

**Company**

Regeneron Pharmaceuticals, Inc. and Sanofi

**Drug or Device Name**

Dupixent® (dupilumab)

**Category**

Biotechnology

**Compound/Technical Name**

dupilumab

**Trade Name**

Dupixent®

**Date of Approval**

09/28/2022

**Therapeutic Categories**

Moderate-to-severe Asthma (eosinophilic or steroid dependent): approved 10/19/2018 for adults and adolescents, 10/20/2021 for children (6 to 11 years) · Moderate-to-severe Atopic Dermatitis: approved 03/28/2017 for adults, 03/11/2019 for adolescents, 05/26/2020 for children (6 to 11 years), 06/07/2022 for infants (6 months to 5 years) · Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP): approved 06/26/2019 for adults · Eosinophilic Esophagitis (EoE): approved 05/20/2022 adults and children (12 years and older) · Prurigo Nodularis (PN): approved 09/28/2022 for adults · Chronic Obstructive Pulmonary Disease (COPD) - Positive Phase 3 data announced

**Indications**

Dupixent® (dupilumab) is a rare example of a true “first-in-class” breakthrough medicine, and an even rarer example of a breakthrough therapeutic that can effectively treat multiple previously uncontrollable serious diseases – from the relatively rare (eosinophilic esophagitis [EoE] and prurigo nodularis [PN]) to the exceedingly common (atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyps [CRSwNP]).

Dupixent’s remarkable efficacy and safety account for its utilization by millions across these indications: efficacy measures show average improvements of 70-80%; unlike other immunomodulators, it is not immunosuppressive, with a safety profile allowing treatment in infants as young as 6 months.

A single biologic approved as a first-in-class treatment for so many seemingly disparate non-oncologic diseases may be unprecedented. Predicting this success was a prospective unifying scientific hypothesis: that many – if not all – allergic and atopic diseases are driven by excess interleukin-4 (IL-4) and interleukin-13 (IL-13). The remarkable efficacy of the first therapeutic blocking IL-4 and IL-13 (i.e.,

Dupixent) across so many allergic disorders validated this unifying scientific hypothesis.

As allergic and atopic diseases steadily rise in prevalence across the world, , this paradigm-changing medicine continues to give hope to millions suffering with chronic, debilitating and burdensome allergic and atopic diseases. As a result, Dupixent continues to have incredible potential: Dupixent recently demonstrated highly positive Phase 3 results in eosinophilic chronic obstructive pulmonary disease (COPD). If approved, Dupixent would become the first biologic to treat this life-threatening disease.

## Background

Millions suffer from severe and uncontrollable allergic and atopic conditions. While it has long been known that many of these diseases occur together in the same patient, it would take decades of scientific discovery and innovation – attributed in significant part to Regeneron and its development of Dupixent – to prove that type 2 inflammation, largely driven by IL-4 and IL-13, is the unifying basis of all of these seemingly disparate diseases.

A key early breakthrough was the discovery of IL-4 in the 1980s by Bill Paul's (NIH) and Bob Coffman's (DNAX) laboratories, and its ability to induce IgE production – a key feature of allergy. Shortly thereafter, IL-13 was discovered and shown to share a receptor system with IL-4, and many biologic properties. These findings prompted efforts by other companies to individually target IL-4 and IL-13, whereas Regeneron scientists focused on simultaneously blocking IL-4 and IL-13, initially by generating a dual-cytokine "Trap". Early individual blockers of IL-4 and IL-13 failed in clinical trials, causing most companies to abandon their interest in the pathway.<sup>2</sup> Unfortunately, Regeneron's Trap had manufacturing and pharmacokinetic limitations. But Regeneron scientists pressed on – leveraging their expertise in cytokine receptors, they decided to target a receptor component, IL-4R, shared by IL-4 and IL-13. Because a first-generation HumAb mouse failed to deliver an effective IL-4R blocking antibody, they invented a better HumAb mouse (i.e., VelocImmune®), to generate the first effective blocking antibodies for IL-4R. They then defined new complexities in the IL-4 and IL-13 receptor system that enabled screening methods to select the most potent of these antibodies, which is Dupixent.

