# Libtayo® (cemiplimab) in Combination with Chemotherapy Approved by European Commission for the First-line Treatment of Advanced PD-L1 Positive Non-small Cell Lung Cancer (NSCLC)

March 29, 2023

**Libtayo-based combination demonstrated superior survival outcomes compared to chemotherapy alone in Phase 3 trial designed to include patients with varied disease presentations seen in everyday clinical practice**

**Approval marks second first-line indication in NSCLC and fifth indication for Libtayo in the European Union (EU)**

TARRYTOWN, N.Y., March 29, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that the European Commission (EC) approved Libtayo® (cemiplimab) in combination with platinum-based chemotherapy for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with ≥1% PD-L1 expression. This includes patients that have no EGFR, ALK or ROS1 aberrations and whose tumors are metastatic or locally advanced and not candidates for definitive chemoradiation.

"Today's approval considerably expands the number of people in Europe with advanced non-small cell lung cancer who are eligible for Libtayo-based first-line treatment, including those with PD-L1 expression ranges most commonly seen in real-world practice," said Israel Lowy, M.D., Ph.D., Senior Vice President, Translational and Clinical Sciences, Oncology at Regeneron. "We are proud that Libtayo continues to distinguish itself among PD-1 pathway blockers, as just one of two PD-1 inhibitors to be approved for use across squamous and non-squamous forms of advanced NSCLC in both combination and monotherapy settings. This marks the fifth approval for Libtayo in Europe."

Lung cancer is the leading cause of cancer death worldwide. In recent years, more than 2.2 million annual new cases have been diagnosed globally. Approximately 80-85% of all lung cancers are NSCLC, with 75% of these cases diagnosed in advanced stages.

"The Phase 3 EMPOWER-Lung 3 trial showed significant improvements across primary and key secondary endpoints, including overall survival in the cemiplimab plus chemotherapy arm," said Prof. Martin Reck, Head of Department of Thoracic Oncology, Lung Clinic Grosshansdorf, Germany. "As a treating physician of this patient population, I welcome a new treatment option for patients in Europe, as we continue to strive for better outcomes for patients with advanced non-small cell lung cancer."

"With lung cancer being the leading cause of cancer mortality globally, ongoing research is imperative to find more treatment options for people impacted by this disease," said Anne-Marie Baird, Ph.D., President, Lung Cancer Europe. "This approval highlights continued progress in first-line treatment options for people impacted by advanced lung cancer in Europe."

Libtayo is currently approved in the EU and other countries for the treatment of certain patients with advanced basal cell carcinoma (BCC), advanced cutaneous squamous cell carcinoma (CSCC), advanced NSCLC and advanced cervical cancer. The Libtayo combination was also approved by the U.S. Food and Drug Administration (FDA) for advanced NSCLC regardless of PD-L1 expression in November 2022.

**About the Phase 3 Trial**
The EC approval is based on data from the global Phase 3 EMPOWER-Lung 3 trial, a randomized, multicenter trial investigating a first-line combination treatment of Libtayo and platinum-doublet chemotherapy (Libtayo combination), compared to platinum-doublet chemotherapy alone. The trial enrolled 466 patients with locally advanced or metastatic NSCLC, as well as squamous or non-squamous histologies across all PD-L1 expression levels and with no EGFR, ALK or ROS1 aberrations. Notably, the trial was designed to closely resemble a patient population with varied disease presentations seen in everyday clinical practice. Among those enrolled, 43% had tumors with squamous histology, 15% had locally advanced disease and 7% had a history of brain metastases.

Patients were randomized 2:1 to receive either Libtayo 350 mg (n=312) or placebo (n=154) administered intravenously every 3 weeks for 108 weeks, plus platinum-doublet chemotherapy administered every 3 weeks for 4 cycles. The trial was stopped early based on a recommendation by the Independent Data Monitoring Committee after the Libtayo combination demonstrated a significant improvement in overall survival (OS). Results of the trial at the primary analysis were published in *Nature Medicine* in August 2022.

