NEWS RELEASE

Press Release: Dupixent is the first and only biologic to achieve significant improvements in disease remission and symptoms in bullous pemphigoid positive pivotal study

2024-09-11

Dupixent is the first and only biologic to achieve significant improvements in disease remission and symptoms in bullous pemphigoid positive pivotal study

- Study met the primary and all key secondary endpoints in adults with moderate-to-severe disease; five times more patients achieved sustained disease remission with Dupixent than placebo
- Dupixent is the first medicine to show significant steroid-sparing effect in this debilitating and life-threatening disease
- If approved, Dupixent would be the first and only targeted medicine to treat BP in the U.S. and European Union

Paris and Tarrytown, NY, September 11, 2024. A Dupixent (dupilumab) pivotal study (ADEPT) in bullous pemphigoid (BP) met the primary and all key secondary endpoints evaluating its investigational use in adults with moderate-to-severe disease. In the study, five times more Dupixent patients achieved sustained disease remission compared to those on placebo. Sustained disease remission was defined as complete clinical remission with completion of oral corticosteroids (OCS) taper by week 16 without relapse and no rescue therapy use during the 36-week treatment period. Dupixent was previously granted Orphan Drug Designation by the U.S. Food and Drug Administration for BP, which applies to investigational medicines intended for the treatment of rare diseases that affect fewer than

200,000 people in the U.S. This study will support regulatory submissions around the world, starting with the U.S. later this year.

BP, a chronic and relapsing disease, is characterized by intense itch and blisters, reddening of the skin, and painful chronic lesions. The blisters and rash can form over much of the body and cause the skin to bleed and crust, resulting in patients being more prone to infection and affecting their daily functioning.

Dietmar Berger, M.D., Ph.D.
Chief Medical Officer, Global Head of Development at Sanofi
"The itchy blisters caused by bullous pemphigoid can be so intense they are debilitating, especially for elderly patients. There is a significant unmet medical need for new medicines for people suffering with this hard-to-treat disease in which the standard of care is oral and topical corticosteroids and immunosuppressants – treatments that have poor clinical outcomes and safety concerns, respectively, and should be used sparingly in an elderly population. These positive pivotal results for bullous pemphigoid add to an immense body of scientific evidence that underscores the important role IL4 and IL13 play in driving diseases characterized by itch. Combined with the consistent safety profile of the other dermatology indications, these results show the potential of Dupixent to transform the treatment paradigm for bullous pemphigoid."

In the ADEPT study, 106 adults with moderate-to-severe BP were randomized to receive Dupixent 300 mg (n=53) every two weeks after an initial loading dose or placebo (n=53), along with standard-of-care OCS. During treatment, all patients underwent a protocol-defined OCS tapering regimen if control of disease activity was maintained.

For the primary endpoint, 20% of Dupixent patients experienced sustained disease remission at 36 weeks compared to 4% for placebo (p=0.0114). For the components comprising the primary endpoint – with patients having to achieve all components – efficacy among patients receiving Dupixent compared to placebo was as follows*:

- Absence of disease relapse after patient completed OCS taper: 59% vs. 16% (nominal p=0.0023)
- Absence of need for rescue therapy during treatment period: 42% vs. 12% (nominal p=0.0004)
- Achievement of complete remission and off OCS by week 16: 38% vs. 27% (not significant)

*Components were not separately included in pre-specified statistical analyses and are therefore nominal

For selected secondary endpoints, results for Dupixent compared to placebo were statistically significant as follows:

- Patients achieving ≥90% reduction in disease severity: 41% vs. 10% (p=0.0003)

- Patients achieving clinically meaningful itch reduction: 40% vs. 11% (p=0.0006)
- Secondary endpoints assessing decreased OCS use, and time to use of rescue medications, also favored Dupixent and were significant (p=0.0220 and p=0.0016, respectively)
- Reduction in disease severity from baseline: 77% vs. 51% (p=0.0021)
- Reduction in itch from baseline: 52% vs. 27% (p=0.0021)
- Days of complete remission off OCS: 40 vs. 13 (p=0.0072)

In this older population, overall rates of adverse events (AEs) were 96% (n=51) for Dupixent and 96% (n=51) for placebo. AEs more commonly observed with Dupixent compared to placebo in more than 3 patients included peripheral edema (n=8 vs. n=5), arthralgia (n=5 vs. n=3), back pain (n=4 vs. n=2), blurred vision (n=4 vs. n=0), hypertension (n=4 vs. n=3), asthma (n=4 vs. n=1), conjunctivitis (n=4 vs. n=0), constipation (n=4 vs. n=1), upper respiratory tract infection (n=3 vs. n=1), limb injury (n=3 vs. n=2), and insomnia (n=3 vs. n=2). There were no AEs leading to death in the Dupixent group and 2 AEs leading to death in the placebo group.

