Regeneron and Sanofi Announce Positive Dupilumab Topline Results from Phase 3 Trial in Uncontrolled Persistent Asthma

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TARRYTOWN, N.Y. and PARIS, Sept. 11, 2017 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that the pivotal Phase 3 LIBERTY ASTHMA QUEST study of dupilumab in a broad population of patients with uncontrolled, persistent asthma met its two primary endpoints. Dupilumab, when added to standard therapies, reduced severe asthma attacks (exacerbations) and improved lung function. At 52 weeks, in the 300 mg dose group, dupilumab reduced severe asthma attacks by 46 percent in the overall population, 60 percent in patients with 150 eosinophilic cells/microliter or greater, and 67 percent in patients with 300 eosinophilic cells/microliter or greater (p less than 0.001 for all groups). At 12 weeks, in the 300 mg dupilumab dose group, mean improvement in lung function over placebo as assessed by forced expiratory volume over one second (FEV_1) was 130 mL (9 percent) in the overall population, 150 mL (11 percent) in patients with 150 eosinophilic cells/microliter or greater, and 240 mL (18 percent) in patients with 300 eosinophilic cells/microliter or greater (p less than 0.001 for all groups). The companies plan to submit a Supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) by the end of this year.

"Approximately one million U.S. adults and adolescents live with uncontrolled, persistent asthma, and continue to experience serious asthma attacks, despite taking an intensive regimen of standard therapies," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "Dupilumab has now demonstrated positive late-stage results in two serious allergic diseases -- asthma and atopic dermatitis -- with robust efficacy and an extensive safety database. These results continue to support our hypothesis that the IL-4/IL-13 pathway is a critical driver of allergic disease, and we remain committed to further investigating the IL-4/IL-13 pathway in other allergic diseases."

The results for the 200 mg and 300 mg dupilumab dose groups were generally comparable on both exacerbations and FEV_1. The extent of patient response correlated with allergic or atopic status as reflected by blood eosinophils and other markers. Less activity was observed in patients with less than 150 eosinophilic cells/microliter. The overall rates of adverse events, deaths, infections, conjunctivitis, herpes and discontinuations were comparable between the dupilumab and placebo groups. Injection site reactions were more common in the dupilumab groups occurring in 17 percent of dupilumab patients compared to 8 percent of placebo patients.

"We believe that therapies like dupilumab, which focus on specific molecular pathways such as the Th2 pathway associated with multiple chronic allergic diseases, are important targets for further investigations," said Elias Zerhouni, M.D., President, Global R&D, Sanofi. "The positive data from this large second pivotal trial in uncontrolled persistent asthma, following the positive results of dupilumab in atopic dermatitis, further support this view in our opinion. We will work diligently with health authorities to bring this new application of dupilumab to the patients who most need it."

The QUEST pivotal Phase 3 trial enrolled 1,902 patients including 1,795 adults and 107 adolescents across 413 study sites worldwide. The four study groups included patients treated with 200 mg every other week with a loading dose of 400 mg, 300 mg every other week with a loading dose of 600 mg, and two separate placebo groups. Patients were randomized in a 2:1 fashion to active drug versus placebo. The two primary endpoints of the study were the annualized rate of severe exacerbation events at 52 weeks and the absolute change from baseline in a standard measure of lung function known as pre-bronchodilator forced expiratory volume over one second (FEV_1) at 12 weeks (changes of 100 to 200 mL are considered clinically relevant). The pre-specified primary analysis included hierarchical evaluation of these endpoints in the overall population, in patients with 150 eosinophilic cells/microliter or greater, and in patients with 300 eosinophilic cells/microliter or greater. In the study, approximately 50 percent of patients had 300 eosinophilic cells/microliter or greater and approximately 70 percent of patients had 150 eosinophilic cells/microliter or greater. Higher eosinophil counts are generally thought to be associated with poorer asthma control and higher rates of exacerbations, as was observed in the placebo patients in this study.

All patients continued on a medium or high dose inhaled corticosteroid (ICS) and up to two additional controller medicines throughout the study. Eosinophil subgroups were classified based on baseline levels.

Detailed results from this study will be submitted for presentation at a future medical congress. QUEST is the second pivotal trial in uncontrolled persistent asthma following a positive Phase 2b pivotal study of dupilumab. Data from another Phase 3 study known as VENTURE examining the ability of dupilumab to reduce oral corticosteroid use in patients with severe steroid-dependent asthma are expected later this year. Also included in the LIBERTY ASTHMA clinical development program is the TRAVERSE trial, a long-term safety extension study. The potential use of dupilumab in asthma is currently under clinical development and the safety and efficacy have not been fully evaluated by any regulatory authority.

In March 2017, the FDA approved DUPIXENT® (dupilumab) in the U.S. for the treatment of moderate-to-severe atopic dermatitis

that is not adequately controlled with topical prescription therapies.

About Uncontrolled Persistent Asthma
People who live with uncontrolled persistent asthma often have severe attacks (exacerbations) that may lead to emergency room visits, hospitalizations and decreased lung function. Despite currently available treatments, there is a need for new medicines that offer comprehensive asthma control including preservation of lung function and reduction in exacerbations. Uncontrolled persistent asthma is often associated with other Type 2 allergic inflammatory diseases including atopic dermatitis, nasal polyps, allergic rhinitis, eosinophilic esophagitis and food allergies. The disease is characterized by an imbalance or overactivity of certain immune cells (including eosinophils) and signaling proteins known as interleukins. Two of these are Interleukin-4 (IL-4) and interleukin-13 (IL-13), which are central drivers of Type 2 inflammation.

About Dupilumab Clinical Programs
Dupilumab is a fully human monoclonal antibody that is designed to simultaneously inhibit overactive signaling of IL-4 and IL-13 cytokines, one of the root causes of Type 2 allergic inflammation. Sanofi and Regeneron are studying dupilumab in a broad range of clinical development programs for diseases that are driven by Type 2 inflammation, including pediatric atopic dermatitis (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.

DUPIXENT® (dupilumab) is the first and only biologic medicine FDA-approved for the treatment of adults with moderate-to-severe atopic dermatitis (AD) whose disease is not adequately controlled with topical prescription therapies.

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

IMPORTANT SAFETY INFORMATION
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.

INDICATION

DUPIXENT is used to treat 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 can be used with or without topical corticosteroids. It is not known if DUPIXENT is safe and effective in children.

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 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, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its proprietary VelociSuite® technologies, including VelocImmune® which yields optimized fully-human antibodies, 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, persistent asthma in adults and adolescents and other potential indications; 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. 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 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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