Regeneron and Sanofi Announce Positive Study Results for DUPIXENT® (dupilumab) in Patients With Moderate-to-Severe Atopic Dermatitis

September 16, 2017

TARRYTOWN, N.Y. and PARIS, Sept. 16, 2017 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced positive results from the Phase 3 CAFÉ study of DUPIXENT® (dupilumab) in adults with moderate-to-severe atopic dermatitis (AD) who are inadequately controlled with or are intolerant to the broad immunosuppressant drug cyclosporine A (CSA), or when this treatment is medically inadvisable. In the study, DUPIXENT with topical corticosteroids (TCS) significantly improved measures of overall disease severity, skin clearing, itching, and patient reported quality of life measures. CSA is approved for the treatment of AD in most European countries and Japan; it is not approved in the U.S. for this use. The results of this study are being presented at the European Academy of Dermatology and Venereology (EADV) Congress in Geneva, Switzerland.

The primary endpoint of the study was the proportion of patients that achieved a 75 percent or greater improvement in the Eczema Area and Severity Index (EASI-75) score at 16 weeks from baseline. EASI is a tool used to measure the extent and severity of the disease. Fifty-nine percent of patients who received DUPIXENT weekly with TCS, and 63 percent of patients who received DUPIXENT every two weeks with TCS achieved EASI-75, compared to 30 percent of those patients who received placebo with TCS (p less than 0.0001). The mean percent change improvement in EASI from baseline at 16 weeks (a secondary endpoint) was 78 percent and 80 percent for patients who received DUPIXENT weekly or every two weeks with TCS, respectively, compared to 47 percent for those who received placebo plus TCS (p less than 0.0001).

"In moderate-to-severe atopic dermatitis, some patients stop cyclosporine therapy due to intolerance or lack of efficacy, or are not candidates because of other medical conditions or contraindicated medications," said Dr. Marjolein De Bruin-Weller, Dermatologist, National Expertise Center for Atopic Dermatitis, University Medical Center Utrecht. "In the CAFÉ study, DUPIXENT with topical corticosteroids significantly improved overall measures of disease severity including lesions, itch, quality of life measures and symptoms of anxiety and depression in these patients. The safety profile in this study was consistent with three previous positive DUPIXENT Phase 3 studies in moderate-to-severe atopic dermatitis."

Other secondary endpoints of the study included measures of the impact of DUPIXENT on the persistent itch caused by the disease, quality of life measures, and symptoms of anxiety and depression. The results for these secondary endpoints at 16 weeks include:

- The mean percent improvement from baseline in the intensity of patient-reported itch, as measured by the pruritus Numerical Rating Scale (NRS), was 52 percent and 54 percent in patients who received DUPIXENT weekly or every two weeks with TCS, respectively, compared to 25 percent for those who received placebo plus TCS (p less than 0.0001).
- The proportion of patients with a greater than or equal to four-point improvement from baseline in aspects of patient quality of life, as measured by the Dermatology Life Quality Index (DLQI), was 78 percent and 88 percent in patients who received DUPIXENT weekly or every two weeks with TCS, respectively, compared to 44 percent of those who received placebo plus TCS (p less than 0.0001).
- The proportion of patients with a greater than or equal to four-point improvement from baseline in the severity of their AD, as measured by the Patient Oriented Eczema Measure (POEM), a tool that quantifies the illness as experienced by the patients, was 76 percent and 83 percent in patients who received DUPIXENT weekly or every two weeks with TCS, respectively, compared to 42 percent for those who received placebo plus TCS (p less than 0.0001).

No new adverse events were reported in the study. The proportion of patients reporting an adverse event was similar among the treatment arms. Conjunctivitis was more frequent in patients who received DUPIXENT with TCS, with 16 percent and 28 percent reported in patients who received DUPIXENT weekly or every two weeks with TCS, respectively, compared to 11 percent for patients who received placebo with TCS. Injection site reactions were reported in 11 percent and 4 percent among patients who received DUPIXENT with TCS weekly or every two weeks, respectively, compared to 5 percent for patients who received placebo with TCS. Skin infections were reported in 4 percent and 2 percent among patients who received DUPIXENT weekly or every two weeks with TCS, respectively, compared to 8 percent for patients who received placebo with TCS.

