



Phase 3 Trial of Libtayo® (cemiplimab) as Monotherapy for First-Line Advanced Non-small Cell Lung Cancer Stopped Early Due to Highly Significant Improvement in Overall Survival

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Libtayo decreased the risk of death by 32.4% compared to chemotherapy

Regeneron and Sanofi plan regulatory submissions in 2020

[Regeneron Pharmaceuticals, Inc.](#) (NASDAQ: **REGN**) and Sanofi today announced the primary endpoint of overall survival (OS) was met in a Phase 3 trial comparing the PD-1 inhibitor Libtayo® (cemiplimab) to platinum-doublet chemotherapy in patients with first-line locally advanced or metastatic non-small cell lung cancer (NSCLC) that tested positive for PD-L1 in ≥50% of tumor cells. Based on a recommendation by the Independent Data Monitoring Committee to stop the trial early, the trial will be modified to allow all patients to receive Libtayo for this investigational use. The data will form the basis of regulatory submissions in the U.S. and European Union (EU) in 2020.

"While demonstrating a survival benefit in first-line NSCLC has been challenging for immunotherapies, the one FDA-approved anti-PD-1 monotherapy has changed the therapeutic paradigm," said George D. Yancopoulos, M.D., Ph.D., Co-Founder, President and Chief Scientific Officer of Regeneron. "We are pleased with the results of this trial that demonstrate the survival benefit of Libtayo in these patients and hope it may become a potential alternative for physicians and patients."

A protocol-specified interim analysis conducted by the Independent Data Monitoring Committee demonstrated that patients treated with Libtayo monotherapy had a significant increase in OS. Libtayo decreased the risk of death by 32.4% (HR=0.676; CI:0.525-0.870, p=0.002), compared to platinum-doublet chemotherapy, despite a third of patients entering the trial within the past six months and all chemotherapy patients being able to crossover to Libtayo if their disease progressed. No new Libtayo safety signal was identified. Detailed trial data will be presented at a future medical meeting.

"This is the largest clinical trial evaluating a PD-1 inhibitor as a first-line monotherapy in patients with advanced non-small cell lung cancer with high PD-L1 expression. These positive results are extremely encouraging, and we look forward to advancing a potential new treatment option for these patients," said John Reed, M.D., Ph.D., Global Head of Research and Development at Sanofi. "We are grateful to all of the investigators and patients who participated in the global trial."

Lung cancer is the leading cause of cancer death worldwide. In 2020, more than 2.2 million new cases are expected to be diagnosed globally, with 228,800 new cases in the U.S. alone. Approximately 85% of all lung cancers are NSCLC, with an estimated 25% to 30% of cases expected to test positive for PD-L1 in ≥50% of tumor cells. While immunotherapies have transformed advanced NSCLC treatment in recent years, there remains an unmet need to optimize the identification and treatment of patients with high PD-L1 expression.

Libtayo is being jointly developed and commercialized by Regeneron and Sanofi under a global collaboration agreement. Libtayo was invented using Regeneron's proprietary *VelocImmune*® technology that utilizes a proprietary genetically-engineered mouse platform endowed with a genetically-humanized immune system to produce optimized fully-human antibodies. *VelocImmune* technology has been used to create multiple antibodies including Dupixent® (dupilumab), Praluent® (alirocumab) and Kevzara® (sarilumab), which are approved in multiple countries around the world. Regeneron previously used these technologies to rapidly develop a treatment for Ebola virus infection, which is currently under review by the FDA, and is now being used in efforts to create preventative and therapeutic medicines for COVID-19.

The use of Libtayo to treat advanced NSCLC is investigational and has not been fully evaluated by any regulatory authority.

