



Sanofi and Regeneron Report Phase 2 Data for Potential First-in-Class Lipid-Lowering PCSK9 Antibody

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PARIS and TARRYTOWN, N.Y., March 26, 2012 /PRNewswire/ -- Sanofi (EURONEXT: SAN and NYSE: SNY) and Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that data from two Phase 2 trials with SAR236553/REGN727, an investigational, high-affinity, subcutaneously administered, fully-human antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9), were presented at the American College of Cardiology's (ACC) 61st Annual Scientific Meeting in Chicago.

To view the multimedia assets associated with this release, please click: <http://www.multivu.com/mnr/55299-sanofi-regeneron-pharmaceuticals-lipid-lowering-medications-pcsk9-antibody>

The data showed that treatment with SAR236553/REGN727 over 8 to 12 weeks significantly reduced mean low-density lipoprotein-cholesterol (LDL-C, or "bad" cholesterol) by 40% to 72% in patients with elevated LDL-C on stable dose of statins.(1),(2)

"Many patients are not able to lower their LDL-C sufficiently by diet and medication despite the availability of statins. As guidelines are evolving, there is a real need for additional lipid-lowering medications," said Dr. James McKenney, President and CEO of National Clinical Research, Inc., Professor Emeritus of the Virginia Commonwealth University School of Pharmacy, USA, and Principal Investigator of the study. *"These trial results suggest that SAR236553/REGN727 may enable patients for whom statins are insufficient to further reduce LDL-C."*

Presented today in a late-breaking clinical trials session at the ACC meeting, "Study DFI11565," the Phase 2 dose-finding clinical trial enrolled 183 patients with elevated LDL-C (greater than or equal to 100 mg/dL) despite being on a stable dose of atorvastatin. The objective of the study was to evaluate the effect of adding SAR236553/REGN727 to existing statin therapy. Across the five different dose regimens tested, patients receiving SAR236553/REGN727 for 12 weeks achieved and sustained a mean LDL-C reduction from baseline of 40% to 72%, compared to 5% in patients receiving placebo (p < 0.0001). Patients in the study were followed for a total of 20 weeks for safety.

The most common adverse events (AEs) with SAR236553/REGN727 were injection site reactions. Serious AEs occurred in one patient receiving placebo and three patients in the active treatment arms, including a patient on active treatment who experienced a skin rash diagnosed as leukocytoclastic vasculitis. Six patients, all on active treatment, prematurely discontinued therapy due to AEs. Muscle complaints were infrequent and similar across all treatment groups. There were no significant elevations in liver enzymes or other lab values in patients on active treatment.

"So far, SAR236553/REGN727 has demonstrated LDL-lowering efficacy and a generally acceptable safety profile," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Research Laboratories. *"PCSK9 inhibition is being investigated for its potential to lower LDL-C in patients who cannot achieve their goals with standard therapies."*

The PCSK9 mechanism is an example of how the study of genetics can identify new targets for developing new therapies.(3),(4) The role of PCSK9 in lipid metabolism was discovered a few years ago based on population studies.(5)

"Genetic data have shown that patients with natural loss-of-function mutations in PCSK9 have significantly lower LDL-C and a lower risk of coronary heart disease," said Dr. Elias Zerhouni, President, Global Research & Development, Sanofi. *"Based on this finding and the results of our Phase 2 trials, Sanofi and Regeneron plan to initiate the SAR236553/REGN727 Phase 3 program in the second quarter."*

Data from a separate trial, "Study DFI11566," were presented yesterday during an oral session of the ACC meeting. The study enrolled patients with primary hypercholesterolemia with elevated LDL-C (greater than or equal to 100 mg/dL) who were on a stable low dose of atorvastatin (10 mg). The primary objective of the study was to compare the effect on LDL-C lowering of switching to a high dose of atorvastatin alone (80 mg) versus a high dose of atorvastatin combined with SAR236553/REGN727. Patients who received SAR236553/REGN727 plus atorvastatin 80 mg achieved a mean reduction of 73% in LDL-C, compared to a mean reduction of 17% for patients who switched to atorvastatin 80 mg alone (p < 0.001) after eight weeks. The study also included a third arm in which SAR236553/REGN727 was added to the stable low dose of atorvastatin. Patients in this arm achieved a 66% reduction in mean LDL-C. Patients in the study were followed for a total of 16 weeks for safety.

In this trial, the most common AE with SAR236553/REGN727 was infection. There was one serious AE in the SAR236553/REGN727 plus atorvastatin 80 mg group (dehydration) that was deemed not to be treatment-related.

A long-term safety and tolerability study of SAR236553/REGN727 (NCT01507831) is ongoing in patients with hypercholesterolemia who are not adequately controlled with their current lipid-modifying therapy.(6) Sanofi and Regeneron are intending to initiate Phase 3 clinical studies for SAR236553/REGN727 in Q2 2012.

Sanofi and Regeneron are co-developing SAR236553/REGN727 as part of their research and development collaboration agreements.

About PCSK9

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

About SAR236553/REGN727 and the Phase 2 primary hypercholesterolemia trials

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

Study 11565 was a randomized, double-blind, multi-dose, placebo-controlled, 183-patient trial in patients with primary hypercholesterolemia and on stable doses of atorvastatin. In this trial, patients on a stable dose of atorvastatin 10, 20 or 40 mg for at least 6 weeks with LDL-cholesterol levels greater than or equal to 100 mg/dL, or who had LDL-cholesterol levels greater than or equal to 100 mg/dL after a run-in period on atorvastatin 10, 20 or 40 mg, were randomized to one of five different dose regimens of SAR236553/REGN727 (i.e. either 50, 100, or 150 mg Q2W, or 200 or 300 mg Q4W alternating with placebo at 2 weeks) plus continued atorvastatin or placebo. The primary endpoint of the study was the change in LDL-cholesterol from baseline over the 12-week study period. Patients were followed for a total of 20 weeks for safety.

Study 11566 was a randomized, double-blind, multi-dose, placebo-controlled, 92-patient trial in patients with primary hypercholesterolemia. In this trial, patients on a stable dose of atorvastatin 10 mg for at least 6 weeks with LDL-cholesterol levels greater than or equal to 100 mg/dL, or who had LDL-cholesterol levels greater than or equal to 100 mg/dL after a run-in period on atorvastatin 10 mg, were randomized to either (a) titration from atorvastatin 10 mg to atorvastatin 80 mg plus SAR236553/REGN727 150 mg Q2W, (b) titration from atorvastatin 10 mg to atorvastatin 80 mg plus placebo, or (c) continued atorvastatin 10 mg plus SAR236553/REGN727 150 mg Q2W. The primary endpoint of the study was the change in LDL-cholesterol from baseline over the 8-week study period. Patients were followed for a total of 16 weeks for safety.

About primary hypercholesterolemia

Hypercholesterolemia, particularly an increase in LDL-C levels, is a major risk factor for the development of cardiovascular disease. LDL-C is identified as the primary target of cholesterol-lowering therapies such as statins, which have significantly helped in managing the risk for cardiovascular disease.⁽⁷⁾ However, despite the availability of statins, many patients with hypercholesterolemia are not reaching their recommended LDL-C goal and need new additional therapy.

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 (EURONEXT: SAN) and in New York (NYSE: SNY).

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, one for the treatment of neovascular (wet) age-related macular degeneration and another for the treatment of a rare inflammatory condition. Additionally, Regeneron has three regulatory applications pending before the U.S. Food and Drug Administration (FDA) and 10 drug candidates in clinical development. More information and recent news releases are available on the Regeneron web site at 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. 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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