



## Sanofi and Regeneron Launch Comprehensive Phase 3 Clinical Program With LDL Cholesterol-Lowering PCSK9 Antibody

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Sanofi (EURONEXT: SAN and NYSE: SNY) and Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) announced today that several trials within ODYSSEY, the Phase 3 clinical program of SAR236553/REGN727, have initiated patient enrollment. SAR236553/REGN727 is a potential first-in-class, subcutaneously administered, fully-human antibody that lowers low-density lipoprotein (LDL) cholesterol by targeting PCSK9 (proprotein convertase subtilisin/kexin type 9), an enzyme which binds LDL receptors, leading to their accelerated degradation and increased LDL-cholesterol (LDL-C) levels.

"We are delighted to lead the field of PCSK9 late stage development with the broad global 22,000 patient ODYSSEY clinical trial program, and would like to thank in advance the patients and physicians who will contribute to the first Phase 3 program evaluating a PCSK9-targeted therapy," said Jay Edelberg M.D., Ph.D., Head of the PCSK9 Development and Launch Unit, Sanofi. "This comprehensive Phase 3 program will test the safety and efficacy of SAR236553/REGN727 administered as one single injection every two weeks in multiple treatment strategies and patient types, such as those who are at elevated cardiovascular risk, are unable to tolerate statin therapy, or have familial hypercholesterolemia."

"Lowering LDL-C remains the primary objective for the management of hypercholesterolemia and has been supported by numerous morbidity and mortality trials. Despite the existence of very effective LDL-C lowering therapies, many patients, such as those with heterozygous familial hypercholesterolemia or those with elevated cardiovascular risk, are unable to achieve their LDL-C goals," said Professor Henry N. Ginsberg, M.D., Columbia University Medical Center, New York and Chair of the ODYSSEY Steering Committee. "Sustained PCSK9 blockade represents a potential new option to further reduce LDL-C on top of standard of care statin therapy and help patients achieve their LDL-C goals."

The ODYSSEY program will enroll more than 22,000 patients. This includes over ten clinical trials evaluating the effect of SAR236553/REGN727 on the lowering of LDL-C and an 18,000 patient cardiovascular outcomes (e.g., heart attack, stroke) study. LDL-C is expected to be the primary efficacy endpoint for regulatory filings. The studies will be conducted in clinical centers around the world including the United States, Canada, Western and Eastern Europe, South America, Australia and Asia. Studies are currently enrolling patients with familial hypercholesterolemia or elevated cardiovascular risk, as well as patients unable to tolerate statin therapy.

"We believe that Regeneron's expertise in antibody discovery and development, combined with Sanofi's experience in clinical development and self-injectable delivery systems, will be an advantage as we work to bring this important new therapy to patients who are unable to reach their LDL-C goals with traditional lipid-modifying therapies, as quickly as possible," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Research Laboratories.

In parallel, Sanofi announced the creation of a dedicated PCSK9 Development & Launch Unit. Jay Edelberg, M.D., Ph.D. has recently been appointed as Head of the Development & Launch Unit, reporting to Elias Zerhouni, President, Global R&D and Hanspeter Spek, President, Global Operations, Sanofi. The creation of a dedicated unit for this new PCSK9 inhibitor underscores Sanofi's commitment to develop this potential first-in-class therapeutic agent.

### 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 in patients with primary hypercholesterolemia and one in 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 the Phase 3 SAR236553/REGN727 Program

The Phase 3 ODYSSEY program will include over ten clinical trials designed to test the efficacy and long-term safety of SAR236553/REGN727 both as monotherapy, and in combination with other lipid-lowering agents. ODYSSEY will enroll several patient populations including patients with heFH who are inadequately controlled by current lipid-modifying therapy, and high cardiovascular risk patients with primary hypercholesterolemia. The

primary efficacy parameter will be LDL-C; however, multiple lipid parameters will be evaluated. The global Phase 3 program will be conducted across more than 2,000 study centers across the United States, Canada, Western and Eastern Europe, South America, Australia and Asia. The Phase 3 ODYSSEY program will include the following studies:

- **ODYSSEY FH I, FH II and HIGH FH:** The primary objective of these three studies is to demonstrate the efficacy and safety of SAR236553/REGN727 as an add-on therapy in patients with heFH who are not adequately controlled with their lipid-modifying therapy.
- **ODYSSEY COMBO I and COMBO II:** The primary objective of these two studies is to demonstrate the safety and efficacy of SAR236553/REGN727 as an add-on therapy in patients with primary hypercholesterolemia at high cardiovascular risk who are not adequately controlled with their lipid-modifying therapy.
- **ODYSSEY MONO:** The primary objective of this study is to demonstrate the safety and efficacy of SAR236553/REGN727 as monotherapy in comparison with ezetimibe in patients with primary hypercholesterolemia.
- **ODYSSEY ALTERNATIVE:** The primary objective of this study is to demonstrate the safety and efficacy of SAR236553/REGN727 in comparison with ezetimibe in patients with primary hypercholesterolemia (heFH and non-familial hypercholesterolemia) who are unable to tolerate statins.
- **ODYSSEY OPTIONS I and OPTIONS II:** The primary objective of these studies is to evaluate the safety and efficacy of SAR236553/REGN727 as an add-on therapy in patients with primary hypercholesterolemia at high cardiovascular risk or with heFH who are not adequately controlled on statins, in comparison to several second line lipid lowering strategies.
- **ODYSSEY LONG TERM:** The primary objective of this study is to evaluate the long-term safety and tolerability of SAR236553/REGN727 in patients with hypercholesterolemia at high cardiovascular risk or patients with heFH inadequately controlled with their current lipid-modifying therapy.

In addition, the ODYSSEY program will also include **ODYSSEY OUTCOMES**, a Phase 3 cardiovascular outcomes trial which will enroll about 18,000 patients and evaluate the effect of SAR236553/REGN727 on the occurrence of cardiovascular events.

Further information about the initiated Phase 3 studies can be found at <http://www.clinicaltrials.gov>.

#### **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, EYLEA<sup>®</sup> (afibercept) Injection and ARCALYST<sup>®</sup> (rilonacept) Injection for Subcutaneous Use. Regeneron has filed regulatory applications with the U.S. Food and Drug Administration (FDA) for second indications for EYLEA and ARCALYST and for the product candidate ZALTRAP<sup>®</sup> (afibercept) Concentrate for Intravenous Infusion. 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 <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 products and 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 products 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.*

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