**DRAFT – PRIX GALIEN 2023**

*Please note that the sections and word limits outlined below are pre-set by Prix Galien.*

**Section 1: CATEGORY**

Category: Best Biotechnology Product

**Section 2: PRODUCT**

Drug or Device Name:Dupixent®

Compound Technical Name:*dupilumab*

Trade Name:Dupixent®

Date of Approval:

* **Moderate-to-severe Asthma (eosinophilic or steroid dependent):** 
  + 10/19/2018 for adults and adolescents
  + 10/20/2021 for children (6 to 11 years)
* **Moderate-to-severe Atopic Dermatitis:**
  + 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):**
  + 06/26/2019 for adults
* **Eosinophilic Esophagitis (EoE):**
  + 05/20/2022 adults and children (12 years and older)
* **Prurigo Nodularis (PN):**
  + 09/28/2022 for adults
* **Chronic Obstructive Pulmonary Disease (COPD)**
  + Positive Phase 3 data announced

**Indications (300 words max); Current word count: 239**

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]).[[1]](#endnote-2)

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.1

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).[[2]](#endnote-3) 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,[[3]](#endnote-4),[[4]](#endnote-5) 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).[[5]](#endnote-6) If approved, Dupixent would become the first biologic to treat this life-threatening disease.[[6]](#endnote-7)

**SECTION 3: BACKGROUND (300 words max)**

*Background information and need for drug/device*

**Current Word Count: 300**

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.[[7]](#endnote-8) Shortly thereafter, IL-13 was discovered and shown to share a receptor system with IL-4, and many biologic properties.[[8]](#endnote-9) 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”.[[9]](#endnote-10),[[10]](#endnote-11) Early individual blockers of IL-4 and IL-13 failed in clinical trials, causing most companies to abandon their interest in the pathway.2 Unfortunately, Regeneron’s Trap had manufacturing and pharmacokinetic limitations. But Regeneron scientists pressed on – leveraging their expertise in cytokine receptors,10 they decided to target a receptor component, IL-4Ra, shared by IL-4 and IL-13. Because a first-generation HumAb mouse failed to deliver an effective IL-4Ra blocking antibody,[[11]](#endnote-12) they invented a better HumAb mouse (i.e., *VelocImmune**®*)[[12]](#endnote-13),[[13]](#endnote-14) to generate the first effective blocking antibodies for IL-4Ra. 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.2

**SECTION 4: DEVELOPMENT (300 words max)**

*History of the development of the drug/device*

**Current Word Count: 267**

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.5
* 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.[[14]](#endnote-15)
* 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*.*[[15]](#endnote-16)

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.1

**SECTION 5: INNOVATION (300 words max)**

*Why this drug or device is innovative, the broad implications for future research and/or how it will improve the human condition*

**Current Word Count: 296**

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.1 Notably, Dupixent succeeded where prior efforts failed.2 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 mouse12,13—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;12,13 genetic engineering of the *VelocImmune* mouse was only possible because of another Regeneron invented technology, *VelociGene*®, that allowed large scale genetic humanizations.[[16]](#endnote-17) 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.

**SECTION 6: PUBMED**

**Pub Med List**

Wenzel S, Ford L, Pearlman D, et al. Dupilumab in persistent asthma with elevated eosinophil levels. *N Engl J Med.*2013;368(26):2455-2466.

Macdonald LE, Karow M, Stevens S, et al. Precise and in situ genetic humanization of 6 Mb of mouse immunoglobulin genes. *Proc Natl Acad Sci USA.* 2014;111(14):5147-52.

Murphy AJ, Macdonald LE, Stevens S, et al. Mice with megabase humanization of their immunoglobulin genes generate antibodies as efficiently as normal mice. *Proc Natl Acad Sci USA.* 2014;111(14):5153-8.

Beck LA, Thaçi D, Hamilton JD, et al. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *N Engl J Med.*2014;371(2):130-139.

Thaçi, D, Simpson EL, Beck LA, et al. Efficacy and safety of dupilumab in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical treatments: a randomised, placebo-controlled, dose-ranging phase 2b trial. *Lancet.*2016;387(10013):40-52.

