

## Press Release

### *Dupixent® late-breaking data from NOTUS confirmatory phase 3 COPD study presented at ATS and published in NEJM*

- \* *NOTUS results confirm landmark data from the phase 3 BOREAS study and show Dupixent significantly reduced exacerbations by 34% and improved lung function, compared to placebo, in uncontrolled chronic obstructive pulmonary disease (COPD) with evidence of type 2 inflammation*
- \* *Data support the potential of Dupixent as the first new treatment approach in more than a decade and first-ever targeted therapy for COPD*

**Paris and Tarrytown, N.Y. May 20, 2024.** Late-breaking data were presented from the NOTUS phase 3 study evaluating the investigational use of Dupixent® (dupilumab) as an add-on maintenance treatment in adults with uncontrolled COPD on maximal standard-of-care inhaled therapy (nearly all on triple therapy) and evidence of type 2 inflammation (i.e., blood eosinophils  $\geq 300$  cells per  $\mu\text{L}$ ). The NOTUS study confirmed the positive results demonstrated in the landmark phase 3 BOREAS study, with its data presented at a late-breaking session of the 2024 American Thoracic Society (ATS) International Conference and simultaneously published in the [New England Journal of Medicine \(NEJM\)](#).

#### ***Surya Bhatt, M.D., MSPH***

Professor at the University of Alabama at Birmingham, Division of Pulmonary, Allergy, and Critical Care Medicine, and a co-principal investigator of the study

*“In my more than 20 years of practice, there have been limited advancements for patients struggling with the debilitating effects of uncontrolled COPD, and too many patients experience a vicious cycle of exacerbations that can result in loss of lung function and greatly diminish their quality of life. In NOTUS, dupilumab reduced exacerbations by a magnitude never seen before with an investigational biologic in a phase 3 COPD clinical study. These comprehensive results reinforce that, if approved, dupilumab could provide a first-of-its-kind medical advancement for the COPD community.”*

As presented and published, the NOTUS study met its primary and key secondary endpoints. All patients were on background maximal standard-of-care inhaled therapy (nearly all on triple therapy). Patients receiving Dupixent (n=470) experienced the following, compared to placebo (n=465):

- **34% reduction in moderate or severe COPD exacerbations** over 52 weeks ( $p < 0.001$ ), the primary endpoint.
- **More than two times greater improvement in lung function** (pre-bronchodilator FEV<sub>1</sub>) from baseline at 12 weeks (139 mL vs. 57 mL;  $p < 0.001$ ), with an improvement maintained at week 52 (115 mL vs. 54 mL;  $p = 0.018$ ), secondary endpoints.

- **Numerically greater improvements in health-related quality of life** from baseline at 52 weeks, a secondary endpoint, as defined by patient-reported outcomes (PRO) in the St. George's Respiratory Questionnaire (SGRQ).
- **Numerically greater reductions in respiratory symptom severity** from baseline to 52 weeks, a secondary endpoint, as defined by PROs in Evaluating Respiratory Symptoms in COPD (E-RS).

The safety results were generally consistent with the known safety profile of Dupixent in its approved indications. Overall rates of adverse events (AEs) were 67% for Dupixent and 66% for placebo. AEs more commonly observed with Dupixent than placebo included COVID-19 (9.4% Dupixent, 8.2% placebo), nasopharyngitis (6.2% Dupixent, 5.2% placebo), and headache (7.5% Dupixent, 6.5% placebo). AEs more commonly observed with placebo than Dupixent included COPD (7.8% placebo, 4.9% Dupixent). AEs leading to deaths were 2.6% for Dupixent and 1.5% for placebo.

Dupixent is currently under Priority Review by the US Food and Drug Administration as an add-on maintenance treatment in certain adult patients with uncontrolled COPD with evidence of type 2 inflammation. The target action date is June 27, 2024. Regulatory submissions are also under review in the European Union and China, and discussions with other regulatory authorities around the world are ongoing.

The potential use of Dupixent in COPD is currently under clinical development, and its safety and efficacy have not been fully evaluated by any regulatory authority in this setting.

### **About COPD**

COPD is a respiratory disease that damages the lungs and causes progressive lung function decline. Symptoms include persistent cough, breathlessness and excessive mucus production that may impair the ability to perform routine daily activities, which may lead to anxiety, depression and sleep disturbances. COPD is also associated with a significant health and economic burden due to recurrent acute exacerbations that require systemic corticosteroid treatment and/or lead to hospitalization. Smoking and exposure to noxious particles are key risk factors for COPD, but even individuals who quit smoking can still develop or continue having the disease. There have been no new treatment approaches approved for more than a decade. In the US, approximately 300,000 people live with uncontrolled COPD with evidence of type 2 inflammation.

### **About the Dupixent COPD phase 3 study program**

BOREAS and NOTUS are replicate, randomized, phase 3, double-blind, placebo-controlled studies that evaluated the efficacy and safety of Dupixent in adults who were current or former smokers with moderate-to-severe COPD. Patients were aged 40 to 80 years in BOREAS and 40 to 85 years in NOTUS. All 1,874 patients enrolled in BOREAS and NOTUS had evidence of type 2 inflammation, as measured by blood eosinophils  $\geq 300$  cells per  $\mu\text{L}$ . Patients with a diagnosis or history of asthma were excluded from the studies.

During the 52-week treatment period, patients in BOREAS and NOTUS received Dupixent or placebo every two weeks added to a maximal standard-of-care inhaled triple therapy of inhaled corticosteroids (ICS), long-acting beta agonists (LABA), and long-acting muscarinic antagonists (LAMA). Double maintenance therapy, which included LABA and LAMA, was allowed if ICS was contraindicated.

