



## **Kevzara® (sarilumab) Data at the 2018 ACR/ARHP Annual Meeting Provide Additional Insight on Safety and Efficacy in Rheumatoid Arthritis**

October 19, 2018

**Among 13 Alliance presentations, a late-breaker poster will highlight potential for IL-6 levels to serve as a biomarker to help predict treatment response**

TARRYTOWN, N.Y. and BRIDGEWATER, N.J., Oct. 19, 2018 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi will present data from analyses of the Kevzara® (sarilumab) Phase 3 clinical development program at the 2018 ACR/ARHP Annual Meeting, which is being held in Chicago from October 19 to 24.

A late-breaking poster presentation will discuss new post-hoc analyses from the positive Phase 3 MONARCH and MOBILITY RA trials, which have previously reported results showing Kevzara significantly improved efficacy over two commonly-used RA therapies. The new analyses show patients with high baseline levels of interleukin-6 (IL-6) had higher disease activity and joint damage at baseline and showed a greater response to Kevzara 200 mg compared to either methotrexate (MTX) alone or adalimumab than patients with low IL-6 levels. In the MOBILITY trial, patients with high IL-6 levels treated with Kevzara were more likely to demonstrate improvement in clinical signs and symptoms and had less joint damage according to radiographic assessment, versus those with high IL-6 levels treated with MTX alone. In the MONARCH trial, patients with high IL-6 levels treated with Kevzara were more than 30 times as likely to achieve a measure of disease remission (disease activity score in 28 joints with an erythrocyte sedimentation rate less than 2.6) at week 24 compared to those treated with adalimumab (odds ratio 33.9 [unadjusted 95% CI 3.5, 328.7]). The incidence of treatment-emergent adverse events was similar in patients in the low, medium and high IL-6 groups. In Phase 3 clinical trials, the most common adverse reactions (incidence at least 2 percent) with Kevzara were neutropenia, increased ALT (a liver enzyme), injection site erythema, upper respiratory infections and urinary tract infections.

"The analysis of these Phase 3 data provides a look at the utility of biomarkers and their potential role in optimizing treatment choices for patients with RA," said Jonathan Sadeh, M.D., Vice President, Immunology and Inflammation Development Franchise, Sanofi. "We look forward to uncovering new insights that can help support physicians in their efforts to identify the right treatment plan for each patient with RA."

"It makes sense that patients with the highest level of IL-6 would respond best to a therapy that specifically inhibits this pathway – however, it's very exciting for the first time to have actual data supporting this concept. The application of biomarkers to predict response to different types of therapy could herald a new precision management approach to RA," said Bolanle Akinlade, M.D., Vice President, Clinical Sciences, Regeneron. "We are initiating additional Kevzara clinical trials in 2019 that will include the prospective evaluation of IL-6 levels as a predictor for treatment response. We believe this may have important future implications for personalized RA patient care."

Use of IL-6 as a biomarker has not been reviewed by any regulatory authority.

Data being presented at ACR also include three oral presentations, describing Kevzara safety and efficacy data for patients with low absolute neutrophil counts; and health economics and outcomes research data focusing on tumor necrosis factor (TNF) inhibitor versus non-TNF inhibitor treatment switching trends; as well as comparative effectiveness of first-line TNF inhibitor treatment versus non-TNF inhibitor treatment in patients who had not been on a biologic disease-modifying antirheumatic drug (bDMARD).

Kevzara is a fully-human monoclonal antibody, derived using Regeneron's proprietary *VelocImmune*® technology, that binds specifically to the IL-6 receptor, and has been shown to inhibit IL-6-mediated signaling. IL-6 is a signaling protein produced in increased quantities in patients with RA and has been associated with disease activity, joint destruction and other systemic problems.