Bachert C, Mannent L, Naclerio RM, et al. Effect of subcutaneous dupilumab on nasal polyp burden in patients with chronic sinusitis and nasal polyposis a randomized clinical trial. *JAMA.* 2016;315(5):469-479.

Wenzel S, Castro M, Corren J, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting beta-agonist: a pivotal dose-ranging study. *Lancet*. 2016;388(10039):31-44.

Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335-2348.

Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled phase 3 trial. *Lancet*. 2017;389(10086):2287-2303.

Castro M, Corren J, Pavord ID, et al. Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma. *N Engl J Med.* 2018;378:2486-2496.

Rabe KF, Nair P, Brusselle G, et al. Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma. *N Engl J Med.* 2018;378:2475-2485.

# Bachert C, Han J, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. *Lancet*. 2019;10209:1638-1650.

# Simpson E, Paller A, Siegfried E, et al. Efficacy and Safety of Dupilumab in Adolescents With Uncontrolled Moderate to Severe Atopic Dermatitis. *JAMA*. 2019;156(1):44-56.

# Cork M, Thaci D, Eichenfield L, et al. A study of dupilumab in the treatment of adolescents with eczema. *BJD*. 2020;182:85-96.

# Beck L, Thaci D, Deleuran M, et al. Dupilumab Provides Favorable Safety and Sustained Efficacy for up to 3 Years in an Open-Label Study of Adults with Moderate-to-Severe Atopic Dermatitis. *Am J Clin Dermatol*. 2020.

# Paller A, Siegfried E, Thaci D, et al. Efficacy and safety of dupilumab with concomitant topical corticosteroids in children 6 to 11 years old with severe atopic dermatitis: a randomized, double-blinded, placebo-controlled phase 3 trial. *JAAD*. 2020.

# Bacharier L, Maspero J, Katelaris C, et al. Dupilumab in children with uncontrolled moderate-to-severe asthma. *N Engl J Med.* 2021; 385: 2230-2240.

# Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet.* 2022; 400 908-919.

# Yosipovitch, Gil, et al. “Dupilumab in patients with prurigo nodularis: two randomized, double-blind, placebo-controlled phase 3 trials.” *Nature medicine*. 2023; 1-11.

# Bhatt, Surya P., et al. "Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts." *New England Journal of Medicine* (2023).

*Reference*

**SUPPLEMENTAL INFORMATION**

**Additional Background Information about Dupixent® and Its Impact**

Type 2 inflammatory diseases are largely chronic, unpredictable, extremely burdensome and life-altering. The impact of these immunological conditions is often more than physical. Across atopic dermatitis (AD), asthma, CRSwNP, EoE, and prurigo nodularis, patients are more likely to suffer from mental health conditions such as anxiety and depression that compound over time.[[17]](#endnote-18),[[18]](#endnote-19),[[19]](#endnote-20),[[20]](#endnote-21),[[21]](#endnote-22)

**Moderate-to-severe AD**

From the very first Dupixent AD studies, Regeneron heard from a number of patients and investigators who reached out to share their stories, often through tears. By addressing the key inflammatory cause of AD, Dupixent was able to significantly improve patients’ eczema – and give many back their lives as the first biologic approved for AD. To this day, Dupixent remains the only biologic approved for patients 6 months of age and older.

In the U.S., moderate-to-severe AD affects approximately 1.6 million adults, an estimated 389,000 adolescents and an estimated 88,000 children aged 6 to 11 years and an estimated 75,000 infants and young children less than 6 years of age.[[22]](#endnote-23)

AD is misunderstood as a superficial skin disease, but it is often associated with a debilitating rash, intense itching and skin lesions covering much of a person’s body, and problems with sleep and daily living.[[23]](#endnote-24),[[24]](#endnote-25),[[25]](#endnote-26),[[26]](#endnote-27) To make others understand the horror of this disease, many patients explain that the disease is like having poison ivy over half your body surface, but which never goes away. People with moderate-to-severe forms of the disease may not be able to control their symptoms with topical medications and need to be prescribed systemic steroids or broad immune-suppressant medicines,[[27]](#endnote-28),[[28]](#endnote-29) which are often ineffective, and also run the risk of serious side effects if used long-term.[[29]](#endnote-30) Because of the constant pain and itch, which also disrupts sleep and working ability, AD imposes a significant economic impact (billions of dollars annually in the U.S. alone)[[30]](#endnote-31) and, even more importantly, has one of the highest rates of associated mental health disorders and suicidal ideation.[[31]](#endnote-32),[[32]](#endnote-33),[[33]](#endnote-34)

