



Dupixent® (dupilumab) Showed Positive Topline Results in Two Phase 3 Trials of Patients with Chronic Rhinosinusitis with Nasal Polyps

October 16, 2018 at 12:59 AM EDT

TARRYTOWN, N.Y. and PARIS, Oct. 16, 2018 /PRNewswire/ --

Dupixent significantly reduced nasal polyp size, nasal congestion severity and need for systemic corticosteroids and/or surgery

Dupixent has now demonstrated positive late-stage results in three Type 2 or allergic inflammatory diseases: atopic dermatitis, asthma and chronic rhinosinusitis with nasal polyps

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that both pivotal Phase 3 placebo-controlled trials evaluating Dupixent® (dupilumab) in adults with inadequately-controlled chronic rhinosinusitis with nasal polyps ("CRSwNP"), met all their primary and secondary endpoints.

On the co-primary endpoints for both trials at 24 weeks, patients treated with Dupixent added to a standard-of-care corticosteroid nasal spray experienced a 51% and 57% improvement in their nasal congestion/obstruction severity compared to a 15% and 19% improvement with nasal spray alone ("placebo") (-1.25 and -1.34 for Dupixent compared to -0.38 and -0.45 for placebo, on a 0-3 scale). Dupixent-treated patients had a 27% and 33% reduction in their nasal polyps score compared to a 4% and 7% increase for placebo (-1.71 and -1.89 for Dupixent compared to 0.10 and 0.17 for placebo, on a 0-8 scale that measures bilateral polyps size by endoscopy). Dupixent also met all secondary endpoints in both trials, including demonstrating a significant reduction in the need for systemic corticosteroids or surgery, and improvements in smell and chronic rhinosinusitis symptoms. In a pre-specified group of patients with comorbid asthma, Dupixent significantly improved lung function and asthma control ($p < 0.0001$ for all primary and secondary endpoints in both trials). Dupixent blocks the IL-4 and IL-13 signaling pathways.

"Dupixent has now demonstrated significant late-stage efficacy in three Type 2 or allergic inflammatory diseases, indicating that IL-4 and IL-13 are required drivers of Type 2 or allergic inflammation in general. With these data, Dupixent has now been shown to address this inflammation across the complete airway, which manifests in the upper respiratory tract as polyps and congestion, and in the lower airway as asthma," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "We look forward to U.S. regulatory action on our moderate-to-severe asthma application later this month, and we are continuing our development program in additional Type 2 or allergic inflammatory diseases with high unmet need including pediatric asthma, pediatric and adolescent atopic dermatitis, eosinophilic esophagitis, and food and environmental allergies."

CRSwNP is a chronic disease in which Type 2 or allergic inflammation causes polyps that obstruct the sinus and nasal passages, leading to severe congestion, nasal discharge, facial pain or pressure, and reduced sense of smell and taste. Persistent symptoms of CRSwNP have a substantial adverse impact on patients' health-related quality of life. Current treatments are limited and include intranasal corticosteroids, oral corticosteroids and surgery, with high recurrence rates after treatment. Among the patients involved in the two Phase 3 Dupixent trials, more than half had previously undergone surgery for their nasal polyps and nearly three-quarters had used systemic corticosteroids within the past two years.

"Living with inadequately controlled nasal polyps carries a heavy burden with patients experiencing pain, nasal discharge, difficulty breathing and the inability to smell. The standard of care, which includes the use of oral and intranasal corticosteroids, often alongside surgery, has not changed for decades," said John Reed, M.D., Executive Vice President, Global Head of Research & Development at Sanofi. "For the first time, we have Phase 3 data showing that a biologic can help address the underlying Type 2 or allergic inflammation that causes chronic rhinosinusitis with nasal polyps and we look forward to working with regulatory authorities around the world to make Dupixent an option for people living with this chronic condition."

The rates of adverse events were generally similar across Dupixent and placebo, and no new or unexpected side effects related to Dupixent were observed. The rates of conjunctivitis were: 1.4% Dupixent versus 0.8% placebo in SINUS-24; 2.7% Dupixent every two weeks and 2.0% Dupixent every two/four weeks versus 1.3% placebo in SINUS-52. Overall rates of serious adverse events were lower with Dupixent: 4.2% Dupixent versus 14.4% placebo in SINUS-24; 5.4% Dupixent every two weeks and 6.8% Dupixent every two/four weeks versus 10.0% placebo in SINUS-52.

The pivotal Phase 3 trials, known as SINUS-24 (n=276) and SINUS-52 (n=448), had the same co-primary endpoints, which were change from baseline in nasal congestion/ obstruction severity based on the patient's daily morning assessment, and change from baseline in nasal polyposis score (a measure of polyp size) after 24 weeks, as assessed by nasal endoscopy. An additional co-primary endpoint in Japan and a key secondary endpoint in other countries was change from baseline in sinus opacification, as assessed by computed tomography scan. The trials were randomized double-blind, placebo-controlled trials evaluating Dupixent

when added to the corticosteroid mometasone furoate nasal spray (MFNS), compared to MFNS alone. The trials enrolled patients who were 18 years or older with bilateral nasal polyps who, despite treatment with systemic corticosteroids in the previous two years or history of surgery, continued to have ongoing moderate or severe symptoms of nasal congestion, blockage, loss of smell or nasal discharge. Consistent with the overlap seen among patients with Type 2 or allergic inflammatory diseases, more than three-quarters also suffered from other conditions, including asthma (approximately 59 percent), allergic rhinitis (approximately 58 percent) and NSAID-exacerbated respiratory disease (approximately 28 percent). Patients with co-morbid asthma and CRSwNP tend to have more severe disease.

