Regeneron to Highlight Progress Across Its Differentiated Oncology Portfolio and Pipeline at WCLC and ESMO

September 9, 2024 at 7:00 AM EDT

At WCLC, five-year survival data to be presented on Libtayo (PD-1 inhibitor) first-line monotherapy in advanced non-small cell lung cancer

At ESMO, longer-term results with investigational fianlimab (LAG-3 inhibitor) plus Libtayo from initial trial in advanced melanoma show high clinical activity, including deepening responses, per blinded independent central review

Regeneron to host virtual investor event to discuss results alongside updates across its oncology portfolio on Monday, September 16 at 8:30 a.m. ET

TARRYTOWN, N.Y., Sept. 09, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the presentation of data from its oncology portfolio at the IASLC 2024 World Conference on Lung Cancer (WCLC) hosted by the International Association for the Study of Lung Cancer (September 7-10) and the European Society for Medical Oncology (ESMO) Annual Meeting (September 13-17). A combined 11 presentations across both congresses highlight Regeneron's commitment to transforming care for people living with difficult-to-treat cancers, including advanced melanoma, advanced non-melanoma skin cancer, and different types of lung cancer.

"The breadth of our presentations at ESMO and WCLC underscore our progress in advancing treatment approaches for cancer that have the potential to be among the best in their class," said Israel Lowy, MD, PhD, Clinical Development Unit Head, Oncology, at Regeneron. "At WCLC, five-year outcomes for Libtayo monotherapy in advanced NSCLC reinforce its position as the anti-PD-1 backbone of our oncology portfolio. At ESMO, the latest two-year data for our LAG-3 inhibitor fianlimab combined with Libtayo show persistent and high clinical activity in advanced melanoma patients. As our portfolio and pipeline mature, the insights from these data are helping us advance our differentiated and novel combination approaches – all with the goal of transforming care for those living with cancer."

Notably, at ESMO, Regeneron will present new, two-year results evaluating the investigational combination of LAG-3 inhibitor fianlimab and Libtayo® (cemiplimab) in adults with advanced melanoma across three independent expansion cohorts of a first-in-human, multi-cohort trial. The combination is being further studied in an ongoing, randomized, placebo-controlled, blinded Phase 3 trial of fianlimab and Libtayo versus pembrolizumab in previously untreated unresectable locally advanced or metastatic melanoma. Additional trials are underway in the adjuvant and perioperative settings, as well as against other first-line, standard-of-care LAG3 and PD-1 combinations.

The longer-term analysis of 98 patients from the initial trial builds on results presented at ASCO 2023, with data assessed per blinded independent central review presented for the first time. With a median follow-up of 23 months and median treatment duration of 35 weeks, the results show persistent and deepening tumor responses across all three independent cohorts. Results were as follows:

- In MM1, the initial cohort (n=40), there was a 23% complete response (CR) rate and a 60% objective response rate (ORR).
- In MM2, the confirmatory cohort (n=40), there was a 25% CR rate and a 63% ORR.
- In MM3, the cohort of patients with prior neoadjuvant or adjuvant systemic therapy (n=18; including 13 patients who had progressed despite prior anti-PD-1 treatments, and thus might be expected to have lower response rates to the combination), there was a 28% CR rate and a 39% ORR.
- In a post-hoc analysis of the three cohorts combined, there was a 25% CR rate (24 of 98 patients) and a 57% ORR (56 of 98 patients).

Initial progression-free survival (PFS) and overall survival (OS) assessments from this single arm trial, which support the ongoing Phase 3 trial designed to evaluate these survival endpoints for the Libtayo and fianlimab combination, were as follows:

- PFS for the MM1, MM2, and MM3 cohorts, respectively: Not reached (95% CI: 8 months to not evaluable [NE]), 19 months (95% CI: 8 months to NE), and 12 months (95% CI: 1 month to NE).
- In a post-hoc analysis of the three cohorts combined, median PFS was 24 months (85% CI: 12 months to NE) and median OS was not reached (95% CI: 42 months to NE). Median OS was also not reached for any individual cohort.

