SANOFI

Press Release

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Positive results presented from two Phase 3 trials of Dupixent® (dupilumab) in severe chronic rhinosinusitis with nasal polyps

- Dupixent showed significant improvement on every primary and secondary endpoint in patients with severe chronic rhinosinusitis with nasal polyps who had failed previous treatment with surgery and/or systemic corticosteroids
- Dupixent also showed significant improvement of co-morbid asthma

PARIS and TARRYTOWN, NY – February 25, 2019 – Detailed results were presented from two Phase 3 trials in patients with recurring severe chronic rhinosinusitis with nasal polyps (CRSwNP) despite previous treatment with surgery and/or systemic corticosteroids. These trials, known as SINUS-24 and SINUS-52, demonstrated that Dupixent® (dupilumab), when added to the standard of care corticosteroid nasal spray, improved nasal polyp size, nasal congestion severity, chronic sinus disease, sense of smell and co-morbid asthma outcomes. In these severe patients, Dupixent reduced the need for systemic corticosteroid use and the need for nasal/sinus surgery. These data were presented in two late-breaking sessions at the 2019 Annual Meeting of the American Academy of Allergy, Asthma & Immunology (AAAAI) in San Francisco.

> *"Dupixent is the first biologic therapy to demonstrate the potential to produce disease-modifying effects in severe CRSwNP, significantly improving all disease measures in the study, including sense of smell, one of the most troublesome and challenging-to-treat symptoms for patients,"* said Claus Bachert, M.D., Professor and Head of Clinics of the Department of Otorhinolaryngology at Ghent University and principal investigator of the trials*. "Patients with co-morbid CRSwNP and asthma are often more difficult to treat so it is encouraging that Dupixent, which targets key drivers of Type 2 inflammation, may address both conditions in these patients."*

Dupixent is a human monoclonal antibody specifically designed to inhibit signaling of interleukin-4 and interleukin-13 (IL-4 and IL-13). The findings from these studies, as well as from prior studies in atopic dermatitis and asthma, demonstrate that these are two key proteins that play a central role in Type 2 inflammation, which seem to underlie CRSwNP as well as several allergic diseases.

CRSwNP is a chronic disease of the upper airway predominantly driven by Type 2 inflammation and characterized by polyps that obstruct the sinuses and nasal passages. Patients may experience severe nasal obstruction with breathing difficulties, nasal

discharge, reduced or loss of sense of smell and taste and facial pain or pressure. Persistent symptoms of CRSwNP have a substantial adverse impact on patients' health-related quality of life, which can be measured by a composite endpoint that includes reduced productivity and activities of daily living, inability to enjoy food, lack of sleep and fatigue.

Current treatment options are intranasal corticosteroids, systemic corticosteroids and surgery, all with suboptimal efficacy and/or high recurrence rates after treatment. Mometasone furoate nasal spray (MFNS) is a standard-of-care intranasal corticosteroid, and the Phase 3 SINUS-24 and SINUS-52 trials evaluated 300 mg Dupixent added to MFNS ("Dupixent group") compared to placebo injection plus MFNS ("placebo group").

The topline results for both trials were announced in October 2018. These trials met their co-primary endpoints of change from baseline in nasal congestion/obstruction severity and change from baseline in nasal polyps score, measured at 24 weeks. Patients treated with Dupixent experienced a:

- 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 (absolute change from baseline of -1.34 and -1.25 for Dupixent compared to -0.45 and -0.38 for placebo; $p<0.0001$ for both)
- 33% and 27% reduction in their nasal polyps score compared to a 7% and 4% increase for placebo in SINUS-24 and SINUS-52, respectively (absolute change from baseline of -1.89 and -1.71 for Dupixent compared to 0.17 and 0.10 for placebo; $p<0.0001$ for both)

New data presented at AAAAI

Dupixent significantly reduced chronic sinus disease in both trials. Dupixent treatment effects began as early as four weeks with progressive improvement up to 24 weeks in SINUS-24, a 24-week trial, and up to 52 weeks in SINUS-52. Both trials evaluated Dupixent treatment every two weeks for up to 24 weeks, and after week 24 through 52 weeks, SINUS-52 included a group of patients treated every four weeks in addition to a group treated every two weeks.

Patients in the Dupixent every two weeks group experienced a:

- 42% and 27% improvement in sinus opacification vs. 4% and 0% with placebo at 24 weeks in SINUS-24 and SINUS-52, respectively (absolute change from baseline of -8.18 and -5.21 for Dupixent vs. -0.74 and -0.09 for placebo; $p<0.0001$ for both). For patients in SINUS-52, a 37% improvement in sinus opacification was achieved with Dupixent treatment vs. 2% with placebo at 52 weeks (absolute change from baseline of -6.83 for Dupixent vs. 0.11 for placebo; nominal $p<0.0001$)
- 146% and 108% improvement in ability to identify different smells vs. 19% and 7% with placebo at 24 weeks in SINUS-24 and SINUS-52, respectively (absolute change from baseline of 11.26 and 9.71 for Dupixent vs. 0.7 and -0.81 for placebo; $p<0.0001$ for both). In both trials, Dupixent-treated patients reported an

improvement in sense of smell as early as four weeks based on a separate daily assessment

