

20 October 2018

LIBERTY ASTHMA TRAVERSE/ LTS12551

Study entitled: Open-label extension study to evaluate the long-term safety and tolerability of dupilumab in patients with asthma who participated in a previous dupilumab asthma clinical study

[Press Release on FDA approval of asthma indication for Dupixent® \(dupilumab\)](#)

Dear Investigator, Study Site Staff and Patients,

We want to express our sincere thanks and appreciation to you for your dedication and tremendous hard work on the Dupilumab Liberty Asthma studies.

Our special thanks and appreciation go out to all the study patients for their commitment and participation in the studies.

The U.S. Food and Drug Administration has approved Dupixent® (dupilumab) as an add-on maintenance therapy in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.

Please see below for the press release.

Should you have any questions or require any additional information please do not hesitate to contact your Sanofi CRA/CPL/Regional CPL.

Thanks again and congratulations to you all!

Sincerely,

Liberty Asthma Traverse Study Team.



FDA approves asthma indication for Dupixent® (dupilumab)

- Only biologic approved for both moderate and severe asthma patients with eosinophilic phenotype
- Only biologic approved for oral corticosteroid-dependent asthma, regardless of phenotype
- Only asthma biologic that offers patient self-administration at home
- Only asthma biologic also approved for adult patients with moderate-to-severe atopic dermatitis, a Type 2 inflammatory disease driven by the IL-4 and IL-13 pathway
- In clinical trials, Dupixent reduced severe exacerbations and oral corticosteroid use, and improved lung function

PARIS and TARRYTOWN, N.Y., Oct. 19, 2018 /PRNewswire/ -- Sanofi (EURONEXT: SAN) (NYSE: SNY)

The U.S. Food and Drug Administration has approved Dupixent® (dupilumab) as an add-on maintenance therapy in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.

Dupixent inhibits the overactive signaling of interleukin-4 (IL-4) and interleukin-13 (IL-13), two key proteins that contribute to the Type 2 inflammation that may underlie moderate-to-severe asthma. This effect is associated with the reduction of inflammatory biomarkers including fractional exhaled nitric oxide (FeNO), immunoglobulin E (IgE) and eotaxin-3 (CCL26).

"Dupixent is now approved in the U.S. for two important groups of uncontrolled asthma patients – those who are moderate-to-severe with an eosinophilic phenotype or those with oral corticosteroid-dependent asthma," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "In the asthma clinical trial program, Dupixent reduced severe exacerbations and oral corticosteroid use, improved quality of life and showed statistically significant and clinically meaningful improvements in lung function. Following the approvals in atopic dermatitis and asthma, and recently announced positive Phase 3 results in chronic rhinosinusitis with nasal polyps, we are committed to advancing our broad development program in additional Type 2 inflammatory diseases."

"Today's approval marks a significant development for certain people with moderate-to-severe asthma aged 12 years and older. For patients dependent on oral corticosteroids, Dupixent improved lung function, reduced oral corticosteroid use and reduced exacerbations regardless of baseline eosinophil levels," said Olivier Brandicourt, M.D., Chief Executive Officer, Sanofi. "Despite the spectrum of treatments for asthma, there continues to be an unmet need for so many patients with moderate-to-severe asthma, and given that Dupixent works differently than other biologics, there is now a new treatment option for some of these patients. Dupixent has already made a difference for many adults with atopic dermatitis, and we now have the opportunity to do the same for certain adults and adolescents with moderate-to severe asthma in the U.S."

Patients with moderate-to-severe asthma often have uncontrolled, persistent symptoms despite standard-of-care therapy that may make them suitable for treatment with a biologic therapy. They live with coughing, wheezing and difficulty breathing, and are at risk of severe asthma attacks that may require emergency room visits or hospitalizations.^{1,2} Oral corticosteroids can provide relief for severe, short-term symptoms. However, their chronic use is limited to the most severe patients due to the potential for serious side effects.^{3,4}

"Despite being compliant with their current medicine, many people with moderate-to-severe asthma, including those with eosinophilic phenotype or with oral steroid dependence, live with persistent symptoms like unpredictable attacks and difficulty breathing," said Kenneth Mendez, President and CEO of the Asthma and Allergy Foundation of America (AAFA). "AAFA supports the availability of innovative new treatment options for people with asthma who struggle with uncontrolled symptoms that impair their quality of life."

For people with asthma, Dupixent comes in two doses (200 mg and 300 mg) given every other week at different injection sites after an initial loading dose.

