



Regeneron and Sanofi Provide Update on Kevzara® (sarilumab) Phase 3 U.S. Trial in COVID-19 Patients

July 2, 2020

TARRYTOWN, N.Y. and PARIS, July 2, 2020 /PRNewswire/ -- [Regeneron Pharmaceuticals, Inc.](#) (NASDAQ: REGN) and Sanofi today announced that the U.S. Phase 3 trial of Kevzara® (sarilumab) 400 mg in COVID-19 patients requiring mechanical ventilation did not meet its primary and key secondary endpoints when Kevzara was added to best supportive care compared to best supportive care alone (placebo).

Minor positive trends were observed in the primary pre-specified analysis group (critical patients on Kevzara 400 mg who were mechanically ventilated at baseline) that did not reach statistical significance, and these were countered by negative trends in a subgroup of critical patients who were not mechanically ventilated at baseline.¹ In the primary analysis group, adverse events were experienced by 80% of Kevzara patients and 77% of placebo patients. Serious adverse events that occurred in at least 3% of patients and more frequently among Kevzara patients were multi-organ dysfunction syndrome (6% Kevzara, 5% placebo) and hypotension (4% Kevzara, 3% placebo).

Based on the results, the U.S.-based trial has been stopped, including in a second cohort of patients who received a higher dose of Kevzara (800 mg). Detailed results will be submitted to a peer-reviewed publication later this year.

The primary analysis group included 194 patients who were critically ill with COVID-19 and were receiving mechanical ventilation at the time of enrollment. The primary endpoint assessed the percentage of patients who achieved at least a 1-point change from baseline on a 7-point scale, which consisted of 1) death; 2) hospitalized, requiring invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) hospitalized, requiring non-invasive ventilation or high-flow oxygen devices; 4) hospitalized, requiring supplemental oxygen; 5) hospitalized, not requiring supplemental oxygen – requiring ongoing medical care (COVID-19 related or otherwise); 6) hospitalized, not requiring supplemental oxygen – no longer requires ongoing medical care; 7) discharged from hospital. A second cohort, which was partially recruited (n=27), compared Kevzara 800 mg versus placebo.

The Kevzara trial was designed after a small (n=21), single-arm study in China ([Xu et al](#)) among mostly severe, febrile, hospitalized COVID-19 patients found elevated IL-6 levels and suggested that inhibiting this pathway with the IL-6 blocker tocilizumab rapidly reduced fever and improved oxygenation in severe patients, allowing for successful hospital discharge. The Phase 3 Kevzara trial was designed to evaluate this hypothesis in a large, placebo-controlled trial. The trial has been funded in part with federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; and Biomedical Advanced Research and Development Authority (BARDA), under OT number: HHSO100201700020C.

A separate Sanofi-led trial outside of the U.S. in hospitalized patients with severe and critical COVID-19 using a different dosing regimen is ongoing. The same Independent Data Monitoring Committee (IDMC) is overseeing both the Regeneron-led U.S. trial and the Sanofi-led trial outside of U.S. and has recommended that the trial outside of the U.S. continue. The companies expect to report results of the trial outside of the U.S. in Q3 2020.

Footnote

1. Clinical trial endpoints that showed positive trends in patients on mechanical ventilation at baseline, and were countered by negative trends in patients who were not mechanically ventilated at baseline included: the proportion of patients with a 1-point improvement on day 22 (primary endpoint for mechanical ventilation group); the proportion of patients who died by day 29; and the proportion of patients who recovered by day 22.

About Kevzara® (sarilumab) Injection

Kevzara is currently approved in multiple countries to treat adults with moderately to severely active rheumatoid arthritis who have not responded to or tolerated previous therapy.

Kevzara binds specifically to the IL-6 receptor, and has been shown to inhibit IL-6-mediated signaling. IL-6 is an immune system protein produced in increased quantities in patients with rheumatoid arthritis and has been associated with disease activity, joint destruction and other systemic problems. Kevzara is being investigated for its ability to reduce the overactive inflammatory immune response associated with COVID-19 based on evidence of markedly elevated levels of IL-6 in critically ill patients infected with coronaviruses.

IMPORTANT SAFETY INFORMATION FOR KEVZARA® (sarilumab) INJECTION

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. Your healthcare provider should test you for TB before starting KEVZARA. Your healthcare provider should monitor you closely for signs and symptoms of TB during treatment with KEVZARA.**
 - 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. Symptoms may include sweats or chills, muscle aches, a cough, shortness of breath, blood in your 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, if you feel very tired, or if you 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. Your healthcare provider should do blood tests 4 to 8 weeks after starting KEVZARA and then every 6 months during treatment to check for an increase in blood cholesterol levels.
 - **TEARS (PERFORATION) OF THE STOMACH OR INTESTINES:** Tell your healthcare provider if you have had a condition known as diverticulitis (inflammation in parts of the large intestine) or ulcers in your stomach or intestines. Some people using KEVZARA had tears in their stomach or intestine. This happens most often in people who also take nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or methotrexate. 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 your lips, tongue or face; moderate or 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 breast milk
 - take any prescription or nonprescription medicines, vitamins or herbal supplements. It is especially important to 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
 - medicines that affect the way certain liver enzymes work. Ask your healthcare provider if you are not sure if your medicine is one of these
- The most common side effects include:
 - injection site redness
 - upper respiratory tract infection
 - urinary tract infection
 - nasal congestion, sore throat, and 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.

WHAT IS KEVZARA?

Kevzara is an injectable prescription medicine called an interleukin-6 (IL-6) receptor blocker. Kevzara is used to treat adult patients with moderately to severely active rheumatoid arthritis (RA) after at least one other medicine called a disease-modifying antirheumatic drug (DMARD) has been used and did not work well or could not be tolerated.

Click [here](#) for full Prescribing Information including risk of SERIOUS SIDE EFFECTS and Medication Guide for KEVZARA.

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 over 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, pain, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*[®] technologies, such as *VelocImmune* which uses unique genetically-humanized mice to produce optimized fully-human antibodies and bispecific antibodies, and through 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 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 impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, suppliers, and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs (including those discussed in this press release), Regeneron's ability to manage its supply chain, net product sales of products marketed by Regeneron and/or its collaborators (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and product candidates and research and clinical programs now underway or planned, including without limitation Kevzara[®] (sarilumab) for the treatment of hospitalized patients with severe or critical respiratory illness caused by COVID-19 and REGN-COV2 (Regeneron's investigational dual antibody cocktail for the prevention and treatment of COVID-19); the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates and new indications for Regeneron's Products; unforeseen safety issues resulting from the administration of Regeneron's Products and product candidates (such as Kevzara and REGN-COV2) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates in clinical trials; 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 and REGN-COV2; ongoing regulatory obligations and oversight impacting Regeneron's Products (such as Kevzara), research and clinical programs, and business, including those relating to patient privacy; 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; the availability and extent of reimbursement of Regeneron's Products 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; competing drugs and product candidates that may be superior to Regeneron's Products and product candidates; 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; 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; 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 and other related proceedings relating to Dupixent[®] (dupilumab) and Praluent[®] (alirocumab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, the ultimate outcome of any such proceedings and investigations, 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-K for the year ended December 31, 2019 and its Form 10-Q for the quarterly period ended March 31, 2020. 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 and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. 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, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties 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, 2019. 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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