

Dupixent® significantly reduced COPD exacerbations in second positive Phase 3 trial, accelerating FDA submission and confirming potential to become first approved biologic for this serious disease



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Dupixent® significantly reduced COPD exacerbations in second positive Phase 3 trial, accelerating FDA submission and confirming potential to become first approved biologic for this serious disease

- NOTUS trial met its primary endpoint with overwhelming efficacy, showing Dupixent significantly reduced exacerbations by 34% compared to placebo in patients with moderate-to-severe COPD with evidence of type 2 inflammation (ie, blood eosinophils ≥ 300 cells per μL), confirming results from the landmark BOREAS pivotal trial
- Dupixent rapidly and significantly improved lung function (139 mL in FEV1) compared to placebo (57 mL in FEV1) at 12 weeks
- Supplemental BLA submission planned by end of 2023
- Approximately 300,000 people in the U.S. alone live with uncontrolled COPD with evidence of type 2 inflammation; no new treatment approaches approved for more than a decade

Paris and Tarrytown, N.Y. November 27, 2023. The second Dupixent® (dupilumab) investigational Phase 3 chronic obstructive pulmonary disease (COPD) trial (NOTUS) has shown that Dupixent significantly reduced (34%) exacerbations, confirming positive published results from the landmark Phase 3 BOREAS trial. The NOTUS trial also confirmed that treatment with Dupixent led to rapid and significant

improvements in lung function by 12 weeks and were sustained at 52 weeks. The NOTUS trial evaluated the investigational use of Dupixent compared to placebo in adults currently on maximal standard-of-care inhaled therapy (triple therapy) with uncontrolled COPD and evidence of type 2 inflammation (i.e., blood eosinophils ≥ 300 cells per μL). These results were from an interim analysis and, given the overwhelming positive efficacy of the primary endpoint, will be considered the primary analysis of the trial. Sanofi and Regeneron plan to submit the data from this replicate trial, along with positive results from the Phase 3 BOREAS trial, to the U.S. Food and Drug Administration (FDA) by the end of the year.

Head of Global Development, Immunology and Inflammation at Sanofi

This is the first and only time an investigational biologic in COPD has shown a significant and clinically meaningful reduction in exacerbations in two Phase 3 trials and we are pleased that we can potentially deliver Dupixent faster to patients in need where no new advancements have been identified in over a decade. These data validate our belief that Dupixent has the potential to transform the treatment of moderate-to-severe COPD and given the significant unmet needs for patients with uncontrolled COPD, we are not stopping with Dupixent. Our second program in COPD, itepekimab, continues with data expected in 2025. If positive, Dupixent and itepekimab could emerge as treatments for approximately 80% of those suffering from moderate-to-severe COPD with recurrent exacerbations.

Earlier this year, the FDA granted Breakthrough Therapy designation for Dupixent as an add-on maintenance treatment in adult patients with uncontrolled COPD associated with a history of exacerbations and an eosinophilic phenotype based on the positive results from BOREAS.

George D. Yancopoulos, M.D., Ph.D.

Board Co-Chair, President and Chief Scientific Officer at Regeneron

We are highly encouraged by these remarkable results from NOTUS showing a 34% reduction in COPD exacerbations compared to placebo, confirming the unprecedented results from our first Phase 3 trial, BOREAS. These results

demonstrate the important role of type 2 inflammation in yet another chronic and debilitating disease, and the ability of Dupixent to address this inflammation. We are working to submit these data rapidly to the FDA.

The NOTUS trial included 935 adults who were current or former smokers aged 40 to 85 years and randomized to receive Dupixent (n=470) or placebo (n=465), which was added to maximal standard-of-care inhaled therapy. Patients receiving Dupixent compared to placebo experienced:

- 34% reduction in moderate or severe acute COPD exacerbations over 52 weeks ($p=0.0002$), the primary endpoint.
- Improved lung function from baseline by 139 mL at 12 weeks compared to 57 mL for placebo ($p=0.0001$), with the benefit versus placebo sustained at week 52 (115 mL for Dupixent versus 54 mL for placebo, $p=0.0182$), both of which were key secondary endpoints.

The safety results were generally consistent with the known safety profile of Dupixent in its approved indications. Overall rates of adverse events (AE) were 67% for Dupixent and 66% for placebo. AEs more commonly observed with Dupixent ($\geq 5\%$ and $\geq 1\%$ imbalance) compared to 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 compared to Dupixent included COPD (7.8% placebo, 4.9% Dupixent). AEs leading to deaths were 2.6% for Dupixent and 1.5% for placebo.

Detailed results from the NOTUS trial are planned for presentation at a future scientific forum.

