FDA to Undertake Priority Review of Dupixent® (dupilumab) for Adults with Inadequately Controlled Severe Chronic Rhinosinusitis with Nasal Polyps

March 8, 2019

TARRYTOWN, N.Y. and PARIS, March 8, 2019 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that the U.S. Food and Drug Administration (FDA) has accepted for Priority Review the supplemental Biologics License Application (sBLA) for Dupixent® (dupilumab) as an add-on maintenance treatment for adults with inadequately controlled severe chronic rhinosinusitis with nasal polyps (CRSwNP). Patients with severe CRSwNP often experience recurrence despite previous treatment with surgery and/or systemic corticosteroids. The target action date for the FDA decision is June 26, 2019.

Currently, there are no FDA-approved biologic medicines to treat CRSwNP, 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, reduction 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 that includes reduced productivity and activities of daily living, inability to enjoy food, lack of sleep and fatigue. People with co-morbid asthma and CRSwNP tend to have more severe disease and are often more difficult to treat.

The sBLA is supported by data from two pivotal Phase 3 trials evaluating the efficacy and safety of Dupixent when combined with standard-of-care corticosteroid nasal spray in patients with recurring severe CRSwNP despite previous treatment with surgery and/or systemic corticosteroids. About 60% of patients in the trials had co-morbid asthma. Data from these trials were presented at the Annual Meeting of the American Academy of Allergy, Asthma & Immunology (AAAAI) in February 2019. In addition to moderate-to-severe atopic dermatitis and moderate-to-severe asthma, this is the third type 2 allergic inflammatory disease in which Dupixent has demonstrated positive Phase 3 results.

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 trials, as well as from prior trials in atopic dermatitis and asthma, demonstrate that both IL-4 and IL-13 are two key proteins that play a central role in type 2 inflammation, which seems to underlie CRSwNP as well as several other allergic diseases.

In the U.S., Dupixent is approved for treatment of adult patients 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 is also approved for use 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 is also approved for use in certain adult patients with moderate-to-severe atopic dermatitis in countries of the European Union (EU), and other countries including Canada and Japan.

On March 1, 2019, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion for the application for Dupixent, recommending its approval in the EU as add-on maintenance treatment for adult and adolescent (12 years and older) severe asthma patients with type 2 inflammation characterized by increased blood eosinophils and/or raised exhaled nitric oxide measured by FeNO test and inadequately controlled by inhaled high dose corticosteroids plus another asthma medicinal product. This indication remains investigational in the EU, pending the adoption of the CHMP opinion by the European Commission.

Other potential uses for Dupixent, including in CRSwNP, are investigational and the safety and efficacy have not been evaluated by the FDA, the EMA or any other regulatory authority. Dupilumab is being developed jointly by Regeneron and Sanofi as part of a global collaboration agreement.

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 chronic rhinosinusitis with nasal polyps (Phase 3 *completed*), adolescent (12 to 17 years of age) atopic dermatitis (Phase 3 *completed*), pediatric (6 to 11 years of age) atopic dermatitis (Phase 3), pediatric (6 months to 5 years of age) atopic dermatitis (Phase 2/3), pediatric (6 to 11 years of age) asthma (Phase 3), eosinophilic esophagitis (Phase 2/3), and food and environmental 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. Dupilumab and REGN3500 were invented using Regeneron's proprietary *VelocImmune*® technology that yields optimized fully human antibodies.

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

U.S. 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.

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 (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 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 injection site reactions, 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.

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

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); the impact of the recent and any potential future U.S. government shutdowns on the anticipated timing of the decision by the U.S. Food and Drug Administration regarding the supplemental Biologics License Application for Dupixent referenced in this press release; the impact of the opinion adopted by the European Medicine Agency'sCommittee for Medicinal Products for Human Use referenced in this press release on the European Commission's decision regarding the Marketing Authorization Application for Dupixent for use as an add-on maintenance treatment in certain adults and adolescents (12 years of age and older) with inadequately controlled severe asthma or oral corticosteroid-dependent asthma; 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).

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.

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