



Regeneron and Sanofi Announce Approval of Praluent® (alirocumab) for the Treatment of Hypercholesterolemia in the European Union

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TARRYTOWN, N.Y. and PARIS, Sept. 28, 2015 /PRNewswire/ -- [Regeneron Pharmaceuticals, Inc.](http://www.regeneron.com) (NASDAQ: **REGN**) and Sanofi today announced that the European Commission (EC) has granted marketing authorization for Praluent® (alirocumab) for the treatment of bad cholesterol, known as low-density lipoprotein (LDL) cholesterol, in certain adult patients with hypercholesterolemia. Praluent is the only EC-approved PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitor that is available in two starting doses as a single 1-milliter (mL) injection (75 mg and 150 mg) once every two weeks, offering two levels of efficacy. Praluent will be available in a single-dose pre-filled pen that patients self-administer.

"The availability of two different Praluent dosing strengths provides for dosing flexibility. In clinical practice, this will enable physicians to tailor treatment based on an individual patient's LDL-cholesterol-lowering needs," said Michel Farnier, M.D., Ph.D., Point Medical, Dijon, France. "In the Phase 3 trials, the majority of patients who started on the lower Praluent 75 mg dose were able to achieve their pre-defined LDL-cholesterol goals, and maintained treatment at this dose throughout the assessment period."

The EC approved Praluent for the treatment of adult patients with primary hypercholesterolemia (heterozygous familial hypercholesterolemia [HeFH] and non-familial) or mixed dyslipidemia as an adjunct to diet: **a)** in combination with a statin, or statin with other lipid-lowering therapies in patients unable to reach their LDL-cholesterol goals with the maximally-tolerated statin or **b)** alone or in combination with other lipid-lowering therapies for patients who are statin intolerant, or for whom a statin is contraindicated. The effect of Praluent on cardiovascular (CV) morbidity and mortality has not yet been determined.

High cholesterol is a significant health concern in Europe. According to the World Health Organization (WHO), Europe has the greatest prevalence per capita of high cholesterol in the world (54 percent) followed by the WHO Region of Americas (48 percent). High LDL-cholesterol is a major risk factor for cardiovascular disease (CVD), which remains the leading cause of death around the world. Unfortunately, despite treatment with current standard-of-care, including statins and and/or other lipid-lowering therapies, many Europeans continue to have poorly controlled LDL-cholesterol including those with HeFH, high CV risk; and/or those with a history of statin-intolerance. For some of these patients, additional treatment options are needed to more aggressively lower their cholesterol.

"Our clinical program focused on patients with the highest unmet needs, most of whom were on maximally-tolerated statins and/or other lipid-lowering therapies," said Olivier Brandicourt, M.D., Chief Executive Officer, Sanofi. "It was very exciting for us to see that the majority of these patients, most of whom continued to have very high LDL-cholesterol despite treatment with other lipid-lowering drugs, were able to achieve their cholesterol-lowering goals within weeks of adding Praluent to their treatment regime."

The EC marketing authorization is based on data from 10 pivotal Phase 3 ODYSSEY trials, including five placebo-controlled and five ezetimibe-controlled. The data showed consistent, robust reductions in LDL-cholesterol for Praluent compared to placebo or ezetimibe, when added to current standard-of-care, which included maximally-tolerated statins. All trials met their primary efficacy endpoint, demonstrating significantly greater reductions from baseline in LDL-cholesterol at week 24, compared to placebo or ezetimibe. In the placebo-controlled trials, the average LDL-cholesterol reductions from baseline at week 24 for the Praluent group ranged from 46 to 61 percent. In the ezetimibe-controlled trial with Praluent added to background statins, the average change in LDL-cholesterol from baseline was 51 percent at week 24. In the ezetimibe trials with patients not on statins, the average LDL-cholesterol reduction from baseline in the Praluent group ranged from 45 to 47 percent at week 24. Additionally, significantly more patients achieved an LDL-cholesterol level of less than 70 mg/dL (< 1.81 mmol/L) in the Praluent group compared to placebo or ezetimibe at week 12 and week 24.

"We are pleased to bring Praluent to European patients in need of further LDL-cholesterol lowering," said Leonard S. Schleifer, M.D., Ph.D., Founder, President, and Chief Executive Officer, Regeneron. "This approval was made possible through the tremendous hard work of our innovative scientists who translated a genetics-based discovery into an important new medicine, as well as thousands of dedicated investigators and patient participants."