Detailed results from these trials will be submitted for presentation at future medical meetings and will form part of the companies' regulatory submissions. The safety and efficacy of Dupixent in CRSwNP is investigational and has not been evaluated by any regulatory authority.

Dupilumab Development Program

In addition to its approved indication in adults with uncontrolled moderate-to-severe atopic dermatitis, Regeneron and Sanofi are also studying dupilumab in a broad range of clinical development programs for diseases driven by allergic or Type 2 inflammation, including asthma (under regulatory review), pediatric asthma (Phase 3), pediatric atopic dermatitis (Phase 3), adolescent atopic dermatitis (Phase 3), eosinophilic esophagitis (Phase 3), grass allergy (Phase 2) and peanut allergy (Phase 2). A future trial is planned for chronic obstructive pulmonary disease. Dupixent is also being studied in combination with REGN-3500, which targets IL-33. These potential uses are investigational and the safety and efficacy have not been evaluated by any regulatory authority. Dupilumab was discovered using Regeneron's proprietary *VelocImmune*[®] technology that yields optimized fully human antibodies, and is being jointly developed by Regeneron and Sanofi under a global collaboration agreement.

For more information on dupilumab clinical trials please visit www.clinicaltrials.gov.

INDICATION

In the U.S., Dupixent is used to treat adult patients with moderate-to-severe atopic dermatitis (eczema) 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.

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
- have asthma
- are scheduled to receive any vaccinations. You should not receive a "live vaccine" if you are treated with Dupixent.
- are pregnant or plan to become pregnant. It is not known whether Dupixent will harm your unborn baby.
- 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. If you have asthma and are taking asthma medicines, do not change or stop your asthma medicine without talking to your healthcare provider.

Dupixent can cause serious side effects, including:

- **Allergic reactions.** Stop using Dupixent and go to the nearest hospital emergency room if you get any of the following symptoms: fever, general ill feeling, swollen lymph nodes, hives, itching, joint pain, or skin rash.
- **Eye problems.** Tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision.

The most common side effects include injection site reactions, eye and eyelid inflammation, including redness, swelling and itching, and cold sores in your mouth or on your lips.

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 may report side effects to FDA at 1-800-FDA-1088.

Use Dupixent exactly as prescribed. If your healthcare provider decides that you or a caregiver can give Dupixent injections, you or your caregiver should receive training on the right way to prepare and inject Dupixent. **Do not** try to inject Dupixent until you have been shown the right way by your healthcare provider.

Please click [here](#) for the full Prescribing Information. The patient information is available [here](#).

About Regeneron

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science

into medicine has led to seven FDA-approved treatments and numerous product candidates in development, 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, neuromuscular diseases, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*[®] technologies, such as *VelocImmune*[®] which produces optimized fully-human antibodies, and ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

Sanofi, Empowering Life

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 Regeneron's products, product candidates, and research and clinical programs now underway or planned, including without limitation Dupixent[®] (dupilumab) Injection; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products, such as dupilumab for the treatment of inadequately-controlled chronic rhinosinusitis with nasal polyps, pediatric and adolescent atopic dermatitis, asthma, pediatric asthma, eosinophilic esophagitis, grass allergy, food allergy (including peanut), chronic obstructive pulmonary disease, and other potential indications; unforeseen safety issues resulting from the administration of products and product candidates (such as dupilumab) in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates in clinical trials; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in other studies and lead to therapeutic applications; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as Dupixent), research and clinical programs, and business, including those relating to patient privacy; 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 product candidates, including without limitation dupilumab; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's products and product candidates; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties to perform filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's products and product candidates; the availability and extent of reimbursement of the Company's products (such as Dupixent) 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; 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 or collaboration agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), to be cancelled or terminated without any further product success; and risks associated with intellectual property of other parties and pending or future litigation relating thereto, including without limitation the patent litigation proceedings relating to EYLEA[®] (afibercept) Injection, Dupixent, and Praluent[®] (alirocumab) Injection, the ultimate outcome of any such litigation proceedings, 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-Q for the quarterly period ended June 30, 2018. 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 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 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 absence of guarantee that the product will 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 conditions, as well as those risks 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, 2017. 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

Hala Mirza

Tel.: +1 914-847-3422

Hala.Mirza@regeneron.com

Investor Relations

Manisha Narasimhan, Ph.D.

Tel: 1 (914) 847-5126

Manisha.Narasimhan@regeneron.com

Sanofi Contacts:

Media Relations

Ashleigh Koss

Tel: +1 (908) 981-8745


Ashleigh.Koss@sanofi.com

Investor Relations

George Grofik

Tel: +33 (0)1 53 77 45 45

ir@sanofi.com

 View original content: <http://www.prnewswire.com/news-releases/dupixent-dupilumab-showed-positive-topline-results-in-two-phase-3-trials-of-patients-with-chronic-rhinosinusitis-with-nasal-polyps-300731373.html>

SOURCE Regeneron Pharmaceuticals, Inc.