Regeneron and Sanofi Announce FDA Approval of Kevzara® (sarilumab) for the Treatment of Moderately to Severely Active Rheumatoid Arthritis in Adult Patients

May 22, 2017

TARRYTOWN, N.Y. and PARIS, May 22, 2017 /PRNewswire/ --

- *Kevzara is now available to U.S. patients*

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced the U.S. Food and Drug Administration (FDA) approval of Kevzara® (sarilumab) 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 disease modifying antirheumatic drugs (DMARDs), such as methotrexate (MTX). Kevzara is a human monoclonal antibody that binds to the interleukin-6 receptor (IL-6R), and has been shown to inhibit IL-6R mediated signaling. IL-6 is a cytokine in the body that, in excess and over time, can contribute to the inflammation associated with RA.

"In the clinical trial program, sarilumab demonstrated statistically significant, clinically-meaningful improvements in adult patients with rheumatoid arthritis by reducing signs and symptoms and improving physical function, resulting in significantly less radiographic progression of structural damage of RA," said Alan Kivitz, M.D., CPI, Founder and Medical Director of the Altoona Center for Clinical Research and Altoona Arthritis and Osteoporosis Center, and an investigator in the global SARIL-RA clinical program for sarilumab. "This is important because not all currently available treatments work in all patients, and some patients may spend years cycling through different treatments without achieving their treatment goals. Sarilumab works differently from the most commonly used biologics, such as those in the anti-TNF class, and is a welcome new option for patients and their physicians."

RA is a chronic inflammatory autoimmune disease, which carries substantial burden. In RA, the immune system attacks the tissues of the joints, causing inflammation, pain, and eventually joint damage and disability. RA affects approximately 1.3 million Americans, with nearly 75 percent being women. It most often strikes people between 30 and 60 years old; however, it can occur in adults at any age.

"Despite the many advances made in the treatment of rheumatoid arthritis, patients continue to need new treatment options," said Olivier Brandicourt, M.D., Chief Executive Officer, Sanofi. "Today's approval in the U.S. not only underscores our ongoing commitment to making a difference in the lives of patients, but also demonstrates our drive to accelerate science and medicine in immunology."

"Today's milestone with Kevzara, which follows closely on the heels of our recent approval of Dupixent (dupilumab), showcases the ability of our internal discovery and science engine to deliver important new medicines by leveraging our leading technologies, such as VelocImmune," said George D. Yancopoulos, M.D., Ph.D., Founding Scientist, President, and Chief Scientific Officer, Regeneron. "This milestone would not have been possible without our important ongoing collaboration with Sanofi, and most importantly, the patients and physicians who participated in our SARIL-RA clinical program, and worked with us to make Kevzara available to those in the U.S. RA community in need of new options."

Kevzara may be used as monotherapy or in combination with MTX or other conventional DMARDs. The recommended dosage of Kevzara is 200 mg once every two weeks given as a subcutaneous injection, which can be self-administered. The dosage can be reduced from 200 mg to 150 mg once every two weeks, as needed, to help manage certain laboratory abnormalities (neutropenia, thrombocytopenia, and liver enzyme elevations).

The approval of Kevzara was based on data from approximately 2,900 adults with moderately to severely active RA who had an inadequate response to previous treatment regimens. In two pivotal Phase 3 clinical trials, Kevzara plus background DMARDs demonstrated statistically significant, clinically-meaningful improvements in patients with moderately to severely active RA.

In the MOBILITY study, treatment with Kevzara plus MTX reduced signs and symptoms, improved physical function, and demonstrated significantly less radiographic progression of structural damage, compared to placebo plus MTX.

- At 24 weeks, patients treated with Kevzara plus MTX achieved a greater improvement in the primary endpoint of signs and symptoms as measured by the proportion of patients achieving a 20 percent improvement in the American College of Rheumatology Criteria (ACR20) (Kevzara 200 mg, 66 percent; Kevzara 150 mg, 58 percent; placebo, 33 percent)
- At 52 weeks, patients treated with Kevzara plus MTX demonstrated significantly less radiographic progression of structural damage as measured by the change in modified Total Sharp Score, a key endpoint of the study (placebo, 2.78; Kevzara 200 mg, 0.25; Kevzara 150 mg, 0.90)
- At 16 weeks, patients treated with Kevzara plus MTX demonstrated greater improvement from baseline in physical function as measured by the Health Assessment Questionnaire - Disability Index (HAQ-DI), a key endpoint of the study (Kevzara 200 mg, -0.58; Kevzara 150 mg, -0.54; placebo, -0.30)

In the TARGET study, treatment with Kevzara plus DMARD reduced signs and symptoms and improved physical function, compared to placebo plus DMARD.