In eight trials, patients initially started on Praluent 75 mg every two weeks, and had their dose up-titrated to 150 mg every two weeks at week 12 if needed to reach protocol-specified LDL-cholesterol targets. Patients who initially started on Praluent 75 mg every two weeks experienced average LDL-cholesterol reductions from baseline ranging from 44.5 percent to 49 percent at week 12. The majority of patients achieved their pre-defined LDL-cholesterol target on the 75 mg dose, and maintained treatment at this dose. In two other trials where patients initially started on Praluent 150 mg every two weeks, the average LDL-cholesterol reduction from baseline was 63 percent at week 12. In ODYSSEY LONG TERM, the largest Phase 3 placebo-controlled trial evaluating Praluent to date, LDL-cholesterol reductions were sustained through 78 weeks.

The ability of Praluent to reduce major CV events is being investigated in the ongoing ODYSSEY OUTCOMES trial, with results anticipated in 2017. In pre-specified final analyses of the ODYSSEY LONG TERM study, major CV events confirmed by adjudication were reported in 1.7 percent of patients in the Praluent group and 3.3 percent of patients in the placebo group. Hazard ratios were calculated post-hoc; HR=0.52 (95 percent CI, 0.31 to 0.90). In pre-specified analyses of pooled Phase 3 studies, major CV events were reported in 1.6 percent of patients in the Praluent group and 1.8 percent of those in the control group, which included either placebo or ezetimibe (HR=0.81; 95 percent CI, 0.52 to 1.25).

Across the Phase 3 trials all-cause mortality was 0.6 percent in the Praluent group and 0.9 percent in the control group, with CV events being the primary cause of death in the majority of these patients.

In clinical trials, Praluent was generally well-tolerated with an acceptable safety profile. Local injection site reactions including erythema/redness, itching, swelling or pain/tenderness where the injection is given were the most common events (6 percent with Praluent versus 4 percent with placebo) in clinical trials. Most injection site reactions were transient and of mild intensity. The discontinuation rate due to local injection site reactions was comparable between the two groups (0.2 percent Praluent and 0.3 percent control groups). Other common adverse events occurring more frequently in the Praluent group than placebo included upper respiratory tract signs and symptoms, and pruritus.

In July, the companies announced that Praluent was approved for use in the U.S. as an adjunct to diet and maximally-tolerated statin therapy for the treatment of adults with HeFH or clinical atherosclerotic CVD (ASCVD), who require additional lowering of LDL-cholesterol. The effect of Praluent on CV morbidity and mortality has not been determined.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Important Safety Information for U.S.

Do not use PRALUENT if you are allergic to alirocumab or to any of the ingredients in PRALUENT. Before you start using PRALUENT, tell your healthcare provider about all your medical conditions, including allergies, and if you are pregnant or plan to become pregnant or if you are breastfeeding or plan to breastfeed.

Tell your healthcare provider or pharmacist about any prescription and over-the-counter medicines you are taking or plan to take, including natural or herbal remedies.

PRALUENT can cause serious side effects, including allergic reactions that can be severe and require treatment in a hospital. Call your healthcare provider or go to the nearest hospital emergency room right away if you have any symptoms of an allergic reaction including a severe rash, redness, severe itching, a swollen face, or trouble breathing.

The most common side effects of PRALUENT include: redness, itching, swelling, or pain/tenderness at the injection site, symptoms of the common cold, and flu or flu-like symptoms. Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

Talk to your doctor about the right way to prepare and give yourself a PRALUENT injection and follow the "Instructions for Use" that comes with Praluent.

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please click [here](#) for the full Prescribing Information

About Sanofi

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in diabetes solutions, human vaccines, innovative drugs, consumer healthcare, emerging markets, animal health and Genzyme. Sanofi is listed in Paris (EURONEXT: [SAN](#)) and in New York (NYSE: [SNY](#)).

About Regeneron Pharmaceuticals, Inc.

Regeneron (NASDAQ: [REGN](#)) is a leading science-based biopharmaceutical company based in Tarrytown, New York that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron commercializes medicines for high LDL cholesterol, eye diseases, and a rare inflammatory condition and has product candidates in development in other areas of high unmet medical need, including oncology, rheumatoid arthritis, asthma, atopic dermatitis, pain, and infectious diseases. For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

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, 2014. 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 and Use of Digital Media

This news release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. 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 Praluent® (alirocumab) Injection; unforeseen safety issues and possible liability resulting from the administration of products (including without limitation Praluent) and product candidates in patients; serious complications or side effects in connection with the use of Regeneron's products and product candidates in clinical trials, such as the ODYSSEY OUTCOMES trial evaluating Praluent; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as Praluent), research and clinical programs, and business, including those relating to the enrollment, completion, and meeting of the relevant endpoints of post-approval studies; 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 product candidates; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's products and product candidates; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its sales or other financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi and Bayer HealthCare LLC, to be cancelled or terminated without any further product success; and risks associated with intellectual property of other parties 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, 2014 and its Form 10-Q for the quarterly period ended June 30, 2015. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update publicly any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (<http://newsroom.regeneron.com>) and its Twitter feed (<http://twitter.com/regeneron>).

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