At the primary analysis (median follow-up: 16 months), the trial showed a statistically significant improvement in the primary endpoint of OS for patients treated with the Libtayo combination compared to chemotherapy alone in the overall population (hazard ratio [HR]: 0.71; 95% confidence interval [CI]: 0.53 to 0.93). Among the 70% of patients in the trial expressing PD-L1 ≥1% (n=327), efficacy results for the Libtayo combination arm (n=217) compared to chemotherapy alone (n=110) showed a:

- 22-month median OS versus 13 months, representing a 45% relative reduction in the risk of death (HR: 0.55; 95% CI: 0.39 to 0.78).
- 9-month median progression-free survival (PFS) versus 6 months (HR: 0.48; 95% CI: 0.36 to 0.63)
- 48% objective response rate (ORR) versus 23%
- 16-month median duration of response (DOR; range: 2 to 19+) versus 5 months (range: 2 to 19+)

At the time of the pre-specified final analysis (median follow up: 28 months), patients with PD-L1 expression ≥1% treated with the Libtayo combination continued to show clinically meaningful survival and PFS benefits compared to chemotherapy alone.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue during or after treatment with Libtayo. Among patients treated with the Libtayo combination evaluated for safety in the trial (n=312), adverse reactions occurring in at least 10% included

anemia (44%), alopecia (37%), musculoskeletal pain (27%), nausea (25%), fatigue (23%), peripheral neuropathy (21%), hyperglycemia (18%), decreased appetite (17%), alanine aminotransferase increased (16%), aspartate aminotransferase increased (15%), neutropenia (15%), constipation (14%), dyspnoea (13%), rash (13%), thrombocytopenia (13%), vomiting (12%), diarrhea (11%), insomnia (11%), weight decreased (11%) and hypoalbuminemia (10%). Adverse reactions were serious in 25% of patients and led to permanent discontinuation of the Libtayo combination in 5% of patients.

In December 2022, Libtayo in combination with chemotherapy was added to the European Society for Medical Oncology (ESMO) Magnitude of Clinical Benefit Scale (score: 4 out of 5), for patients with advanced NSCLC across squamous and non-squamous histologies, and irrespective of PD-1 expression levels.

**About Regeneron in Oncology**
At Regeneron, we're applying more than three decades of scientific innovation with the goal of developing paradigm-changing therapies for patients with cancer. Our oncology portfolio is built around two foundational approaches – our approved PD-1 inhibitor Libtayo and investigational bispecific antibodies – which are being evaluated both as monotherapies and in combination with emerging therapeutic modalities. Together, they provide us with unique combinatorial flexibility to develop potentially synergistic treatments for a wide range of solid tumors and blood cancers.

If you are interested in learning more about our clinical trials, please contact us (clinicaltrials@regeneron.com or 844-734-6643) or visit our clinical trials website.

**About Libtayo**
Libtayo is a fully human monoclonal antibody targeting the immune checkpoint receptor PD-1 on T cells and was invented using Regeneron's proprietary *VelocImmune*® technology. By binding to PD-1, Libtayo has been shown to block cancer cells from using the PD-1 pathway to suppress T-cell activation. In the U.S. and other countries, Libtayo is indicated in certain patients with advanced BCC, advanced CSCC and advanced NSCLC, as well as in advanced cervical cancer in the EU, Canada and Brazil. As of July 1, 2022, Regeneron is responsible for the development and marketing of Libtayo globally. In the EU, Libtayo is currently marketed by Sanofi on Regeneron's behalf over the course of a defined transition period.

In the U.S., the generic name for Libtayo in its approved indications is cemiplimab-rwlc, with rwlc as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the FDA. Outside of the U.S. the generic name of Libtayo in its approved indications is cemiplimab.

The extensive clinical program for Libtayo is focused on difficult-to-treat cancers. Libtayo is currently being investigated in trials as a monotherapy, as well as in combination with either conventional or novel therapeutic approaches for other solid tumors and blood cancers. These potential uses are investigational, and their safety and efficacy have not been evaluated by any regulatory authority.

