



Regeneron and Sanofi Announce Positive Topline Phase 2 Results for IL-33 Antibody in Asthma

June 21, 2019

TARRYTOWN, N.Y. and PARIS, June 21, 2019 /PRNewswire/ --

REGN3500 monotherapy significantly reduced loss of asthma control and improved lung function compared to placebo

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that a Phase 2 proof-of-concept trial evaluating the investigational IL-33 antibody REGN3500 (SAR440340) met the primary endpoint of improvement in loss of asthma control when comparing REGN3500 monotherapy to placebo. The trial also met a key secondary endpoint, demonstrating REGN3500 monotherapy significantly improved lung function compared to placebo.

In the trial, the greatest improvement was observed in patients with blood eosinophil levels ≥ 300 cells/microliter. Patients treated with Dupixent[®] (dupilumab) monotherapy did numerically better than REGN3500 across all endpoints, although the trial was not powered to show differences between active treatment arms. The combination of REGN3500 and Dupixent also did not demonstrate increased benefit compared to Dupixent monotherapy in this trial. More detailed results will be presented at an upcoming medical meeting.

"This trial suggests that REGN3500 may provide an alternative targeted approach for patients suffering from asthma," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "We look forward to working with Sanofi to advance REGN3500 through our asthma clinical trial program, as well as continuing our ongoing trials in atopic dermatitis and chronic obstructive pulmonary disease."

Adverse events (AEs) occurred in 61.6% of patients who received REGN3500, 66.2% of patients receiving both REGN3500 and Dupixent, 56.8% of patients who received Dupixent and 64.9% of patients who received placebo. The incidence of serious AEs and AEs leading to treatment discontinuations was low.

Despite standard-of-care treatment with inhaled corticosteroid (ICS) and long-acting beta-agonist (LABA) therapy, people with moderate-to-severe asthma often have inadequately controlled, persistent symptoms that may make them suitable for treatment with a biologic therapy. These people live with coughing, wheezing and difficulty breathing, and are at risk of severe asthma attacks that may require emergency room visits or hospitalizations.

"Asthma is a heterogeneous disease and not everyone experiences it in the same way. Therefore, there is value in evaluating new therapies with distinct and novel mechanisms such as anti-IL-33," said Steve Pascoe, M.D., Head of Immuno-Inflammation Development at Sanofi. "We have ongoing studies for REGN3500 in atopic dermatitis and chronic obstructive pulmonary disease. We will evaluate the results of these studies as well as the findings in asthma to determine the best path forward for this therapy."

REGN3500 is a fully-human monoclonal antibody that inhibits interleukin-33 (IL-33), a protein that is believed to play a key role in type 1 and type 2 inflammation. Preclinical research showed REGN3500 blocked several markers of both types of inflammation. In moderate-to-severe asthma, there can be multiple sources of underlying inflammation that new therapies may help address.

About the Phase 2 Trial

The trial was a randomized, double-blind, placebo-controlled, 12-week proof-of-concept trial that enrolled 296 adult patients with moderate-to-severe asthma who were not well controlled on LABA and ICS therapy. Patients were randomized into four treatment groups: REGN3500 plus placebo, REGN3500 plus Dupixent, Dupixent plus placebo, and placebo. All patients received fluticasone/salmeterol as the ICS/LABA maintenance therapy, which was withdrawn during the trial. At four weeks post-randomization, the LABA was withdrawn, and between six and nine weeks the ICS was tapered to withdrawal. Patients continued without ICS/LABA maintenance therapy until 12 weeks. If a patient experienced loss of asthma control (LOAC) during the trial, they resumed their prescreening ICS/LABA maintenance therapy and entered the safety follow-up period.

The primary endpoint was the proportion of patients who experienced LOAC on REGN3500 with or without Dupixent, compared to placebo.

About the REGN3500 Development Program

Regeneron and Sanofi are currently studying REGN3500 in respiratory and dermatological diseases where inflammation is thought to play an underlying role. REGN3500 is being studied in Phase 2 trials for asthma, chronic obstructive pulmonary disease and atopic dermatitis. These potential uses are investigational and the safety and efficacy have not been evaluated by any regulatory authority. REGN3500 was invented using Regeneron's proprietary *VelocImmune*[®] technology that yields optimized fully-human antibodies, and is being developed jointly by Regeneron and Sanofi as part of a global collaboration agreement.

About Dupixent[®] (dupilumab)

Dupixent is a fully-human monoclonal antibody specifically designed to inhibit the signaling of interleukin-4 (IL-4) and interleukin-13 (IL-13), two key proteins that may play a central role in the type 2 inflammation that underlies asthma as well as other allergic and atopic diseases.

Dupixent is approved in the U.S. for the treatment of people 12 years of age and older with moderate-to-severe atopic dermatitis (eczema) that is not well controlled with prescription therapies used on the skin (topical), or who cannot use topical therapies; and for use with other asthma medicines for the maintenance treatment of moderate-to-severe asthma in people aged 12 years and older whose asthma is not controlled with their current asthma medicines. Dupixent is also approved for certain patients with moderate-to-severe atopic dermatitis and severe asthma in the European Union and Japan.

In addition to the currently approved indications, Regeneron and Sanofi are also studying dupilumab for additional diseases driven by allergic and other type 2 inflammation, including chronic rhinosinusitis with nasal polyps (Phase 3 *completed*), pediatric asthma and atopic dermatitis (6 to 11 years

of age, Phase 3), pediatric atopic dermatitis (6 months to 5 years of age, Phase 2/3), eosinophilic esophagitis (Phase 3), chronic obstructive pulmonary disease (Phase 3), and food and environmental allergies (Phase 2). These potential uses, and its use in combination with REGN3500, are investigational and the safety and efficacy have not been evaluated by any regulatory authority.

