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Press Release

Source: Sanofi (EURONEXT: SAN) (NYSE: SNY)

New England Journal of Medicine publishes two positive Phase 3 trials showing Dupixent® (dupilumab) improved moderate-to-severe asthma

- Results showed Dupixent demonstrated a significant improvement in multiple asthma endpoints in two Phase 3 clinical trials in a broad population of patients with uncontrolled asthma, irrespective of minimum baseline eosinophil levels or other biomarkers of Type 2 inflammation
- Greater benefit observed in patients with higher levels of markers of Type 2 inflammation, as evidenced by eosinophils or exhaled nitric oxide levels
- In steroid-sparing VENTURE trial, Dupixent-treated patients substantially reduced use of oral corticosteroids, yet had fewer exacerbations and improved lung function compared to placebo.
- In both trials, Dupixent treated patients showed significant lung function improvement two weeks after first dose that was sustained over 52 weeks

Paris and Tarrytown, NY – May 21, 2018 –The *New England Journal of Medicine* (NEJM) today published detailed results from two Phase 3 trials for the investigational use of Dupixent® (dupilumab) in moderate-to-severe asthma. The results showed that Dupixent significantly reduced the risk of severe asthma attacks (exacerbations), improved lung function and reduced dependence on oral corticosteroids (OCS). The trials, known as QUEST and VENTURE, are part of the pivotal clinical trial program that evaluated Dupixent in uncontrolled asthma patients. These data were simultaneously presented at the American Thoracic Society 2018 International Conference.

Dupixent demonstrated significant improvements in the key primary and secondary endpoints across the overall populations in both QUEST and VENTURE, with the largest benefit experienced in patients with more severe Type 2 inflammatory asthma, as evidenced by elevated blood eosinophils or exhaled nitric oxide levels. Type 2 asthma can also be characterized by other parameters, including elevated Immunoglobulin E (IgE). Dupixent blocks the IL-4/IL-13 pathway, which is emerging as a central driver of Type 2 allergic inflammation in asthma, as well as in a range of other allergic or atopic diseases.

The investigational use of Dupixent as an add-on maintenance treatment of adults and adolescents with uncontrolled moderate-to-severe asthma is currently under regulatory review in several countries, including the U.S., Japan and in the European Union (EU), and

the safety and efficacy for this use have not been evaluated by any regulatory authority. In the U.S., the target action date is October 20, 2018. Dupixent is currently approved in a number of countries for the treatment of adults with uncontrolled moderate-to-severe atopic dermatitis.

About LIBERTY ASTHMA QUEST

The Phase 3 QUEST trial showed that a broad population of adults and adolescents with moderate-to-severe asthma (no minimum blood eosinophil level requirement or other biomarker requirement at baseline) benefited when Dupixent was added to their standard therapies. Dupixent reduced severe asthma attacks and improved lung function compared to placebo. Lung function improvements were observed from the first measurement two weeks after receiving the first dose of Dupixent, and improvements were sustained throughout the 52-week trial. Patients also reported improved asthma control and quality of life, as measured by the 5-item Asthma Control Questionnaire (ACQ-5) and Asthma Quality of Life Questionnaire (AQLQ).

> *"About 20 percent of people with asthma continue to have uncontrolled moderate-to-severe symptoms despite available treatments," said Mario Castro, M.D., Alan A. and Edith L. Wolff Professor of Pulmonary and Critical Care Medicine at Washington University School of Medicine in St. Louis. "The results published today in the New England Journal of Medicine show evidence from a Phase 3 trial that a biologic may have the potential to help a broad population of patients improve multiple key asthma treatment goals when added to standard treatments. Dupixent was designed to inhibit signaling from two important proteins (IL-4 and IL-13) involved in Type 2 inflammation that contribute to uncontrolled symptoms in many people with moderate-to-severe asthma."*

The QUEST trial enrolled 1,902 patients worldwide including 1,795 adults and 107 adolescents. The four study groups included patients treated with 200 mg every other week (loading dose of 400 mg), 300 mg every other week (loading dose of 600 mg) and two separate placebo groups. All patients continued on a medium- or high-dose inhaled corticosteroid (ICS) and up to two additional controller medicines throughout the study.

