Regeneron and Sanofi Provide Update on U.S. Phase 2/3 Adaptive-Designed Trial of Kevzara® (sarilumab) in Hospitalized COVID-19 Patients

April 27, 2020 at 6:58 AM EDT

TARRYTOWN, N.Y. and PARIS, April 27, 2020 /PRNewswire/ --

Independent Data Monitoring Committee recommended continuing ongoing Phase 3 trial only in the more advanced "critical" group with Kevzara higher-dose versus placebo and discontinuing less advanced "severe" group

Phase 3 trial will be amended to enroll only "critical" patients

Phase 3 trial will also be amended to discontinue lower-dose Kevzara (200 mg); all new patients to receive either higher-dose Kevzara (400 mg) or placebo

No new safety findings were observed for Kevzara use in COVID-19 patients

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced the preliminary results from the Phase 2 portion of an ongoing Phase 2/3 trial evaluating Kevzara® (sarilumab), an interleukin-6 (IL-6) receptor antibody, in hospitalized patients with "severe" or "critical" respiratory illness caused by COVID-19. Following a review by the Independent Data Monitoring Committee (IDMC) of all available Phase 2 and Phase 3 data, the trial will be immediately amended so that only "critical" patients continue to be enrolled to receive Kevzara 400 mg or placebo.

The randomized Phase 2 portion of the trial compared intravenously-administered Kevzara higher dose (400 mg), Kevzara lower dose (200 mg) and placebo. It assessed 457 hospitalized patients, who were categorized at baseline as having either "severe" illness (28% of patients), "critical" illness (49% of patients) or "multi-system organ dysfunction" (MSOD) (23% of patients). Patients were classified as "severe" if they required oxygen supplementation without mechanical or high-flow oxygenation; or "critical" if they required mechanical ventilation or high-flow oxygenation or required treatment in an intensive care unit.

Preliminary analysis of the Phase 2 portion of the trial demonstrated that Kevzara rapidly lowered C-reactive protein (CRP), a key marker of inflammation, meeting the primary endpoint (see table below). Baseline levels of IL-6 were elevated across all treatment arms, with higher levels observed in "critical" patients compared to "severe" patients. Additionally, no new safety signals were observed with the use of Kevzara in COVID-19 patients.

Analysis of clinical outcomes in the Phase 2 trial was exploratory and pre-specified to focus on the "severe" and "critical" groups. In the preliminary Phase 2 analysis, Kevzara had no notable benefit on clinical outcomes when combining the "severe" and "critical" groups, versus placebo. However, there were negative trends for most outcomes in the "severe" group, while there were positive trends for all outcomes in the "critical" group (see table below). Subsequent to the IDMC review, Regeneron and Sanofi reviewed the discontinued "severe" group data, which revealed that the negative trends in the Phase 2 trial (n=126) were not reproduced in Phase 3 trial (n=276), and that clinical outcomes were balanced across the Kevzara and placebo treatment arms. Outcomes for the "severe" group were better than expected based on prior reports, regardless of treatment assignment: for example, in the Phase 2 portion, approximately 80% were discharged, 10% of patients died and 10% remain hospitalized.

"Even in a pandemic setting, it's both crucial and possible to obtain controlled data in adequately-sized trials to provide the evidence needed to inform optimal medical care," said George D. Yancopoulos, M.D., Ph.D., Regeneron Co-Founder, President and Chief Scientific Officer. "Emerging evidence with Kevzara and other repurposed drugs in the COVID-19 crisis highlight the challenges of making decisions about existing medicines for new viral threats using small, uncontrolled studies. We await results of the ongoing Phase 3 trial to learn more about COVID-19, and better understand whether some patients may benefit from Kevzara treatment. In addition, there is an acute need for tailored approaches that specifically target this virus. To that end, Regeneron is rapidly advancing our targeted anti-SARS-CoV-2 antibody cocktail and we plan to initiate clinical trials in June."

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. These uncontrolled findings require confirmation in adequately-sized and well-controlled trials. Last month, Regeneron and Sanofi moved rapidly to evaluate Kevzara in a prospective, randomized, placebo-controlled adaptively-designed U.S. Phase 2/3 trial in collaboration with U.S. groups including the Biomedical Advanced Research and Development Authority (BARDA, part of the office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services), the Food and Drug Administration (FDA) and hospitals across the country.

"At Sanofi, we are committed to help combat the global COVID-19 pandemic. As we quickly follow the science to better

understand this disease and explore how to best treat patients, these initial results from the randomized clinical trial setting provide physicians much needed insights and information regarding the potential of Kevzara for patients with COVID-19 treatment," said John Reed, M.D., Ph.D., Sanofi's Global Head of Research and Development. "While our evaluation of the use of Kevzara for COVID-19 treatment remains an investigational approach, Sanofi continues to stay at the forefront of multiple initiatives to fight this disease, including researching other potential treatment options, developing vaccine candidates that can be manufactured at large-scale, and a potential collaboration for an innovative SARS-CoV-2 smartphone-based self-testing solution."

The Phase 2 numerical results are presented in the table below, including exploratory clinical endpoints for the "critical" group, which is the focus of the ongoing Phase 3 trial.

U.S. Kevzara Trial – Phase 2 Efficacy Results

	Placebo	**Kevzara 200 mg**	**Kevzara 400 mg**
PRIMARY ENDPOINT (REDUCTION IN C-REACTIVE PROTEIN)			
	(n=77)	*(n=136)*	*(n=145)*
% change from baseline in CRP (Patients with high baseline IL-6, where data was available)	-21%	-77%	-79%
EXPLORATORY CLINICAL ENDPOINTS IN "CRITICAL" GROUP			
	(n=44)	*(n=94)*	*(n=88)*
Died or "On a ventilator"	24 (55%)	43 (46%)	28 (32%)
Died	*12 (27%)*	*34 (36%)*	*20 (23%)*
On a ventilator	*12 (27%)*	*9 (10%)*	*8 (9%)*
Clinical improvement (Achieved ³2 point improvement on 7-point scale)[1]	18 (41%)	48 (51%)	52 (59%)
Off oxygenation	18 (41%)	40 (43%)	51 (58%)
Discharged	18 (41%)	37 (39%)	47 (53%)

1. 7-point scale consists 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.

The ongoing portion of the Phase 3 trial, which is continuing to enroll, currently includes more than 600 patients in the "critical" group. Regeneron and Sanofi remain blinded to the ongoing portion of the Phase 3 trial and expect to report results by June.

In addition, the companies are also conducting a second trial in countries outside of the U.S. The Phase 3 trial of Kevzara in approximately 400 patients hospitalized with COVID-19 infection is currently enrolling in Italy, Spain, Germany, France, Canada, Russia, Israel and Japan. Initial results from this second trial are expected in the third quarter of 2020. The findings from the U.S. trial will be shared immediately with the IDMC and similar amendments to the trial outside the U.S. will be considered.

The U.S. Kevzara 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 BARDA, under OT number: HHSO100201700020C.

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

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 that utilizes a genetically-engineered mouse platform endowed with a genetically-humanized immune system to produce optimized fully-human antibodies. *VelocImmune* technology has been used to create multiple antibodies including Dupixent® (dupilumab), Praluent® (alirocumab) and Libtayo® (cemiplimab), which are approved in multiple countries around the world. Regeneron previously used its *VelociSuite*® technologies to rapidly develop an investigational treatment for Ebola virus infection (currently under review by the FDA) and is now using these same technologies to create novel preventative and therapeutic antibodies for COVID-19.

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 severely 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.regneron.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 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 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 (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, 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 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 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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