

Dupixent® (dupilumab) Phase 3 trial shows positive results in children 1 to 11 years of age with eosinophilic esophagitis

- * First and only investigational Phase 3 trial to show positive results in these young children; results follow recent approval of Dupixent in people with eosinophilic esophagitis aged 12 years and older who weigh at least 40 kilograms
- * Trial met its primary endpoint, with 68% of patients on higher dose Dupixent and 58% on lower dose Dupixent achieving histological disease remission at 16 weeks
- * Of the approximately 21,000 children under the age of 12 in the U.S. currently being treated for EoE, about 9,000 do not satisfactorily respond to the unapproved therapies they have been treated with
- * Fifth pediatric pivotal trial across three type 2 inflammatory diseases to reinforce the well-established efficacy and safety profile of Dupixent

Paris and Tarrytown, N.Y. July 14, 2022 A Phase 3 trial assessing the investigational use of Dupixent® (dupilumab) in children aged 1 to 11 years with eosinophilic esophagitis (EoE) met its primary endpoint of histological disease remission at 16 weeks with both higher and lower dose weight-tiered regimens. There are no approved treatments for children with EoE under 12 years of age.

Naimish Patel, M.D.

Senior Vice President, Head of Global Development, Immunology and Inflammation, Sanofi

“We are incredibly excited to share results from this Phase 3 pivotal trial evaluating Dupixent in young children suffering from eosinophilic esophagitis – the first ever to show positive results across a variety of primary and secondary endpoints. The lack of treatment options for children living with eosinophilic esophagitis leaves many caregivers with the stress and burden of adapting their child’s meals and their entire family’s daily schedules to ensure healthy growth and development. In some cases, they must resort to off-label use of poorly studied treatments like steroids that can pose serious health risks when used long term. The faster and larger than anticipated enrollment in this trial further emphasizes the unmet treatment needs for children with EoE and underscores the significance of these first-ever positive results.”

EoE is a chronic inflammatory disease that damages the esophagus and prevents it from working properly. The results seen with Dupixent in adults and children with EoE demonstrate that IL-4 and IL-13 are key drivers of the type 2 inflammation underlying this disease. In children, common symptoms of eosinophilic esophagitis include acid reflux, vomiting, abdominal discomfort, trouble swallowing, and a failure to thrive. These symptoms can impact growth and development, and can cause food-related fear and anxiety which can persist through adulthood. Diet adjustments, which oftentimes include the elimination of many foods, is the standard treatment for EoE, as well as the use of treatments not approved for the disease. These include proton pump inhibitors, swallowed topical corticosteroids, or in severe cases, a feeding tube, which may be used to ensure proper caloric intake and weight gain. Of the approximately 21,000 children under the age of 12 in the U.S. currently being treated for EoE, about 9,000 do not satisfactorily respond to the unapproved therapies they have been treated with and potentially require advanced therapy.

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

President and Chief Scientific Officer, Regeneron

“Dupixent is the first medicine to alleviate key signs of eosinophilic esophagitis in children as young as 1 year of age in a Phase 3 trial. The efficacy of Dupixent demonstrates that, in this age group, as in adults, IL-4 and IL-13 are key drivers of the type 2 inflammation underlying this

debilitating disease. Eosinophilic esophagitis can turn the basic and life-sustaining act of eating into a painful experience at a point in children's lives when proper nutrition and achieving a healthy weight is critical to ensuring they grow and thrive. The positive results from this Phase 3 pediatric trial show Dupixent has the potential to improve signs of eosinophilic esophagitis and support healthy weight gain in children from their first birthday."

In the Phase 3 trial, 102 children aged 1 to 11 were randomized to receive Dupixent, in either a higher dose (n=37) or lower dose (n=31) regimen based on body weight, or placebo (n=34). At 16 weeks, 68% of children on higher dose and 58% of patients on lower dose Dupixent achieved the primary endpoint of significant histological disease remission (peak esophageal intraepithelial eosinophil count of ≤ 6 eosinophils [eos]/high power field [hpf]) compared to 3% of children on placebo ($p < 0.0001$ for both). Additionally, children receiving higher dose Dupixent experienced the following changes at week 16:

- 86% reduction in peak esophageal intraepithelial eosinophil count from baseline compared to a 21% increase for placebo ($p < 0.0001$).
- 0.88 and 0.84 reduction from baseline in disease severity and extent, respectively, as measured at the microscopic level in biopsy specimens compared to a 0.02 and 0.05 increase for placebo (both $p < 0.0001$).
- 3.5-point reduction in abnormal endoscopic findings from baseline compared to a 0.3-point increase for placebo ($p < 0.0001$).
- A numerical improvement in the proportion of days children experienced symptoms of EoE from baseline, as reported by caregivers (Pediatric EOE signs/symptoms questionnaire [PESQ-C]), compared to placebo, though not statistically significant. The PESQ-C is a novel endpoint developed by Sanofi and Regeneron used for the first time in this trial, designed to assess symptoms in young children through their caregivers (as signs), as children may have difficulty verbalizing their symptoms themselves.
- As part of a prespecified exploratory analysis a 3.09 percentile increase in body weight for age percentile from baseline compared to 0.29 for placebo.