Dupixent has revolutionized the treatment of this disease. In AD clinical studies, heavily pre-treated patients saw a remarkable, approximately 75% improvement from baseline on average and significantly improved sleep, anxiety, depression and quality of life.[[34]](#endnote-35),[[35]](#endnote-36) Dupixent was well tolerated, without the immunosuppressive side effects common to other classes of systemic medicines.

**Moderate-to-severe asthma**

Additionally, Dupixent is the only biologic approved for oral corticosteroid-dependent asthma, regardless of phenotype, and is the first available in the U.S. for at-home use – providing a critical new option for patients at serious risk for asthma attacks. Dupixent is also approved for use with other asthma medicines as a maintenance treatment of moderate-to-severe eosinophilic or oral steroid-dependent asthma in patients aged 6 years and older whose asthma is not controlled with their current asthma medicines.

Moderate-to-severe asthma affects approximately 900,000 people aged 12 years and older in the U.S. and an estimated 75,000 children aged 6 to 11.6 These patients experience difficulty breathing and are at risk of severe asthma attacks (exacerbations) requiring emergency room visits or hospitalizations.[[36]](#endnote-37)

Oral corticosteroids (OCS) can provide relief for severe, short-term symptoms. However, current asthma guidelines suggest limiting chronic use to the most severe patients due to the potential for serious side effects.[[37]](#endnote-38),[[38]](#endnote-39),[[39]](#endnote-40)

After its initial approval in October 2018, Dupixent became the first biologic approved for both moderate and severe asthma patients with an eosinophilic phenotype (raised blood eosinophils), oral corticosteroid-dependent asthma (regardless of biomarkers), and with the potential for self-administration at home.18 In clinical studies, Dupixent significantly reduced asthma exacerbations, improved lung function and reduced or eliminated OCS use. In children aged 6 to 11 years, Dupixent is the only biologic medicine to improve lung function in a randomized Phase 3 trial.

**CRSwNP**

Dupixent was the first FDA-approved medicine for adults with CRSwNP, changing the treatment paradigm and giving new hope to the many patients for whom systemic corticosteroids and surgery did not provide relief.

An estimated 90,000 people have CRSwNP in the U.S., and they suffer from a range of debilitating symptoms caused by obstruction of their sinuses and nasal passages.6 These patients can have other type 2 inflammatory diseases as well, which adds to their overall burden of disease.[[40]](#endnote-41) Common care for these patients includes systemic steroids or nasal surgery, which often do not provide complete disease control.24

In clinical studies, Dupixent significantly reduced nasal polyp size, improved congestion and loss of smell while also reducing the need for surgery and systemic corticosteroids.18 With its approval in CRSwNP, another condition with underlying type 2 inflammation, Dupixent’s ability to target this important biological driver of disease was further cemented.

**Eosinophilic esophagitis**

Last year, Dupixent became the first and only FDA-approved medicine indicated to treat eosinophilic esophagitis. About 160,000 patients with EoE in U.S. are currently being treated with therapies not specifically approved for the disease, of whom approximately 48,000 continue to experience symptoms despite multiple treatments.6

Common treatments for patients with EoE include disruptive and strict elimination diets to avoid food triggers, with some having to resort to invasive procedures or feeding tubes to ensure proper nutrition.[[41]](#endnote-42),[[42]](#endnote-43)

In clinical trials, Dupixent reduced disease symptoms and esophageal inflammation compared to placebo.14 With this first approval for Dupixent in a gastrointestinal disease, its role in addressing diseases with underlying type 2 inflammation across body systems was further established.