The primary endpoint for BOREAS and NOTUS evaluated the annualized rate of acute moderate or severe COPD exacerbations. Moderate exacerbations were defined as those

requiring systemic steroids and/or antibiotics. Severe exacerbations were defined as those requiring hospitalization; requiring more than a day of observation in an emergency department or urgent care facility; or resulting in death. Key secondary endpoints included change from baseline in lung function (assessed by pre-bronchodilator forced expiratory volume [FEV1]) at 12 and 52 weeks, change from baseline at 52 weeks in SGRQ total score compared to placebo, and safety.

Data from BOREAS were also [published](#) in the *New England Journal of Medicine*.

### **About Sanofi and Regeneron's COPD Clinical Research Program**

Sanofi and Regeneron are motivated to transform the treatment paradigm of COPD by examining the role different types of inflammation play in the disease progression through the investigation of two potentially first-in-class biologics, Dupixent and itepekimab.

Dupixent inhibits the signaling of the interleukin-4 (IL-4) and interleukin-13 (IL-13) pathways and the program focuses on a specific population of people with evidence of type 2 inflammation. Itepekimab is a fully human monoclonal antibody that binds to and inhibits interleukin-33 (IL-33), an initiator and amplifier of broad inflammation in COPD.

Itepekimab is currently under clinical investigation, with two phase 3 studies currently enrolling, and its safety and efficacy have not been evaluated by any regulatory authority.

### **About Dupixent**

Dupixent is a fully human monoclonal antibody that inhibits the signaling of the interleukin-4 (IL-4) and interleukin-13 (IL-13) pathways and is not an immunosuppressant. The Dupixent development program has shown significant clinical benefit and a decrease in type 2 inflammation in phase 3 studies, establishing that IL-4 and IL-13 are two of the key and central drivers of the type 2 inflammation that plays a major role in multiple related and often co-morbid diseases.

Dupixent has received regulatory approvals in more than 60 countries in one or more indications including certain patients with atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyposis (CRSwNP), eosinophilic esophagitis (EoE), prurigo nodularis and chronic spontaneous urticaria (CSU) in different age populations. More than 850,000 patients are being treated with Dupixent globally.

### **Dupilumab Development Program**

Dupilumab is being jointly developed by Sanofi and Regeneron under a global collaboration agreement. To date, dupilumab has been studied across more than 60 clinical studies involving more than 10,000 patients with various chronic diseases driven in part by type 2 inflammation.

In addition to the currently approved indications, Sanofi and Regeneron are studying dupilumab in a broad range of diseases driven by type 2 inflammation or other allergic processes in phase 3 studies, including chronic spontaneous urticaria, chronic pruritus of unknown origin, chronic obstructive pulmonary disease with evidence of type 2 inflammation and bullous pemphigoid. These potential uses of dupilumab are currently under clinical investigation, and the safety and efficacy in these conditions have not been fully evaluated by any regulatory authority.

### **About Regeneron**

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents, develops and

commercializes life-transforming medicines for people with serious diseases. Founded and led by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to numerous approved treatments and product candidates in development, most of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, neurological diseases, hematologic conditions, infectious diseases, and rare diseases.

Regeneron pushes the boundaries of scientific discovery and accelerates drug development using our proprietary technologies, such as *VelociSuite*<sup>®</sup>, which produces optimized fully human antibodies and new classes of bispecific antibodies. We are shaping the next frontier of medicine with data-powered insights from the Regeneron Genetics Center<sup>®</sup> and pioneering genetic medicine platforms, enabling us to identify innovative targets and complementary approaches to potentially treat or cure diseases.

For more information, please visit [www.Regeneron.com](http://www.Regeneron.com) or follow Regeneron on [LinkedIn](#), [Instagram](#), [Facebook](#) or [X](#).

### *About Sanofi*

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across the world, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Sanofi is listed on Euronext: SAN and NASDAQ: SNY

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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 fact that product may not 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 and market conditions, and the impact that pandemics or other global crises may have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. The risks and uncertainties also include the uncertainties 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, 2023. 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 press 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 products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products") and product candidates being developed by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation Dupixent<sup>®</sup> (dupilumab) and itepekimab; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products, such as Dupixent for the treatment of uncontrolled chronic obstructive pulmonary disease with evidence of type 2 inflammation as discussed in this press release (including the impact of the previously disclosed request by the U.S. Food and Drug Administration to provide additional analyses regarding sub-populations from the BOREAS and NOTUS pivotal studies) as well as for the treatment of chronic spontaneous urticaria, chronic pruritus of unknown origin, bullous pemphigoid, and other potential indications; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary), including the studies discussed or referenced in this press release, on any of the foregoing or any potential regulatory approval of Regeneron's Products (such as Dupixent) and Regeneron's Product Candidates (such as itepekimab); the ability of Regeneron's collaborators, licensees, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and Regeneron's Product Candidates; the ability of Regeneron to manage supply chains for multiple products and product candidates; safety issues resulting from the administration of Regeneron's Products (such as Dupixent) and Regeneron's Product Candidates (such as itepekimab) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's Product Candidates in clinical trials; 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 Regeneron's Product Candidates; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license, collaboration, or supply agreement, including Regeneron's agreements with Sanofi and Bayer (or their respective affiliated companies, as applicable) to be cancelled or terminated; the impact of public health outbreaks, epidemics, or pandemics (such as the COVID-19 pandemic) on Regeneron's business; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA<sup>®</sup> (afibercept) Injection), other litigation and other proceedings and government investigations relating to the Company and/or its operations (including the pending civil proceedings initiated or joined by the U.S. Department of Justice and the U.S. Attorney's Office for the District of Massachusetts), the ultimate outcome of any such proceedings and investigations, 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 U.S. Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2023 and its Form 10-Q for the quarterly period ended March 31, 2024. 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 or otherwise) 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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