



Dupixent® (dupilumab) Approved by European Commission as the First and Only Targeted Medicine Indicated for Prurigo Nodularis

December 15, 2022

Approval based on direct-to-Phase 3 program showing more than three times as many Dupixent patients (60% and 58%) experienced clinically meaningful itch reduction at 24 weeks compared to placebo (18% and 20%)

Dupixent also significantly reduced skin lesions and improved health-related quality of life compared to placebo

In Europe, about 70,000 adults living with prurigo nodularis are most in need of new treatment options

Dupixent now approved to treat four chronic inflammatory diseases in the EU

TARRYTOWN, N.Y. and PARIS, Dec. 15, 2022 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) and Sanofi today announced that the European Commission (EC) has expanded the marketing authorization for Dupixent® (dupilumab) in the European Union to treat adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy. Prurigo nodularis is a chronic, debilitating skin disease with underlying type 2 inflammation and its impact on quality of life is one of the highest among inflammatory skin diseases. With this approval, Dupixent is the first and only targeted medicine specifically indicated to treat prurigo nodularis in Europe and the [U.S.](#)

"For the first time, patients with prurigo nodularis in Europe have a medicine that can help relieve the burden of itchy and painful nodules covering their skin, which can have a devastating impact on their day-to-day lives, both physically and mentally," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron, and a principal inventor of Dupixent. "Dupixent is now approved for its second dermatological disease and fourth disease overall. We remain committed to further investigating this innovative medicine for diseases – such as chronic urticarias and chronic obstructive pulmonary disease – in which type 2 inflammation may play a role."

"As the first and only targeted medicine approved to treat people living with prurigo nodularis, Dupixent has the potential to transform the standard-of-care for people in Europe living with this debilitating skin disease. In the pivotal trials, patients treated with Dupixent experienced significant improvements in key hallmarks of the disease, such as reduction in itch and achieving clearer skin, as well as broader impacts on their daily lives," Naimish Patel, M.D. Head of Global Development, Immunology and Inflammation at Sanofi. "This approval of Dupixent underscores our continued commitment to bringing Dupixent to patients suffering from chronic skin diseases with underlying type 2 inflammation as quickly as possible."

The EC decision is based on data from two Phase 3 trials, [PRIME](#) and [PRIME2](#), evaluating the efficacy and safety of Dupixent (PRIME n=75; PRIME2 n=78) in adults with uncontrolled prurigo nodularis compared to placebo (PRIME n=76; PRIME2 n=82). In these trials, 44% and 37% of Dupixent patients experienced a clinically meaningful reduction in itch at 12 weeks, compared to 16% and 22% for placebo, respectively. The improvement further increased at 24 weeks, with approximately three times as many Dupixent patients (60% and 58%) experiencing a clinically meaningful reduction in itch from baseline, compared to placebo (18% and 20%).

In PRIME and PRIME2, more than twice as many Dupixent patients (48% and 45%) also achieved clear or almost clear skin at 24 weeks, compared to placebo (18% and 16%). Dupixent also significantly improved health-related quality of life, while reducing measures of skin pain and symptoms of anxiety/depression from baseline at 24 weeks compared to placebo.

The safety results of the trial were generally consistent with the known safety profile of Dupixent in its approved indications, with the most common side effects across indications including injection site reactions, conjunctivitis, conjunctivitis allergic, arthralgia, oral herpes and eosinophilia. Adverse events more commonly observed in prurigo nodularis with Dupixent compared to placebo included conjunctivitis (4% Dupixent and 1% placebo).

About Prurigo Nodularis

Prurigo nodularis is a chronic, debilitating skin disease with underlying type 2 inflammation and has one of the highest impacts on a patient's quality of life among inflammatory skin diseases due to the extreme itch it causes. Those with prurigo nodularis experience intense, persistent itch with thick skin lesions (called nodules) that can cover most of the body. The disease is often painful – with burning, stinging and tingling of the skin – and can negatively affect mental health, activities of daily living and social interactions. High-potency topical steroids are commonly prescribed but are associated with safety risks if used long-term. In Europe, about 70,000 adults living with prurigo nodularis are most in need of new treatment options.

About the Dupixent Prurigo Nodularis Trials

The PRIME and PRIME2 Phase 3 double-blind, placebo-controlled trials evaluated the efficacy and safety of Dupixent in 311 adults with uncontrolled prurigo nodularis. In PRIME and PRIME2, the primary endpoint evaluated the proportion of patients with clinically meaningful improvement in itch from baseline (measured by a ≥4-point reduction in Worst-Itch Numeric Rating Scale [WI-NRS] on a 0-10 scale) at 24 and 12 weeks, respectively.

Additional endpoints included the proportion of patients with clear or almost clear skin of nodules at 24 weeks (measured by a score of 0 or 1 on the Investigator's Global Assessment PN-Stage [IGA PN-S] on a 0-4 scale), the proportion of patients who achieved a clinically meaningful response in both WI-NRS and IGA PN-S, improvement from baseline in health-related quality of life (measured by the Dermatology Life Quality Index [DLQI] on a 0-30 scale), improvement from baseline in skin pain (measured by a Numerical Rating Scale from 0-10), and improvement from baseline in symptoms of anxiety and depression (measured by the Hospital Anxiety and Depression Scale [HADS] from 0-42).