**Prurigo nodularis**

In late 2022, Dupixent became the first FDA-approved treatment specifically indicated for prurigo nodularis. About 75,000 adults in the U.S. living with prurigo nodularis are in need of new treatment options.6 High-potency topical steroids are commonly prescribed but are associated with safety risks if used long-term.[[43]](#endnote-44)

In clinical trials, Dupixent reduced itch and skin lesions compared to placebo.18 The approval of Dupixent for prurigo nodularis was its second in a dermatological disease, and established the effectiveness of targeting underlying type 2 inflammation to address both less common and prevalent chronic, inflammatory skin diseases.

Across all approved indications globally, more than 600,000 patients are being treated with Dupixent,[[44]](#endnote-45) with the potential for many more to benefit from this innovative medicine in the coming years.

**Personal connections to atopic and allergic diseases**

Many people who have been involved in the development of Dupixent have a personal connection to atopic and allergic diseases, which bolsters their commitment to addressing the unmet needs of people with diseases exacerbated by type 2 inflammation.

In the early 1990s, the father of George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron, developed severe AD while undergoing lung cancer treatment, and Dr. Yancopoulos witnessed the severity of this disease first-hand. It was, in part, this experience that motivated Dr. Yancopoulos to initiate and relentlessly lead the Dupixent program for more than 30 years.

Remarkably, his own daughter subsequently developed serious atopic dermatitis and asthma, and she is currently a successful responder to Dupixent treatment. The person who confirmed Dupixent’s action in living cells was Jamie Orengo, Ph.D., Director of Immunology and Inflammation at Regeneron, who is a caregiver to her three children with AD and other allergic diseases.

This commitment to developing a safe and effective first-of-its-kind treatment for AD has been shown in the more than 52 completed and ongoing clinical trials of Dupixent in AD, including an extensive Phase 3 clinical program of 15 trials in nearly 5,000 patients worldwide.28

**Regeneron and Sanofi are committed to bring Dupixent to younger patients with severe AD because of stories like the following from a physician who reached out in a letter.**

“*I met this family when she was first admitted to my children’s hospital (transferred by ambulance from a community hospital ~3 hours away). Prior treatment had been cycles of prednisone, oral anti-Staph antibiotics, pound jars of triamcinolone and chronic daily sedating antihistamines.*

*The family was in crisis. During hospitalizations from November through February, this girl was miserable, and unable to interact with hospital staff….THIS IS A TRULY HORRIBLE DISEASE...we had to restrain her so wouldn’t scratch herself constantly and bleed and get infections.*”This is how she looked when she was admitted:



“*After three doses of dupilumab, she is a pistol*…*THIS IS WHAT DUPILUMAB CAN DO*:”



*“We all want you to know how grateful we are for dupilumab...[My patient’s] quality of life has vastly improved, and so has mine…* *As a scientist, I don’t think there is anything more rewarding than seeing that you can use the power of science to do this, to change a little girl’s life…and I think that’s why many of us do what we do…”*

**Many patients with AD have proactively contacted Regeneron and Sanofi to tell us how Dupixent has changed their lives or shared their experiences publicly:**

*“Getting access to Dupixent remains the single most significant thing that has ever happened to me. It has changed the course of my life in ways that were unimaginable only a few years ago.” –Sirish (adult with AD), via email28*

*Images provided by Sirish during the clinical trial:*



*“…I am so passionate about Dupixent. This drug has been life changing for me…” –Sue (adult with AD), via emai28*

*“After two weeks my old skin started to shed, and I had new, normal skin for the first time in my life…I don’t think I slept a full night in my entire adolescence…This medicine [Dupixent] has totally changed my way of life.” –Anne (adult with AD), via email28*

*"Dupixent has been life changing for me. I was diagnosed at age 6 and I am currently 32 years of age. I have severe eczema and typically dress completely covered to prevent the stares, questions and comments. I have not been able to wear my wedding ring for 7 years because of the dyshidrotic eczema on my hands. I have never been bowling with my children, the oldest being 12. I have a hard time allowing anyone to touch me because my skin is so hypersensitive; it drives me insane. I have never slept all the way through the night. My self-esteem is highly affected, and exercise is nearly impossible with the sweat pouring and irritating the wounds. Sometimes, just getting out of bed, walking, or taking a shower is enough to send me to tears. Dupixent has given me a new life. It has given me life back. I now know what all eczema took from me, and I am forever grateful for the opportunity to be on this medication." –Nicole**[[45]](#endnote-46)*