- 60% and 51% improvement in health-related quality of life vs. 18% and 18% with placebo at 24 weeks in SINUS-24 and SINUS-52, respectively (absolute change from baseline of -30.43 and -27.77 for Dupixent vs. -9.31 and -10.4 for placebo; $p<0.0001$ for both). At 52 weeks, there was a 58% improvement in health-related quality of life with Dupixent vs. 14% with placebo (absolute change from baseline of -29.84 for Dupixent vs. -8.88; $p<0.0001$)
- 0.21L improvement in lung function vs. placebo at 24 weeks in SINUS-24 in the subset of patients with asthma at baseline (absolute change from baseline of 0.15L for Dupixent vs. -0.06L for placebo; nominal $p=0.0004$) and 0.21L improvement in lung function vs. placebo at 24 weeks in SINUS-52 (absolute change from baseline of 0.17L for Dupixent vs. -0.015L for placebo; nominal $p<0.0001$). In the trials, approximately 60% of patients had co-morbid asthma, most of them receiving asthma controller medication
- 73% reduction in rescue treatment with systemic corticosteroids or nasal polyp surgery compared with placebo at 24 weeks in SINUS-24 and 76% reduction in rescue treatment compared with placebo at 52 weeks in SINUS-52 (Kaplan-Meier estimates at 24 weeks were 7% for Dupixent vs. 23% for placebo in SINUS-24, HR 0.27 [95% CI: 0.13 to 0.55], nominal $p=0.0003$; and Kaplan-Meier estimates at 52 weeks were 13% for Dupixent vs. 44% for placebo in SINUS-52, HR 0.24 [0.16 to 0.36]; nominal $p<0.0001$)

Overall, rates of adverse events were generally similar between the Dupixent-treated group and placebo. Treatment-emergent adverse events occurred less frequently in the Dupixent group compared to placebo (65% vs. 71% in SINUS-24; 83% vs. 91% in SINUS-52). Adverse events that were observed more frequently in the Dupixent group compared with placebo included epistaxis (nosebleeds) in SINUS-24 (8% vs. 3%) and bronchitis (6% vs. 5%), cough (6% vs. 5%) and injection site reactions (3% vs. 2%) in SINUS-52. The rate of serious adverse events was 4% with Dupixent vs. 14% with placebo in SINUS-24, and 5% with Dupixent vs. 10% with placebo in SINUS-52. Adverse events leading to discontinuation occurred in 4% with Dupixent vs. 2% with placebo in SINUS-24 and 4% with Dupixent vs. 11% with placebo in SINUS-52.

Other Dupixent presentations at AAAAI included analyses on allergic rhinitis, CRSwNP and other sino-nasal outcomes in patients with co-morbid asthma or atopic dermatitis.

In the U.S., Dupixent is approved for treatment of adult patients with moderate-to-severe atopic dermatitis that is not well controlled by topical prescription therapies, or who cannot use topical therapies; Dupixent is also approved in the U.S for use with other asthma medicines for maintenance treatment of moderate-to-severe asthma in people aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. Other potential uses for Dupixent are investigational and the safety and efficacy have not been evaluated by the U.S. Food and Drug Administration, the European Medicines Agency or any other regulatory authority. Dupilumab is being developed jointly by Sanofi and Regeneron as part of a global collaboration agreement.

About the SINUS-24 and SINUS-52 trials

SINUS-24 (n=276) and SINUS-52 (n=448) were randomized double-blind, placebo-controlled pivotal Phase 3 trials in patients with severe CRSwNP. SINUS-24 included two treatment groups added to nasal spray: 300 mg Dupixent every two weeks for 24 weeks or placebo every two weeks for 24 weeks. SINUS-52 included three treatment groups added to nasal spray: 300 mg Dupixent every two weeks for 52 weeks, 300 mg Dupixent every two weeks for 24 weeks and then every four weeks until 52 weeks, or placebo every two weeks for 52 weeks. The co-primary and secondary endpoints of the trials included change from baseline in: nasal congestion/obstruction severity, a 0-3 scale, at 24 weeks (co-primary); nasal polyps score (a measure of polyp size), as assessed by nasal endoscopy, a 0-8 scale, at 24 weeks (co-primary); Lund-Mackay score, a 0-24 scale, as assessed by computed tomography (CT) scans at 24 weeks; University of Pennsylvania Smell Identification Test (UPSIT), 0-40 scale, at 24 weeks; severity of decreased or loss of smell by patient daily assessment on a 0-3 scale at 24 weeks; 22-item Sino-Nasal Outcome Test (SNOT-22), a 0-110 scale at 24 weeks; and the previous endpoints up to 52 weeks in SINUS-52.

Other pre-specified endpoints included the: change from baseline to 24 weeks in forced expiratory volume over one second (FEV1) in patients with co-morbid asthma; and proportion of patients during trial treatment who received rescue treatment with systemic corticosteroids and/or nasal polyp surgery.

The trials enrolled patients who were 18 years or older with bilateral nasal polyps who, despite treatment with systemic corticosteroids in the previous two years or history of surgery, continued to have ongoing moderate or severe symptoms of nasal congestion, blockage, loss of smell or nasal discharge. Consistent with the overlap seen among patients with Type 2 or allergic inflammatory diseases, more than three-quarters also suffered from other conditions, including asthma (approximately 59%), allergic rhinitis (approximately 58%) and NSAID-exacerbated respiratory disease (approximately 28%). Patients with co-morbid asthma and CRSwNP tend to have more severe disease.

Dupilumab development program

In addition to the approved indications in moderate-to-severe atopic dermatitis and moderate-to-severe asthma, 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 (6 to 11 years of age) atopic dermatitis (Phase 3), pediatric (6 months to 5 years of age) atopic dermatitis (Phase 2/3), adolescent (12 to 17 years of age) atopic dermatitis (Phase 3 completed), pediatric (6 to 11 years of age) asthma (Phase 3), eosinophilic esophagitis (Phase 2/3) and food and environment allergies (Phase 2). A future trial is planned for chronic obstructive pulmonary disease. 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.

For more information on dupilumab clinical trials please visit 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 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 atopic dermatitis, pediatric asthma, eosinophilic esophagitis, grass allergy, food allergy (including peanut), 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 manufacturing, 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® (aflibercept) 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).