

May 26, 2012

Sanofi and Regeneron Announce Publication of Positive Phase 2 Results for Lipid-Lowering PCSK9 Antibody in The Lancet

PARIS and TARRYTOWN, New York, May 26, 2012 /PRNewswire/ --

Global Phase 3 program of SAR236553/REGN727 to be initiated in June across multiple patient populations

Sanofi and Regeneron Pharmaceuticals, Inc. today announced additional positive results from a Phase 2 trial of SAR236553/REGN727 (Study 1003, NTC01266876) in patients with heterozygous familial hypercholesterolemia (heFH). SAR236553/REGN727 is a subcutaneously administered, fully-human antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9) in clinical development. The results from this study were published online in The Lancet,[1] and also presented at a late-breaking oral session at the 80th European Atherosclerosis Society Congress (EAS) in Milan, Italy.[2] Positive, top-line results from this study were announced in November 2011.[3]

The trial randomized 77 patients with heFH whose LDL-cholesterol (LDL-C) levels remained uncontrolled on statin therapy with or without ezetimibe. Across the four different dosing regimens tested, patients receiving SAR236553/REGN727 for 12 weeks achieved a mean LDL-C reduction from baseline of 28.9% to 67.9%, compared to 10.7% in patients receiving placebo ($p < 0.05$). In addition, in the most intense dose regimen tested where the greatest LDL-C reduction was observed (150 milligrams [mg] every two weeks), 93.8% of patients achieved LDL-C levels lower than 100 mg/dL (2.59 mmol/L), compared to 13.3% of patients on placebo, and 81.3% reached LDL-C levels lower than 70 mg/dL (1.81 mmol/L), compared to none on placebo.

There were no serious adverse events (SAE) on active treatment, while a single SAE was recorded for a patient in the placebo group. There were no elevations in liver function tests (LFT) > 3 times the upper limit of normal (ULN) and no cases of elevated creatinine kinase (CK) were reported. The most common adverse event reported was injection-site reaction.

"Heterozygous familial hypercholesterolemia is a common, serious, and often undiagnosed cause of early heart disease. There remains a high degree of unmet need in these patients as a large percentage are unable to reach optimal LDL-C goals despite being on maximal lipid-lowering therapy," said Evan A. Stein, M.D., Ph.D., Director of the Metabolic and Atherosclerosis Research Center in Cincinnati, Ohio, and Principal Investigator of the study. "These data suggest that SAR236553/REGN727 may provide a new option, on top of existing therapies, to lower LDL-cholesterol and finally reach LDL-C goals for these difficult-to-treat patients."

Sanofi and Regeneron also announced today that based on discussions with the U.S. and European regulatory authorities, they intend to initiate a global Phase 3 program with SAR236553/REGN727 in June. This will be the first Phase 3 program of an investigational drug targeting PCSK9.

"These data, along with recently presented data in patients with hypercholesterolemia, further support our belief that blocking PCSK9 with our antibody has the potential to offer a novel mechanism for lowering LDL-cholesterol in a broad range of patients," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. Dr. Elias Zerhouni, President, Global Research & Development, Sanofi, added: "Our global Phase 3 program will include patients with high unmet medical need, such as patients with familial hypercholesterolemia or with elevated cardiovascular risk who cannot reach their LDL-cholesterol goals with current standard therapies. The program reflects our excitement and commitment to develop this potential therapeutic option for these patients."

About PCSK9

PCSK9 is known to be a determinant of circulating LDL-C levels, as it binds to LDL receptors resulting in their degradation so that fewer are available on liver cells to remove excess LDL-C from the blood.[4] Moreover, traditional LDL-lowering therapies such as statins actually stimulate the production of PCSK9, which limits their own ability to lower LDL-C.[5] Blocking the PCSK9 pathway is therefore a potentially novel mechanism for lowering LDL-C.

About SAR236553/REGN727 and the Phase 2 Heterozygous Familial Hypercholesterolemia trial

SAR236553/REGN727 is a fully human monoclonal antibody directed against PCSK9, administered via subcutaneous injection. By inhibiting PCSK9, a determinant of circulating LDL-C levels in the blood, SAR236553/REGN727 increases the number of free LDL receptors which can bind to circulating LDL-C and clear it from the bloodstream. SAR236553/REGN727 was created using Regeneron's VelocImmune(R) technology.

Study 1003 was a randomized, double-blind, placebo-controlled, dose-finding study in patients with heFH. The primary objective of the trial was to assess the efficacy of various subcutaneous doses and dosing regimens of SAR236553/REGN727 on LDL-C in patients with heFH. Seventy-seven patients were randomized to either placebo or one of four active dose regimens of 150 mg at four-week intervals (Q4W), 200 mg Q4W, 300 mg Q4W, or 150 mg at two-week intervals (Q2W). At baseline, all patients had LDL-C greater than or equal to 100 mg/dL (2.59 mmol/L) and were on stable daily statin therapy (the type and dosage of statin was at the discretion of the investigator) with or without ezetimibe, for at least six weeks prior to screening. The majority of patients, 77%, were taking a high intensity dose of a statin, and 71% were also taking ezetimibe 10 mg at the time of the screening visit and throughout the trial. Despite this aggressive therapy, the mean baseline LDL-C for all study participants was approximately 155 mg/dL (4 mmol/L). The primary endpoint of the study was the change in LDL-C from baseline over the 12-week study period. Patients were followed for a total of 20 weeks for safety.[2]

About Heterozygous Familial Hypercholesterolemia

HeFH is an inherited disease that is characterized by very high LDL-C levels and familial patterns of increased risk of premature coronary artery disease and heart disease-related death due to these elevated LDL-C levels. 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 leads to high levels of LDL-C in the blood that can accelerate the initiation and progression of atherosclerosis.[6] As a result of the severe elevations in LDL-C, many of these patients cannot reach treatment goals with existing therapies. A recent analysis of 1,249 heFH patients found that only 21% were able to achieve a treatment goal of < 2.5 mmol/L (< 97 mg/dL).[7] It is estimated that 1 in 500 people worldwide carries a genetic mutation that is responsible for heFH. [6]

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, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris and in New York .

About Regeneron Pharmaceuticals, Inc.

Regeneron is a fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron markets two products in the United States, ARCALYST(R) (rilonacept) Injection for Subcutaneous Use and EYLEA(R) (aflibercept) Injection, and has filed regulatory applications with the U.S. Food and Drug Administration (FDA) for second indications for each of these products. A regulatory application has also been submitted to the FDA for the product candidate ZALTRAP(R) (aflibercept) Concentrate for Intravenous Infusion. Phase 3 studies are in progress with EYLEA(R) in a third indication, and with product candidate sarilumab. Earlier-stage clinical programs are underway with nine additional monoclonal antibodies. Regeneron has active research and development programs in many disease areas, including ophthalmology, inflammation, cancer, and hypercholesterolemia. Additional information and recent news releases are available on the Regeneron web site at <http://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 labelling and other matters that could affect the availability or commercial potential of such product candidates, the absence of guarantee that the product 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, trends in exchange rates and prevailing interest rates, the impact of cost containment policies and subsequent changes thereto, the average number of shares outstanding 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, 2011. 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 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, including without limitation SAR236553/REGN727, unforeseen safety issues resulting from the administration of products and product candidates in patients, 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 Regeneron's 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 the Sanofi Group 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, 2011 and Form 10-Q for the quarter ended March 31, 2012. 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.

References

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