The remarkable efficacy of Dupixent across so many allergic and type 2 disorders has validated the unifying basis of allergic diseases, and is a testament to the power of tailoring treatment options to critical inflammatory processes that drive disease.

## Development

Following the insights by Regeneron around type 2 inflammation and the IL-4 and IL-13 receptor system, alongside the generation of Dupixent (dupilumab) using the new VelocImmune technology, Sanofi was compelled to partner with Regeneron in 2007. Together, Regeneron and Sanofi have studied Dupixent in over 10,000 patients across more than 60 clinical trials in various chronic diseases driven in part by type 2 inflammation – and demonstrated unprecedented clinical efficacy in seven diseases to date.

The development of Dupixent continues to this day. In addition to its approved indications, it is being studied to treat COPD with evidence of type 2 inflammation, pediatric EoE and chronic spontaneous urticaria (CSU).

We are already seeing definitive Phase 3 results:

- In COPD, where no new treatment approaches have been approved in over a decade, Dupixent is the first and only biologic to demonstrate exacerbation reduction (by 30%), and significantly improve lung function, health-related quality of life, and respiratory symptoms.<sup>5</sup>
- In pediatric EoE, a majority (up to 68%) of patients treated with Dupixent experienced histological disease remission compared to placebo, the first and only Phase 3 trial to show positive results in this patient population.
- In CSU, a debilitating chronic skin condition, Dupixent significantly reduced itch and hives by more than 60% in those who did not respond to standard-of-care antihistamines.

Dupixent has resulted in strong, paradigm-changing efficacy in virtually every type 2 inflammatory condition for which results have been available, paired with a well-established and consistent safety profile across different diseases and age groups that includes those as young as 6 months old.

### **Innovation**

Dupixent is the first and only approved biologic that simultaneously inhibits IL-4 and IL-13, thereby transforming the treatment of multiple allergic and atopic conditions. Notably, Dupixent succeeded where prior efforts failed. While high-profile failures resulted in a loss of interest in this pathway, Regeneron believed in the biology and that a better antibody could be made, which required invention of an entirely new technology – the VelocImmune HumAb mouse—Regeneron’s unique platform for generating fully human antibodies.

VelocImmune involved the largest genetic humanization ever performed, resulting in mice engineered to have genetically humanized immune systems, overcoming limitations of prior HumAb mice; genetic engineering of the VelocImmune mouse was only possible because of another Regeneron invented technology, VelociGene, that allowed large scale genetic humanizations. Notably, VelocImmune overcomes limitations of prior platforms by allowing nature (i.e. the mouse) to generate fully human antibodies that tightly bind to therapeutic targets, requiring no further optimization or artificial engineering.

If these efforts had not been undertaken, and if Dupixent had not been brought forward, the world would still be in the dark on the fundamental shared drivers of type 2 inflammatory conditions. In fact, the many successful Phase 3 clinical trials with Dupixent – across multiple atopic and allergic conditions – provide the first definitive proof that IL-4 and IL-13 are indeed THE central drivers of type 2 inflammation, which include the prominent type 2 diseases of asthma, atopic dermatitis and CRSwNP.

This relentless commitment to scientific discovery and innovation has resulted in an impact few medicines have ever achieved: Dupixent is emerging as the major weapon to fight back against the epidemic of allergic diseases, with five indications approved across 60+ countries, and three additional indications anticipated, resulting in millions treated and the potential to improve the lives of millions more.

### **Pubmed**

Pub Med List

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#### **Attachments**

- 1624479255Background\_US\_Dupixent\_Prix\_Galien\_Submission\_2021.docx
- 1624479268Development\_US\_Dupixent\_Prix\_Galien\_Submission\_2021.docx
- 1624479281Innovation\_US\_Dupixent\_Prix\_Galien\_Submission\_\_2021.docx
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