Promising Anti-tumor Activity of Novel Costimulatory Bispecific Antibody REGN7075 (EGFRxCD28) in Combination with Libtayo® (cemiplimab) to be Reported at ASCO

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Oral presentation to highlight activity of REGN7075 in combination with Libtayo from dose-escalation portion of trial in patients with microsatellite stable colorectal cancer, which has historically proven unresponsive to immunotherapy

Ongoing REGN7075 Phase 1/2 trial is investigating a potentially first-in-class combination across a range of advanced solid tumors

TARRYTOWN, N.Y., May 23, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive new results from an ongoing Phase 1/2 trial evaluating its first-in-class costimulatory bispecific antibody, REGN7075 (EGFRxCD28), in combination with Libtayo® (cemiplimab) in patients with advanced solid tumors. Data from the dose-escalation portion of the trial showed the investigational combination led to anti-tumor responses in patients with microsatellite stable colorectal cancer (MSS CRC). REGN7075 is one of the first immunotherapies to demonstrate clinical activity in MSS CRC, including in a patient with liver metastases. The results will be shared during an oral session at the American Society of Clinical Oncology (ASCO) 2024 Annual Meeting in Chicago.

“Microsatellite stable colorectal cancer has historically been unresponsive to immunotherapy,” said Neil H. Segal, M.D., Ph.D., Medical Oncologist and Research Director in the Division of Gastrointestinal Oncology at Memorial Sloan Kettering Cancer Center, and a trial investigator. “The early results for this novel investigational EGFRxCD28 costimulatory bispecific in combination with Libtayo are encouraging, showing anti-tumor responses in a highly difficult-to-treat cancer. This combination is one of the first immunotherapy regimens to show clinical activity in microsatellite stable colorectal cancer, and we are excited to advance this trial in additional tumor types.”

In the dose-escalation portion of the trial, patients with metastatic and locally advanced solid tumors – who had exhausted standard treatment options, and most of whom also had liver metastases – received combination therapy with REGN7075 and Libtayo, following a REGN7075 monotherapy lead-in dose. Among 94 patients treated as of data cutoff, 65% (n=61) had MSS CRC, of which 51 MSS CRC patients were treated at an active dose level. Efficacy results among these 51 patients were as follows:

- 6% (n=3) overall response rate (ORR) and 29% (n=15) disease control rate (DCR). This included one complete response (CR), two partial responses (PR), and 12 patients with stable disease. At data cutoff, all responders were without liver metastases.
- Among the subset of 15 patients without liver metastases, there was a 20% ORR (n=3) and 80% DCR (n=12).
- Among the subset of 36 patients with liver metastases, three patients had stable disease as of data cutoff, and one patient achieved a PR following data cutoff.

Safety was assessed in 84 patients across multiple solid tumor types at a variety of doses of REGN7075. REGN7075 and Libtayo showed an acceptable safety profile, and the maximum tolerated dose was not reached. Treatment-emergent adverse events (TEAEs) of any grade occurred in 98% of patients; Grade 3 and 4 TEAEs occurred in 35% of patients. Treatment-related adverse events (TRAEs) occurred in 90% of patients, with 7% of cases reported as grade 3 or 4. The majority of TRAEs were Grade 1 to 2 (83%), with the most common being infusion-related reactions (58%) that were manageable with premedication and dosing adjustments. TRAEs led to discontinuation in 5% of patients, and three patients discontinued treatment due to Grade 2 infusion-related reactions. As of data cutoff, there have been no dose-limiting toxicities, no reports of cytokine release syndrome, and no treatment-related deaths.

“Regeneron is focused on developing a unique investigational portfolio of oncology medicines including checkpoint inhibitors, CD3 bispecifics and CD28 costimulatory bispecifics. Over the past several years, we have made progress in our programs across checkpoint inhibitors and the CD3 class and are now showing promising activity with two costimulatory bispecific antibodies,” said Israel Lowy, M.D., Ph.D., Senior Vice President, Translational and Clinical Oncology at Regeneron. “Our costimulatory bispecifics were designed with the goal of turning cancer cells into antigen presenting cells, thereby converting historically immunotherapy unresponsive tumors from ‘cold’ to ‘hot’. These early data speak to the potential of REGN7075 in combination with Libtayo and add to a growing body of evidence supporting novel costimulatory bispecifics that are in clinical trials for a range of solid tumors and blood cancers.”

The combination of REGN7075 and Libtayo is currently under clinical development, and its safety and efficacy have not been fully evaluated by any regulatory authority. While the dose escalation portion of the trial across multiple solid tumor types including

non-small cell lung cancer, colorectal cancer, head and neck cancer and other tumor types is ongoing, expansion cohorts in several tumor types have also been initiated.

About the Phase 1/2 Trial
The Phase 1/2, first-in-human, open-label trial investigating REGN7075 in combination with Libtayo is currently enrolling patients with metastatic and locally advanced solid tumors who have exhausted standard treatment options. The trial includes an ongoing Phase 1 dose-escalation portion and a Phase 2 dose-expansion period. In the Phase 1 dose-escalation portion, patients first receive a weekly lead-in dose of REGN7075 monotherapy for three weeks to assess its safety and efficacy alone. This is followed by treatment with combination therapy, with Libtayo dosed once every three weeks and REGN7075 dosed either every week or every three weeks. The primary endpoints are assessing safety and tolerability, while the secondary endpoints are assessing efficacy, pharmacokinetics and immunogenicity. Expansion cohorts in several tumor types have been initiated. For more information, visit the Regeneron clinical trials website, or contact via clinicaltrials@regeneron.com or 844-734-6643.

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 non-small cell lung cancer (NSCLC), as well as in advanced cervical cancer in the European Union, Canada and Brazil. 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 (NASDAQ: REGN) is a leading biotechnology company that invents, develops and commercializes life-transforming medicines for people with serious diseases. Founded and led by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to numerous approved treatments and product candidates in development, most 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, neurological diseases, hematologic conditions, infectious diseases, and rare diseases.

Regeneron pushes the boundaries of scientific discovery and accelerates drug development using our proprietary technologies, such as *VelociSuite*®, which produces optimized fully human antibodies and new classes of bispecific antibodies. We are shaping the next frontier of medicine with data-powered insights from the Regeneron Genetics Center® and pioneering genetic medicine platforms, enabling us to identify innovative targets and complementary approaches to potentially treat or cure diseases. For more information, please visit www.Regeneron.com or follow Regeneron on LinkedIn, Instagram, Facebook or X.

Dr. Segal has financial interests related to Regeneron Pharmaceuticals.

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 REGN7075 in combination with Libtayo® (cemiplimab) and other of Regeneron's Product Candidates 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 REGN7075 in combination with Libtayo in patients with advanced solid tumors and the other clinical programs discussed or referenced in the press release; 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 or any potential regulatory approval of Regeneron's Products and Regeneron's Product Candidates (such as REGN7075 in combination with Libtayo); 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 and Regeneron's Product Candidates (such as REGN7075 in combination with Libtayo) 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 March 31, 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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