About Dupixent

Dupixent is an injection under the skin (subcutaneous injection) at different injection sites. In the EU for adults with prurigo nodularis, Dupixent is administered at 300 mg every two weeks, following a loading dose. It is available as both a pre-filled pen and pre-filled syringe at the 300 mg dose.

Dupixent is intended for use under the guidance of a healthcare professional and can be given in a clinic or at home by self-administration after training by a healthcare professional.

Dupixent, which was invented using Regeneron's proprietary *VelocImmune*[®] technology, 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 polyposis (CRSwNP) and prurigo nodularis, as well as investigational disease eosinophilic esophagitis (EoE) in the EU.

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. More than 500,000 patients have been treated with Dupixent globally.

About Regeneron's *VelocImmune* Technology

Regeneron's *VelocImmune* technology utilizes a proprietary genetically engineered mouse platform endowed with a genetically humanized immune system to produce optimized fully human antibodies. When Regeneron's co-Founder, President and Chief Scientific Officer George D. Yancopoulos was a graduate student with his mentor Frederick W. Alt in 1985, they were the first to [envision](#) making such a genetically humanized mouse, and Regeneron has spent decades inventing and developing *VelocImmune* and related *VelociSuite*[®] technologies. Dr. Yancopoulos and his team have used *VelocImmune* technology to create approximately one in five of all original, FDA-approved or authorized fully human monoclonal antibodies. This includes REGEN-COV[®] (casirivimab and imdevimab), Dupixent, Libtayo[®] (cemiplimab-rwlc), Praluent[®] (alirocumab), Kevzara[®] (sarilumab), Evkeeza[®] (evinacumab-dgnb) and Inmazeb[®] (atoltivimab, maftivimab and odesivimab-ebgn).

Dupilumab Development Program

Dupilumab is being jointly developed by Regeneron and Sanofi 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, Regeneron and Sanofi 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, hand and foot atopic dermatitis, chronic inducible urticaria-cold, chronic spontaneous urticaria, chronic pruritus 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.

U.S. INDICATIONS

DUPIXENT is a prescription medicine used:

- to treat adults and children 6 months of age and older with moderate-to-severe eczema (atopic dermatitis or AD) that is not well controlled with prescription therapies used on the skin (topical), or who cannot use topical therapies. DUPIXENT can be used with or without topical corticosteroids. It is not known if DUPIXENT is safe and effective in children with atopic dermatitis under 6 months of age.
- with other asthma medicines for the maintenance treatment of moderate-to-severe eosinophilic or oral steroid dependent asthma in adults and children 6 years of age and older whose asthma is not controlled with their current asthma medicines. DUPIXENT helps prevent severe asthma attacks (exacerbations) and can improve your breathing. DUPIXENT may also help reduce the amount of oral corticosteroids you need while preventing severe asthma attacks and improving your breathing. DUPIXENT is not used to treat sudden breathing problems. It is not known if DUPIXENT is safe and effective in children with asthma under 6 years of age.
- with other medicines for the maintenance treatment of chronic rhinosinusitis with nasal polyposis (CRSwNP) in adults whose disease is not controlled. It is not known if DUPIXENT is safe and effective in children with chronic rhinosinusitis with nasal polyposis under 18 years of age.
- to treat adults and children 12 years of age and older, who weigh at least 88 pounds (40 kg), with eosinophilic esophagitis (EoE). It is not known if DUPIXENT is safe and effective in children with eosinophilic esophagitis under 12 years of age and who weigh at least 88 pounds (40 kg).
- to treat adults with prurigo nodularis (PN). It is not known if DUPIXENT is safe and effective in children with prurigo nodularis under 18 years of age.

IMPORTANT SAFETY INFORMATION

Do not use if you are allergic to dupilumab or to any of the ingredients in DUPIXENT[®].

Before using DUPIXENT, tell your healthcare provider about all your medical conditions, including if you:

- have eye problems.
- have a parasitic (helminth) infection.
- are scheduled to receive any vaccinations. You should not receive a "live vaccine" right before and during treatment with DUPIXENT.
- are pregnant or plan to become pregnant. It is not known whether DUPIXENT will harm your unborn baby.

- A pregnancy registry for women who take DUPIXENT during pregnancy collects information about the health of you and your baby. To enroll or get more information call 1-877-311-8972 or go to <https://mothertobaby.org/ongoing-study/dupixent/>.
- are breastfeeding or plan to breastfeed. It is not known whether DUPIXENT passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Especially tell your healthcare provider if you are taking oral, topical, or inhaled corticosteroid medicines; have asthma and use an asthma medicine; or have atopic dermatitis, chronic rhinosinusitis with nasal polyposis, eosinophilic esophagitis, or prurigo nodularis and also have asthma. **Do not** change or stop your corticosteroid medicine or other asthma medicine without talking to your healthcare provider. This may cause other symptoms that were controlled by the corticosteroid medicine or other asthma medicine to come back.