The efficacy results in NOTUS were consistent with the previously announced results in BOREAS. BOREAS results showed:

- 30% reduction in moderate or severe acute COPD exacerbations over 52 weeks ($p=0.0005$), the primary endpoint.
- Improved lung function from baseline by 160 mL at 12 weeks compared to 77 mL for placebo (p

The safety results in NOTUS were also consistent with those

previously announced in BOREAS. Overall rates of AEs in BOREAS were 77% for Dupixent and 76% for placebo. AEs more commonly observed with Dupixent compared to placebo included headache (8.1% Dupixent, 6.8% placebo), diarrhea (5.3% Dupixent, 3.6% placebo) and back pain (5.1% Dupixent, 3.4% placebo). AEs more commonly observed with placebo compared to Dupixent included upper respiratory tract infection (9.8% placebo, 7.9% Dupixent), hypertension (6.0% placebo, 3.6% Dupixent) and COVID-19 (5.7% placebo, 4.1% Dupixent). AEs leading to deaths were 1.5% for Dupixent and 1.7% for placebo.

The European Medicines Agency is reviewing Sanofi and Regeneron's application for Dupixent for the treatment of uncontrolled COPD with type 2 inflammation; this application is based on results from the BOREAS trial. Discussions with other regulatory authorities around the world are ongoing.

The safety and efficacy of Dupixent in COPD are currently under clinical investigation and have not been evaluated by any regulatory authority.

COPD is the third leading cause of death worldwide and a life-threatening respiratory disease that damages the lungs and causes progressive lung function decline. Symptoms include persistent cough, breathlessness and excessive mucus production that may not only impair the ability to perform routine daily activities, but can also 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 or even death. 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. In the U.S. alone, approximately 300,000 people live with uncontrolled COPD with evidence of type 2 inflammation.

About the Dupixent COPD Phase 3 Trial Program

NOTUS and BOREAS are replicate, randomized, Phase 3, double-blind, placebo-controlled trials that evaluated the efficacy and safety of Dupixent in adults who were current or former smokers with moderate-to-severe COPD aged 40 to 85 years in NOTUS and 40 to 80 years in BOREAS. Enrolling a total of 1,874 patients, all patients in NOTUS and BOREAS had evidence of type 2 inflammation, as

measured by blood eosinophils ≥ 300 cells per μL . Patients with a diagnosis or history of asthma were excluded from the trials.

During the 52-week treatment period, patients in NOTUS and BOREAS 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 NOTUS and BOREAS 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.

Data from BOREAS were 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. Across both programs, four Phase 3 trials are ongoing and designed to inform next-generation treatments for people with COPD who might not have other options.

Itepekimab is currently under clinical investigation and its safety and efficacy have not been evaluated by any regulatory authority.

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 trials, establishing that IL-4 and IL-13 are key and central drivers of the type 2 inflammation that plays a major role in multiple related and often co-morbid diseases. These diseases include approved indications for Dupixent, such as atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), eosinophilic esophagitis (EoE) and prurigo nodularis.

Dupixent has received regulatory approvals in one or more countries around the world for use in certain patients with atopic dermatitis, asthma, CRSwNP, EoE or prurigo nodularis in different age populations. Dupixent is currently approved for one or more of these indications in more than 60 countries, including in Europe, the U.S. and Japan. Approximately 750,000 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 trials 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 trials, including pediatric EoE, 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.

Regeneron is a leading biotechnology company that invents, develops, and commercializes life-transforming medicines for people with serious diseases. Founded and led for 35 years by physician-scientists, Regeneron's unique ability to repeatedly and consistently translate science into medicine has led to numerous FDA-approved

treatments and product candidates in development, almost all of which were homegrown in Regeneron's laboratories. Regeneron's medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, hematologic conditions, infectious diseases, and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its proprietary VelociSuite® technologies, such as VelocImmune®, which uses unique genetically humanized mice to produce optimized fully human antibodies and bispecific antibodies, and through 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 Regeneron, please visit www.regeneron.com or follow Regeneron on

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 some 100 countries, 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 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 fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi’s ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with

intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, 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, 2022. 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® (dupilumab) and itepekimab; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron’s Product Candidates (such as itepekimab for the treatment of chronic obstructive pulmonary disease

(“COPD

)) and new indications for Regeneron’s Products (such as Dupixent for the treatment of COPD with evidence of type 2 inflammation as well as for the treatment of pediatric eosinophilic esophagitis, 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® (aflibercept) Injection and REGEN-COV® (casirivimab and imdevimab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, 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, 2022 and its Form 10-Q for the quarterly period ended September 30, 2023. 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.

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 (<https://investor.regeneron.com>) and its LinkedIn page (<https://www.linkedin.com/company/regeneron-pharmaceuticals>).

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