



Regeneron Provides Updates on Phase 3 Libtayo® (cemiplimab) Development Program in Advanced Non-small Cell Lung Cancer

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TARRYTOWN, N.Y., Nov. 5, 2019 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today provided an update on the ongoing Phase 3 development program evaluating Libtayo® (cemiplimab), a PD-1 inhibitor, as monotherapy and combination therapy in first-line patients with advanced non-small cell lung cancer (NSCLC). Regeneron is currently recruiting patients in two Phase 3 trials in first-line NSCLC.

The first trial, an open-label randomized trial that compares Libtayo monotherapy to standard-of-care platinum-based chemotherapy in patients with high PD-L1 expression (tumor proportion score [TPS] $\geq 50\%$):

- The trial has enrolled 90% of the 700 planned patients and is expected to be fully enrolled by year's end.
- The independent data monitoring committee recently conducted an interim analysis for overall survival (OS) based on approximately 34% of anticipated events and recommended the trial should continue as planned. The next event-driven interim analysis for OS is anticipated in 2020.
- In the first 361 randomized patients (minimum 6 months of follow-up), the confirmed objective response rate (ORR), as determined by investigators, is currently 42% for Libtayo patients and 22% for patients treated with chemotherapy.

The second trial, which consists of two parts, evaluates Libtayo in combination with platinum-based chemotherapy:

- Part 1 is fully enrolled (n=323), and evaluates patients with PD-L1 expression of $<50\%$ in three treatment groups: chemotherapy, chemotherapy with Libtayo, and chemotherapy in combination with Libtayo and ipilimumab.
- Part 2, a randomized, double-blind, placebo-controlled Phase 3 trial (n=450), has enrolled approximately 20% of patients, and is expected to complete enrollment in the second half of 2020. The trial evaluates patients with all PD-L1 expression levels in two treatment groups: chemotherapy alone or chemotherapy in combination with Libtayo.

Libtayo is being jointly developed by Regeneron and Sanofi under a global collaboration agreement. Libtayo is a PD-1 inhibitor that was invented by Regeneron using the company's proprietary *VelocImmune*® technology, which uses a genetically-humanized mouse to produce optimized fully-human antibodies.

About the Phase 3 Libtayo NSCLC Trials

The primary endpoints of the randomized, open-label Phase 3 monotherapy trial are OS and progression-free survival (PFS). Patients receive either Libtayo 350 mg every 3 weeks or investigator's choice of a standard-of-care platinum-based doublet chemotherapy regimen (with or without maintenance therapy). Patients in the trial have stage IIIB, IIIC or stage IV squamous or non-squamous NSCLC, are not candidates for definitive chemotherapy and radiation, have not received prior systemic treatment for their advanced disease, and have high PD-L1 expression (TPS $\geq 50\%$). As part of a separate internal research effort assessing the effect of baseline patient variables, an unintended aggregation of open-label ORR data by treatment group occurred for the first 361 enrolled patients. In NSCLC, regulatory authorities do not consider ORR a validated surrogate endpoint.

In the Phase 3 combination trial, the Part 1 primary endpoint is ORR and the Part 2 primary endpoints are OS and PFS. Patients in the Libtayo treatment groups receive 350 mg every 3 weeks. Trial patients have either stage IIIB or IIIC squamous or non-squamous NSCLC and are not candidates for treatment with definitive concurrent chemoradiation, or have stage IV disease and have not received prior systemic treatment for recurrent or metastatic NSCLC.

About Libtayo

Libtayo is a fully-human monoclonal antibody targeting the immune checkpoint receptor PD-1 (programmed cell death protein-1). It is approved in the U.S., European Union, Canada and Brazil for adult patients 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 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.

In addition to NSCLC, Libtayo is also being investigated in potential registrational trials in basal cell carcinoma and cervical cancer, along with additional trials in squamous cell carcinoma of the head and neck, melanoma, colorectal cancer, prostate cancer, multiple myeloma, Hodgkin lymphoma and non-Hodgkin lymphoma. These trials are designed to investigate Libtayo as monotherapy; in combination with conventional treatments like chemotherapy; or in combination with other investigational agents, including vaccines, oncolytic viruses and bispecific antibodies, among others. 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 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.

Please see accompanying [full Prescribing Information](#), including Medication Guide.

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.

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 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.

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 Libtayo® (cemiplimab) as a monotherapy and combination therapy in first-line patients with advanced non-small cell lung cancer ("NSCLC") and as a monotherapy or in combination with conventional treatments or other investigational agents for the treatment of basal cell carcinoma, cervical cancer, squamous cell carcinoma of the head and neck, melanoma, colorectal cancer, prostate cancer, multiple myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, and other potential indications; the likelihood and timing of achieving any of Regeneron's anticipated clinical development milestones; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates (such as Libtayo) in clinical trials (including the clinical trials referenced in this press release); the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed 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, cervical cancer, squamous cell carcinoma of the head and neck, melanoma, colorectal cancer, prostate cancer, multiple myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, and other potential indications; 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 Libtayo), 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; 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; 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; the availability and extent of reimbursement of the Company'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; 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), the ultimate outcome of any such 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-K for the fiscal year ended December 31, 2018 and its Form 10-Q for the quarterly period ended September 30, 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, 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>).

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