



## Press Release

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

### Dupixent® (dupilumab) Approved for Severe Asthma by European Commission

- \* Only biologic approved in the EU for severe asthma with type 2 inflammation, as characterized by raised blood eosinophils and/or raised fractional exhaled nitric oxide (FeNO)
- \* In clinical trials, Dupixent improved lung function and quality of life, and reduced severe exacerbations and oral corticosteroid use

**PARIS and TARRYTOWN, NY – May 7, 2019** – The European Commission has approved Dupixent® (dupilumab) for use in adults and adolescents 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.

*“People whose severe asthma is inadequately controlled on current therapy continue to have trouble breathing and suffer potentially life-threatening exacerbations. This daily burden and unpredictability can significantly diminish quality of life, causing missed days of school, work and social activities,” said Tonya Winders, President, Global Allergy and Asthma Patient Platform (GAAPP). “GAAPP welcomes the addition of new treatments such as Dupixent, designed to help those with severe asthma take control of their symptoms and get on with their daily lives.”*

Despite standard-of-care treatment, people with severe asthma often have inadequately controlled, persistent symptoms that may make them suitable for treatment with a biologic therapy. These patients live with coughing, wheezing and difficulty breathing, and are at risk of severe asthma attacks that may require emergency room visits or hospitalizations. In addition to taking maintenance ICS treatment, patients with severe asthma often rely on oral corticosteroids (OCS) when their symptoms worsen. While OCS can provide relief for severe symptoms, current asthma guidelines suggest limiting their chronic use to the most severe patients due to the potential for serious side effects.

*“Type 2 inflammation is responsible for many of the hallmark symptoms of asthma – and Dupixent is the first and only treatment approved for patients in the European Union with severe asthma characterized by multiple biomarkers of type 2 inflammation,” said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. “Dupixent is now approved in asthma and atopic*

*dermatitis, and we continue to study this novel treatment in younger populations with these diseases, as well as other conditions driven by type 2 inflammation, including chronic rhinosinusitis with nasal polyps and food and environmental allergies.”*

Dupixent is a human monoclonal antibody that inhibits the signaling of interleukin-4 (IL-4) and interleukin-13 (IL-13), two key proteins that play a central role in type 2 inflammation that underlies specific types of asthma as well as several other allergic diseases. This effect is associated with the reduction of type 2 inflammatory biomarkers including FeNO, immunoglobulin E (IgE) and eotaxin-3 (CCL26).

*“Today’s approval marks an important moment for adolescents and adults in the European Union who suffer from severe asthma with type 2 inflammation,” said John Reed, M.D., Ph.D., Head of Research and Development at Sanofi. “In clinical trials, Dupixent not only reduced exacerbations and oral corticosteroid use, but it also improved lung function and patients’ overall quality of life. Dupixent offers a new treatment option for those who remain inadequately controlled with current medications, including those dependent on oral corticosteroids – which may have potentially serious side effects when used chronically.”*

### **About the LIBERTY ASTHMA Clinical Program**

The EC approval is based on clinical data from 2,888 adults and adolescents who participated in three pivotal trials from the global LIBERTY ASTHMA program, including the Phase 3 QUEST and VENTURE trials and a Phase 2b trial. QUEST enrolled 1,902 patients with persistent asthma and evaluated whether adding Dupixent to standard-of-care therapy could reduce severe exacerbations and improve lung function (measured by FEV<sub>1</sub>). VENTURE enrolled 210 patients with severe oral corticosteroid-dependent asthma and evaluated whether adding Dupixent to standard-of-care therapy could reduce the use of maintenance oral corticosteroids. The Phase 2b trial enrolled 776 adult patients with moderate-to-severe asthma and evaluated whether adding Dupixent to standard-of-care therapy could improve lung function.

In these trials, Dupixent:

- **Reduced severe exacerbations:** In QUEST, by week 52 exacerbations were reduced by up to 67% compared to placebo in patients with eosinophils  $\geq 300$  cells/microliter and up to 65% for those with FeNO levels  $\geq 25$  parts per billion. In the Phase 2b trial, by week 24 exacerbations were reduced by up to 81% compared to placebo in patients with eosinophils  $\geq 300$  cells/microliter.
- **Improved lung function:** In QUEST, by week 12 Dupixent improved FEV<sub>1</sub> by up to 33% (vs. up to 16% for placebo) in patients with blood eosinophils of  $\geq 300$  cells/microliter and up to 30% (vs. up to 14% for placebo) in patients with FeNO  $\geq 25$  parts per billion. In the Phase 2b trial, by week 12 Dupixent improved FEV<sub>1</sub> by up to 26% (vs. 10% for placebo) in patients with blood eosinophils of  $\geq 300$  cells/microliter.
- **Reduced oral corticosteroid use:** In VENTURE, by week 24 more than half of Dupixent patients completely eliminated oral corticosteroids, and overall use reduced by 70% (vs. 42% for placebo).

- **Safety:** In asthma clinical trials, the most common adverse reaction was injection site erythema (redness). Anaphylactic reaction has been reported very rarely in the asthma development program.

All trials enrolled patients irrespective of minimum baseline type 2 inflammatory biomarkers, such as eosinophils or FeNO levels. Recently updated Global Initiative for Asthma (GINA) guidelines characterize type 2 inflammation by eosinophils  $\geq 150$  cells/microliter or FeNO  $\geq 20$  parts per billion. In these pivotal trials, patients with eosinophils  $\geq 150$  cells/microliter or FeNO  $\geq 25$  parts per billion benefited most from Dupixent. In the Phase 2b trial and QUEST, the greatest improvements in exacerbations and lung function were observed in patients with higher baseline levels of type 2 disease. In VENTURE the effect of Dupixent on oral corticosteroid use, exacerbations and lung function, was similar irrespective of baseline levels of type 2 inflammation.

### About Dupixent

Dupixent is also approved in the EU for the treatment of adults with moderate-to-severe atopic dermatitis who are candidates for systemic therapy. In October 2018, Dupixent was approved in the U.S. 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. It is also approved in the U.S. for adults and adolescents (12 to 17 years of age) with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent is being developed jointly by Regeneron and Sanofi as part of a global collaboration agreement.

Dupixent comes in a 200 mg pre-filled syringe for patients with severe asthma or a 300 mg pre-filled syringe for those who have severe asthma and are on oral corticosteroids or with co-morbid moderate-to-severe atopic dermatitis. It is given as a subcutaneous injection every other week at different injection sites after the initial loading dose. Dupixent can be given in a clinic or at home by self-administration after training by a healthcare professional.

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 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). Dupilumab is also being studied in combination with REGN3500, 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 were invented using Regeneron's proprietary *VelocImmune*<sup>®</sup> technology that yields optimized fully-human antibodies.

For more information on dupilumab clinical trials please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

## 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*<sup>®</sup> technologies, such as *VelocImmune*<sup>®</sup> 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](http://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 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 Forward-Looking Statements**

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 atopic dermatitis, pediatric asthma, chronic rhinosinusitis with nasal polyps, eosinophilic esophagitis, food and environmental allergies, chronic obstructive pulmonary disease, 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; 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® (afibbercept) 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-K for the year ended December 31, 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>).