Efficacy and safety results from the pivotal clinical trial program

The pivotal trial program evaluated 2,888 adult and adolescent patients with moderate-to-severe asthma in three randomized, placebo-controlled, multicenter trials (Trial 1, Trial 2 and Trial 3) for six months to one year (24 to 52 weeks). All trials enrolled patients irrespective of minimum baseline eosinophil levels.

In Trial 2 (the largest trial), Dupixent reduced exacerbations and improved lung function in the overall population. Benefits in exacerbations were seen in patients with eosinophil counts greater than or equal to 150 cells/microliter, which represented 70% of the patients enrolled. Efficacy improved in patients with higher eosinophil counts. For example, in patients with blood eosinophils of 300 cells/microliter or greater, Dupixent reduced severe exacerbations by 67% compared to placebo and improved FEV₁ (lung function) by 29%-33% compared to 14%-16% for placebo. In patients with eosinophil counts less than 150 cells/microliter, there was no difference in severe exacerbation rates for Dupixent versus placebo.

In Trial 3, which evaluated severe, oral corticosteroid-dependent patients, Dupixent reduced average daily oral corticosteroid use by 70% compared to 42% with placebo. More than half of patients treated with Dupixent completely eliminated use of oral corticosteroids. Effects on lung function and on oral steroid and exacerbation reduction were similar for Dupixent irrespective of baseline blood eosinophil levels.

In the asthma clinical trials, the adverse reactions that occurred with Dupixent at a rate of at least 1% and more frequently than the respective comparator were injection site reactions, sore throat, and an increase in the number of eosinophils, a type of white blood cell, in the blood.

Additional data can be found in the prescribing information. Data from Trial 1 were published in *The Lancet* in April 2016 and data from Trials 2 and 3 were published in the *New England Journal of Medicine* in May 2018.

About Dupixent

Dupixent comes in a pre-filled syringe and is intended for injection under the skin (subcutaneous injection) under the guidance of a healthcare provider. It can be given in a clinic or, for convenience, at home by self-administration after training by a healthcare professional.

Dupixent is also approved 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, or when those therapies are not advisable. In the U.S., Dupixent is marketed by Sanofi Genzyme, the specialty care global business unit of Sanofi, and Regeneron.

The wholesale acquisition cost of Dupixent remains unchanged and will be the same for both asthma doses. Sanofi and Regeneron are committed to helping patients in the U.S. who are prescribed Dupixent gain access to the medicine and receive the support they may need with the *DUPIXENT MyWay*[®] program. For more information, please call 1-844-DUPIXENT (1-844-387-4936) or visit www.DUPIXENT.com.

Dupixent is currently under regulatory review for moderate-to-severe asthma in several other countries, including Japan and in the European Union (EU).

Dupilumab development program is ongoing

Sanofi and Regeneron are also studying dupilumab in a broad range of clinical development programs for diseases driven by Type 2 inflammation, including chronic rhinosinusitis with nasal polyps (Phase 3), pediatric asthma (Phase 3), pediatric atopic dermatitis (Phase 3), adolescent atopic dermatitis (Phase 3), eosinophilic esophagitis (Phase 3), grass allergy (Phase 2) and peanut allergy (Phase 2). A future trial is planned for chronic obstructive pulmonary disease. Dupixent is also being studied in combination with REGN-3500, which targets IL-33. These potential uses are investigational and the safety and efficacy have not been evaluated by any regulatory authority. Dupilumab and REGN-3500 are being jointly developed by Sanofi and Regeneron under a global collaboration agreement.

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

IMPORTANT SAFETY INFORMATION AND INDICATIONS FOR U.S. PATIENTS

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 usually, but not always, happens in people who also take a steroid medicine by mouth that is being stopped or the dose is being lowered. 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 reaction, 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. 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 with asthma 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.

INDICATIONS

DUPIXENT is a prescription medicine used:

- to treat adults 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 18 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.

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 diseases, 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

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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 absence of guarantee that the product will 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 conditions, 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, 2017. 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 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 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 dupilumab for the treatment of chronic rhinosinusitis with nasal polyps, pediatric asthma, pediatric and adolescent atopic dermatitis, eosinophilic esophagitis, grass allergy, food allergy (including peanut), chronic obstructive pulmonary disease, and other potential indications; unforeseen safety issues resulting from the administration of products and product candidates (such as dupilumab) in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates in clinical trials; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as Dupixent), 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, including without limitation dupilumab; the availability and extent of reimbursement of the Company's products (such as Dupixent) 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; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates (such as Dupixent) and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of any such products and product candidates; 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 to perform 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 proceedings relating to EYLEA® (afibercept) Injection, Dupixent, and Praluent® (alirocumab) Injection, the ultimate outcome of any such litigation 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-Q for the quarterly period ended June 30, 2018. 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>).