George D. Yancopoulos, M.D., Ph.D.
Board co-Chair, President, and Chief Scientific Officer at Regeneron
“Bullous pemphigoid is a debilitating skin disease with a high mortality rate due to infection. Dupixent is the first medication to show significant and robust impacts in this patient population. These latest pivotal results reaffirm the underlying role type-2 inflammation plays in driving multiple skin diseases. We look forward to further advancing this research and sharing the positive results from the bullous pemphigoid pivotal trial with regulatory authorities.”

Additionally, a small separate phase 3 study (Study A) evaluating the investigational use of Dupixent in adults with uncontrolled and severe chronic pruritus of unknown origin (CPUO) did not achieve statistical significance in its primary itch responder endpoint (despite favorable numerical improvements), but showed nominally significant improvements in all other itch endpoints including: change from baseline; percent of patients achieving no/mild itch; and change in itch-related quality of life from baseline. Safety results were generally consistent with the known safety profile of Dupixent in its approved dermatological indications. The Dupixent phase 3 study program in CPUO consists of Study A and Study B. Study B is planned to initiate as a subsequent pivotal study.
Detailed efficacy and safety results for both BP and CPUO studies are planned for presentation at a forthcoming medical meeting.

The safety and efficacy of Dupixent in BP and CPUO are currently under clinical investigation and have not been evaluated by any regulatory authority.

About the Dupixent BP pivotal study
ADEPT is a randomized, phase 2/3, double-blind, placebo-controlled study evaluating the efficacy and safety of

Dupixent in 106 adults with moderate-to-severe BP for a 52-week treatment period. After randomization, patients received Dupixent or placebo every two weeks, with OCS treatment. During treatment, OCS taper was initiated after patients experienced two weeks of sustained control of disease activity. OCS tapering could start between four to six weeks after randomization and was continued as long as disease control was maintained, with the intent of completion by 16 weeks. After OCS tapering, patients were only treated with Dupixent or placebo for at least 20 weeks, unless rescue treatment was required.

The primary endpoint evaluated the proportion of patients achieving sustained disease remission at 36 weeks. Sustained disease remission was defined as complete clinical remission with completion of OCS taper by 16 weeks without relapse and no rescue therapy use during the 36-week treatment period. Relapse was defined as appearance of ≥3 new lesions a month or ≥1 large lesion (>10cm in diameter) that did not heal within a week. Rescue therapy could include treatment with high-potency topical corticosteroids, OCS (including increase of OCS dose during the taper or re-initiation of OCS after completion of the OCS taper), systemic non-steroidal immunosuppressive medications, or immunomodulating biologics.

Select secondary endpoints evaluated at 36 weeks included:

- Proportion of patients achieving ≥90% reduction in Bullous Pemphigoid Disease Area Index (BPDAI; scale:0-360)
- Proportion of patients with ≥4-point reduction in Peak Pruritus Numerical Rating Scale (PP-NRS; scale 0-10)
- Total cumulative OCS dose
- Time to first use of rescue medication
- Percent change from baseline in BPDAI
- Percent change in weekly average of daily PP-NRS
- Duration of complete remission while not requiring OCS

About the Dupixent CPUO phase 3 program

The Dupixent phase 3 program in CPUO consists of Study A and Study B. Study A was a randomized, phase 3, double-blind, placebo-controlled study evaluating the efficacy and safety of Dupixent in adults with uncontrolled, severe CPUO. During the 4-week run-in period, patients received a standard-of-care regimen comprised of a non-sedative antihistamine and moisturizer to confirm they were refractory to available options. During the following 24-week treatment period, patients received Dupixent or placebo every two weeks added to the standard-of-care regimen.