The NEJM publication provides data on key endpoints, including data in the table below.

QUEST Data Summary		
Placebo-adjusted reduction in annualized rate of severe asthma exacerbations over 52 weeks		
	200 mg Dupixent (n=631) vs. Placebo (n=317)	**300 mg Dupixent (n=633) vs. Placebo (n=321)**
Overall population[1]	48 percent*	46 percent*
	200 mg Dupixent (n=264) vs. Placebo (n=148)	**300 mg Dupixent (n=277) vs. Placebo (n=142)**
Patients with 300 eosinophils/microliter or greater	66 percent[±]*	67 percent*

Placebo-adjusted absolute (percent) change in lung function (measured by $FEV_{1)}$ from baseline to week 12[2]		
	200 mg Dupixent (n=611) vs. Placebo (n=307)	**300 mg Dupixent (n=610) vs. Placebo (n=313)**
Overall population[1]	140 mL* (9 percent)	130 mL* (9 percent)
	200 mg Dupixent (n=256) vs. Placebo (n=144)	**300 mg Dupixent (n=266) vs. Placebo (n=139)**
Patients with 300 eosinophils/microliter or greater	210mL[±] (13 percent)	240mL* (18 percent)

[1] Co-primary endpoint, * p-value <0.001, [±] p-value nominal
[2] Number of patients with FEV_1 measurement at week 12

For the 52-week treatment period, the overall rate of adverse events was similar across treatment groups (81 percent in the combined Dupixent-treated group and 83 percent in the combined placebo-treated group). The rate of serious adverse events was 8 percent in the combined Dupixent-treated group and 8 percent in the combined placebo-treated group. The most frequent adverse events that occurred more frequently with Dupixent treatment vs. placebo were injection site reactions (17 percent vs. 8 percent, respectively), back pain (4 percent, both groups) and eosinophilia (4 percent vs. 1 percent, respectively).

About LIBERTY ASTHMA VENTURE

The Phase 3 VENTURE trial also did not require minimum biomarker levels for enrollment. The study showed that adults and adolescents with severe, steroid-dependent asthma who were treated with Dupixent, when added to standard therapies, could reduce their use of OCS medications while improving asthma control compared to placebo at 24 weeks. With Dupixent, OCS use decreased by 70 percent in the overall population (vs. 42 percent for placebo), and 80 percent for patients with baseline eosinophil levels 300 cells/microliter or greater (vs. 43 percent for placebo). Despite reductions in OCS, patients treated with Dupixent reduced the risk of severe asthma attacks and improved their lung function.

> *"Up to 45 percent of people with severe asthma rely on systemic corticosteroids to control their symptoms but potential long-term side-effects should be taken into account according to global asthma treatment guidelines," said Klaus Rabe, MD, Director of the Department of Pneumology at LungenClinic Grosshansdorf and Professor of Medicine at Christian Albrechts University, Kiel, Germany. "In the Phase 3 VENTURE trial, a majority of patients treated with Dupixent and standard therapies significantly reduced their use of oral steroids, and nearly half of patients completely stopped using oral steroids, while improving their asthma."*

The 24-week VENTURE study enrolled 210 patients (103 in the Dupixent group and 107 in the placebo group) with severe asthma who regularly used maintenance OCS in the six months prior to enrollment in the study. The two study groups were 300 mg Dupixent every other week (loading dose of 600 mg) and placebo. All patients continued on a high-dose ICS and up to two additional controller medicines throughout the study. The prescribed OCS in the study was prednisone or prednisolone.

The NEJM publication provides data on key endpoints, including data in the tables below.

