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Sanofi and Regeneron Announce Publication of Positive Phase 2a Results of Dupilumab in Asthma in the New England Journal of Medicine

Phase 2a study of the IL-4R alpha inhibitor, dupilumab, demonstrated 87% reduction in risk of asthma exacerbations in moderate-to-severe asthma patients with elevated eosinophils

PARIS and TARRYTOWN, N.Y., May 21, 2013 /PRNewswire/ -- Sanofi (EURONEXT: **SAN** and NYSE: **SNY**) and Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the *New England Journal of Medicine* published online the positive Phase 2a study results of dupilumab (SAR231893/REGN668) in patients with moderate-to-severe allergic asthma. Dupilumab is an investigational monoclonal antibody targeting the alpha subunit of the interleukin 4 receptor (IL-4R alpha), which modulates signaling of both IL-4 and IL-13, drivers of Th2 (Type 2 helper T cell) immune response. The study results will also be presented today at a late-breaking clinical trials session at the American Thoracic Society 2013 International Conference.

The proof-of-concept study enrolled 104 patients with moderate-to-severe, persistent asthma that was not well controlled with inhaled glucocorticosteroids (ICS) and long-acting beta agonist (LABA) therapy, and who had elevated blood or sputum eosinophils (immune cells used as a marker of Th2 asthma in this study).

The primary objective of the trial was to assess the effect of dupilumab, dosed subcutaneously, weekly at 300 milligrams (mg) for twelve weeks. Patients were treated with dupilumab (N=52) or placebo (N=52) on top of ICS and LABA therapy for the first four weeks of the study. The LABA was withdrawn at week four and the ICS was tapered to withdrawal between weeks six and nine. Patients were treated for 12 weeks or until they experienced a protocol-defined asthma exacerbation, the primary endpoint of the study. 23 patients (44.2%) receiving placebo experienced an asthma exacerbation compared to three patients (5.8%) receiving dupilumab, resulting in an 87% reduction in the incidence of asthma exacerbations for the dupilumab arm compared to placebo ($p < 0.0001$).

Clinically meaningful and statistically significant improvements were observed for lung function and other asthma control parameters, such as forced expiratory volume over one second (FEV_1) (difference from baseline to week 12 between dupilumab and placebo of 0.27 L, $p < 0.001$).

Treatment-emergent adverse events (AEs) were reported by a similar proportion of patients in both groups (76.9% placebo; 80.8% dupilumab). AEs were generally non-specific and of mild-to-moderate intensity. The most common AEs for placebo and dupilumab were injection-site reaction (9.6% and 28.8%), nasopharyngitis (3.8% and 13.5%), upper respiratory tract infection (17.3% and 13.5%), headache (5.8% and 11.5%) and nausea (1.9% and 7.7%).

"Despite existing therapies, a significant number of patients with moderate-to-severe, persistent allergic asthma are not optimally controlled, which puts them at risk of poor clinical outcomes. These patients contribute to the significant economic burden of asthma," said Sally Wenzel, M.D., Professor of Medicine and Director of the Asthma Institute at the University of Pittsburgh and lead investigator of this trial. "These encouraging data support the potential role of IL-4/IL-13 blockade in an important subset of asthma patients and warrant continued clinical investigation."

"Through blockade of IL-4R alpha, dupilumab modulates signaling of both the IL-4 and IL-13 pathways, which have been implicated in the pathophysiology of Th2 mediated, or allergic, diseases such as asthma," said George D. Yancopoulos, M.D., Ph. D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "These data, combined with our previously-reported positive proof-of-concept clinical results of dupilumab in atopic dermatitis, support the idea that blocking the IL-4/IL-13 pathway may be an effective mechanism to treat multiple allergic conditions. We look forward to initiating Phase 2b studies in both asthma and atopic dermatitis shortly."

These data will be presented by Dr. Sally Wenzel this morning at the American Thoracic Society 2013 International Conference in a presentation entitled, "Efficacy and safety of SAR231893/REGN668 in patients with moderate-to-severe, persistent asthma and elevated eosinophil levels."

About IL-4R and the IL-4/IL-13 Pathway

Atopic dermatitis and some types of asthma are characterized by the induction of a specific type of an immune response that is 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. IL-4 and IL-13 signaling occurs through Type I and II IL-4 receptors (IL-4 through both receptors and IL-13 through Type II receptors), which both contain a common IL-4R alpha subunit.

About Dupilumab (SAR231893/REGN668)

Dupilumab is a fully human monoclonal antibody directed against IL-4R alpha and is administered via subcutaneous injection. By blocking IL-4R alpha dupilumab modulates signaling of both IL-4 and IL-13, drivers of a Th2 immune response. Dupilumab was created using Regeneron's pioneering VelocImmune[®] technology and is being co-developed with Sanofi. Dupilumab is currently being studied in both atopic dermatitis and asthma.

About Asthma

Asthma is a chronic inflammatory disease of the airways characterized by airway sensitivity to environmental and biologic factors such as dust, chemicals, smoke, allergens, and viral infections leading to an acute and chronic narrowing of the airway and increased mucus production. Patients with asthma can experience wheezing, shortness of breath, cough and chest tightness, and in severe cases, these symptoms can be life-threatening. For most asthma patients, currently available treatments can control the disease. However, an estimated 10% to 20% of asthmatic patients are less than optimally controlled despite existing therapies. Moderate-to-severe asthma can negatively impact the lives of patients and is associated with a high burden to society both in terms of direct costs of medical care and prescription drugs, as well as loss of productivity. Moderate-to-severe asthma is recognized as a heterogeneous disease; the Th2 inflammation pathway is believed to play a role in disease pathogenesis in approximately 50% of these patients. It is estimated that approximately 25 million people in the United States are known to have asthma. The worldwide estimates are between 235-300 million people, with 180,000 deaths annually.

About Sanofi

Sanofi, an integrated 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, 2012. 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. 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; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates; 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 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, to be cancelled or terminated without any further product success; and risks associated with third party intellectual property 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, 2012 and our Form 10-Q for the quarter ended March 31, 2013. 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, unless required by law.

Contacts:

Sanofi:

Media Relations

Marisol Peron

Tel: +33 (0) 1 53 77 45 02

Mobile: +33 (0) 6 08 18 94 78

E-mail: marisol.peron@sanofi.com

Investor Relations

Sebastien Martel

Tel: +33 (0)1 53 77 45 45

E-mail: IR@sanofi.com

Regeneron:

Media Relations

Peter Dworkin

Tel: 1 (914) 847-7640

peter.dworkin@regeneron.com

Investor Relations

Manisha Narasimhan, Ph.D.

Tel: 1 (914) 847-5126

manisha.narasimhan@regeneron.com

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