

# REGENERON®

## FDA Approves Praluent® (alirocumab) to Prevent Heart Attack, Stroke and Unstable Angina Requiring Hospitalization

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- Praluent is the first PCSK9 inhibitor that has shown a meaningful reduction in death from any cause
- Praluent treatment effect was observed in patients already receiving other lipid-lowering therapies, including maximally-tolerated statins

[Regeneron Pharmaceuticals, Inc.](#) (NASDAQ: **REGN**) and Sanofi today announced that the U.S. Food and Drug Administration (FDA) has approved Praluent® (alirocumab) to reduce the risk of heart attack, stroke and unstable angina requiring hospitalization in adults with established cardiovascular (CV) disease.

"Heart disease accounts for one quarter of all American deaths each year and many others are at risk for heart attack and stroke due to uncontrolled LDL-C levels," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer, Regeneron. "The Phase 3 ODYSSEY OUTCOMES trial showed that people who received Praluent significantly reduced their risk for serious cardiovascular events. There was also a clinically-meaningful reduction in death from any cause with Praluent treatment. With this approval, and the recent introduction of a lower U.S. Praluent list price, we hope that more patients in need will be able to access Praluent."

High levels of "bad" cholesterol, also known as low-density lipoprotein cholesterol (LDL-C), increase patients' risk for serious CV events such as heart attack or stroke. Adults who experience a heart attack or stroke have an approximately one in three chance to have another CV event.

"Today's FDA approval marks a significant achievement in the treatment of adults with established cardiovascular disease, who are among those at greatest risk of death or disability caused by serious cardiovascular events," said John Reed, M.D., Ph.D., Global Head of Research & Development, Sanofi. "Praluent has already helped many adults lower their LDL-C levels, and this new indication provides an opportunity to help appropriate patients by reducing the risk of serious, life-threatening cardiovascular events, including heart attacks and stroke."

The FDA approval is based on data from ODYSSEY OUTCOMES, which was published in the [New England Journal of Medicine](#) in November 2018, assessing the effect of adding Praluent to maximally-tolerated statins on CV outcomes in 18,924 patients who had an acute coronary syndrome (ACS) within a year of enrolling in the trial. Patients who received Praluent in the trial experienced:

- A 15% reduced risk for major CV events. The primary endpoint included time to first heart attack, stroke, death from coronary heart disease (CHD), or unstable angina requiring hospitalization (HR 0.85; 95% CI, 0.78 to 0.93; p=0.0003).
- A 27% reduced risk of stroke, 14% reduced risk of non-fatal heart attack and 39% reduced risk of unstable angina requiring hospitalization.\*
- A 15% reduced risk of death from any cause (also called all-cause mortality; HR 0.85; 95% CI, 0.73 to 0.98; nominal p=0.026) was also observed.\*

\*Because statistical testing of these endpoints was performed outside of the hierarchy, the results are not considered statistically significant.

Adverse events were similar between the Praluent and placebo groups, except for injection site reactions (Praluent 3.8%, placebo 2.1%). In ODYSSEY OUTCOMES, the adverse events that occurred in ≥5% of patients included: non-cardiac chest pain (7.0% Praluent, 6.8% placebo), nasopharyngitis (6.0% Praluent, 5.6% placebo) and myalgia (5.6% Praluent, 5.3% placebo).

The FDA also approved Praluent as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce LDL-C.

Praluent was the first PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitor approved by the FDA and is the only PCSK9 inhibitor available in two doses with two levels of efficacy as a single 1 mL injection (75 mg and 150 mg) once every two weeks. It can also be administered as 300 mg once every four weeks (monthly), enabling physicians to tailor treatment based on an individual patient's LDL-C-lowering needs.

### About ODYSSEY OUTCOMES

ODYSSEY OUTCOMES, the longest CV outcomes trial of any PCSK9 inhibitor to date, assessed the effect of Praluent on the occurrence of major adverse CV events in patients who had experienced an ACS before enrolling in the trial, and who were already on intensive or maximally-tolerated statin treatment. Patients were randomized to receive Praluent (n=9,462) or a placebo (n=9,462) and were assessed for a median of 2.8 years, with some patients being treated for up to five years. Approximately 90% of patients were on high-intensity statins prior to randomization.

The trial was designed to maintain patients' LDL-C levels between 25-50 mg/dL (0.65-1.29 mmol/L), using two different doses of Praluent (75 mg and 150 mg). Praluent-treated patients started the trial on 75 mg every two weeks and switched to 150 mg every two weeks if their LDL-C levels remained above 50 mg/dL (n=2,615). Some patients who switched to 150 mg switched back to 75 mg if their LDL-C fell below 25 mg/dL (n=805), and patients who experienced two consecutive LDL-C measurements below 15 mg/dL (0.39 mmol/L) while on the 75 mg dose (n=730) stopped active Praluent therapy for the remainder of the trial.

### **About Praluent**

Praluent® (alirocumab) inhibits the binding of PCSK9 to the LDL receptor and thereby increases the number of available LDL receptors on the surface of liver cells to clear LDL, which lowers LDL-C levels in the blood. Praluent was developed by Regeneron and Sanofi under a global collaboration agreement and invented by Regeneron using the company's proprietary *VelocImmune*® technology that yields optimized fully-human monoclonal antibodies.

Praluent is approved in more than 60 countries worldwide, including the U.S., European Union (EU), Japan, Canada, Switzerland, Mexico and Brazil. In the U.S., Praluent is approved to reduce the risk of heart attack, stroke and unstable angina requiring hospitalization in adults with established CV disease. Praluent is also approved as an adjunct to diet, alone or in combination with other lipid lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce LDL-C.

### **Important Safety Information for the U.S.**

Do not use Praluent if you are allergic to alicumab 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.

### **About Regeneron Pharmaceuticals, Inc.**

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to seven FDA-approved treatments and numerous product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, neuromuscular diseases, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies, such as *VelocImmune*® which produces optimized fully-human antibodies, and ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit [www.regeneron.com](http://www.regeneron.com) or follow @Regeneron on Twitter.

### **About Sanofi**

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

Sanofi, Empowering Life

### **Regeneron Forward-Looking Statements and Use of Digital Media**

*This press 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; 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; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates, such as Praluent (including any impact of the U.S. Food and Drug Administration approval discussed in this press release on the commercialization of Praluent); 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 availability and extent of reimbursement of the Company's products (such as Praluent) from third-party payers, such as private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid (including any impact of the pricing strategy for Praluent referenced in this press release); coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates in clinical trials; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in other studies and lead to therapeutic applications; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as Praluent), research and clinical programs, and business, including those relating to patient privacy; 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, including without limitation Praluent; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's products and product candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; risks associated with intellectual property of other parties and pending or future litigation relating thereto, including without limitation the patent litigation and other proceedings relating to Praluent, EYLEA® (afibercept) Injection, and Dupixent® (dupilumab) Injection, the ultimate outcome of any such proceedings, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition; and the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), to be cancelled or terminated without any further product success. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2018. 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>).*

### **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 regarding the marketing and other potential of the product, or regarding potential future revenues from the product. 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, unexpected regulatory actions or delays, or government regulation generally, that could affect the availability or commercial potential of the product, the absence of guarantee that the product will be commercially successful, the uncertainties inherent in research and development, including future clinical data and analysis of existing clinical data relating to the product, including post marketing, unexpected safety, quality or manufacturing issues, competition in general, risks associated with intellectual property and any related future litigation and the ultimate outcome of such litigation, and volatile economic conditions, as well as those risks 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, 2018. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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