For more information on dupilumab clinical trials please visit www.clinicaltrials.gov.

U.S. INDICATIONS OF DUPIXENT

DUPIXENT is a prescription medicine used:

- to treat people 12 years of age and older with moderate-to-severe atopic dermatitis (eczema) that is not well controlled with prescription therapies used on the skin (topical), or who cannot use topical therapies. DUPIXENT can be used with or without topical corticosteroids. It is not known if DUPIXENT is safe and effective in children with atopic dermatitis under 12 years of age.
- with other asthma medicines for the **maintenance treatment of moderate-to-severe asthma** in people aged 12 years and older whose asthma is not controlled with their current asthma medicines. DUPIXENT helps prevent severe asthma attacks (exacerbations) and can improve your breathing. DUPIXENT may also help reduce the amount of oral corticosteroids you need while preventing severe asthma attacks and improving your breathing. DUPIXENT is not used to treat sudden breathing problems. It is not known if DUPIXENT is safe and effective in children with asthma under 12 years of age.

IMPORTANT SAFETY INFORMATION FOR U.S. PATIENTS TAKING DUPIXENT

Do not use if you are allergic to dupilumab or to any of the ingredients in DUPIXENT®.

Before using DUPIXENT, tell your healthcare provider about all your medical conditions, including if you:

- have eye problems (if you also have atopic dermatitis)
- have a parasitic (helminth) infection
- are taking oral, topical, or inhaled corticosteroid medicines. **Do not** stop taking your corticosteroid medicines unless instructed by your healthcare provider. This may cause other symptoms that were controlled by the corticosteroid medicine to come back.
- are scheduled to receive any vaccinations. You should not receive a "live vaccine" if you are treated with DUPIXENT.
- are pregnant or plan to become pregnant. It is not known whether DUPIXENT will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known whether DUPIXENT passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. If you are taking asthma medicines, do not change or stop your asthma medicine without talking to your healthcare provider.

DUPIXENT can cause serious side effects, including:

- **Allergic reactions (hypersensitivity), including a severe reaction known as anaphylaxis.** Stop using DUPIXENT and tell your healthcare provider or get emergency help right away if you get any of the following symptoms: breathing problems, fever, general ill feeling, swollen lymph nodes, swelling of the face, mouth and tongue, hives, itching, fainting, dizziness, feeling lightheaded (low blood pressure), joint pain, or skin rash.
- **Eye problems.** If you have atopic dermatitis, tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision.
- **Inflammation in your blood vessels:** Rarely, this can happen in people with asthma who receive DUPIXENT. This may happen in people who also take a steroid medicine by mouth that is being stopped or the dose is being lowered. It is not known whether this is caused by DUPIXENT. Tell your healthcare provider right away if you have: rash, shortness of breath, persistent fever, chest pain, or a feeling of pins and needles or numbness of your arms or legs.

The most common side effects include injection site reactions, pain in the throat (oropharyngeal pain) and cold sores in your mouth or on your lips. Eye and eyelid inflammation, including redness, swelling and itching have been seen in patients who have atopic dermatitis.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of DUPIXENT. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Use DUPIXENT exactly as prescribed. DUPIXENT is an injection given under the skin (subcutaneous injection). If your healthcare provider decides that you or a caregiver can give DUPIXENT injections, you or your caregiver should receive training on the right way to prepare and inject DUPIXENT. **Do not** try to inject DUPIXENT until you have been shown the right way by your healthcare provider. In adolescents 12 years of age and older, it is recommended that DUPIXENT be administered by or under supervision of an adult.

Please see accompanying [full Prescribing Information](#) including Patient Information.

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 disease, 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*[®] technologies, such as *VelocImmune*[®] 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 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 Regeneron's products, product candidates, and research and clinical programs now underway or planned, including without limitation REGN3500 (as a monotherapy or in combination with Dupixent[®] (dupilumab) Injection, as applicable) for the treatment of asthma, chronic obstructive pulmonary disease ("COPD"), atopic dermatitis, and other potential indications, as well as dupilumab as a monotherapy for the treatment of chronic rhinosinusitis with nasal polyps, pediatric asthma and atopic dermatitis, eosinophilic esophagitis, COPD, food and environmental allergies, and other potential indications; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates (such as REGN3500 and dupilumab, either as a monotherapy or in combination) in clinical trials; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators (including those discussed in this press release) may be replicated in other studies and lead to therapeutic applications; 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; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, 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; 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; 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; the availability and extent of reimbursement of the Company'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; 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 EYLEA[®] (afibercept) Injection, Dupixent, and Praluent[®] (alirocumab) Injection, the ultimate outcome of any such 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-K for the fiscal year ended December 31, 2018 and its Form 10-Q for the quarterly period ended March 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 absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities 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 conditions, the impact of cost containment initiatives and subsequent changes thereto, the average number of shares outstanding as well as those 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, 2018. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

Regeneron Contacts:

Media Relations

Sharon Chen

Tel: +1 (914) 847-1546

Sharon.Chen@regeneron.com

Investor Relations

Justin Holko

Tel: +1 (914) 847-7786

Justin.Holko@regeneron.com

Sanofi Contacts:

Media Relations

Ashleigh Koss

Tel: +1 (908) 981-8745

Ashleigh.Koss@sanofi.com

Investor Relations

George Grofik

Tel: +33 (0)1 53 77 45 45

ir@sanofi.com

 View original content: <http://www.prnewswire.com/news-releases/regeneron-and-sanofi-announce-positive-topline-phase-2-results-for-il-33-antibody-in-asthma-300872459.html>

SOURCE Regeneron Pharmaceuticals, Inc.