



## Regeneron and Sanofi Announce New Positive Praluent® (alirocumab) Phase 3 Data Presented at ESC Congress 2015

September 1, 2015

TARRYTOWN, N.Y., and PARIS, Sept. 1, 2015 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that, in a new pooled analysis of heterozygous familial hypercholesterolemia (HeFH) patients included in the ODYSSEY clinical trial program, Praluent® (alirocumab) significantly reduced bad cholesterol, known as low-density lipoprotein cholesterol (LDL-C).<sup>1</sup> This analysis included 1,257 HeFH patients, the largest group of HeFH patients ever studied in a Phase 3 program. At week 24, when the primary efficacy endpoint was assessed, patients treated with Praluent had an average 56 percent greater reduction in LDL-C compared to placebo (p less than 0.0001) in both arms.<sup>1</sup> Reductions were observed as early as week 4 and were maintained for the duration of therapy, until week 78.<sup>1</sup>

Results of this analysis were presented today at the ESC Congress 2015 in London, and the 78 week results from two of the four trials included in the analysis, ODYSSEY FH I and II, were concurrently published online in the European Heart Journal.

"Approximately 20 percent of HeFH patients achieve LDL-C less than 100 mg/dL with statins. In this analysis, up to 75 percent of patients who added Praluent to standard-of-care achieved their LDL-C goals by week 24," said John J. P. Kastelein, M.D., Ph.D., FESC, Professor of Medicine, Department of Vascular Medicine, Academic Medical Center/University of Amsterdam, the Netherlands. "Both Praluent 75 mg and 150 mg significantly reduced LDL-C levels below 100 mg/dL and sustained these lower levels through 78 weeks, offering patients and their doctors a flexible approach to treatment, with adverse events comparable to placebo."

Across the pooled analysis, the most common adverse events (occurring in at least five percent of patients in any Praluent group) were nasopharyngitis, injection site reaction, influenza, headache, upper respiratory tract infection, arthralgia, back pain, urinary tract infection and myalgia.<sup>1</sup>

People with HeFH have an inherited form of high cholesterol and are unable to process the body's natural supply of cholesterol in the liver, leading to very high levels of LDL-C that can block arteries (atherosclerosis) and can lead to a heart attack or stroke.<sup>3,4</sup> If left untreated, people with HeFH typically have LDL-C levels of 200-400 milligrams/deciliter (mg/dL),<sup>5</sup> are at high risk for premature atherosclerosis and cardiovascular (CV) events, and are at 20 times greater risk of developing heart disease.<sup>3,4</sup>

The analysis presented at ESC Congress 2015 evaluated the efficacy and safety of Praluent compared to placebo in 1,257 patients with HeFH. Data from four Phase 3 ODYSSEY trials, LONG TERM (HeFH patients only), HIGH FH, FH I, and FH II, were included in the analysis. In these trials, patients either received Praluent or placebo, in addition to standard-of-care, which included maximally-tolerated statins with or without other lipid-lowering therapies such as ezetimibe. In ODYSSEY LONG TERM and HIGH FH, patients were treated with Praluent 150 mg (n=348) every two weeks administered as a single 1-milliliter (mL) injection or placebo (n=174).<sup>1</sup> In these patients, the average LDL-C at baseline was 168 mg/dL and 162 mg/dL in the Praluent and placebo groups respectively.<sup>1</sup> In ODYSSEY FH I and FH II, patients were treated with Praluent 75 mg (n=490) every two weeks administered as a single 1-mL injection or placebo (n=245).<sup>1</sup> In ODYSSEY FH I and FH II, patients had their dose adjusted to 150 mg at week 12 if they did not achieve their pre-specified LDL-C goal at week 8. In these patients, the average LDL-C level at baseline was 141 mg/dL in both the Praluent and placebo groups.<sup>1</sup>

Across all primary and secondary endpoints assessed, there were statistical differences in favor of Praluent compared to placebo.<sup>1</sup> Patients treated with Praluent achieved average LDL-C levels of less than 85 mg/dL at week 12,<sup>6</sup> and maintained reductions through 78 weeks of therapy.<sup>1</sup>

### Summary of Primary and Select Secondary Endpoints

		Baseline LDL-C	% LDL-C reduction from baseline (week 24) <sup>a</sup>	% achieved LDL-C goal <sup>b</sup> (week 24)	Greater % reduction for Praluent vs. placebo groups (on-treatment analysis) <sup>c</sup>		
					Week 24	Week 52	Week 78
Initially treated with 75 mg (FH I and FH II)	Praluent	141	49 <sup>d</sup>	75 <sup>d</sup>	56 <sup>d</sup>	58 <sup>d</sup>	56 <sup>d</sup>
	Placebo	141	-7	5			
Initially treated with 150 mg (LONG TERM and HIGH FH)	Praluent	168	55	64.5	57	60	63
	Placebo	162	-1	4			

Note: p less than 0.0001 vs. placebo for all data points

<sup>a</sup> Primary efficacy endpoint

<sup>b</sup> LDL-C goal either 70 mg/dL or 100 mg/dL depending on baseline CV risk

<sup>c</sup> On-treatment analysis (all other data is intention-to-treat)

<sup>d</sup> Includes 42 percent of patients treated with Praluent who had their dose adjusted to 150 mg at week 12

Praluent, a human monoclonal antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9), is 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 CV disease (ASCVD), who require



additional lowering of LDL-C. The effect of Praluent on CV morbidity and mortality has not been determined. In July, the European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) recommended the approval of Praluent in certain adult patients with hypercholesterolemia, and a final decision from the European Commission is anticipated in September.

#### **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](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

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

#### **References**

1. Kastelein JJP, Farnier M, Hovingh GK, et al. Efficacy and safety of the PCSK9 monoclonal antibody alirocumab vs placebo in 1257 patients with heterozygous familial hypercholesterolaemia: analyses up to 78 weeks from four ODYSSEY trials. Oral presentation at ESC Congress 2015 (#5772): 29 August-2 September 2015.
2. Kastelein JJP, Ginsberg HN, Langslet G, et al. ODYSSEY FH I and FH II: 78 week results with alirocumab treatment in 735 patients with heterozygous familial hypercholesterolaemia. *European Heart Journal* 2015: doi:10.1093/eurheartj/ehv370.
3. FH Foundation. *What is FH?* Available from: <http://thefhfoundation.org/about-fh/what-is-fh/> Last accessed 6 August 2015.
4. Goldberg AC, Hopkins PN, Toth PP et al. Familial Hypercholesterolemia: Screening, diagnosis and management of pediatric and adult patients. *J Clin Lipidol*. 2011;5:S1-S8.
5. Reiner Z, Catapano AL, De Backer G, et al. The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS): ESC/EAS Guidelines for the management of dyslipidaemias. *European Heart Journal* 2011: 32;1769-1818.
6. Kastelein JJP, Farnier M, Hovingh GK, et al. Efficacy and safety of the PCSK9 monoclonal antibody alirocumab vs placebo in 1257 patients with heterozygous familial hypercholesterolaemia: analyses up to 78 weeks from four ODYSSEY trials. Abstract from the ESC Congress 2015: 29 August-2 September 2015.

#### **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 have 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](http://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, including without limitation Praluent; the impact of the opinion adopted by the European Medicine Agency's Committee for Medicinal Products for Human Use discussed in this news release on the European Commission's decision regarding the Marketing Authorization Application for Praluent in the European Union; 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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