



Dupilumab Significantly Reduced Steroid Use, Asthma Attacks, and Improved Lung Function in Phase 3 Study of People with Severe Steroid-Dependent Asthma

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TARRYTOWN, N.Y. and PARIS, Oct. 31, 2017 /PRNewswire/ -- [Regeneron Pharmaceuticals, Inc.](#) (NASDAQ: **REGN**) and [Sanofi](#) today announced that the Phase 3 investigational study evaluating dupilumab in adults and adolescents with severe, steroid-dependent asthma met its primary endpoint and key secondary endpoints. For the primary endpoint, at 24 weeks in the overall population, dupilumab added to standard therapies significantly reduced the use of maintenance oral corticosteroids (OCS) by 70 percent on average (median reduction of 100 percent) compared to 42 percent with placebo (median reduction of 50 percent) (p less than 0.0001). In prespecified analyses of patients with baseline eosinophil counts greater than or equal to 300 cells/microliter, adding dupilumab significantly reduced OCS use by 80 percent on average (median reduction of 100 percent) compared to 43 percent for placebo (median reduction of 50 percent) (nominal p equals 0.0001).

At 24 weeks, despite the reduced use of OCS, patients treated with dupilumab had 59 percent fewer attacks (exacerbations) in the overall population (p less than 0.0001) and 71 percent fewer attacks in patients with eosinophil counts greater than or equal to 300 cells/microliter. Also at 24 weeks, compared to placebo, dupilumab improved lung function, as assessed by forced expiratory volume over one second (FEV₁) by 220ml (15 percent) in the overall population (p equals 0.0007) and by 320ml (25 percent) in patients with eosinophil counts greater than or equal to 300 cells/microliter (nominal p equals 0.0049).

"This Phase 3 study showed that most severe asthma patients could substantially reduce their dependence on oral corticosteroids, with half completely eliminating their use of oral corticosteroids, which are not recommended for long-term use and can carry significant and potentially irreversible safety risks. Importantly, despite a reduction in oral corticosteroid use, dupilumab was associated with an improvement in lung function. This is the third study in which dupilumab has demonstrated a reduction in asthma attacks and improvement in lung function in a broad group of patients with uncontrolled asthma - this effect was most profound in patients with elevated markers of Type 2 allergic inflammation, such as an eosinophil count over 300," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "Dupilumab blocks the IL-4/IL-13 pathway, which is emerging as a central driver of Type 2 allergic inflammation. We remain committed to investigating dupilumab in other Type 2 inflammatory diseases including eosinophilic esophagitis, nasal polyps, pediatric atopic dermatitis and food allergy."

"This Phase 3 study enrolled severe steroid-dependent asthma patients regardless of eosinophil levels or other biomarkers at baseline, and the results showed improvements compared to placebo on lung function and exacerbations across patient subgroups - those with baseline eosinophil counts above 300 cells/microliter, above 150 cells/microliter and below 150 cells/microliter," said Elias Zerhouni, M.D., President, Global R&D, Sanofi. "It is striking that dupilumab has demonstrated a consistent improvement in lung function across the asthma program as this is critically important for patients with severe asthma struggling with declines in their everyday breathing ability."

The safety and tolerability profile of dupilumab in this study was consistent with previous studies. There were more dupilumab-treated patients with injection site reactions (9 percent dupilumab vs. 4 percent placebo). There were more dupilumab-treated patients with an increase in eosinophil counts (14 percent dupilumab vs. 1 percent placebo), most of which were mild and the vast majority of which resolved. The overall rates of adverse events, including infections, conjunctivitis, and herpes were comparable between the dupilumab and placebo groups.

Patients with severe chronic asthma live with a profound decrease in their lung function, approximately 52 percent of predicted normal for those in this study at baseline, which impacts their ability to breathe normally, and may lead to frequent exacerbations that require acute treatment and hospitalization. These problems occur even in patients who are treated with chronic OCS to manage their symptoms.

In the Phase 3 study, known as LIBERTY ASTHMA VENTURE, additional secondary endpoint results at 24 weeks included the following:

- In the overall population, 80 percent of patients who received dupilumab reduced their OCS dose by at least half while maintaining overall asthma control compared to 50 percent of patients who received placebo (p less than 0.0001). In patients with eosinophil counts greater than or equal to 300 cells/microliter (high EOS), dupilumab allowed for a reduction in the OCS dose by at least half in 88 percent of patients compared to 52 percent for placebo (nominal p equals 0.0011).
- In the overall population, 69 percent of patients who received dupilumab reduced their OCS dose to less than 5 mg per day while maintaining asthma control compared to 33 percent of patients who received placebo (p less than 0.0001); in the high EOS group, 84 percent of dupilumab patients reduced their OCS dose to less than 5 mg per day compared to 40 percent for placebo (nominal p equals 0.0002).

"Severe, uncontrolled asthma can lead to a dependence on oral corticosteroids, with systemic steroid exposure potentially leading to serious short- and long-term adverse effects, including weight gain, diabetes, osteoporosis, glaucoma, anxiety, depression, cardiovascular disease and immunosuppression," said Professor Mario Castro, M.D., MPH, FCCP, Washington University School of Medicine in St. Louis. "There is an urgent need for new therapies that can decrease or eliminate chronic oral corticosteroid use, as well as reduce severe asthma attacks and improve lung function in this difficult-to-treat patient population."