**U.S. FDA-approved Indications**
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.
- People with a type of skin cancer called basal cell carcinoma (BCC):
  - That cannot be removed by surgery (locally advanced BCC) and have received treatment with a hedgehog pathway inhibitor (HHI), or cannot receive treatment with an HHI.
  - That has spread (metastatic BCC) and have received treatment with an HHI, or cannot receive treatment with an HHI. This use is approved based on how many patients responded to treatment and how long they responded. Studies are ongoing to provide additional information about clinical benefit.
- Adults with a type of lung cancer called NSCLC:
  - Libtayo may be used in combination with chemotherapy that contains a platinum medicine as your first treatment when your lung cancer has not spread outside your chest (locally advanced lung cancer) and you cannot have surgery or chemotherapy with radiation, OR your lung cancer has spread to other areas of your body (metastatic lung cancer), AND your tumor does not have an abnormal "EGFR", "ALK" or "ROS1" gene.
  - Libtayo may be used alone as your first treatment when your lung cancer has not spread outside your chest (locally advanced lung cancer) and you cannot have surgery or chemotherapy with radiation, OR your lung cancer has spread to other areas of your body (metastatic lung cancer), AND your tumor tests positive for high "PD-L1", AND your tumor does not have an abnormal "EGFR", "ALK "or "ROS1" gene.

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

**IMPORTANT SAFETY INFORMATION FOR U.S. PATIENTS**

**What is the most important information I should know about Libtayo?**
Libtayo is a medicine that may treat certain cancers 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. You can have more than one of these problems at the same time. 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 new or worsening signs or symptoms, including:**

- **Lung problems:** cough, shortness of breath, or chest pain
- **Intestinal problems:** diarrhea (loose stools) or more frequent bowel movements than usual, stools that are black, tarry, sticky or have blood or mucus, or severe stomach-area (abdomen) pain or tenderness

- **Liver problems:** yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), dark urine (tea colored), or bleeding or bruising more easily than normal
- **Hormone gland problems:** headache that will not go away or unusual headaches, eye sensitivity to light, eye problems, rapid heartbeat, increased sweating, extreme tiredness, weight gain or weight loss, feeling more hungry or thirsty than usual, urinating more often than usual, hair loss, feeling cold, constipation, your voice gets deeper, dizziness or fainting, or changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness
- **Kidney problems:** decrease in your amount of urine, blood in your urine, swelling of your ankles, or loss of appetite
- **Skin problems:** rash, itching, skin blistering or peeling, painful sores or ulcers in mouth or nose, throat, or genital area, fever or flu-like symptoms, or swollen lymph nodes
- **Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with Libtayo. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:** chest pain, irregular heartbeat, shortness of breath or swelling of ankles, confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs, double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight, persistent or severe muscle pain or weakness, muscle cramps, low red blood cells, or bruising
- **Infusion reactions that can sometimes be severe.** Signs and symptoms of infusion reactions may include: nausea, chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, feel like passing out, fever, back or neck pain, or facial swelling
- **Rejection of a transplanted organ.** Your healthcare provider should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had
- **Complications, including graft-versus-host disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with Libtayo. Your healthcare provider will monitor you for these complications

**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 also need to delay or completely stop treatment with Libtayo 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 received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- 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 when used alone include muscle or bone pain, tiredness, rash, and diarrhea. The most common side effects of Libtayo when used in combination with platinum-containing chemotherapy include hair loss, muscle or bone pain, nausea, tiredness, numbness, pain, tingling, or burning in your hands or feet, and decreased appetite. 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 at 1-877-542-8296.

**Please see full Prescribing Information, including Medication Guide.**

**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 a substantial proportion of all original, FDA-approved or authorized fully human monoclonal antibodies. This includes REGEN-COV® (casirivimab and imdevimab), Dupixent® (dupilumab), Libtayo®, Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza®

(evinacumab-dgnb) and Inmazeb® (atoltivimab, maftivimab and odesivimab-ebgn).

**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 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.

**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 Libtayo® (cemiplimab) in combination with platinum-based chemotherapy for the first-line treatment of adult patients with advanced non-small cell lung cancer; 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; 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 Libtayo (as a monotherapy or in combination with conventional or novel therapeutic approaches, as applicable) for other solid tumors and blood cancers as well as Regeneron's investigational bispecific antibodies referenced in this press release; safety issues resulting from the administration of Regeneron's Products (such as Libtayo) 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 (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, 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 (including those discussed or referenced in this press release) may be replicated in other studies and/or lead to advancement of product candidates to clinical trials or therapeutic applications; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; 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; 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 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® (aflibercept) Injection, Praluent® (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, 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).*

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