VENTURE Data Summary		
Reduction in OCS dose at 24 weeks		
	300 mg Dupixent (n=103)	**Placebo (n=107)**
Overall population[1]	70 percent*	42 percent
	300 mg Dupixent (n=48)	**Placebo (n=41)**
Patients with 300 eosinophils/microliter or greater	80 percent*	43 percent
Proportion of patients with 50 percent or greater reduction in OCS		
Overall population	80 percent*	50 percent
Proportion of patients who reduced their OCS dose to less than 5 mg per day		
Overall population	69 percent*	33 percent

[1] Primary endpoint, * p-value vs. placebo <0.001

VENTURE Data Summary, Continued		
	Difference between 300 mg DUPIXENT (n=103) vs. Placebo (n=107) (Overall population)	**Difference between 300 mg DUPIXENT (n=48) vs. Placebo (n=41)** (Patients with 300 eosinophils/ microliter or greater)
Change in annualized rate of severe asthma exacerbations over 24 weeks	59 percent reduction*	71 percent reduction[±]
Absolute (percent) change in FEV_1 from baseline to 24 weeks	220 mL (15 percent***) improvement*	320 mL (25 percent***) improvement[±]

* Nominal p-value vs. placebo < 0.001
[±]Nominal p-value vs. placebo < 0.005
*** Data not included in NEJM publication

For the 24-week treatment period, the overall rate of adverse events was similar across treatment groups (62 percent in the Dupixent-treated group and 64.5 percent in the placebo-treated group). The rate of serious adverse events was 9 percent in the Dupixent-treated group and 6 percent in the placebo-treated group. The most frequent adverse events that occurred more frequently with Dupixent treatment vs. placebo were injection site reaction (9 percent vs. 4 percent, respectively), bronchitis (7 percent vs. 6 percent, respectively), sinusitis (7 percent vs. 4 percent, respectively) and eosinophilia (14 percent vs. 1 percent, respectively).

Dupilumab Development Program

Sanofi and Regeneron are also studying dupilumab in a broad range of clinical development programs for diseases driven by Type 2 inflammation, including pediatric atopic dermatitis (Phase 3), nasal polyps (Phase 3) and eosinophilic esophagitis (Phase 2). Future trials are planned for chronic obstructive pulmonary disease, grass allergy and food allergy (including peanut). These potential uses are investigational and the safety and efficacy have not been evaluated by any regulatory authority. Dupilumab is being jointly developed by Sanofi and Regeneron under a global collaboration agreement.

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

About Dupixent® (dupilumab)

Dupixent is currently approved 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 also approved for use in certain patients with moderate-to-severe atopic dermatitis in the EU and a number of other countries, including Canada, and Japan.

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. Dupixent is administered by subcutaneous injection at different injection sites every two weeks after an initial loading dose. Dupixent is intended for use under the guidance of a healthcare provider. A patient may self-inject Dupixent after training in subcutaneous injection technique using the pre-filled syringe.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

Sanofi, Empowering Life

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 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to six FDA-approved treatments and numerous 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 our proprietary *VelociSuite*® technologies, such as *VelocImmune*® which produces optimized fully-human antibodies, and ambitious research initiatives such as the Regeneron Genetics Center, which is conducting 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.

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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, 2017. 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 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 dupilumab for the treatment of inadequately controlled moderate-to-severe asthma (including possible regulatory approval of dupilumab in the United States, Japan and the European Union referenced in this news release), pediatric atopic dermatitis, nasal polyps, eosinophilic esophagitis, chronic obstructive pulmonary disease, food allergy, and 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 dupilumab; serious complications or side effects in connection with the use of Regeneron's products and product candidates (such as dupilumab) 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 proceedings relating to Praluent® (alirocumab) Injection, the ultimate outcome of any such litigation proceedings, 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, 2017 and its Form 10-Q for the quarterly period ended March 31, 2018. 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).