Media Update

ERS: Dupixent data reinforce clinically meaningful benefit from pooled analysis of two COPD phase 3 studies

- Pooled results from the BOREAS and NOTUS studies show meaningful clinical benefit with 31% reduction in exacerbations along with lung function improvement
- Data from these two phase 3 studies supported Dupixent as the first-ever biologic approved for certain patients with uncontrolled COPD in the EU

Paris, September 10, 2024. A pooled analysis from the BOREAS and NOTUS phase 3 studies showed that Dupixent reduced exacerbations and improved lung function compared to placebo in adults with uncontrolled chronic obstructive pulmonary disease (COPD) and evidence of type 2 inflammation (i.e., raised blood eosinophils). The results were presented today, in collaboration with Regeneron, for the first time at the 2024 European Respiratory Society (ERS) International Congress.

The European Medicines Agency was the first regulatory authority in the world to approve Dupixent as an add-on maintenance treatment for adults with uncontrolled COPD characterized by raised blood eosinophils. Specifically, the approval covers patients already on a combination of an inhaled corticosteroid (ICS), a long-acting beta2-agonist (LABA) and a long-acting muscarinic antagonist (LAMA), or on a combination of a LABA and a LAMA if ICS is not appropriate. Dupixent has also been approved by ANVISA (the Brazilian health regulatory agency) and the Russian Ministry of Health for certain adults with uncontrolled COPD associated with type 2 inflammation. Regulatory submissions are under review with other authorities around the world, including in the US, China, and Japan.

> ***Surya Bhatt, M.D., MSPH***
> Professor at the University of Alabama at Birmingham, US, Division of Pulmonary, Allergy, and Critical Care Medicine, and a co-principal investigator of the study
> *"For far too long, I have watched patients with uncontrolled COPD struggle with a relentless cycle of exacerbations that diminish lung function, with no new treatment approaches to help alleviate this downward spiral. The pooled analysis of the pivotal BOREAS and NOTUS phase 3 studies provide more comprehensive examination of the unprecedented efficacy and safety data, which reinforce the benefit of dupilumab for patients on maximal inhaled therapy and limited additional options."*

As presented, this pooled analysis reinforces previous positive results from the BOREAS and NOTUS phase 3 studies. All patients were on background maximal standard-of-care inhaled therapy (with nearly all on triple therapy). Dupixent patients (n=938) achieved the following compared to placebo (n=936):

- 31% reduction in the annualized rate of moderate or severe COPD exacerbations over 52 weeks (nominal $p<0.0001$).
- Improvement in lung function (pre-bronchodilator FEV_1) from baseline by 147 mL compared to 64 mL at 12 weeks (nominal $p<0.0001$). These improvements were observed as early as two weeks and sustained at 52 weeks (nominal $p<0.0001$).

Safety results in this pooled analysis were generally consistent with the known safety profile of Dupixent in its approved indications. Overall rates of adverse events (AEs) were 72% for Dupixent and 71% for placebo. AEs more commonly observed with Dupixent than placebo included nasopharyngitis (7.8% Dupixent, 7.4% placebo) and headache (7.8% Dupixent, 6.6%placebo). AEs leading to deaths were 2% for Dupixent and 1.6% for placebo.

The potential use of Dupixent and its safety and efficacy in COPD have not been fully evaluated by any regulatory authorities outside of the EU, Brazil, and Russia.

About COPD
COPD is a respiratory disease that damages the lungs and causes progressive lung function decline and is the fourth leading cause of death worldwide. Symptoms include persistent cough, excessive mucus production and shortness of breath that may impair the ability to perform routine daily activities, which may lead to sleep disturbances, anxiety, and depression. 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. Prior to the approval of Dupixent in the EU, there had been no new treatment approaches approved for more than a decade.

About the Dupixent COPD phase 3 study program
BOREAS and NOTUS were 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 with evidence of type 2 inflammation, as measured by blood eosinophils ≥300 cells per µL. The trials enrolled 1,874 patients who were aged 40 to 80 years in BOREAS and 40 to 85 years in NOTUS.

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 ICS, LABA and LAMA. Double maintenance therapy, which included LABA and LAMA, was allowed if ICS was not appropriate.

The primary endpoint for BOREAS and NOTUS evaluated the annualized rate of 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 [FEV_1]) at 12 and 52 weeks, change from baseline at 52 weeks in St. George's Respiratory Questionnaire total score compared to placebo, change from baseline at 52 weeks in Evaluating Respiratory Symptoms in COPD total score compared to placebo, and safety.

The p-values for the pooled analysis were nominal because there was no hierarchical testing procedure for the pooled data.

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 (IL4) and interleukin-13 (IL13) 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 (IL33), an initiator and amplifier of broad inflammation in COPD.

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

About Dupixent
Dupixent (dupilumab) is a fully human monoclonal antibody that inhibits the signaling of the interleukin-4 (IL4) and interleukin-13 (IL13) 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 IL4 and IL13 are 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, eosinophilic esophagitis, prurigo nodularis, chronic spontaneous urticaria, and COPD in different age populations. More than 900,000 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 pruritus of unknown origin 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 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.
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Sanofi Forward-Looking Statements
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