Additional analyses on difficult-to-treat subgroups, including patients who had received prior adjuvant anti-PD-1 therapy, will be presented.

The safety profile of the fianlimab and Libtayo combination was generally consistent with the safety profile of Libtayo monotherapy and other anti-PD-(L)1 agents, except for higher rates of treatment-related adrenal insufficiency (12% of patients; 5% were ≥Grade 3). Adverse events (AEs) of any grade occurred in 95% of patients. Grade 3 or greater AEs, serious AEs, and immune-mediated AEs (IMAEs) occurred in 47%, 36%, and 13% of patients, respectively. AEs leading to death occurred in seven patients; two were considered treatment related.

An overview of all data presentations at both congresses is summarized below:

Regeneron presentations at WCLC:

Medicine	Abstract title	Abstract	Presenter	Presentation date/time (all PDT)
Libtayo	Cemiplimab monotherapy for first line advanced NSCLC patients with PD-L1 expression ≥50%: 5-year outcomes of EMPOWER-Lung 1	**#OA11.06** Oral Session: Shifting the Bar in the Front Line Immunotherapy Setting	Ana Baramidze	Monday, September 9 2:32 p.m. – 2:42 p.m.
	Prognostic utility of peripheral myeloid cells for clinical outcomes in patients with NSCLC treated with cemiplimab	# P2.11A.26 Poster Presentation Session: Metastatic Non-small Cell Lung Cancer —Immunotherapy —Immunobiology	Rolando J. Acosta	Sunday, September 8 6:15 p.m. – 7:45 p.m
	Real-world comparative effectiveness in advanced NSCLC and high PD-L1 with 1L immune checkpoint inhibitors ± chemotherapy	#EP.11A.08 e-Poster Presentation	Melinda L. Hsu	N/A
Fianlimab	Fianlimab-based combination therapies in patients with advanced non-small cell lung cancer: Trials in progress updates	# P4.11D.09 Poster Presentation Session: Metastatic Non-small Cell Lung Cancer —Immunotherapy—Clinica Trials in Progress	Ana Baramidze	Monday, September 9 6:30 p.m. – 8:00 p.m.
	Phase 2 peri-operative study of fianlimab + cemiplimab + chemotherapy vs cemiplimab + chemotherapy in resectable early-stage NSCLC	#P4.07D.03 Poster Presentation Session: Early-Stage Non-small Cell Lung Cancer —Clinical Trials in Progress	Luis Paz-Ares	Monday, September 9 6:30 p.m. – 8:00 p.m.
REGN7075, Libtayo	A Phase 1/2 Study of REGN7075 (EGFR×CD28) Combined with Cemiplimab (anti–PD-1) in NSCLC: Trial in Progress Update	#P4.11D.04 Poster Presentation Session: Metastatic Non-Small Cell Lung Cancer —Immunotherapy—Clinica Trials in Progress	Melissa Johnson	Monday, September 9 6:30 p.m. – 8:00 p.m.

Regeneron presentations at ESMO:

Medicine	Abstract title	Abstract	Presenter	Presentation date/time (all CDT)
Skin Cancer				
Libtayo	Neoadjuvant Cemiplimab for Stage II–IV Cutaneous Squamous Cell Carcinoma (CSCC): 2-year Follow-up and Biomarker Analyses	#1091 Poster Session	Danny Rischin	Saturday, September 14 9:00 a.m. – 5:00 p.m.
Fianlimab	Long-term follow-up of advanced melanoma (unresectable/metastatic - aMel) patients (pts) treated with fianlimab (FIAN) + cemiplimab (CEMI): Results from blinded	#1097 Poster Session	Meredith McKean	Saturday, September 14 9:00 a.m. – 5:00 p.m.

