



Regeneron and Sanofi Announce First Approval of Kevzara™ (sarilumab) for the Treatment of Moderately to Severely Active Rheumatoid Arthritis in Adult Patients by Health Canada

February 1, 2017

TARRYTOWN, N.Y. and PARIS, Feb. 1, 2017 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that Health Canada approved Kevzara™ (sarilumab), an interleukin-6 (IL-6) receptor antibody, for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more biologic or non-biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs).¹

"With Kevzara, we have a promising new therapy in Canada, which has shown clinically-meaningful and statistically significant improvements in adult patients with moderately to severely active rheumatoid arthritis," said Dr. William Bensen, Clinical Professor of Rheumatology, Department of Medicine at McMaster University, Ontario, Canada. "Kevzara represents a welcome new treatment option that works differently from the most commonly used biologics."

Kevzara is a fully human monoclonal antibody that binds specifically to both soluble and membrane-bound IL-6 receptors, and has been shown to inhibit IL-6-mediated signalling through these receptors.¹ Local production of IL-6 by synovial and endothelial cells in joints affected in chronic inflammatory disease, such as RA, may play an important role in development of the inflammatory processes.¹

"While there have been advances in the treatment of rheumatoid arthritis, not all available therapies work for every patient and there remains an unmet need for new therapeutic options," said David Meeker, M.D., Executive Vice President and Head of Sanofi Genzyme. "The approval of Kevzara in Canada represents an important advancement in treating adult patients with moderately to severely active RA."

RA is a systemic inflammatory disease that can affect multiple joints in the body. In RA, inflammation manifests in the lining of the joints causing pain, swelling, joint damage and can lead to deformity. RA impacts 70 million adults worldwide.^{2,3} In Canada alone, RA affects approximately 300,000 people. RA is most common in people between 40 and 60 years old; however, it can occur in adults at any age.⁴

The Health Canada approval of Kevzara was based on data from the global SARIL-RA clinical trial program which includes approximately 2,900 adults with moderately to severely active RA who had an inadequate response to previous treatment regimens. Kevzara demonstrated clinically-meaningful improvements, either as monotherapy or in combination with conventional DMARDs, including methotrexate, in reducing signs and symptoms, improving physical function, and inhibiting radiographic progression of structural damage of RA in approximately 1,743 patients with moderately to severely active RA.^{5,6,7,8,9,10} Kevzara should be used in combination with methotrexate or other traditional DMARDs, or may be given as monotherapy in cases of intolerance or contraindication to methotrexate or DMARDs.¹ The recommended dose of Kevzara is 200 mg once every two weeks given as a subcutaneous injection; dosage can be reduced from 200 mg to 150 mg once every two weeks to help manage certain laboratory abnormalities.¹

Patients treated with Kevzara are at increased risk for developing serious infections that may lead to hospitalization or death.¹ The most frequent adverse reactions (occurring in at least 3% of patients treated with Kevzara in combination with DMARDs) observed with Kevzara in the clinical studies were neutropenia (6-10%), increased alanine aminotransferase (4-5%), injection site erythema (3-4%), and upper respiratory tract infections (3%).¹

Kevzara is expected to be available to patients in Canada soon and there will be a patient support program at the time of product availability. The companies are committed to helping patients who are prescribed Kevzara gain access to the medicine and receive the support they may need. In Canada, Kevzara will be marketed by Sanofi Genzyme, the specialty care global business unit of Sanofi. The full Product Monograph in Canada is available [here](#).

Update on U.S. and European Regulatory Submissions

The resubmission of the sarilumab Biologics License Application (BLA) to the United States Food and Drug Administration (FDA) is expected in the first quarter of 2017. This resubmission is subject to successful completion of an inspection by FDA of Sanofi's Le Trait fill and finish facility, with an anticipated action date in the second quarter.

The European Medicines Agency accepted for review the Marketing Authorization Application for sarilumab in July 2016 and a decision is expected later this year.

