reductions observed were in addition to those achieved with the patients' existing therapeutic regimens. Additional detail from these studies was presented at the European Society of Cardiology's Congress last year and the American College of Cardiology's 60th Annual Scientific Session this year.

“The findings presented at EAS highlight mipomersen's potential to treat the unique needs of patients with severe forms of FH,” said Paula Soteropoulos, Vice President and General Manager of Genzyme's Cardiovascular Business. *“Other than apheresis, there is no approved treatment that addresses the*



specific challenges faced by severe FH patients, which include elevated Lp(a) in addition to LDL-C. We believe mipomersen could play an important role as a targeted treatment for these patients.”

In a presentation entitled “Mipomersen, an ApoB Synthesis Inhibitor, Might Reduce Necessity for Lipid Apheresis in CAD,” K.G. Parhofer, M.D. of Ludwig-Maximilians University, Munich, Germany focused on mipomersen’s potential to reduce the necessity for lipid-apheresis by lowering LDL-C values below thresholds for apheresis eligibility. Patients with severe forms of FH may be eligible for this treatment, a dialysis-like procedure where blood is filtered through a machine to remove excess cholesterol. Country-specific LDL-C thresholds to determine eligibility for apheresis can range from ≥ 100 mg/dL to ≥ 160 mg/dL. However, many eligible patients are not on apheresis because of lack of availability, high cost and negative impact on quality of life.

In the phase 3 trial in HeFH patients with CAD, an additional analysis revealed that mipomersen reduced the percentage of patients with LDL-C levels ≥ 160 mg/dL by 95 percent (from 39 percent to 2 percent); with LDL-C levels ≥ 130 mg/dL by 74 percent (from 62 percent to 16 percent); and with LDL-C levels ≥ 100 mg/dL by 45 percent (from 98 percent to 54 percent). The reductions observed were in addition to those achieved with the patients’ existing therapeutic regimens. No significant changes in LDL-C were observed in placebo-treated patients.

“These results suggest that the impact of mipomersen on the treatment landscape could be quite significant, both in countries such as Germany, where apheresis is more widely available and the eligibility threshold is relatively low, and in places like the United States, where apheresis is not as widely available,” said Dr. Parhofer. *“Mipomersen has the potential to reduce the necessity for apheresis in a considerable number of patients, and also become an important new treatment option for those who are eligible for apheresis but cannot access it or tolerate its impact on their quality of life.”*

Genzyme expects to file for EU marketing approval of mipomersen for the treatment of patients with homozygous (Ho) FH and severe HeFH early in the third quarter of this year. Genzyme also expects to file for U.S. approval for the HoFH indication in the second half of this year.

Genzyme and Isis have completed the four phase 3 studies that are planned to be included in the initial U.S. and EU filings. As previously reported, the phase 3 study of mipomersen in HoFH patients met its primary endpoint with 25 percent LDL-C reduction, and the phase 3 study in patients with high cholesterol at high risk for coronary heart disease met its primary endpoint with a 37 percent LDL-C reduction. These studies also met all of their secondary and tertiary endpoints, which included percent reduction in Lp(a).

In the four phase 3 studies, the most commonly observed adverse events were injection site reactions and flu-like symptoms. Persistent elevations in liver transaminases (ALTs) above 3X ULN (three times the upper limit of normal) were observed in 8 percent of mipomersen-treated patients across all four studies. Persistent is defined as consecutive elevations at least one week apart. Mipomersen-treated patients who were evaluated by MRI had moderate median increases in liver fat. No patients had changes in other laboratory tests to indicate hepatic dysfunction. In general, increases in ALT levels and liver fat appeared to be associated with rapid and larger drops in LDL-C.

“Mipomersen is a great example of the potential antisense technology holds to address major unmet medical needs,” said Stan C. Crooke, President and CEO of Isis Pharmaceuticals. *“We look forward to the upcoming filings this year as they will move us closer to our goal of making mipomersen available to patients who are in the greatest need of new treatments.”*



About Mipomersen

Mipomersen is a first-in-class apo-B synthesis inhibitor currently in late-stage development for the reduction of LDL cholesterol (LDL-C). It is intended to reduce LDL-C by preventing the formation of atherogenic lipoproteins, the particles that carry cholesterol through the bloodstream. Mipomersen acts by blocking the production of apolipoprotein B (apoB), the protein that provides the structural core for these atherogenic particles, including LDL and lipoprotein-a (Lp(a)).

About Familial Hypercholesterolemia

FH is a genetic disease that results in elevated LDL-C levels and family patterns of increased risk of premature heart disease and heart disease-related death. FH patients have inherited abnormalities in liver cells that are responsible for clearing LDL particles from the blood. FH is autosomal dominant, which means that all first-degree relatives of FH patients have a 50 percent chance of having the disease as well, making early detection through family screening critically important.

The most severe FH patients have LDL-C levels that are two to four times higher than recommended levels, even when taking multiple cholesterol-lowering medications. These people, who are characterized as having severe FH, include: those who have inherited the disease from both parents (homozygous FH (HoFH)) and those who have inherited it from only one parent, and have a severe form of the disease (severe heterozygous FH (severe HeFH)).

For more information about FH and mipomersen, please visit:

<http://www.multimedianewscenter.com/genzyme/mipomersen-data-portal>

About Genzyme, a Sanofi Company

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 that have provided new hope for patients. The company's areas of focus are rare genetic diseases, multiple sclerosis, cardiovascular disease, and endocrinology. Genzyme is a Sanofi company. Genzyme's press releases and other company information are available at www.genzyme.com.

About Sanofi

Sanofi, a global and diversified healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth platforms: diabetes solutions, human vaccines, innovative drugs, rare diseases, consumer healthcare, emerging markets and animal health. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

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



Sanofi Forward Looking Statement

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’s 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, 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 labeling 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, including those listed under “Risk Factors” and “Cautionary Statement Regarding Forward-Looking Statements” in Sanofi’s annual report on Form 20-F for the year ended December 31, 2010. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

Isis Forward Looking 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 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 Media Contact:

Erin Emlock

617-768-6923

Isis Contacts:

Amy Blackley, Ph.D.,

760-603-2772 (Media)

Kristina Lemonidis, 760-603-2490 (Investors)