DUPIXENT can cause serious side effects, including:

- **Allergic reactions. DUPIXENT can cause allergic reactions that can sometimes be severe.** Stop using DUPIXENT and tell your healthcare provider or get emergency help right away if you get any of the following signs or symptoms: breathing problems or wheezing, swelling of the face, lips, mouth, tongue or throat, fainting, dizziness, feeling lightheaded, fast pulse, fever, hives, joint pain, general ill feeling, itching, skin rash, swollen lymph nodes, nausea or vomiting, or cramps in your stomach-area.
- **Eye problems.** Tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision, such as blurred vision. Your healthcare provider may send you to an ophthalmologist for an exam if needed.
- **Inflammation of your blood vessels.** Rarely, this can happen in people with asthma who receive DUPIXENT. This may happen in people who also take a steroid medicine by mouth that is being stopped or the dose is being lowered. It is not known whether this is caused by DUPIXENT. Tell your healthcare provider right away if you have: rash, chest pain, worsening shortness of breath, a feeling of pins and needles or numbness of your arms or legs, or persistent fever.
- **Joint aches and pain.** Some people who use DUPIXENT have had trouble walking or moving due to their joint symptoms, and in some cases needed to be hospitalized. Tell your healthcare provider about any new or worsening joint symptoms. Your healthcare provider may stop DUPIXENT if you develop joint symptoms.

The most common side effects include:

- **Eczema:** injection site reactions, eye and eyelid inflammation, including redness, swelling, and itching, sometimes with blurred vision, cold sores in your mouth or on your lips, and high count of a certain white blood cell (eosinophilia).
- **Asthma:** injection site reactions, high count of a certain white blood cell (eosinophilia), pain in the throat (oropharyngeal pain), and parasitic (helminth) infections.
- **Chronic Rhinosinusitis with Nasal Polyposis:** injection site reactions, eye and eyelid inflammation, including redness, swelling, and itching, sometimes with blurred vision, high count of a certain white blood cell (eosinophilia), gastritis, joint pain (arthralgia), trouble sleeping (insomnia), and toothache.
- **Eosinophilic Esophagitis:** injection site reactions, upper respiratory tract infections, cold sores in your mouth or on your lips, and joint pain (arthralgia).
- **Prurigo Nodularis:** eye and eyelid inflammation, including redness, swelling, and itching, sometimes with blurred vision, herpes virus infections, common cold symptoms (nasopharyngitis), dizziness, muscle pain, and diarrhea.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of DUPIXENT. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Use DUPIXENT exactly as prescribed by your healthcare provider. It's an injection given under the skin (subcutaneous injection). Your healthcare provider will decide if you or your caregiver can inject DUPIXENT. **Do not** try to prepare and inject DUPIXENT until you or your caregiver have been trained by your healthcare provider. In children 12 years of age and older, it's recommended DUPIXENT be administered by or under supervision of an adult. In children 6 months to less than 12 years of age, DUPIXENT should be given by a caregiver.

Please see accompanying full [Prescribing Information](#) including Patient Information.

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 nine FDA-approved treatments and numerous 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.

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) for the treatment of adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy; 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 and Regeneron's Product Candidates; 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 pediatric eosinophilic esophagitis, 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; 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 and Bayer (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, Praluen[®] (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 September 30, 2022. 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 (<http://newsroom.regeneron.com>) and its Twitter feed (<http://twitter.com/regeneron>).

Sanofi Disclaimers or 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 regarding the marketing and other potential of the product, or regarding potential future revenues from the product. 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, unexpected regulatory actions or delays, or government regulation generally, that could affect the availability or commercial potential of the product, the fact that product may not be commercially successful, the uncertainties inherent in research and development, including future clinical data and analysis of existing clinical data relating to the product, including post marketing, unexpected safety, quality or manufacturing issues, competition in general, risks associated with intellectual property and any related future litigation

and the ultimate outcome of such litigation, and volatile economic and market conditions, and the impact that COVID-19 will 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. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. 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, 2021. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

Regeneron Contacts:

Media Relations

Hannah Kwagh

Tel: +1 914-847-6314

Hannah.Kwagh@regeneron.com

Investor Relations

Vesna Tosic

Tel: +1 914-847-5443

Vesna.Tosic@regeneron.com

Sanofi Contacts:

Media Relations

Sally Bain

Tel: +1 617-834-6026

Sally.Bain@sanofi.com

Investor Relations

Eva Schaefer-Jansen

Tel: +33 7 86 80 56 39

eva.schaefer-jansen@sanofi.com

Arnaud Delepine

Tel: +33 (0)6 73 69 36 93

arnaud.delepine@sanofi.com

Corentine Driancourt

Tel: +33 (0)6 40 56 92

corentine.driancourt@sanofi.com

Felix Lauscher

Tel: +1 908-612-7239

felix.lauscher@sanofi.com

Priya Nanduri

Tel: +1 617-764-6418

priya.nanduri@sanofi.com

Nathalie Pham

Tel: +33 (0)7 85 93 30 17

nathalie.pham@sanofi.com

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