About the Phase 3 Trial

The open-label, randomized, multi-center Phase 3 trial investigated the first-line treatment of Libtayo monotherapy compared to platinum-doublet chemotherapy in squamous or non-squamous advanced NSCLC that tested positive for PD-L1 in ≥50% of tumor cells. The trial included 712 patients (of whom 710 were included in the interim analysis) with locally advanced NSCLC (Stage IIIB/C), who were not candidates for surgical resection or definitive chemoradiation or had progressed after treatment with definitive chemoradiation, or previously untreated metastatic NSCLC (Stage IV). The trial offers the largest data set from a pivotal trial currently available for this patient population.

Patients were randomized 1:1 to receive either Libtayo 350 mg administered intravenously every three weeks for up to 108 weeks, or an investigator-selected, platinum-doublet chemotherapy regimen for four to six cycles (with or without maintenance pemetrexed chemotherapy). The primary endpoints are OS and progression-free survival (PFS), and secondary endpoints include overall response rate, duration of response and quality of life.

The trial was designed to reflect current and emerging treatment paradigms. Inclusion criteria allowed patients with NSCLC that had: controlled hepatitis B, hepatitis C or HIV; pre-treated and stable brain metastases; and/or locally advanced disease that had progressed on definitive chemoradiation. Patients whose disease progressed in the trial were able to change their therapy: those in the chemotherapy arm were allowed to crossover into the Libtayo arm, while those in the Libtayo arm were allowed to combine Libtayo treatment with four to six cycles of chemotherapy.

A separate Phase 3 trial evaluating a first-line combination of Libtayo and chemotherapy in patients with advanced NSCLC irrespective of PD-L1 expression is also underway and expected to be fully enrolled in 2020.

About Libtayo

Libtayo is a fully-human monoclonal antibody targeting the immune checkpoint receptor PD-1 on T-cells. By binding to PD-1, Libtayo has been shown to block cancer cells from using the PD-1 pathway to suppress T-cell activation.

Libtayo is approved in the U.S., EU, and other countries for adults with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. In the U.S., the generic name for Libtayo in its approved indication is cemiplimab-rwlc, with rwlc as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the U.S. Food and Drug Administration.

The extensive clinical program for Libtayo is focused on difficult-to-treat cancers. In skin cancer, this includes a potentially registrational Phase 2 trial in basal cell carcinoma and additional trials in adjuvant and neoadjuvant CSCC. Libtayo is also being investigated in a potentially registrational Phase 3 trial in cervical cancer, as well as in trials combining Libtayo with novel therapeutic approaches for both solid tumors and blood cancers. These potential uses are investigational, and their safety and efficacy have not been evaluated by any regulatory authority.

IMPORTANT SAFETY INFORMATION AND INDICATION FOR U.S. PATIENTS

What is Libtayo?

Libtayo is a prescription medicine used to treat people with a type of skin cancer called cutaneous squamous cell carcinoma (CSCC) that has spread or cannot be cured by surgery or radiation.

It is not known if Libtayo is safe and effective in children.

What is the most important information I should know about Libtayo?

Libtayo is a medicine that may treat a type of skin cancer by working with your immune system. Libtayo can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse:

- **Lung problems (pneumonitis).** Signs and symptoms of pneumonitis may include new or worsening cough, shortness of breath, and chest pain.
- **Intestinal problems (colitis) that can lead to tears or holes in your intestine.** Signs and symptoms of colitis may include diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, sticky or that have blood or mucus; and severe stomach-area (abdomen) pain or tenderness.
- **Liver problems (hepatitis).** Signs and symptoms of hepatitis may include yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual.
- **Hormone gland problems** (especially the adrenal glands, pituitary, thyroid and pancreas). Signs and symptoms that your hormone glands are not working properly may include headaches that will not go away or unusual headaches, rapid heartbeat, increased sweating, extreme tiredness, weight gain or weight loss, dizziness or fainting, feeling more hungry or thirsty than usual, hair loss, feeling cold, constipation, deeper voice, very low blood pressure, urinating more often than usual, nausea or vomiting, stomach-area (abdomen) pain, and changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.
- **Kidney problems**, including nephritis and kidney failure. Signs of these problems may include decrease in your amount of urine, blood in your urine, swelling in your ankles, and loss of appetite.
- **Skin problems.** Signs of these problems may include rash, itching, skin blistering, and painful sores or ulcers in the mouth, nose, throat, or genital area.
- **Problems in other organs.** Signs of these problems may include headache, tiredness or weakness, sleepiness, changes in heartbeat (such as beating fast, seeming to skip a beat, or a pounding sensation), confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, seizures (encephalitis), swollen lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis), seeing or hearing things that are not there (hallucinations), severe muscle weakness, low red blood cells (anemia), bruises on the skin or bleeding, and changes in eyesight.
- **Rejection of a transplanted organ.** Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.
- **Infusion (IV) reactions that can sometimes be severe and life-threatening.** Signs of these problems may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, fever, feeling of passing out, back or neck pain, and facial swelling.