- At 24 weeks, patients treated with Kevzara plus DMARD achieved a greater improvement in the primary endpoint of signs and symptoms as measured by the proportion of patients achieving an ACR20 response (Kevzara 200 mg, 61 percent; Kevzara 150 mg, 56 percent; placebo, 34 percent)

- At 12 weeks, patients treated with Kevzara plus DMARD demonstrated greater improvement from baseline in physical function as measured by HAQ-DI, a key endpoint of the study (Kevzara 200 mg, -0.49; Kevzara 150 mg, -0.50; placebo, -0.29)

Patients treated with Kevzara are at increased risk of developing serious infections that may lead to hospitalization or death. The most common adverse reactions (occurring in at least 3 percent of patients treated with Kevzara in combination with DMARDs vs. placebo in combination with DMARDs) observed with Kevzara in the clinical studies were neutropenia (7-10 percent vs. 0.2 percent), increased alanine aminotransferase (5 percent vs. 2 percent), injection site erythema (4-5 percent vs. 0.9 percent), upper respiratory infections (3-4 percent vs. 2 percent) and urinary tract infections (3 percent vs. 2 percent).

Sanofi and Regeneron are committed to helping patients in the U.S. who are prescribed Kevzara gain access to the medicine and receive the support they may need. The companies have launched KevzaraConnect®, a comprehensive and specialized program that provides support services to patients throughout every step of the treatment process. KevzaraConnect will also help eligible patients who are uninsured, lack coverage, or need assistance with their out-of-pocket copay costs. Additionally, KevzaraConnect offers personalized support from registered nurses and other specialists who are available 24/7 to speak with patients and help them navigate the complex insurance process. For more information, please call 1-844-Kevzara (1-844-538-9272) or visit www.Kevzara.com.

The U.S. Wholesale Acquisition Cost (WAC) of Kevzara is $39,000/year for the 200 mg and 150 mg doses, and is approximately 30 percent lower than the WAC for the two most widely used TNF-alpha inhibitors. Actual costs to patients, payers and health systems are anticipated to be lower as WAC does not reflect discounts, rebates or copay support.

In the U.S., Kevzara will be marketed by Regeneron and Sanofi Genzyme, the specialty care global business unit of Sanofi. Kevzara was approved in Canada in January 2017. In April 2017, the European Medicine Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion for the marketing authorization of Kevzara recommending its approval for use in adult patients with moderately to severely active RA. A final decision on the Marketing Authorization Application (MAA) for Kevzara in the European Union will be made by the European Commission in the coming months. The companies are also seeking approvals in a number of other countries globally.

IMPORTANT SAFETY INFORMATION

Kevzara can cause serious side effects including:

- **SERIOUS INFECTIONS**: **Kevzara is a medicine that affects your immune system. Kevzara can lower the ability of your immune system to fight infections. Some people have serious infections while using Kevzara, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses that can spread throughout the body. Some people have died from these infections.**
    - Before starting Kevzara, tell your healthcare provider if you:
        - think you have an infection or have symptoms of an infection, with or without a fever, such as sweats or chills, muscle aches, cough, shortness of breath, blood in phlegm, weight loss, warm, red or painful skin or sores on your body, diarrhea or stomach pain, burning when you urinate or urinating more often than normal or feel very tired; or are being treated for an infection, get a lot of infections or have repeated infections
        - have diabetes, HIV, or a weakened immune system.
        - have TB, or have been in close contact with someone with TB
        - live or have lived, or have traveled to certain parts of the country (such as the Ohio and Mississippi River valleys and the Southwest) where there is an increased chance of getting certain fungal infections (histoplasmosis, coccidioidomycosis, or blastomycosis)
        - have or have had hepatitis
    - After starting Kevzara, call your healthcare provider right away if you have any symptoms of an infection.
- **CHANGES IN CERTAIN LABORATORY TEST RESULTS:** Your healthcare provider should do blood tests before and after starting Kevzara to check for low neutrophil (white blood cells that help the body fight off bacterial infections) counts, low platelet (blood cells that help with blood clotting and stop bleeding) counts, and an increase in certain liver function tests. Changes in test results are common with Kevzara and can be severe. You may also have changes in other laboratory tests, such as your blood cholesterol levels.
- **TEARS (PERFORATION) OF THE STOMACH OR INTESTINES:** Some people using Kevzara get tears in their stomach or intestine. Call your healthcare provider right away if you have fever and stomach (abdominal) pain that does not go away.
- **CANCER:** Kevzara may increase your risk of certain cancers by changing the way your immune system works. Tell your healthcare provider if you have ever had any type of cancer.
- **SERIOUS ALLERGIC REACTIONS:** Serious allergic reactions can happen with Kevzara. Get medical attention right away if you have any of the following signs: shortness of breath or trouble breathing; feeling dizzy or faint; swelling of the lips, tongue or face; moderate to severe stomach (abdominal) pain or vomiting; or chest pain.