The primary endpoint evaluated the proportion of patients with a clinically meaningful improvement in itch from baseline at 24 weeks, measured by a ≥4-point reduction in the worst-itch numerical rating scale (WI-NRS; scale: 0-

10). The key secondary endpoint evaluated the proportion of patients with a ≥4-point reduction in WI-NRS at 12 weeks. Additional secondary endpoints included:

- Proportion of patients achieving no/mild pruritus on Patient Global Impression of Severity (PGIS) of pruritus
- Absolute change and percent change from baseline in the weekly average of daily itch-related sleep disturbances at 24 weeks measured by the sleep disturbance NRS (scale: 0-10)
- Absolute change from baseline in itch-related quality of life measured by the ItchyQoL (scale: 22-110)
- Absolute change from baseline in health-related quality of life at 24 weeks measured by the Dermatology Life Quality Index (scale: 0-30)

Study B is planned to initiate as a subsequent pivotal study.

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 chronic obstructive pulmonary disease in different age populations. More than 1,000,000 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 Regeneron

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents, develops and commercializes life-

transforming medicines for people with serious diseases. Founded and led by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to numerous approved treatments and product candidates in development, most 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, neurological diseases, hematologic conditions, infectious diseases, and rare diseases.

Regeneron pushes the boundaries of scientific discovery and accelerates drug development using our proprietary technologies, such as VelociSuite®, which produces optimized fully human antibodies and new classes of bispecific antibodies. We are shaping the next frontier of medicine with data-powered insights from the Regeneron Genetics Center® and pioneering genetic medicine platforms, enabling us to identify innovative targets and complementary approaches to potentially treat or cure diseases.

For more information, please visit **www.Regeneron.com** or follow Regeneron on **LinkedIn**, **Instagram**, **Facebook** or **X**.

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.
Sanofi is listed on EURONEXT: SAN and NASDAQ: SNY

Sanofi Media Relations
Sandrine Guendoul | + 33 6 25 09 14 25 | **sandrine.guendoul@sanofi.com**
Evan Berland | + 1 215 432 0234 | **evan.berland@sanofi.com**
Victor Rouault | + 33 6 70 93 71 40 | **victor.rouault@sanofi.com**
Timothy Gilbert | + 1 516 521 2929 | **timothy.gilbert@sanofi.com**

Sanofi Investor Relations
Thomas Kudsk Larsen |+ 44 7545 513 693 | **thomas.larsen@sanofi.com**
Alizé Kaisserian | + 33 6 47 04 12 11 | **alize.kaisserian@sanofi.com**
Arnaud Delépine | + 33 6 73 69 36 93 |**arnaud.delepine@sanofi.com**
Felix Lauscher | + 1 908 612 7239 | **felix.lauscher@sanofi.com**
Keita Browne | + 1 781 249 1766 | **keita.browne@sanofi.com**
Nathalie Pham | + 33 7 85 93 30 17 | **nathalie.pham@sanofi.com**
Tarik Elgoutni | + 1 617 710 3587 | **tarik.elgoutni@sanofi.com**

Thibaud Châtelet | + 33 6 80 80 89 90 | **thibaud.chatelet@sanofi.com**

Regeneron Media Relations
Ilana Yellen | +1 914-330-9618| **ilana.yellen@regeneron.com**

Regeneron Investor Relations
Vesna Tosic | + 914-847-5443 | **vesna.tosic@regeneron.com**

Sanofi 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 and their underlying assumptions, statements regarding plans, objectives, intentions, and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. 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, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi’s ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that pandemics or other global crises may 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. 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, 2023. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

All trademarks mentioned in this press release are the property of the Sanofi group apart from VelociSuite and Regeneron Genetics Center.

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 nature, timing, and possible success and therapeutic applications of products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "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 bullous pemphigoid and/or chronic pruritus of unknown origin as discussed in this press release as well as 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 studies discussed or referenced in this press release, on any of the foregoing or any potential regulatory approval of Regeneron's Products (such as Dupixent) 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 (including the studies discussed or referenced in this press release) may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; 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; 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; 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; the impact of public health outbreaks, epidemics, or pandemics (such as the COVID-19 pandemic) on Regeneron's business; 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® (aflibercept) Injection), other litigation and other proceedings and government investigations relating to the Company and/or its operations (including the pending civil proceedings initiated or joined by the U.S. Department of Justice and the U.S. Attorney's Office for the District of Massachusetts), 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, 2023 and its Form 10-Q for the quarterly period ended June 30, 2024. 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 (**https://investor.regeneron.com**) and its LinkedIn page (**https://www.linkedin.com/company/regeneron-pharmaceuticals**).

Attachment

- **Press Release**

Source: Sanofi - Aventis Groupe