Regeneron and Sanofi presentations include the following 10 poster presentations and three oral presentations:

### **Sunday, October 21 to Tuesday, October 23 (Late-Breaker Poster)**

- **High Baseline Serum IL-6 Identifies a Subgroup of Rheumatoid Arthritis Patients with Rapid Joint Damage and Clinical Progression and Predicts Increased Sarilumab Treatment Response**

Anita Boyapati, 9:00-11:00AM UTC (Late-breaking abstract poster presentation 9:00-11:00AM UTC on Tuesday, October 23)

### **Monday, October 22**

- **Exploring the Effects of Depressive Symptoms on the Efficacy of Sarilumab and Improvements in Health-Related Quality of Life**  
Vibeke Strand, 9:00-11:00AM UTC
- **Unique Changes in Hemoglobin with Sarilumab Versus Adalimumab Are Independent of Better Disease Control in Patients with Rheumatoid Arthritis (RA)**  
Gerd R. Burmester, 9:00-11:00AM UTC
- **Pain Is Improved in Around 50% of Patients and Fatigue in 40% of Patients with Rheumatoid Arthritis Treated with**

### **Sarilumab in the Target, Mobility and Monarch Trials**

Laure Gossec, 9:00-11:00AM UTC

- **The Relationship between Lipid Profile Changes and Inflammation across the Phase 3 Sarilumab Rheumatoid Arthritis (RA) Developmental Program**

Christina Charles-Schoeman, 9:00-11:00AM UTC

- **Reductions in Absolute Neutrophil Count (ANC) with Sarilumab Resulting in Dose Delays or Dose Decreases: Effects on Efficacy and Safety**

Jeffrey R. Curtis, 5:45-6:00PM UTC

### **Tuesday, October 23**

- **Long-Term Safety with Sarilumab Plus Conventional Synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs) and Sarilumab Monotherapy in Rheumatoid Arthritis (RA): An Integrated Analysis with 9,000 Patient-Years (Pt-Yrs) of Follow-up**

Roy Fleischmann, 9:00-11:00AM UTC

- **Long-Term Treatment with Sarilumab Plus Conventional Synthetic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs): Pooled Safety and Efficacy with over 4 Years' Treatment**

Mark C. Genovese, 9:00-11:00AM UTC

- **Liver Function Test Levels with Sarilumab Treatment in Phase 3 Trials: Analysis By Baseline Liver Function Test (LFT) Level**

John Tesser, 9:00-11:00AM UTC

- **Patient-Reported Benefits of Sarilumab Monotherapy in Adult Patients with Active Rheumatoid Arthritis: Results from an Open-Label Extension Study**

Vibeke Strand, 9:00-11:00AM UTC

- **The Impact of Rheumatoid Arthritis on Patient-Reported Outcomes: Comparison between Sarilumab Clinical Trials and Real-World Patient Data**

Vibeke Strand, 9:00-11:00AM UTC

- **Identifying Trends in Lines of Therapy Following Initial Biologic Disease-Modifying Antirheumatic Drug in Patients with Rheumatoid Arthritis**

Jay Lin, 4:45-5:00PM UTC

- **The Comparative Effectiveness of First-Line Tumor Necrosis Factor Inhibitor (TNFi) Compared with Non-TNFi Agents in Patients with Rheumatoid Arthritis: Results from the Corrona Registry**

Dimitrios A. Pappas, 5:15-5:30PM UTC

In the U.S., Kevzara is indicated for the treatment of adult patients with moderately to severely active RA who have had an inadequate response or intolerance to one or more disease modifying antirheumatic drugs, such as methotrexate. Kevzara is developed and commercialized under a collaboration between Regeneron and Sanofi.

### **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](http://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](http://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 Regeneron**

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*<sup>®</sup> technologies, such as *VelocImmune*<sup>®</sup> 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 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, timing, and scope of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products (such as Kevzara); unforeseen safety issues resulting from the administration of products and product candidates (such as Kevzara) 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 Kevzara), 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 Kevzara; 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; 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, labeling, distribution, and other steps related to Regeneron's products and product candidates; the availability and extent of reimbursement of the Company's products (such as Kevzara) from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; 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; 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 proceedings relating to EYLEA® (afibercept) Injection, Dupixent® (dupilumab) Injection, and Praluent® (alirocumab) Injection, the ultimate outcome of any such litigation proceedings, 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 U.S. Securities and Exchange Commission, including its Form 10-Q for the quarterly period ended June 30, 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, 2017. 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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