- Do not use Kevzara if you are allergic to Sarilumab or any of the ingredients of Kevzara.

- Before using Kevzara, tell your healthcare provider if you:
    - have an infection
    - have liver problems
    - have had stomach (abdominal) pain or a condition known as diverticulitis (inflammation in parts of the large intestine) or ulcers in your stomach or intestines
    - recently received or are scheduled to receive a vaccine. People who take Kevzara should not receive live vaccines.
    - plan to have surgery or a medical procedure
    - are pregnant or plan to become pregnant. It is not known if Kevzara will harm your unborn baby
    - are breastfeeding or plan to breastfeed. Talk to your healthcare provider about the best way to feed your baby if you use Kevzara. It is not known if Kevzara passes into your breastmilk.
    - take any medicines, including prescription and nonprescription medicines, vitamins, and herbal supplements. Especially tell your healthcare provider if you use any other medicines to treat your RA. Using Kevzara with these medicines may increase your risk of infection.

- The most common side effects include:
    - injection site redness
    - upper respiratory tract infection
    - urinary tract infection
    - nasal congestion, sore throat, runny nose

These are not all the possible side effects of Kevzara. Tell your doctor about any side effect that bothers you or does not go away. You are encouraged to report negative side effects of prescription drugs to the FDA at www.fda.gov/medwatch or call 1-800-FDA-1088 or to Sanofi-Aventis at 1-800-633-1610.

To learn more, talk about Kevzara with your healthcare provider or pharmacist. The FDA-approved Medication Guide and Prescribing Information can be found at Kevzara.com or by calling 1-844-Kevzara (1-844-538-9272).

Please click here for full prescribing information including risk of SERIOUS SIDE EFFECTS and Medication Guide

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).

Sanofi Genzyme focuses on developing specialty treatments for debilitating diseases that are often difficult to diagnose and treat, providing hope to patients and their families.

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. All Regeneron commercialized medicines were discovered and developed by our own scientists, including therapies for eye diseases, high LDL cholesterol, atopic dermatitis, rheumatoid arthritis, and a rare inflammatory condition. Regeneron also has product candidates in development in other areas of high unmet medical need, including asthma, pain, cancer and infectious diseases. Regeneron invented the leading VelociSuite® technologies, which are a suite of complementary genetics-based technologies that accelerate, improve and disrupt the traditional drug discovery and development process and established the Regeneron Genetics Center, one of the largest genetic sequencing efforts in the world. 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 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, 2016. 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 Kevzara® (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 disease modifying antirheumatic drugs or other potential indications; the impact of the opinion adopted by the European Medicine Agency's Committee for Medicinal Products for Human Use referenced in this news release on the European Commission's decision regarding the Marketing Authorization Application for Kevzara in the European Union; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates, such as the possible regulatory approval and commercial launch of Kevzara in additional jurisdictions; 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; 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; the ability of Regeneron's collaborators, suppliers, or other third parties to perform filling, finishing, packaging, labelling, 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 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, Bayer, and Teva Pharmaceutical Industries Ltd. (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, including without limitation the patent litigation relating to Praluent® (alirocumab) Injection, the permanent injunction granted by the United States District Court for the District of Delaware that, if upheld on appeal, would prohibit Regeneron and Sanofi from marketing, selling, or commercially manufacturing Praluent in the United States, the outcome of any appeals regarding such injunction, the ultimate outcome of such litigation, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. 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, 2016 and its Form 10-Q for the quarterly period ended March 31, 2017. 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).

Contacts Sanofi:

Media Relations
Ashleigh Koss
Tel: 908-981-8745
ashleigh.koss@sanofi.com

Investor Relations
George Grofik
Tel. +33 (0)1 53 77 45 45
ir@sanofi.com

U.S. Communications
Carrie Brown
Tel: 908-981-6486
Mobile: 908-247-6006
carrie.brown@sanofi.com

Contacts Regeneron:

Media Relations
Arleen Goldenberg
Tel: 1 (914) 847-3456
Mobile: +1 (914) 260-8788
arleen.goldenberg@regeneron.com

Investor Relations
Manisha Narasimhan, Ph.D.
Tel: 1 (914) 847-5126
Manisha.narasimhan@regeneron.com