



Regeneron and Sanofi Begin Global Kevzara® (sarilumab) Clinical Trial Program in Patients with Severe COVID-19

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U.S. Phase 2/3 trial initiated and will begin enrolling patients immediately

Regeneron is leading U.S. trials, Sanofi will lead upcoming ex-U.S. trials

[Regeneron Pharmaceuticals, Inc.](#) (NASDAQ: REGN) and Sanofi today announced they have started a clinical program evaluating Kevzara® (sarilumab) in patients hospitalized with severe COVID-19 infection. Kevzara is a fully-human monoclonal antibody that inhibits the interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor. IL-6 may play a role in driving the overactive inflammatory response in the lungs of patients who are severely or critically ill with COVID-19. The role of IL-6 is supported by preliminary data from a single-arm [study in China](#) using another IL-6 receptor antibody.

This U.S.-based trial will begin at medical centers in New York, one of the epicenters of the U.S. COVID-19 outbreak, and will assess the safety and efficacy of adding Kevzara to usual supportive care, compared to supportive care plus placebo. The multi-center, double-blind, Phase 2/3 trial has an adaptive design with two parts and is anticipated to enroll up to 400 patients. The first part will recruit patients with severe COVID-19 infection across approximately 16 U.S. sites, and will evaluate the impact of Kevzara on fever and patients' need for supplemental oxygen. The second, larger part of the trial will evaluate the improvement in longer-term outcomes including preventing death and reducing the need for mechanical ventilation, supplemental oxygen and/or hospitalization.

"To initiate this trial quickly, so that the results may inform evidence-based treatment of this ongoing pandemic, Regeneron and Sanofi have worked closely with the U.S. Food and Drug Administration and the Biomedical Advanced Research and Development Authority, also known as the FDA and BARDA," said George D. Yancopoulos, M.D., Ph.D., Co-founder, President and Chief Scientific Officer of Regeneron. "Data from China suggest that the IL-6 pathway may play an important role in the overactive inflammatory response in the lungs of patients with COVID-19. Despite this encouraging finding, it's imperative to conduct a properly designed, randomized trial to understand the true impact. Our trial is the first controlled trial in the U.S. to evaluate the effect of IL-6 inhibition prospectively in COVID-19 patients. In addition to our Kevzara program, Regeneron is also rapidly advancing a novel antibody cocktail for the prevention and treatment of COVID-19, which we hope to have available for human testing this summer. Both of these programs are made possible by our unprecedented end-to-end antibody discovery, development and manufacturing technologies, starting with our proprietary *VelocImmune* human antibody mouse, and incorporating our associated rapid manufacturing technologies designed to select and produce the best neutralizing antibodies. Collectively, these technologies expedite a typically years-long process into a matter of months. This same technology was applied to the Ebola virus, where our therapy, REGN-EB3, was shown to dramatically improve survival in infected patients last year."

Scientists have preliminary evidence that IL-6 may play a key role in driving the inflammatory immune response that causes acute respiratory distress syndrome (ARDS) in patients critically ill from COVID-19. Initial non-peer reviewed results from a single-arm, 21-patient Chinese trial found COVID-19 patients experienced rapidly reduced fevers and 75% of patients (15 out of 20) reduced their need for supplemental oxygen within days of receiving a different IL-6 receptor antibody (tocilizumab). Based on these results, China recently updated its COVID-19 treatment guidelines and approved the use of that IL-6 inhibitor to treat patients with severe or critical disease.

"At Sanofi, we are taking a leading role in addressing the global challenge of COVID-19 disease. Scientific evidence has emerged to suggest that Kevzara may be a potentially important treatment option for critically-ill COVID-19 patients, and this trial will provide the well-controlled, rigorous scientific data we need to determine if IL-6 receptor inhibition with Kevzara is better than current supportive care alone. Additionally, we expect to rapidly initiate trials outside the U.S. in the coming weeks, including areas most affected by the pandemic such as Italy," said John Reed, M.D., Ph.D., Sanofi's Global Head of Research and Development. "In addition to Kevzara, Sanofi Pasteur, the vaccines global business unit of Sanofi, is leveraging previous development work for a SARS vaccine as part of our goal to quickly develop a COVID-19 vaccine."

In late 2019, Regeneron and Sanofi [announced](#) their intent to simplify the joint collaboration for Kevzara, which is expected to be finalized in the first quarter of 2020. The companies will continue to collaborate on COVID-19 and other related ARDS development, with Regeneron leading U.S.-based work and Sanofi leading work outside of the U.S.

The use of Kevzara to treat the symptoms of COVID-19 is investigational and has not been fully evaluated by any regulatory authority.

About the Trial

This Phase 2/3, randomized, double-blind, placebo-controlled trial uses an adaptive design to evaluate the safety and efficacy of Kevzara in adults hospitalized with serious complications from COVID-19. To enter the trial, patients must be hospitalized with laboratory-confirmed COVID-19 that is classified as severe or critical, or who are suffering from multi-organ dysfunction. All patients must have pneumonia and fever. After receiving the study dose, patients will be assessed for 60 days, or until hospital discharge or death.

In the Phase 2 part of the trial, patients will be randomized 2:2:1 into three groups: Kevzara high dose, Kevzara low dose and placebo. The primary endpoint is reduction of fever and the secondary endpoint is decreased need for supplemental oxygen.

The Phase 2 findings will be utilized in an adaptive manner to determine transition into Phase 3, helping to determine the endpoints, patient numbers and doses. The second, larger part of the trial will evaluate the improvement in longer-term outcomes including preventing death and reducing the need for mechanical ventilation, supplemental oxygen and/or hospitalization.

If the trial continues with all three treatment arms to the end, it is expected to enroll approximately 400 patients, depending on the status of the COVID-19 outbreak and the proportion of patients with severe COVID-19 and high levels of IL-6.

About Kevzara® (sarilumab) Injection

Kevzara was jointly developed by Regeneron and Sanofi under a global collaboration agreement. Kevzara is a fully-human monoclonal antibody that was invented using Regeneron's proprietary *VelocImmune*® technology, which uses a unique genetically-humanized mouse to produce optimized fully human antibodies. Kevzara 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 rheumatoid arthritis and has been associated with disease activity, joint destruction and other systemic problems. It is also being investigated for its ability to reduce the overactive inflammatory immune response associated with COVID-19.

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

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

About Regeneron

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 nature, timing, and possible success and therapeutic applications of products marketed by Regeneron and/or its collaborators (collectively, "Regeneron's Products") and Regeneron's product candidates and research and clinical programs now underway or planned, including without limitation Kevzara[®] (sarilumab) for the treatment of patients with severe COVID-19 and Regeneron's novel antibody cocktail for the prevention and treatment of COVID-19 (the "COVID-19 Multi-antibody Therapy"); the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates and new indications for Regeneron's Products, such as Kevzara for the treatment of patients with severe COVID-19 and the COVID-19 Multi-antibody Therapy; unforeseen safety issues resulting from the administration of Regeneron's Products and product candidates (such as Kevzara and the COVID-19 Multi-antibody Therapy) 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 the COVID-19 Multi-antibody Therapy; ongoing regulatory obligations and oversight impacting Regeneron's Products, 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. 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 fact that product may not 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 and market conditions, the risk of global disruption, including pandemics, 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, 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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