The VENTURE study enrolled 210 patients (103 in the dupilumab group and 107 in the placebo group) with severe asthma and regular use of maintenance OCS in the six months prior to enrollment in the study. In the study, the prescribed OCS was prednisone or prednisolone. Patients were randomized using a 1:1 ratio and treated with either dupilumab (300 mg every other week with a loading dose of 600 mg) or placebo. The median baseline eosinophil count in the study was 260 eosinophils/microliter.

Detailed results from this study will be submitted for presentation at a future medical congress. VENTURE is the third trial in the uncontrolled persistent asthma pivotal clinical program and follows positive results from the [Phase 3 QUEST study](#) and [Phase 2b pivotal study of dupilumab](#). The companies plan to submit a Supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) by the end of this year. Also included in the LIBERTY ASTHMA clinical development program is the TRAVERSE trial, a long-term safety extension study. The potential use of dupilumab in asthma is currently under clinical development and the safety and efficacy have not been fully evaluated by any regulatory authority.

In March 2017, the U.S. Food and Drug Administration (FDA) approved Dupixent® (dupilumab) in the U.S. for the treatment of adults with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies. The European Commission (EC) also granted marketing authorization for Dupixent for use in adults with moderate-to-severe atopic dermatitis who are candidates for systemic therapy in September 2017.

About Uncontrolled Persistent Asthma

People who live with uncontrolled, persistent asthma often experience decreased lung function and have severe attacks (exacerbations) that may lead to emergency room visits or hospitalizations. Despite currently available treatments, there is a need for new medicines that offer comprehensive asthma control including preservation of lung function and reduction in exacerbations. Uncontrolled, persistent asthma is often associated with other Type 2 allergic inflammatory diseases including atopic dermatitis, nasal polyps, allergic rhinitis, eosinophilic esophagitis and food allergies. The disease is characterized by an imbalance or over activity of certain immune cells (including eosinophils) and signaling proteins known as interleukins. Two of these are interleukin-4 (IL-4) and interleukin-13 (IL-13), which are central drivers of Type 2 inflammation.

About Dupilumab

Dupilumab is a fully human monoclonal antibody that is designed to simultaneously inhibit overactive signaling of IL-4 and IL-13 cytokines. Sanofi and Regeneron are studying dupilumab in a broad range of clinical development programs for diseases that are driven by Type 2 inflammation, including pediatric atopic dermatitis (Phase 3), nasal polyps (Phase 3) and eosinophilic esophagitis (Phase 2). These potential uses are investigational and the safety and efficacy have not been evaluated by any regulatory authority. Dupilumab was discovered using Regeneron's proprietary VelocImmune® technology that yields optimized fully-human antibodies, and is being jointly developed by Regeneron and Sanofi under a global collaboration agreement.

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

IMPORTANT SAFETY INFORMATION

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
- have a parasitic (helminth) infection
- have asthma
- 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 have asthma and 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.** Stop using DUPIXENT and go to the nearest hospital emergency room if you get any of the following symptoms: fever, general ill feeling, swollen lymph nodes, hives, itching, joint pain, or skin rash.
- **Eye problems.** Tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision.

The most common side effects include injection site reactions, eye and eyelid inflammation, including redness, swelling and itching, and cold sores in your mouth or on your lips.

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 may report side effects to FDA at 1-800-FDA-1088.

Use DUPIXENT exactly as prescribed. 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.

Please click [here](#) for the full Prescribing Information. The patient information is available [here](#).

INDICATION

DUPIXENT is used to treat adult patients 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. DUPIXENT is administered by subcutaneous injection every two weeks after an initial loading dose.

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

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 by physician-scientists for the past 30 years, our unique ability to repeatedly and consistently translate science into medicine has led to six FDA-approved treatments and over a dozen product candidates, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye disease, heart disease, allergic and inflammatory diseases, pain, cancer, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its proprietary *VelociSuite*® technologies, including *VelocImmune*® to yield optimized fully human antibodies, and ambitious initiatives such as The Regeneron Genetics Center, 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.

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, 2016. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

Regeneron Forward-Looking Statements and Use of Digital Media

This news release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the nature, timing, and possible success and therapeutic applications of Regeneron's products, product candidates, and research and clinical programs now underway or planned, including without limitation Dupixent® (dupilumab) Injection; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products, such as Dupixent for the treatment of severe, steroid-dependent asthma and other potential indications; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in later studies and lead to therapeutic applications; unforeseen safety issues and possible liability resulting from the administration of products and product candidates in patients, including without limitation Dupixent; serious complications or side effects in connection with the use of Regeneron's products and product candidates (such as Dupixent) in clinical trials; coverage and reimbursement determinations by third-party payers, including Medicare, Medicaid, and pharmacy benefit management companies; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, research and clinical programs, and business, including those relating to the enrollment, completion, and meeting of the relevant endpoints of post-approval studies; 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, such as Dupixent; 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; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its sales or other 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 relating to Praluent® (alirocumab) Injection, the ultimate outcome of such litigation, 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 United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2016 and its Form 10-Q for the quarterly period ended June 30, 2017. 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>).

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