Histological, anatomic and cellular secondary endpoints were also analyzed for the lower dose group, with all being nominally significant and generally comparable with the higher dose. More detailed results will be shared at an upcoming medical meeting, including additional data for the endpoints in the lower dose group.

Safety results were generally consistent with the known safety profile of Dupixent in its approved EoE indication for children and adults aged 12 years and older who weigh at least 40 kg. For the 16-week treatment period, overall rates of adverse events (AEs) were 79% for Dupixent and 91% for placebo. AEs more commonly ($\geq 5\%$) observed with Dupixent compared to placebo included COVID-19 (21% Dupixent, 0% placebo; all cases were mild or moderate and did not lead to study discontinuation), rash (9% Dupixent, 6% placebo), headache (8% Dupixent, 3% placebo), viral gastroenteritis (6% Dupixent, 3% placebo), diarrhea (6% Dupixent, 3% placebo) and nausea (6% Dupixent, 0% placebo). Rates of treatment discontinuation due to AEs prior to week 16 were 0% for Dupixent and 6% for placebo.

In May 2022, the U.S. Food and Drug Administration (FDA) [approved](#) Dupixent 300 mg weekly to treat patients with EoE aged 12 years and older and weighing at least 40 kg after granting the medicine Priority Review.

The potential use of Dupixent in children with EoE aged 1 to 11 years is currently under clinical development, and the safety and efficacy have not been fully evaluated by any regulatory authority. These data will be discussed with regulatory authorities around the world, starting with the U.S. later this year.

About the Dupixent Pediatric Eosinophilic Esophagitis Trial

The Phase 3, randomized, double-blind, placebo-controlled trial evaluated the efficacy and safety of Dupixent in young children aged 1 to 11 years with EoE, as determined by histological and patient- or caregiver-reported measures. At baseline, 98% of these patients had at least one co-

existing type 2 inflammatory disease such as food allergy, allergic rhinitis, asthma and atopic dermatitis.

Patients received Dupixent subcutaneously at either a higher dose or lower dose regimen based on their weight (ranging from ≥ 5 kg to < 60 kg) over a 16-week period, at which point all endpoints were assessed. The dosing frequency ranged between every two weeks and every four weeks, based on weight.

The primary endpoint was histological disease remission. Secondary endpoints included histopathologic measures of the severity and extent of tissue scarring in the esophagus (EoE-HSS grade and stage scores, which measure changes in eight cellular and tissue features on 0-3 scales, respectively), and abnormal endoscopic findings (EoE Endoscopic Reference Score [EoE-EREFS] on a 0-18 scale), as well as changes in caregiver-reported symptoms (proportion of days with 1 or more EoE signs [e.g. stomach pain, vomiting, food refusal] by the Pediatric EoE Sign/Symptom Questionnaire-caregiver version [PESQ-C]). An exploratory endpoint assessed change from baseline in body weight for age percentile.

The trial is ongoing with a 36-week extended active treatment period to evaluate long-term outcomes.

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 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 asthma, atopic dermatitis, chronic rhinosinusitis with nasal polyposis (CRSwNP) and EoE, as well as investigational diseases such as prurigo nodularis.

Dupixent has received regulatory approvals around the world for use in certain patients with atopic dermatitis, asthma, CRSwNP or EoE in different age populations. Dupixent is currently approved across these indications in the U.S. and for one or more of these indications in more than 60 countries, including in the European Union and Japan. More than 400,000 patients have been 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 prurigo nodularis, pediatric EoE, hand and foot atopic dermatitis, chronic inducible urticaria-cold, chronic spontaneous urticaria, chronic pruritis of unknown origin, chronic obstructive pulmonary disease with evidence of type 2 inflammation, chronic rhinosinusitis without nasal polyposis, allergic fungal rhinosinusitis, allergic bronchopulmonary aspergillosis 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 is a leading biotechnology company that invents, develops and commercializes life-transforming medicines for people with serious diseases. Founded and led for nearly 35 years by physician-scientists, our 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 our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, hematologic conditions, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our 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 more information, please visit www.Regeneron.com or follow @Regeneron on Twitter.

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 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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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

impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of 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); 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 children aged 1 to 11 years with eosinophilic esophagitis as discussed in this press release as well as for the treatment of prurigo nodularis, hand and foot atopic dermatitis, chronic inducible urticaria-cold, chronic spontaneous urticaria, chronic pruritis of unknown origin, chronic obstructive pulmonary disease with evidence of type 2 inflammation, chronic rhinosinusitis without nasal polyposis, allergic fungal rhinosinusitis, allergic bronchopulmonary aspergillosis, 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 study discussed in this press release, on any of the foregoing or any potential regulatory approval of Regeneron's Products and Regeneron's Product Candidates (such as Dupixent); 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 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, including without limitation Dupixent; 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, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable) to be cancelled or terminated; 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® (afibercept) Injection, Dupixent, Praluent® (alirocumab), 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, 2021 and its Form 10-Q for the quarterly period ended March 31, 2022. 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