Regeneron and Sanofi Announce Approval of Kevzara® (sarilumab) to Treat Adult Patients with Moderately to Severely Active Rheumatoid Arthritis in the European Union

June 27, 2017

TARRYTOWN, N.Y. and PARIS, June 27, 2017 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that the European Commission (EC) has granted marketing authorization for Kevzara® (sarilumab) in combination with methotrexate (MTX) for the treatment of moderately to severely active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs (DMARDs), such as MTX. Kevzara may be used as monotherapy in case of intolerance to MTX or when treatment with methotrexate is inappropriate.

Kevzara is a human monoclonal antibody that binds to the interleukin-6 receptor (IL-6R), and blocks pro-inflammatory IL-6 mediated signaling. Elevated levels of IL-6 are found in the synovial fluid of patients with RA and play an important role in both the pathologic inflammation and joint destruction which are hallmarks of RA. Kevzara was developed using Regeneron's proprietary VelocImmune® technology that yields optimized fully-human antibodies.

"RA is a difficult-to-treat, lifelong disease and many healthcare providers are challenged with finding a treatment that works for their patients," said Elias Zerhouni, M.D., President, Global R&D, Sanofi. "Kevzara works differently from some of the other most commonly used biologics, and its approval is good news for the many patients where a high unmet need remains."

RA affects approximately 2.9 million people in Europe alone. In RA, the immune system attacks the tissues of the joints, causing inflammation, joint pain, swelling, stiffness, fatigue and eventually joint damage and disability. RA is most common in those aged 35-50 years old.

"We are pleased to bring Kevzara to European patients who may not be responding to the most commonly used biologics such as TNF inhibitors, or who may be seeking an effective monotherapy to reach their treatment goals," said George D. Yancopoulos, M.D., Ph.D., Founding Scientist, President, and Chief Scientific Officer, Regeneron. "This approval was made possible through the hard work of our innovative scientists, as well as thousands of dedicated investigators and patients around the world who participated in the SARIL-RA clinical trial program."

The EC approval is based upon receipt of a positive opinion by European Medicine Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP), which evaluated results from seven Phase 3 trials in the global SARIL-RA clinical development program. These studies incorporate data from more than 3,300 adults with moderately to severely active RA who have had an inadequate response or intolerance to one or more biologic or non-biologic DMARDs.

The program includes the Phase 3 MONARCH study, in which treatment with Kevzara 200 mg monotherapy was superior to adalimumab 40 mg (marketed by AbbVie as HUMIRA®) monotherapy in reducing disease activity and improving physical function, with more patients achieving clinical remission over 24 weeks.

- At 24 weeks, patients treated with Kevzara demonstrated greater reduction in disease activity as measured by change from baseline in the Disease Activity Score with 28 joint count and erythrocyte sedimentation rate (DAS28-ESR), the primary endpoint of the study (Kevzara, -3.28; adalimumab, -2.20; p less than 0.0001)
- At 24 weeks, patients treated with Kevzara demonstrated greater improvement from baseline in physical function as measured by the Health Assessment Questionnaire - Disability Index (HAQ-DI), a secondary endpoint of the study (Kevzara, -0.61; adalimumab, -0.43; p=0.0036)
- At 24 weeks, patients treated with Kevzara achieved higher rates of DAS28-ESR remission (score &#60 2.6), a secondary endpoint of the study (Kevzara, 26.6 percent; adalimumab, 7.0 percent; p less than 0.0001)
- At 24 weeks, patients treated with Kevzara demonstrated a greater improvement in signs and symptoms of RA as measured by the proportion of patients achieving a 20 percent improvement in the ACR criteria (ACR20) (Kevzara, 71.7 percent; adalimumab, 58.4 percent; p=0.0074). The proportion of patients achieving ACR50 was also higher with Kevzara (Kevzara, 45.7 percent; adalimumab, 29.7 percent; p=0.0017) as well as for ACR70 (Kevzara, 23.4 percent; adalimumab, 11.9 percent; p=0.0036). ACR20, ACR50, and ACR70 response at week 24 were secondary endpoints of the study.

In the Phase 3 MOBILITY study, treatment with Kevzara plus MTX reduced signs and symptoms, improved physical function, and at week 52, inhibited the progression of structural damage by 91 percent for the Kevzara 200 mg dose and 68 percent for the Kevzara 150 mg dose, compared to placebo plus MTX. In the Phase 3 TARGET study, treatment with Kevzara plus DMARD reduced signs and symptoms and improved physical function, compared to placebo plus DMARD. Detailed results from the MOBILITY and TARGET studies are available in the Kevzara (sarilumab) FDA approval press release here.

The recommended dose of Kevzara is 200 mg once every 2 weeks administered as a subcutaneous injection with a prefilled syringe or prefilled pen.[1] If necessary, reduction of dose from 200 mg once every 2 weeks to 150 mg once every 2 weeks is recommended to help manage certain laboratory abnormalities (neutropenia, thrombocytopenia, and liver enzyme elevations).

The most frequent adverse reactions observed with Kevzara in clinical studies as indicated were neutropenia, increased alanine aminotransferase, injection site erythema, upper respiratory infections, and urinary tract infections. The most common serious adverse reactions were infections.

Treatment with Kevzara should be withheld in patients who develop a serious infection until the infection is controlled. Initiating treatment with Kevzara is not recommended in patients with a low neutrophil count, i.e., absolute neutrophil count (ANC) &#60 2 x 10^9/L and in patients with a platelet count below 150 x 10^3/µL.

Kevzara is also approved in the United States and Canada. The companies are also seeking approvals in a number of other countries globally.

Important Safety Information for U.S.

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 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 biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led by physician-scientists for nearly 30 years, our unique ability to repeatedly and consistently translate science into medicine has led to six FDA-approved treatments and over a dozen product candidates, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye disease, heart disease, allergic and inflammatory diseases, pain, cancer, and infectious and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its unique VelociSuite® technologies, including VelocImmune® which yields optimized fully-human antibodies, and ambitious initiatives such as the Regeneron Genetics Center, one of the largest genetics 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 moderately to severely active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to, one or more disease modifying anti-rheumatic drugs or other potential indications; 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).

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