



Sanofi and Regeneron Report Positive Preliminary Phase 2 Program Results for Anti-PCSK9 Antibody in Hypercholesterolemia

November 10, 2011

PARIS and TARRYTOWN, N.Y., Nov. 10, 2011 /PRNewswire/ -- Sanofi (EURONEXT: SAN and NYSE: SNY) and Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive preliminary results from the Phase 2 study program in which patients with elevated low-density lipoprotein cholesterol (LDL-C) were treated with REGN727/SAR236553.

REGN727/SAR236553 is a novel, high-affinity, subcutaneously administered, fully-human antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9). Blocking the PCSK9 pathway is a novel mechanism for lowering LDL-C, the leading known risk factor for coronary artery disease.

One Phase 2 trial studied patients with heterozygous familial hypercholesterolemia (heFH) with elevated cholesterol (LDL-C $\geq$ 100mg/dL) despite lipid lowering therapy (statins with or without ezetimibe). The objective of the study was to compare the effect of adding REGN727/ SAR236553 to the existing lipid lowering therapy in heFH patients. In the primary efficacy analysis of the study, after 12 weeks of treatment, patients who received different dosing regimens of REGN727/SAR236553 achieved mean LDL-C reductions from baseline ranging from approximately 30% to greater than 65% depending on the dosing regimen of REGN727/SAR236553 compared to a mean reduction of 10% with placebo ($p < 0.05$ for all dose groups). Patients in the study are being followed for a total of 20 weeks for safety.

In this trial, REGN727/SAR236553 was generally well tolerated over 12 weeks. There were no elevations in LFTs >3 times the upper limit of normal (ULN) and no cases of elevated CPK reported. The most common adverse event was injection site reaction. There were no serious adverse events on active treatment. Full safety data from the 8-week post-treatment monitoring period will be presented at a future medical congress upon final analysis.

Another Phase 2 trial studied patients with primary hypercholesterolemia with elevated cholesterol (LDL-C $\geq$ 100mg/dL) who were on a stable low dose of atorvastatin (10 mg). The primary objective of the study was to compare the effect of switching to a high dose of atorvastatin alone (80mg) versus a high dose of atorvastatin combined with REGN727/SAR236553. In the primary endpoint of the study, after eight weeks of treatment, patients who received REGN727/SAR236553 plus atorvastatin 80mg achieved a greater than 65% reduction in mean LDL-C compared to a mean reduction of 17% for atorvastatin 80mg only ($p < 0.001$). The study also included a third arm in which REGN727/SAR236553 was added to the stable low dose of atorvastatin and the patients achieved a greater than 65% reduction in mean LDL-C. Patients in the study were followed for a total of 16 weeks for safety.

In this trial, REGN727/SAR236553 was generally well tolerated over 16 weeks. There was one serious adverse event of dehydration in the REGN727/SAR236553 + atorvastatin 80mg group that was deemed not treatment related. One patient in the REGN727/SAR236553 + atorvastatin 80mg group with mildly elevated AST prior to randomization ($>ULN$ and $\leq 3ULN$) experienced an elevation of AST $>3ULN$ and $\leq 5ULN$ and one patient discontinued therapy due to a hypersensitivity reaction (rash).

A third study of this Phase 2 program is still ongoing.

"The preliminary Phase 2 results with our anti-PCSK9 antibody are very encouraging," said Elias Zerhouni, President, Global Research & Development, Sanofi. "We look forward to analyzing and presenting the complete data set and remain committed to advancing this program into Phase 3 development as soon as possible."

"Despite the availability of statins, elevated cholesterol and coronary artery disease remain a leading cause of morbidity and mortality in the U.S. and the rest of the world," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Research Laboratories. "We are encouraged that blocking PCSK9 with our anti-PCSK9 antibody has the potential to offer a novel mechanism for lowering LDL-C in a broad range of patients. We look forward to further exploring the safety and efficacy of REGN727/SAR236553 in our Phase 3 clinical program."

More detailed data from these Phase 2 trials, as well as from the third ongoing Phase 2 trial, will be submitted for presentation at an upcoming scientific conference.

About REGN727/SAR236553

REGN727/SAR236553 is the first fully human monoclonal antibody directed against proprotein convertase subtilisin/kexin type 9 (PCSK9). REGN727/SAR236553 is a high affinity, sub-cutaneously delivered, specific inhibitor of PCSK9. It blocks the binding of PCSK9 to the low density lipoprotein (LDL) receptor and interrupts the resultant internalization and degradation of the LDL receptor. In a 15-year retrospective epidemiological analysis from the Atherosclerosis Risk in Communities (ARIC) study, patients with nonsense mutations in PCSK9 had a 28% reduction in mean LDL cholesterol and an 88% reduction in the risk of coronary heart disease(1). REGN727/SAR236553 was developed using Regeneron's VelocImmune® antibody technology.

About the REGN727/SAR236553 Phase 2 Program

The REGN727/SAR236553 Phase 2 program consists of three Phase 2 clinical trials. These are:

1. A randomized, double-blind, multi-dose, placebo-controlled, 75-patient trial in patients with heterozygous familial hypercholesterolemia (heFH). In this trial, patients must meet the World Health Organization criteria for heFH, be on a stable daily statin regimen for at least 6-weeks before entering the trial, and have serum LDL-C levels $\geq$ 100mg/dL.

Patients could be taking ezetimibe in addition to a daily statin. Patients were randomized to one of four different dose regimens of REGN727/SAR236553 or placebo. The primary endpoint of the study is the change in LDL-C from baseline over the 12-week study period. Patients will be followed for a total of 20 weeks for safety.