*"I have had AD for at least 67 years of my 70 years on this earth. My life as a child was hell because of weeping medicated baths and teasing by other children. My adult life has also been equally affected by the use of corticosteroids on my skin, which is now permanently affected due to chronic steroids. When my new dermatologist brought up Dupixent about six months ago I was skeptical and scared. I started March 22. I STOPPED itching in 24 hours. It has been a MIRACLE.” –Pinkas28*

*"I love Dupixent! Before I started injections I was beyond miserable. If there’s a worse word for it... I’ve been using Dupixent since January 17, 2018, and within the first day of taking it, I noticed a drastic change. The itch started to cease quickly, and all of my eczema patches started to dry up and peel off. After about a month, many of my active spots healed. The hyperpigmentation on my face, hands and legs have lightened up. My derm said hyperpig can take a year to go away. I’m fine with that because I never thought I’d be able to look myself in the mirror and not cry. I rejoice quite often because I have a normal life again. I can cook, clean and go to work consistently without having to book an appointment.” –Sam29*

*"I’ve been suffering from eczema my entire life. In the past few years, I’ve had major break outs, really major. You know, the ones when you can’t sleep, stop scratching, and you’re covered in sores. Nothing works, not even rounds and rounds of prednisone where the only thing you get are horrible side effects. Ugh! No fun. I’ve taken Dupixent 5 times so far, one being the initial dose of 2 units and the other 3 self-administered and it’s been a miracle for me. I also suffer from hideous asthma (of course) and my side effect from Dupixent has been NO asthma episodes! I feel like I’d imagine [how] a normal person feels. I CAN BREATHE AND DO THINGS! And I’m not dying of asthma attacks all the time…There aren’t enough stars to rate Dupixent as high as I want to. It really is magical unicorn fairy dust!!" –Zia29*

*“We were following the success of dupilumab in teen and adult AD sufferers for a while and eagerly awaiting for it to be approved in Ella’s age group… at 5 and a half years old, she was approved. Within 4 weeks, we began to see a noticeable decrease in her AD symptoms, particularly her itching. A child that had been spending 5 and a half years itching relentlessly was sitting quietly, reading a book, something she never was able to sit through prior to this, and engaging in normal childhood activities. This was a huge change for us. 2 months in and we weren’t using any topicals to control her AD and she wasn’t needing bleach baths, and we weren’t using any wet wraps. On February 6 2021, just shy of her 6th birthday, Ella slept through the night for the first time in her entire life. I cannot overstate the miracle that this was for us. Ella’s skin was healing, her body was healing, our family was healing. We had finally found a therapy that worked for Ella, and it truly changed the course of her life. It gave us our child back.” –Amy (mother of child with AD)[[46]](#endnote-47)*

**U.S. physicians have also spoken of impressed they are that Dupixent has lived up to its promise as the first biologic medicine to target the underlying type 2 inflammation in AD:**

*“We heard many times that patients even considered suicide because their disease was so bad. Some said they were about to destroy their marriage; and one patient was about to close his law office. But this drug basically enabled them to have a life.” -Dr. Emma Guttman-Yassky, Mount Sinai[[47]](#endnote-48)*

*“…patients mostly are bothered a lot of times by the itching, and improvement can be seen as quickly as two weeks…Patients just say 'this has changed my life. For the first time, I don't itch at night. For the first time, I can leave my house. I can wear shorts.” –Dr. Anabelle Garcia, Sonterra Dermatology[[48]](#endnote-49)*

**Dupixent has also been shown to improve lung function in moderate-to-severe asthma patients. The reaction from patients and U.S. physicians to Dupixent has been overwhelmingly positive.**

“*My son has poorly controlled asthma despite adhering to his medication regime and being extremely well cared for by his consultant. [Dupixent] offers him the chance to live with improved breath – breathing is overlooked by those of us fortunate enough to enjoy good health!” –Natalie[[49]](#endnote-50)*

*"This medication appears to have efficacy in a much broader range of patients than the currently available biologics. It has the potential to be a game changer for some patients, but we won't really know until it is out in the real world." –Dr. Sally Wenzel, University of Pittsburgh[[50]](#endnote-51)*

