



Dupixent® (dupilumab) Now Approved in European Union for Severe Chronic Rhinosinusitis with Nasal Polyposis

October 29, 2019

TARRYTOWN, N.Y. and PARIS, Oct. 29, 2019 /PRNewswire/ --

First biologic approved in the European Union for adults with severe chronic rhinosinusitis with nasal polyposis (CRSwNP)

Dupixent now approved in the EU for three type 2 inflammatory diseases: severe CRSwNP, severe asthma and moderate-to-severe atopic dermatitis

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that the European Commission (EC) has approved a new indication for Dupixent® (dupilumab) in chronic rhinosinusitis with nasal polyposis (CRSwNP). Dupixent is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.

"People living with severe CRSwNP are often desperate to find new treatment options, given that current standard treatments such as intermittent courses of systemic corticosteroids or sinonasal surgery are associated with disease recurrence," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "Dupixent significantly improved the signs and symptoms of severe CRSwNP, and also eliminated the need for further surgery or corticosteroid use in approximately three-quarters of patients. Today's approval provides patients in Europe with the first biologic treatment to address the type 2 inflammation that underlies most CRSwNP. This is the third type 2 disease in which Dupixent has been approved, and we continue to investigate Dupixent in a broad range of type 2 inflammatory diseases."

CRSwNP is a chronic disease of the upper airway that obstructs the sinuses and nasal passages. It can lead to persistent breathing difficulties, nasal congestion and discharge, reduced or loss of sense of smell and taste, and facial pressure or pain.

"Many patients with CRSwNP have co-morbid asthma, and those patients tend to have more severe disease that is often more difficult to treat," said John Reed, M.D., Ph.D., Global Head of Research and Development at Sanofi. "These particular patients may have an increased risk of asthma attacks, high symptom burden and a substantial adverse impact on health-related quality of life. Nearly 60 percent of the patients in the CRSwNP trials had asthma, and the data showed Dupixent provided an additional benefit of improved lung function in these patients."

The EC approval is based on two pivotal Phase 3 trials (the 24-week SINUS-24 and 52-week SINUS-52) that evaluated Dupixent 300 mg every two weeks plus standard-of-care intranasal corticosteroids compared to placebo plus intranasal corticosteroids. In these trials, Dupixent significantly improved key disease measures and met all primary and secondary endpoints. At 24 weeks, patients treated with Dupixent achieved statistically significant improvements in all primary and secondary endpoints, including:

- Co-primary endpoints:
 - 57% and 51% improvement in their nasal congestion/obstruction severity compared to a 19% and 15% improvement with placebo in SINUS-24 and SINUS-52, respectively (least squares [LS] mean change from baseline of -1.34 and -1.25 for Dupixent compared to -0.45 and -0.38 for placebo; difference between Dupixent and placebo: -0.89 and -0.87).
 - 33% and 27% reduction in their nasal polyps score compared to a 7% and 4% increase with placebo in SINUS-24 and SINUS-52, respectively (LS mean change from baseline of -1.89 and -1.71 for Dupixent compared to 0.17 and 0.10 for placebo; difference between Dupixent and placebo: -2.06 and -1.80).
- Secondary endpoints:
 - 42% and 27% improvement in sinus opacification compared to 4% and 0% with placebo in SINUS-24 and SINUS-52, respectively (LS mean change from baseline of -8.18 and -5.21 for Dupixent compared to -0.74 and -0.09 for placebo).
 - 52% and 45% improvement in loss of smell compared to a 12% and 10% improvement for placebo in SINUS-24 and SINUS-52, respectively (LS mean difference in Dupixent compared to placebo of -1.12 and -0.98 in SINUS-24 and SINUS-52, respectively).

In a pre-specified pooled analysis of the two trials up to 52 weeks, Dupixent treatment resulted in a significant reduction of systemic corticosteroid use and the need for sino-nasal surgery compared to placebo.

- The proportion of patients who required systemic corticosteroids was reduced by 74% with Dupixent compared to placebo.
- The proportion of patients who required surgery was reduced by 83% with Dupixent compared to placebo.

In a pre-specified analysis of the 59% of patients who also had asthma, treatment with Dupixent:

- Improved lung function by 0.21 L compared with placebo as measured by forced expiratory volume over one second

(FEV₁).

- Improved asthma control as measured by the 6-item Asthma Control Questionnaire (ACQ-6).

Treatment effects on nasal congestion and loss of smell were observed with the first assessment at 4 weeks and showed continued improvement for the duration of the trials.

In the CRSwNP clinical trials, the common (at least 1%) adverse events in the Dupixent group were inflammation of the eye and eyelids (conjunctivitis), high count of certain white blood cells (eosinophilia), injection site reactions and injection site swelling.

