# Sanofi and Regeneron Announce Positive Results from Phase 2b Study of Dupilumab in Patients with Moderate-to-Severe Atopic Dermatitis

***- Results from Earlier Clinical Trials Published Today in the New England Journal of Medicine –***

**Paris and Tarrytown, NY – July 9, 2014** - Sanofi (EURONEXT : SAN and NYSE : SNY) and Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive results from a Phase 2b dose-ranging study of dupilumab, an investigational therapy, in adult patients with moderate-to-severe atopic dermatitis (AD), a serious, chronic form of eczema. All doses of dupilumab met the primary endpoint of a greater improvement in Eczema Area and Severity Index (EASI) scores from baseline compared to placebo. In addition, the companies also announced that four earlier clinical studies of dupilumab in moderate-to-severe atopic dermatitis were published today in the New England Journal of Medicine (NEJM). Dupilumab is an investigational monoclonal antibody that blocks signaling of IL-4 and IL-13, two cytokines that play a key role in the pathogenesis of moderate-to-severe atopic dermatitis.

"*These clinical data, coupled with our mid-stage phase 2a results in asthma last year, support the growing scientific evidence that the IL4/IL-13 pathway may be a fundamental driver in allergic diseases*," said George D. Yancopoulos, M.D., Ph. D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "*Blocking IL-4/IL-13 signaling may provide an important new approach to atopic conditions, including asthma, atopic dermatitis and nasal polyposis, where we have ongoing clinical programs*."

In the Phase 2b trial, all five subcutaneous doses of dupilumab showed a dose-dependent improvement in the primary endpoint, the mean percent change in EASI score from baseline to week 16. The improvements in EASI score ranged from a high of 74 percent for patients in the highest dose group, who received 300 milligrams (mg) weekly, to a low of 45 percent in patients who received the lowest dose of 100 mg monthly, compared to 18 percent for patients in the placebo group ($p<0.0001$ for all doses).

The most common adverse event in the Phase 2b study was nasopharyngitis, which was balanced across dupilumab treatment groups (18.5 to 23 percent) compared to placebo (21 percent). Injection site reactions were more frequent in the dupilumab group (5 to 9.5 percent) compared to placebo (3 percent), as was headache (12 to 15 percent) compared to placebo (8 percent).

Dupilumab-treated patients showed highly statistically significant and dose-dependent improvements in additional key efficacy measures compared to placebo after 16 weeks of treatment:

- 12 percent to 33 percent of dupilumab-treated patients achieved clearing or near-clearing of skin lesions, as measured by an investigator's global assessment (IGA) score of 0 or 1, compared to 2 percent with placebo. ($p=0.02$ to $p<0.0001$)

- Dupilumab-treated patients experienced a 16.5 percent to 47 percent mean reduction in itching, as measured by the pruritus numerical-rating scale (NRS) score, compared to an increase of 5 percent in the placebo group. ($p=0.0005$ to $p<0.0001$)

"*Atopic dermatitis is known to have a profoundly negative effect on quality of life and people with more severe forms of this disease have limited therapeutic choices,*" said Elias Zerhouni, MD, President, Global R&D, Sanofi. "*These latest results are consistent with what was observed in the earlier clinical studies and add to the body of evidence that investigational dupilumab may have a role to play for patients with moderate-to-severe atopic dermatitis*. *We are now able to select the optimal doses for the phase 3 studies, which we anticipate to begin later this year.*"

This Phase 2b double-blind, placebo-controlled, 16-week, dose-ranging study randomized 380 patients with moderate-to-severe atopic dermatitis, who could not be adequately controlled with topical medication or for whom topical treatment was not advisable. Patients were randomized to receive one of five doses of dupilumab (300 mg weekly, 300 mg every other week, 300 mg monthly, 200 mg every other week, 100 mg monthly) or placebo. Patients in the study had approximately 50 percent of their skin affected by atopic dermatitis at baseline. Within the past year, approximately 35 percent of patients received an oral corticosteroid and approximately 20 percent received a systemic immunosuppressant for AD. Approximately 60 percent of patients had another allergic condition, including approximately 40 percent of patients who had a history of asthma. The follow-up period of the study is ongoing and patients will be followed for 16 weeks after treatment.

### The NEJM Dupilumab Moderate-to-Severe Atopic Dermatitis Publication

The New England Journal of Medicine publication includes data from four placebo-controlled studies, which all evaluated weekly subcutaneous doses of dupilumab. This included a Phase 2a 12-week monotherapy study, a Phase 2a, four-week study of dupilumab in combination with topical glucocorticoids and two Phase 1 four-week monotherapy studies. In these studies, the most common AEs were nasopharyngitis and headache, which occurred with a higher frequency in the dupilumab group. Treatment with dupilumab, either as a monotherapy or in combination, was associated with improvement in skin lesions and substantial improvements in pruritus (itching). The full publication is available at www.nejm.org.

"*The New England Journal of Medicine publication brings important attention to moderate-to-severe atopic dermatitis, a common, chronic skin condition characterized by severe itching that can have a significant negative impact on a patient's ability to lead a full and active life*," said Lisa Beck, M.D., Department of Dermatology, University of Rochester Medical Center and lead author of the NEJM paper. "*We are encouraged by the consistent findings across these earlier studies and look forward to further clinical investigation with dupilumab*."

### About the IL-4/IL-13 Pathway and Atopic Dermatitis

Moderate-to-severe atopic dermatitis, a serious, chronic form of eczema, is a systemic inflammatory disease characterized by an allergic response driven by a subset of immune cells called Type 2 helper T cells, or Th2 cells. IL-4 and IL-13 are key cytokines that are required for the initiation and maintenance of this Th2 immune response. Moderate-to-severe forms of atopic dermatitis can be characterized by pronounced cutaneous dryness, and skin lesions marked by redness, infiltration/papulation, crusting/oozing, and lichenification (skin thickening), with periods of lesion exacerbation accompanied by intense itching, scratching, and skin damage that can lead to secondary infections. Moderate-to-severe atopic dermatitis can negatively impact patients' lives and is associated with a high burden to society in terms of direct costs of medical care and prescription drugs and loss of productivity.

### About Dupilumab

Dupilumab, a fully-human monoclonal antibody, is directed against the shared IL-4R alpha subunit, which blocks signaling from both IL-4 and IL-13. Dupilumab was created using Regeneron's pioneering VelocImmune® technology and is being co-developed with Sanofi in atopic dermatitis, asthma and nasal polyposis. Dupilumab is an investigational agent under clinical development and its safety and efficacy have not been fully evaluated by any regulatory authority.

### About Sanofi

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth

platforms: diabetes solutions, human vaccines, innovative drugs, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

## About Regeneron Pharmaceuticals, Inc.

Regeneron 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 markets medicines for eye diseases, colorectal cancer, and a rare inflammatory condition and has product candidates in development in other areas of high unmet medical need, including hypercholesterolemia, oncology, rheumatoid arthritis, allergic asthma, and atopic dermatitis. For additional information about the company, please visit www.regeneron.com.

***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 policies 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, 2013. 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***

*This news release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron, 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 contemplated Phase 3 study of dupilumab in patients with moderate-to-severe atopic dermatitis; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates, including without limitation dupilumab for the treatment of atopic dermatitis; ongoing regulatory obligations and oversight impacting Regeneron's 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; 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; 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, 2013 and its Form 10-Q for the quarter ended March 31, 2014. 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.*

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