Getting medical treatment right away may help keep these problems from becoming more serious.

Your healthcare provider will check you for these problems during your treatment with Libtayo.

Your healthcare provider may treat you with corticosteroid or hormone replacement medicines.

Your healthcare provider may delay or completely stop treatment if you have severe side effects.

Before you receive Libtayo, tell your healthcare provider about all your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus;
- have had an organ transplant;

- have lung or breathing problems;
- have liver or kidney problems;
- have diabetes;
- are pregnant or plan to become pregnant; Libtayo can harm your unborn baby.

Females who are able to become pregnant:

- Your healthcare provider will give you a pregnancy test before you start treatment.
- You should use an effective method of birth control during your treatment and for at least 4 months after your last dose of Libtayo. Talk with your healthcare provider about birth control methods that you can use during this time.
- Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with Libtayo.
- are breastfeeding or plan to breastfeed. It is not known if Libtayo passes into your breast milk. Do not breastfeed during treatment and for at least 4 months after the last dose of Libtayo.

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

The most common side effects of Libtayo include tiredness, rash, and diarrhea. These are not all the possible side effects of Libtayo. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Regeneron Pharmaceuticals and Sanofi at 1-877-542-8296.

For more information, please see [full Prescribing Information](#), including Medication Guide.

About Regeneron Pharmaceuticals, Inc.

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for over 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, pain, 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 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 impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, suppliers, and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs (including those discussed in this press release), Regeneron's ability to manage its supply chain, net product sales of products marketed by Regeneron and/or its collaborators (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and Regeneron's product candidates and research and clinical programs now underway or planned, including without limitation Libtayo[®] (cemiplimab) as a monotherapy and combination therapy in patients with first-line locally advanced or metastatic non-small cell lung cancer ("NSCLC") and as a monotherapy or in combination with conventional treatments or other investigational agents (as applicable) for the treatment of basal cell carcinoma, adjuvant and neoadjuvant cutaneous squamous cell carcinomas, cervical cancer, blood cancers, and other potential indications; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators may be replicated in other studies and lead to therapeutic applications; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates and new indications for Regeneron's Products, including without limitation any possible regulatory approval of Libtayo (as a monotherapy or in combination with conventional treatments or other investigational agents, as applicable) for the treatment of NSCLC, basal cell carcinoma, adjuvant and neoadjuvant cutaneous squamous cell carcinomas, cervical cancer, blood cancers, and other potential indications; unforeseen safety issues resulting from the administration of Regeneron's Products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates (such as Libtayo) in clinical trials (including those referenced in this press release); 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; ongoing regulatory obligations and oversight impacting Regeneron's Products (such as Libtayo), research and clinical programs, and business, including those relating to patient privacy; 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 availability and extent of reimbursement of Regeneron's Products (such as Libtayo) 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 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 (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and 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 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 and other related proceedings relating to Dupixent® (dupilumab) and Praluent® (alirocumab)), 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, 2019. 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 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 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, 2019. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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