Dupixent is a fully-human monoclonal antibody that inhibits the signaling of the interleukin-4 (IL-4) and interleukin-13 (IL-13) proteins. Dupixent was invented using Regeneron's proprietary *VelocImmune*[®] technology, which uses a unique genetically-humanized mouse to produce optimized fully-human antibodies. Data from Dupixent clinical trials have shown that IL-4 and IL-13 are key drivers of the type 2 inflammation that plays a major role in CRSwNP, asthma and atopic dermatitis.

About Dupixent

Dupixent comes in a 300 mg pre-filled syringe for patients with CRSwNP. It is given as a subcutaneous injection every other week at different injection sites. Dupixent is intended for use under the guidance of a healthcare professional and can be given in a clinic or at home by self-administration after training by a healthcare professional.

In addition to severe CRSwNP, Dupixent is approved in the EU for patients 12 years and older as an add-on maintenance treatment for severe asthma with type 2 inflammation characterized by raised blood eosinophils and/or raised fractional exhaled nitric oxide (FeNO), who are inadequately controlled with high dose inhaled corticosteroid (ICS) plus another medicinal product for maintenance treatment. It is also approved in the EU for use in patients 12 years and older with moderate-to-severe atopic dermatitis who are candidates for systemic therapy.

Outside of the EU, Dupixent is approved for use in specific patients with moderate-to-severe atopic dermatitis and certain patients with asthma in a number of other countries around the world, including the U.S. and Japan. Dupixent is also approved in the U.S. for use with other medicines to treat CRSwNP in adults whose disease is not controlled.

Dupilumab Development Program

In addition to the currently approved indications, Regeneron and Sanofi are also studying dupilumab in a broad range of clinical development programs for diseases driven by allergic and other type 2 inflammation, including pediatric asthma (6 to 11 years of age, Phase 3), pediatric atopic dermatitis (6 months to 5 years of age, Phase 2/3 and 6 to 11 years of age, Phase 3), eosinophilic esophagitis (Phase 2/3), chronic obstructive pulmonary disease (Phase 3) and food and environmental allergies (Phase 2). Dupilumab is also being studied in combination with REGN3500 (SAR440340), which targets IL-33. These potential uses are investigational and the safety and efficacy have not been evaluated by any regulatory authority. Dupilumab and REGN3500, are being jointly developed by Regeneron and Sanofi under a global collaboration agreement.

U.S. INDICATIONS

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.
- with other medicines to treat chronic rhinosinusitis with nasal polyposis in adults whose disease is not controlled. It is not known if DUPIXENT is safe and effective in children with chronic rhinosinusitis with nasal polyposis under 18 years of age.

IMPORTANT SAFETY INFORMATION 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
- 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.** Tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision.
- **Inflammation of 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:

- **Atopic dermatitis:** injection site reactions, eye and eyelid inflammation, including redness, swelling, and itching, and cold sores in your mouth or on your lips.
- **Asthma:** injection site reactions, pain in the throat (oropharyngeal pain), and high count of a certain white blood cell (eosinophilia).
- **Chronic rhinosinusitis with nasal polyposis:** injection site reactions, eye and eyelid inflammation, including redness, swelling, and itching, high count of a certain white blood cell (eosinophilia), trouble sleeping (insomnia), toothache, gastritis, and joint pain (arthralgia).

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 children 12 years of age and older, it is recommended that DUPIXENT be administered by or under supervision of an adult.

Please see 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 diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, infectious diseases, pain and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*[®] technologies, including *VelocImmune*[®] which uses a unique genetically-humanized mouse to produce optimized fully-human antibodies and bispecific antibodies, and through ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

Sanofi, Empowering Life

Regeneron Forward-Looking Statements and Use of Digital Media

This press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the nature, timing, and possible success and therapeutic applications of 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 pediatric asthma and pediatric atopic dermatitis,

eosinophilic esophagitis, chronic obstructive pulmonary disease, food and environmental allergies, and other potential indications (as well as in combination with REGN3500); 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; 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; 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; 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 (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; 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 year ended December 31, 2018 and its Form 10-Q for the quarterly period ended June 30, 2019. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update publicly any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (<http://newsroom.regeneron.com>) and its Twitter feed (<http://twitter.com/regeneron>).

Sanofi Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates regarding the marketing and other potential of the product, or regarding potential future revenues from the product. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, unexpected regulatory actions or delays, or government regulation generally, that could affect the availability or commercial potential of the product, the 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, 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) 847-5018

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/dupixent-dupilumab-now-approved-in-european-union-for-severe-chronic-rhinosinusitis-with-nasal-polyposis-300947130.html>

SOURCE Regeneron Pharmaceuticals, Inc.