	independent central review (BICR) efficacy assessment			
Lung Cancer				
Libtayo	Efficacy of Cemiplimab as Monotherapy or in Combination with Chemotherapy in Japanese Patients with Advanced Non-Small Cell Lung Cancer (aNSCLC)	#1384PPoster Session	Yuki Sato	Saturday, September 14 9:00 a.m. – 5:00 p.m.
	Risk model for overall survival (OS) based on composite patient-reported outcomes (PROs) in aNSCLC patients treated with first-line (1L) cemiplimab-based therapy	#1853P Poster Session	David Gandara	Sunday, September 15 9:00 a.m. – 5:00 p.m.
METxMET	MET×MET bispecific antibody davutamig (REGN5093) for MET-altered advanced non-small cell lung cancer (aNSCLC): Update from a first-in-human (FIH) study	#1302P Poster Session	Byoung Chul Cho	Saturday, September 14 9:00 a.m. – 5:00 p.m.

The potential uses of Libtayo in neoadjuvant CSCC, fianlimab and Libtayo, davutamig, and REGN7075 described above are investigational, and their safety and efficacy have not been fully evaluated by any regulatory authority. Fianlimab, davutamig, and REGN7075 are not currently approved for use in any indication.

About Regeneron in Cancer
We aspire to turn revolutionary discoveries into medicines that can transform the lives of those impacted by cancer. Our team around the world is driven to solve the needs and challenges of those affected by one of the most serious diseases of our time.

Backed by our legacy of scientific innovation and a deep understanding of biology, genetics and the immune system, we're pursuing potential therapies across more than 30 types of solid tumors and blood cancers. Our cancer strategy is powered by cutting-edge technologies and therapies that can be flexibly combined to investigate potentially transformative treatments for patients. Oncology assets in clinical development comprise nearly half of Regeneron's pipeline, and include checkpoint inhibitors, bispecific antibodies and costimulatory bispecific antibodies. Our approved PD-1 inhibitor Libtayo serves as the backbone of many of our investigational combinations.

To complement our extensive in-house capabilities, we collaborate with patients, healthcare providers, governments, biopharma companies and each other to further our shared goals. Together, we are united in the mission to serve as a beacon of transformation in cancer care.

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 basal cell carcinoma (BCC), advanced cutaneous squamous cell carcinoma (CSCC) and advanced NSCLC, as well as in advanced cervical cancer in the European Union, Canada and Brazil. As of July 1, 2022, Libtayo is developed and marketed globally by Regeneron.

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 U.S. Food and Drug Administration (FDA). Outside of the U.S., the generic name of Libtayo in its approved indication 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) when your BCC cannot be removed by surgery (locally advanced BCC) or when it has spread (metastatic BCC) and have received treatment with a hedgehog pathway inhibitor (HHI), or cannot receive treatment with a HHI.

- Adults with a type of lung cancer called non-small cell lung cancer (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 or life-threatening.** Signs and symptoms of infusion reactions may include: nausea, vomiting, 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
- 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

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 to 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

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 tiredness, muscle or bone pain, rash, diarrhea, and low levels of red blood cells (anemia). 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 spend 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), Inmazeb® (atoltivimab, maftivimab and odesivimab-ebgn) and Veopoz® (pozelimab-bbfg).

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, Regeneron's unique ability to repeatedly and consistently translate science into medicine has led to numerous FDA-approved treatments and product candidates in development, almost all of which were homegrown in Regeneron's laboratories. Regeneron's medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, hematologic conditions, infectious diseases, and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its 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 Regeneron, please visit www.regeneron.com or follow Regeneron on LinkedIn.

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 Libtayo® (cemiplimab), fianlimab in combination with Libtayo, REGN7075 in combination with Libtayo, davutamig (REGN5093), and the other programs discussed or referenced in this press release; 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 fianlimab in combination with Libtayo in advanced melanoma, REGN7075 in combination with Libtayo in non-small cell lung cancer ("NSCLC") , davutamig (REGN5093) in MET-altered advanced NSCLC, and the other programs discussed or referenced in this press release; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products (such as Libtayo for the treatment of advanced NSCLC) and Regeneron's Product Candidates (such as those referenced above) 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 and Regeneron's 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; 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 Libtayo) and Regeneron's Product Candidates (such as those referenced above) 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; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; 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).

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