"Regeneron and Sanofi look forward to resubmitting the U.S. BLA for Kevzara later this quarter and anticipate a new U.S. action date in the second quarter of 2017," said Robert Terifay, Executive Vice President, Commercial, Regeneron. "We are especially grateful for the commitment of the patients and investigators who participated in our SARIL-RA clinical program, and have helped to bring this important new therapy to RA patients."

About Sanofi

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi is organized into five global business units: Diabetes and Cardiovascular, General Medicines and Emerging Markets, Sanofi Genzyme, Sanofi Pasteur and Consumer Healthcare. 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 that discovers, invents, develops, manufactures and commercializes medicines for the treatment of serious medical conditions. Regeneron commercializes medicines for eye diseases, high LDL

cholesterol and a rare inflammatory condition and has product candidates in development in other areas of high unmet medical need, including rheumatoid arthritis, atopic dermatitis, asthma, pain, cancer and infectious diseases. For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

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", "looks forward" 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, 2015. 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 KevzaraTM (sarilumab) for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more biologic or non-biologic Disease-Modifying Anti-Rheumatic Drugs or other potential indications; the timing and effectiveness of the corrective measures taken or planned to be taken by Sanofi in response to the Complete Response Letter from the U.S. Food and Drug Administration (the "FDA") regarding the biologics license applications for Kevzara, as well as Sanofi's ability to resolve the previously identified deficiencies timely or at all; 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, such as Kevzara; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates, including without limitation Kevzara (including possible regulatory approval of Kevzara by the FDA and by the European Medicines Agency); 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, such as Kevzara; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as Kevzara), research and clinical programs, and business, including those relating to patient privacy; 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, including without limitation Kevzara; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; 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 (or their respective affiliated companies, as applicable), 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, 2015 and its Form 10-Q for the quarterly period ended September 30, 2016. 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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¹ Kevzara (sarilumab) Product Monograph Health Canada. January 2017.

² Gibofsky, A. Overview of Epidemiology, Pathophysiology, and Diagnosis of Rheumatoid Arthritis. *Am J Manag Care*. 2012 Dec;18(13)

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³ United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Prospects: The 2015 Revision, Key Findings and Advance Tables. Working Paper No. ESA/P/WP.241.

⁴ The Arthritis Society. Rheumatoid Arthritis. Available at: <https://arthritis.ca/understand-arthritis/types-of-arthritis/rheumatoid-arthritis>. Last Accessed January 2017 .

⁵ Genovese, MC. Sarilumab Plus Methotrexate in Patients With Active Rheumatoid Arthritis and Inadequate Response to Methotrexate: Results of a Phase III Study. *Arthritis Rheumatology*. 2015 Jun 67(6):1424-37..

⁶ Fleischmann, R. Sarilumab and Non-Biologic Disease-Modifying Antirheumatic Drugs in Patients With Active RA and Inadequate Response or Intolerance to TNF Inhibitors. *Arthritis Rheumatology*. 2016 Nov 10.1002/art.39944..

⁷ Sanofi. To Evaluate Sarilumab - SAR153191 (REGN88) - Auto-injector Device In Patients With Rheumatoid Arthritis (SARIL-RA-EASY). In: [ClinicalTrials.gov](https://clinicaltrials.gov) [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 28 May 2015]. Available from: <https://clinicaltrials.gov/ct2/show/NCT02057250> NLM Identifier: NCT02057250.

⁸ Emery P, Rondon J, Garg A, et al. Safety and tolerability of subcutaneous sarilumab compared to intravenous tocilizumab in patients with RA. *Arthritis Rheumatol*. 2015;67(suppl 10): 971..

⁹ Burmester G, Garg A, van Hoogstraten H, et al. Sarilumab dose reduction to manage laboratory abnormalities in an open-label extension study in RA patients. *Arthritis Rheumatol*. 2015;67 (suppl 10): 2762..

¹⁰ Sanofi. To Evaluate the Immunogenicity and Safety of Sarilumab Administered as Monotherapy in Patients With Rheumatoid Arthritis (RA) (SARIL-RA-ONE). In: [ClinicalTrials.gov](https://clinicaltrials.gov) [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 28 May 2015].

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