A total of 325 patients in Europe were randomized into three treatment groups in the 16-week study to receive either DUPIXENT 300 mg weekly with TCS, DUPIXENT 300 mg every two weeks with TCS or placebo with TCS.

About DUPIXENT (dupilumab)
DUPIXENT is a human monoclonal antibody that is designed to simultaneously inhibit overactive signaling of IL-4 and IL-13 cytokines. In addition to moderate-to-severe atopic dermatitis, Sanofi and Regeneron are studying dupilumab in a broad range of clinical development programs including uncontrolled persistent asthma (phase 3), nasal polyps (phase 3) and eosinophilic esophagitis (phase 2). These potential uses are investigational and the safety and efficacy have not been evaluated by any regulatory authority. Dupilumab was discovered using Regeneron's proprietary *VelocImmune*® technology that yields optimized fully-human antibodies, and is being jointly developed by Regeneron and Sanofi under a global collaboration agreement.

In March 2017, the U.S. Food and Drug Administration (FDA) approved DUPIXENT® (dupilumab) in the U.S. for the treatment of adults 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 given as one, 300 mg injection under the skin (subcutaneous injection) every 2 weeks after an initial loading dose (600 mg). The European Commission (EC) is expected to adopt a final decision on the Marketing Authorization Application (MAA) for DUPIXENT in the European

Union, following the Committee for Medicinal Products for Human Use (CHMP) adopting a positive opinion on July 21, 2017.

About Atopic Dermatitis
Atopic dermatitis, a form of eczema, is a chronic inflammatory disease with symptoms often appearing as a rash on the skin. Moderate-to-severe atopic dermatitis is characterized by rashes often covering much of the body, and can include intense, persistent itching and skin dryness, cracking, redness, crusting, and oozing. Itch is one of the most burdensome symptoms for patients and can be debilitating. In addition, patients with moderate-to-severe atopic dermatitis experience a substantial burden of disease, including skin lesions, intense pruritus, and impact on quality of life components, such as sleep and symptoms of anxiety and depression.

IMPORTANT SAFETY INFORMATION for U.S.

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.
- Have asthma.
- 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 have asthma and 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.** Stop using Dupixent and go to the nearest hospital emergency room if you get any of the following symptoms: fever, general ill feeling, swollen lymph nodes, hives, itching, 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.

The most common side effects include injection site reactions, eye and eyelid inflammation, including redness, swelling and itching, and cold sores in your mouth or on your lips.

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 may report side effects to FDA at 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.

Please click here for the full Prescribing Information. The patient information is available here.

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 nearly 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to six FDA-approved treatments and over a dozen product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye disease, heart disease, allergic and inflammatory diseases, pain, cancer, and infectious and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its unique *VelociSuite*® technologies and ambitious initiatives such as The Regeneron Genetics Center, 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, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi is organized into five global business units: Diabetes and Cardiovascular, General Medicines and Emerging Markets, Sanofi Genzyme, Sanofi Pasteur and Consumer Healthcare. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

Sanofi Genzyme focuses on developing specialty treatments for debilitating diseases that are often difficult to diagnose and treat, providing hope to patients and their families.

Regeneron Forward-Looking Statements and Use of Digital Media
This news 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 Dupixent for the treatment of uncontrolled moderate-to-severe atopic dermatitis in the European Union and other potential jurisdictions, as well as other potential indications; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in later studies and lead to therapeutic applications; unforeseen safety issues and possible liability resulting from the administration of products and product candidates in patients, including without limitation Dupixent; serious complications or side effects in connection with the use of Regeneron's products and product candidates (such as Dupixent) in clinical trials; coverage and reimbursement determinations by third-party payers, including Medicare, Medicaid, and pharmacy benefit management companies; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, research and clinical programs, and business, including those relating to the enrollment, completion, and meeting of the relevant endpoints of post-approval studies; 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, such as Dupixent; 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; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its sales or other 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 relating to Praluent® (alirocumab) Injection, the permanent injunction granted by the United States District Court for the District of Delaware that, if upheld on appeal, would prohibit Regeneron and Sanofi from marketing, selling, or manufacturing Praluent in the United States, the outcome of any appeals regarding such injunction, the ultimate outcome of such litigation, 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 United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2016 and its Form 10-Q for the quarterly period ended June 30, 2017. 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, 2016. 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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