2. A randomized, double-blind, single-dose, placebo-controlled, 90-patient trial in combination with atorvastatin in patients with primary hypercholesterolemia. In this trial, patients on a stable dose of atorvastatin 10mg for at least 6-weeks with LDL-C levels ≥ 100 mg/dL or who had LDL-C levels ≥ 100 mg/dL after a run-in period on atorvastatin 10mg, were randomized to either (a) titration from atorvastatin 10mg to atorvastatin 80mg plus REGN727/SAR236553, (b) titration from atorvastatin 10mg to atorvastatin 80mg plus placebo, or (c) continued atorvastatin 10mg plus REGN727/SAR236553. The primary endpoint of the study is the change in LDL-C from baseline over the 8-week study period. Patients were followed for a total of 16 weeks for safety.
3. A randomized, double-blind, multi-dose, placebo-controlled, 180-patient trial in combination with atorvastatin in patients with primary hypercholesterolemia and on stable doses of atorvastatin. In this trial, patients on a stable dose of atorvastatin 10mg, atorvastatin 20mg, or atorvastatin 40mg for at least 6-weeks with LDL-C levels ≥ 100 mg/dL or who had LDL-C levels ≥ 100 mg/dL after a run-in period on atorvastatin 10mg, atorvastatin 20mg, or atorvastatin 40mg were randomized to one of five different dose regimens of REGN727/SAR236553 plus continued atorvastatin or placebo plus continued atorvastatin. The primary endpoint of the study is the change in LDL-C from baseline over the 12-week study period. Patients will be followed for a total of 20 weeks for safety.

About Heterozygous Familial Hypercholesterolemia

Heterozygous Familial Hypercholesterolemia (heFH) is an inherited disease that is characterized by elevated LDL-C levels and family patterns of increased risk of premature coronary artery disease and heart disease-related death. The majority of these patients have inherited abnormalities in the gene for the LDL receptor. This results in a decreased ability to clear LDL-C from the blood and consequently, high levels of LDL-C. Because of the severe elevations in LDL-C, many of these patients cannot reach treatment goals with existing therapies. It is estimated that 1 in 500 people carries the genetic mutation that is responsible for heterozygous familial hypercholesterolemia(2).

About Primary Hypercholesterolemia

Hypercholesterolemia, particularly an increase in LDL-C levels, is a major risk factor for the development of atherosclerosis and cardiovascular disease. It is estimated that there are approximately 63 million people in the US with elevated levels of LDL-C. LDL-C is identified as the primary target of cholesterol lowering therapies such as statins. Statins have significantly helped in managing the risk for cardiovascular disease. However, since guidelines have established more stringent goals for very high risk patients due to their CV profiles, more than 60% of this patient group does not reach goal and needs new therapeutic options (3,4,5).

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 Regeneron Pharmaceuticals

Regeneron is a fully integrated biopharmaceutical company that discovers, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. In addition to ARCALYST® (rilonacept) Injection for Subcutaneous Use, which is approved for the treatment of a rare inflammatory condition, Regeneron has completed Phase 3 clinical trials of rilonacept for a new indication and of product candidates EYLEA™ (aflibercept injection; VEGF Trap-Eye) in diseases of the eye and ZALTRAP® (aflibercept; VEGF Trap) in a cancer indication. EYLEA is currently under review with U.S. and European regulatory authorities. Additional therapeutic candidates developed from proprietary Regeneron technologies for creating fully human monoclonal antibodies are in earlier stage development programs in rheumatoid arthritis, pain, cholesterol reduction, allergic and immune conditions, and cancer. Additional information about Regeneron and recent news releases are available on www.regeneron.com

Sanofi 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'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.

Regeneron Forward Looking Statements

This news release includes forward-looking statements that involve risks and uncertainties relating to future events and the future financial performance of Regeneron, and actual events or results may differ materially from these forward-looking statements. These statements concern, and these risks and uncertainties include, among others, the nature, timing, and possible success and therapeutic applications of Regeneron's product candidates and research and clinical programs now underway or planned, the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates, determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize its product and drug candidates, competing drugs that may be superior to Regeneron's product and drug candidates, uncertainty of market acceptance of Regeneron's product and drug candidates, unanticipated expenses, the availability and cost of capital, the costs of developing, producing, and selling products, the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi and Bayer HealthCare, to be canceled or terminated without any product success, and risks associated with third party intellectual property and pending or future litigation relating thereto. A more complete description of these and other material risks can be found in Regeneron's filings with the United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2010 and Form 10-Q for the quarter ended September 30, 2011. Regeneron does not undertake any obligation to update publicly any forward-looking statement, whether as a result of new information, future events, or otherwise, unless required by law.

Contacts:

Sanofi:

Media Relations

Marisol Peron

Tel: +33 (0) 1 53 77 45 02

Mobile: +33 (0) 6 08 18 94 78

E-mail: marisol.peron@sanofi.com

Investor Relations

Sebastien Martel

Tel: +33 (0)1 53 77 45 45

E-mail: IR@sanofi.com

Regeneron:

Media Relations

Peter Dworkin

Tel: 1 (914) 345-7640

peter.dworkin@regeneron.com

Investor Relations

Michael Aberman, M.D.

Tel: 1 (914) 345-7799

michael.aberman@regeneron.com

(1) Cohen JC et al. N Engl J Med 2006;354(12):1264-72

(2) NCEP ATP III guidelines Circulation 2002, 106:3143

(3) NCETP ATPIII guidelines update Circulation 2004;110;227-239

(4) ESC/EAS guidelines for the management of dyslipidemia European Heart Journal (2011) 32, 1769–1818

(5) Virani S. et al Am Heart J 2011;161:1140-6

SOURCE Regeneron Pharmaceuticals, Inc.