**Dupixent is the first and only FDA-approved medicine indicated for eosinophilic esophagitis. Although it is a rare disease, EoE has a large impact on patients’ lives. People with EoE are more likely to have depression and anxiety, especially as they get older, which can be related to fears about disease progression and difficulties with managing their disease, such as adapting eating habits to adhere to strict diets.5,25**,[[51]](#endnote-52)

**Patients with EoE saw a remarkable 69% reduction in disease symptoms with Dupixent, compared to 32% for placebo.18 Dupixent is the first and only biologic to show positive and clinically-meaningful results in this population as part of a Phase 3 trial. Dupixent may improve underlying biological processes related to tissue damage in EoE, as shown by the normalization in the expression of genes association with scarring and barrier function in these patients.[[52]](#endnote-53)**

“*The hardest part, I would say, of this disease on my life probably was in high school. I was extremely small for my age. I was 15 and was about 60 pounds and I was around 4’5” or 4’6”, so I clearly looked very different than the rest of my friends. And as a freshman in high school, it’s hard in general. Everyone has a tough time, but having a disease that makes you look and feel so isolated and different. That was a really big challenge.” –Jori, person with EoE28*

*“My husband has EoE. And then three of our four kids. Charlie is eleven; and Gage is nine; and Tinley is six. The kids definitely have different takes on the disease. With Charlie not having a feeding tube, he has a lot more in his diet; it’s easier for him. Gage hates all of it. He hates the disease, and he hates that he has a feeding tube, and he wants it to all go away.” –Kara, caregiver to family with EoE28*

**Visuals of esophageal impact before and after Dupixent:**

**Before**

**Graphical user interface

Description automatically generatedGraphical user interface

Description automatically generated with low confidence**

**After**

**A picture containing calendar

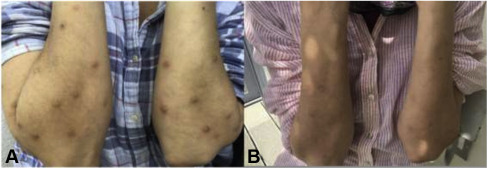
Description automatically generatedMap

Description automatically generated with low confidence**

**Dupixent is the first and only treatment indicated for prurigo nodularis.**.**Although it is a rare disease, it has one of the highest impacts on quality of life amongst inflammatory skin diseases due to the extreme itch it causes.[[53]](#endnote-54),[[54]](#endnote-55) Patients with prurigo nodularis saw significant reductions in itch and skin lesions, two of the key signs and symptoms of disease.18**

*A 51-year-old woman with prurigo nodularis was experiencing intense itch, had multiple skin lesions and reported negative impact on daily life activities and sleep impairment* *in the last 20 years, during which multiple topical and immunosuppressive treatments had been unsuccessful. After three months of treatment with Dupixent, she had a substantial reduction in itch with only two active skin lesions. The clinical benefit continued up to 18 months, at which point she was asymptomatic and had no side effects from treatment. [[55]](#endnote-56)*

**Before Dupixent Treatment After 18 Months**



*A 65-year-old man with prurigo nodularis presented with lesions on his lower extremities, groin and trunk had been previously and unsuccessfully treated with phototherapy, thalidomide, and topical corticosteroids. After one month of treatment with Dupixent, he had significant improvement in itch and skin lesions, and did not report any adverse events.[[56]](#endnote-57)*

A close-up of a person's legs

Description automatically generated with low confidence

**Additionally, Dupixent has as shown positive and clinically meaningful results in an additional skin disease in patients with chronic spontaneous urticaria who have failed standard-of-care antihistamines, characterized by the sudden onset of hives on the skin and/or swelling deep under the skin. Based on these results, the FDA has accepted for review the supplemental Biologics License Application for Dupixent to treat adults and adolescents aged 12 years and older with CSU that is not adequately controlled with the current standard of care, H1 antihistamine treatment.[[57]](#endnote-58)**

We believe that future generations will look back and regard Dupixent as a significant landmark in the management of chronic type 2 inflammatory conditions. This biological treatment is a tangible demonstration of how addressing the root cause of a problem can lead to the invention of exciting, multi-tasking and innovative therapies for diseases with high unmet medical needs.

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