



## Sanofi and Regeneron Announce Publication of Phase 2 Results with LDL Cholesterol-Lowering PCSK9 Antibody in the New England Journal of Medicine

October 31, 2012

PARIS and TARRYTOWN, N.Y., Oct. 31, 2012 /PRNewswire/ -- Sanofi (EURONEXT: SAN and NYSE: SNY) and Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that results from a Phase 2 trial of SAR236553/REGN727 in patients with primary hypercholesterolemia were published in the October 31, 2012 issue of the *New England Journal of Medicine*.

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 administered in a 1ml injection every two weeks.

Patients who received SAR236553/REGN727 administered in a 1ml injection every two weeks 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. Ninety percent (90%) of patients achieved a pre-specified level of 70mg/dL compared to 17.2% for patients who switched to atorvastatin 80 mg alone ( $p < 0.001$ ).

The study also included a third arm in which SAR236553/REGN727 150mg administered in a 1ml injection every two weeks was added to the stable 10 mg of atorvastatin. Ninety-six percent (96.6%) of patients achieved the pre-specified goal of 70mg/dL in this treatment group.

In this trial, the most common adverse events (AE) reported in patients treated with SAR236553/REGN727 plus atorvastatin were headache, dizziness, and diarrhea. There was one serious AE in the SAR236553/REGN727 plus atorvastatin 80 mg group (dehydration) that was deemed not to be treatment-related.

This study was part of the Phase 2 program of SAR236553/REGN727, an investigational, subcutaneously administered, fully-human antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9) that is currently being studied in the ODYSSEY Phase 3 trials for the lowering of low-density lipoprotein cholesterol (LDL-C). Preclinical studies have shown that inhibiting PCSK9 leads to an increase in LDL receptors, which bind to LDL-C and clear it from the blood stream. The publication can be accessed at <http://www.nejm.org>.

Additionally, new data from the Phase 2 studies of SAR236553/REGN727 will be presented at oral sessions at the American Heart Association's Scientific Sessions 2012 (AHA). Results of these presentations are embargoed until the times listed below. The presentations are:

*Embargoed until November 6, 2012 at 9:30 AM PST:*

- Effect of SAR236553/REGN727 Fully Human Monoclonal Anti-Proprotein Convertase Subtilisin/Kexin Type 9 Antibody on Plasma Lipoprotein(a) Concentrations: Pooled Analysis from Three Phase 2 Studies. Tuesday, November 6, 2012, 9:30-9:45 AM PST. Presenter: Daniel Gaudet, M.D., Professor of Medicine, University of Montreal. [Abstract No. 14725]

*Embargoed until November 6, 2012 at 4:45 PM PST :*

- Effect of REGN727/SAR236553 Anti-Proprotein Convertase Subtilisin/Kexin Type 9 Fully Human Monoclonal Antibody in Patients with Elevated Triglycerides/Low High-Density Lipoprotein Cholesterol: Data from Three Phase 2 Studies. Tuesday, November 6, 2012, 4:45-5:00 PM PST. Presenter: Robert Dufour, M.D., M.Sc., Associate Director, Institut de Recherches Cliniques de Montreal. [Abstract No. 16127]

### About PCSK9

PCSK9 is known to contribute to circulating LDL-C levels, as it binds to LDL receptors resulting in their degradation so that fewer are available on liver cells to remove LDL-C 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-C. Inhibiting the PCSK9 pathway is therefore a potentially novel mechanism for lowering LDL-C.

### About SAR236553/REGN727 and the Phase 2 Program

SAR236553/REGN727, created using Regeneron's VelocImmune<sup>®</sup> technology, 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 clear circulating LDL-C from the bloodstream.

SAR236553/REGN727 has been studied in three Phase 2 clinical studies: Two dose ranging studies in patients with hypercholesterolemia; one with 183-patients, and another with 92-patients, and one study of 77 patients with heterozygous familial hypercholesterolemia (heFH). In the primary hypercholesterolemia trials treatment with different dose regimens of SAR236553/REGN727 on top of statin therapy significantly reduced LDL-C from baseline by 40% to 72% over the 8 or 12-week treatment period. A third Phase 2 study was in patients with heFH whose LDL-C levels remained elevated despite statin therapy with or without ezetimibe. Across the four tested doses of SAR236553/REGN727 administered for up to 12 weeks, patients achieved a mean reduction in LDL-C from baseline of 28% to 68%. In the Phase 2 program, injection site reactions were the most common adverse events with SAR236553/REGN727. Rare cases of hypersensitivity reaction were also reported. There were five serious adverse events (SAE) in the active treatment arms (1.8%, 5/275) and two SAEs in the placebo groups (2.6%, 2/77).

## **About Regeneron Pharmaceuticals**

Regeneron is a fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron markets three products in the United States, EYLEA<sup>®</sup> (afibercept) Injection, ZALTRAP<sup>®</sup> (ziv-afibercept) Injection for Intravenous Infusion, and ARCALYST<sup>®</sup> (rilonacept) Injection for Subcutaneous Use; ZALTRAP is co-commercialized with Sanofi. Phase 3 studies are in progress with EYLEA in two additional indications and with product candidates sarilumab and REGN727. 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 [www.regeneron.com](http://www.regeneron.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, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

## **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 products, 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 products and drug candidates, competing drugs that may be superior to Regeneron's products and drug candidates, uncertainty of market acceptance of Regeneron's products and drug candidates, unanticipated expenses, 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, 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 its Form 10-Q for the quarter ended September 30, 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.*

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