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## **Regeneron and Sanofi Announce Positive Dupilumab Topline Results from Two Phase 3 Trials in Inadequately Controlled Moderate-to-Severe Atopic Dermatitis Patients**

**Dupilumab is first systemic therapy to show positive Phase 3 results in patients with moderate-to-severe atopic dermatitis, a serious, chronic inflammatory skin disease marked by widespread rash, itching and associated psychosocial comorbidities**

**U.S. regulatory submission for dupilumab planned for Q3 of 2016**

TARRYTOWN, N.Y and PARIS, April 1, 2016 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) and Sanofi today announced that two placebo-controlled Phase 3 studies evaluating investigational dupilumab in adult patients with inadequately controlled moderate-to-severe atopic dermatitis (AD) met their primary endpoints. In the studies, known as LIBERTY AD SOLO 1 and SOLO 2, treatment with dupilumab as monotherapy significantly improved measures of overall disease severity, skin clearing, itching, quality of life, and mental health.

"These are the first Phase 3 studies of a systemic therapy to demonstrate a significant improvement in moderate-to-severe atopic dermatitis, a chronic, debilitating inflammatory disease that impacts over one million Americans," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "These data provide strong evidence that the IL-4 and IL-13 signaling pathway is a fundamental driver of inflammation in atopic dermatitis. Dupilumab is the first in a new class of immunotherapies - in these 16 week trials, dupilumab blocked the aberrant activation of this pathway, resulting in significant efficacy without evidence of immune-suppressing side effects. We continue to evaluate the role of IL-4 and IL-13 signaling in related inflammatory conditions, including asthma and nasal polyposis, where we have ongoing dupilumab clinical development."

"There are no approved systemic therapies in the U.S. for people with moderate-to-severe atopic dermatitis, underscoring the clear unmet need. These results may bring new hope to atopic dermatitis patients, many of whom have suffered for years," said Elias Zerhouni, M.D., President, Global R&D, Sanofi. "In the U.S., where dupilumab in AD has been granted Breakthrough Therapy designation by the U.S. FDA, we plan to submit a regulatory application in the third quarter of this year and will work to bring this innovative therapy to patients as quickly as possible."

A total of 1,379 adult patients with moderate-to-severe AD were enrolled in the identically-designed SOLO 1 and SOLO 2 trials. Patients were enrolled if they were not adequately controlled with topical medications, or if topical treatment was not medically advisable. All patients were assessed via the 5-point Investigator's Global Assessment (IGA) scale, ranging from 0 (clear) to 4 (severe); entry criteria required a baseline score of 3 or 4. Patients were also assessed using the Eczema Area and Severity Index (EASI) and other measures. Patients were randomized into one of three treatment groups: dupilumab 300 mg subcutaneously once per week, dupilumab 300 mg subcutaneously every two weeks, or placebo for 16 weeks following an initial dupilumab loading dose of 600 mg subcutaneously, or placebo. Results at 16 weeks included the following:

- | For SOLO 1 and SOLO 2, respectively, 37 and 36 percent of patients who received dupilumab 300 mg weekly, and 38 and 36 percent of patients who received dupilumab 300 mg every two weeks, achieved clearing or near-clearing of skin lesions (IGA 0 or 1), compared to 10 and 8.5 percent with placebo (p less than 0.0001). This was the primary endpoint of the study in the U.S. and one of the primary endpoints in the EU.
- | For SOLO 1 and SOLO 2, respectively, the percent improvement in EASI from baseline was 72 and 69 percent in patients who received the 300 mg weekly dose, and 72 and 67 percent for patients who received dupilumab 300 mg every two weeks, compared to 38 and 31 percent for placebo (p less than 0.0001).
- | For SOLO 1 and SOLO 2, respectively, 52.5 and 48 percent of patients who received dupilumab 300 mg weekly, and 51 and 44 percent of patients who received dupilumab 300 mg every two weeks, achieved EASI-75 compared to 15 and 12 percent with placebo (p less than 0.0001). This was the key secondary endpoint in the US and one of the primary endpoints in the EU.

For the 16-week treatment period, the overall rate of adverse events (65-73 percent dupilumab and 65-72 percent placebo) was comparable between the dupilumab groups and the placebo groups. The proportion of patients who completed the treatment period was 88-94 percent for dupilumab and 80.5-82 percent for placebo. The rate of serious adverse events was 1-3 percent for dupilumab and 5-6 percent for placebo. Serious and severe infections were also numerically higher in the placebo groups in both studies (0.5-1 percent dupilumab and 2-3 percent placebo). Adverse events that were noted to have a higher rate with dupilumab treatment across both studies included injection site reactions (10-20 percent dupilumab; 7-8

percent placebo) and conjunctivitis (7-12 percent dupilumab; 2 percent placebo); approximately 26 percent of patients in both studies reported a history of allergic conjunctivitis at study entry. No patient discontinued therapy due to injection site reactions and only one patient discontinued therapy due to conjunctivitis.

More detailed results from SOLO 1 and SOLO 2 will be submitted for presentation at a future medical congress.

The U.S. Food and Drug Administration (FDA) granted dupilumab Breakthrough Therapy designation in AD in November 2014. Dupilumab is currently under clinical development and its safety and efficacy have not been fully evaluated by any regulatory authority.

The LIBERTY AD Phase 3 clinical program consists of five trials of patients with moderate-to-severe AD at sites worldwide.

### **About Atopic Dermatitis**

Atopic dermatitis - a serious form of eczema - is a chronic inflammatory disease characterized by itchy, inflamed skin that can be present on any part of the body. Though symptoms appear externally, atopic dermatitis is characterized by underlying systemic inflammation. Atopic dermatitis affects approximately 7-8 million adults in the U.S. and 1-3 percent of adults worldwide. Based on a survey of 200 physicians, there are approximately 1.6 million moderate-to-severe diagnosed and treated patients in the U.S. with uncontrolled disease. About 70 percent of people with atopic dermatitis have a family history of other common atopic diseases, such as asthma or hay fever. The intense itching, scratching and skin damage associated with the disease can sometimes lead to infections, caused by bacteria, such as *Staphylococcus aureus*. In addition, the physical manifestations of the disease can lead to anxiety, depression, and feelings of social isolation.

### **About Sanofi**

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in diabetes solutions, human vaccines, innovative drugs, consumer healthcare, emerging markets, animal health and Genzyme. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

### **About Regeneron Pharmaceuticals, Inc.**

Regeneron (NASDAQ: REGN) is a leading science-based biopharmaceutical company based in Tarrytown, New York that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron commercializes medicines for high LDL cholesterol, eye diseases, and a rare inflammatory condition and has product candidates in development in other areas of high unmet medical need, including oncology, rheumatoid arthritis, asthma, atopic dermatitis, pain, and infectious diseases. For additional information about the company, please visit [www.regeneron.com](http://www.regeneron.com) or follow @Regeneron on Twitter.

### **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, the Group's ability to benefit from external growth opportunities, trends in exchange rates and prevailing interest rates, 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, 2015. 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 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 dupilumab; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates in clinical trials, such as the clinical development programs evaluating dupilumab; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates, such as dupilumab for atopic dermatitis or other indications; 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 dupilumab; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, research and clinical programs, and business, including those relating to patient privacy; 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; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; 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 and Bayer HealthCare LLC, 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. 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, 2015. 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>).

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