SANOFI

Press Release

Source: Sanofi (EURONEXT: SAN) (NASDAQ: SNY)

FDA approves Dupixent® (dupilumab) for chronic rhinosinusitis with nasal polyposis

- First biologic medicine for adults with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP)
- Dupixent significantly reduces nasal polyp size, improves congestion and loss of smell, while reducing the need for surgery and systemic corticosteroids
- 59% of clinical trial patients had co-morbid asthma, and experienced improvements in their lung function
- Dupixent now approved for three conditions with underlying type 2 inflammation : moderate-to-severe atopic dermatitis, moderate-to-severe asthma and CRSwNP

PARIS and TARRYTOWN, NY – June 26, 2019 – The U.S. Food and Drug Administration (FDA) has approved Dupixent® (dupilumab) for use with other medicines to treat chronic rhinosinusitis with nasal polyposis (CRSwNP) in adults whose disease is not controlled. CRSwNP can be a debilitating condition, with many patients opting for systemic steroids or nasal surgery which often cannot control this disease. Moreover, CRSwNP often occurs in combination with severe asthma.

> *"Dupixent is the first FDA approved medicine for adults with chronic rhinosinusitis with nasal polyposis, and the only approved therapy shown to shrink nasal polyp size and also improve the signs and symptoms of the associated chronic rhinosinusitis. In fact, approximately three-quarters of patients treated with Dupixent no longer required either corticosteroids or surgery, the current standards of care,"* said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. *"Importantly, many patients with CRSwNP also suffer from asthma, and Dupixent was shown to improve lung function in these patients as well. This approval further reinforces that IL-4 and IL-13 are key drivers of type 2 inflammation, and we continue to study Dupixent in other type 2 inflammatory diseases, including eosinophilic esophagitis, and food and environmental allergies."*

The FDA evaluated the CRSwNP Dupixent application under Priority Review, which is reserved for medicines that represent potentially significant improvements in efficacy or safety in treating serious conditions.

Dupixent is a fully-human monoclonal antibody that inhibits the signalling of interleukin-4 (IL-4) and interleukin-13 (IL-13), two proteins that play a central role in type 2 inflammation. Data from Dupixent clinical trials have shown that inhibiting IL-4 and IL-13

helps address the type 2 inflammation that plays a major role in CRSwNP, asthma and atopic dermatitis.

> *"Chronic rhinosinusitis with nasal polyposis can be a debilitating condition. Today's standard of care – which includes intranasal and systemic corticosteroids and sinus surgery – often leaves patients with CRSwNP with recurring symptoms,"* said John Reed, M.D., Ph.D., Head of Research and Development at Sanofi. *"In two Phase 3 trials, Dupixent helped patients significantly reduce their nasal congestion, and many patients experienced significant improvement in their sense of smell in as quickly as four weeks. Treatment with Dupixent also reduced the need for systemic steroids and surgery, and led to improvements in health-related quality of life. Importantly, these patients with co-morbid asthma now have a treatment that can help improve their breathing."*

CRSwNP is a chronic disease of the upper airway that obstructs the sinuses and nasal passages. It can lead to breathing difficulties, nasal congestion and discharge, reduced or loss of sense of smell and taste, and facial pressure. Many patients with CRSwNP have other type 2 inflammatory diseases like asthma, and these patients often have more severe asthma and are often more difficult to treat. In the Dupixent CRSwNP clinical trials, 59% of patients also had asthma. These co-morbid diseases can lead to an increased risk of asthma attacks, high symptom burden and a substantial adverse impact on health-related quality of life.

Efficacy and safety from pivotal clinical trials

The FDA approval is based on two pivotal trials (the 24-week SINUS-24 and 52-week SINUS-52) that are part of the Phase 3 LIBERTY clinical trial program. These trials evaluated Dupixent 300 mg every two weeks with standard-of-care mometasone furoate nasal spray (MFNS) compared to placebo injection plus MFNS. 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 include:
  - 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 with 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 pre-specified pooled analyses 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 sino-nasal surgery was reduced by 83% with Dupixent compared to placebo.

In the 59% of patients who also had asthma, the improvements in lung function were similar to patients in the Dupixent asthma program.

Treatment effects on nasal congestion and loss of smell were observed with the first assessment as early as 4 weeks and showed continued improvement for the duration of the trial. In the 52 week SINUS-52 trial, patients continued to do well through the 52 week treatment period.

In the CRSwNP clinical trials, adverse events that occurred in at least 2% of Dupixent patients and greater than placebo were injection site reactions (6% Dupixent, 4% placebo), conjunctivitis (2% Dupixent, 1% placebo), arthralgia (3% Dupixent, 2% placebo) and gastritis (2% Dupixent, 1% placebo).

Another indication for 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 CRSwNP, Dupixent is approved in the U.S. for use with other asthma medicines for the maintenance treatment of moderate-to-severe asthma in certain patients aged 12 years and older whose asthma is not controlled with their current asthma medicines; and to treat patients aged 12 years 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.

The wholesale acquisition cost of Dupixent remains unchanged with the addition of this indication. 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.

Outside of the U.S., Dupixent is approved in a number of countries for use in certain adults with moderate-to-severe atopic dermatitis. Dupixent is also approved in a number of other countries, including those in the European Union (EU), Japan and Australia, to treat certain patients aged 12 years and older with severe asthma. Dupixent is currently under regulatory review for patients with CRSwNP in the EU, and for adolescents with moderate-to-severe atopic dermatitis in several countries, including Japan, and in the EU.

Dupilumab development program

In addition to the currently approved indications, Sanofi and Regeneron 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 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). 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 is being jointly developed by Sanofi and Regeneron under a global collaboration agreement.

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 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, 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 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 atopic dermatitis, eosinophilic esophagitis, chronic obstructive pulmonary disease, food and environmental allergies, 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; 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® (aflibercept) 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 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).