REGENERON

Novel Regeneron Bispecific Antibodies Show Encouraging Anti-tumor Activity in Two Advanced Solid Tumors

September 10, 2022

First-in-class Phase 1 data presented at ESMO for ubamatamab (REGN4018; MUC16xCD3) in recurrent ovarian cancer and REGN5093 (METxMET) in MET-altered advanced non-small cell lung cancer

TARRYTOWN, N.Y., Sept. 10, 2022 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive early data for two novel and investigational bispecific antibodies – ubamatamab (REGN4018; MUC16xCD3) in recurrent ovarian cancer and REGN5093 (METxMET) in MET-altered advanced non-small cell lung cancer (NSCLC). The initial safety and efficacy results are from the dose-escalation portions of two Phase 1/2 trials and are being presented at the European Society for Medical Oncology (ESMO) Congress 2022 in Paris.

"Bispecific antibodies are an important component of our oncology pipeline because of their flexibility to potentially address a variety of cancers," said Israel Lowy, M.D., Ph.D., Senior Vice President, Translational and Clinical Sciences, Oncology at Regeneron. "At ESMO, we're showcasing this flexibility with ubamatamab and REGN5093, two novel bispecific antibodies that are initially being investigated as monotherapies for recurrent ovarian cancer and MET-altered advanced lung cancer, respectively. They were among the first in our pipeline to progress into clinical trials for solid tumors, and we're encouraged to see both showing anti-tumor activity in dose escalation. These first-in-class results give us confidence in our *VelociBi*® bispecific development platform, and we look forward to investigating ubamatamab and REGN5093 further."

As shared in a mini-oral at ESMO, ubamatamab is a CD3-targeting bispecific under investigation for recurrent ovarian cancer and designed to bridge MUC16 on cancer cells with CD3-expressing T cells to facilitate local T-cell activation. Dose-escalation results were presented for 78 patients with recurrent ovarian cancer who had received a median of 4.5 prior treatments, including platinum-based chemotherapy and a median duration of exposure to ubamatamab was 12 weeks (range: <1 to 145 weeks).Within 42 patients who received ≥1 full doses of ≥20 mg ubamatamab, a 14% (6 of 42 patients) overall response rate (ORR) was achieved across dose levels. The ORR increased to 21% (6 of 29 patients) in those without visceral metastases (exploratory subset) and 31% (4 of 13 patients) in those with high MUC16-expressing tumors (preliminary exploratory subset). Across dose levels, the disease control rate was 57% (24 of 42 patients), and the median duration of response was 12 months per Kaplan-Meier estimates (range: 4 to ≥24 months).

Safety was assessed in 78 ubamatamab-treated patients, with the most common adverse events (AEs) in ≥15% being cytokine release syndrome (74%, all ≤grade 2), pain (87%) and anemia (51%). AEs that were ≥grade 3 occurred in 65% of patients with those in >5% including anemia (24%), pain (23%) and neutropenia (8%). There was one instance of a dose-limiting toxicity (neutropenia) and three deaths due to AEs, none of which were considered related to treatment by sponsor assessment. Based on these efficacy and safety data, the Phase 2 portion of the trial is enrolling patients with platinum-resistant ovarian cancer to further investigate ubamatamab as a monotherapy and in combination with Regeneron's PD-1 inhibitor Libtayo® (cemiplimab).

Preliminary first-in-human results for REGN5093 were also published in an ESMO scientific abstract, with updated data and additional response rates to be detailed in a poster session on Monday, September 12. REGN5093 is a tumor-targeting bispecific designed to bind to the MET receptor in two places and trigger rapid internalization of this complex into cancer cells to degrade the MET receptor and block its ability to support cell proliferation. As highlighted in the abstract, among 36 patients with MET-altered advanced NSCLC who received the highest dose tested to date, 6 experienced a partial response with 5 of these responses occurring in patients who had received prior anti-PD-1 treatment. Total exposure to treatment was approximately 467 patient-weeks.

AEs that were ≥grade 3 occurred in 25% (n=11) of REGN5093-treated patients, with pneumonia and pulmonary embolism each occurring in 2 patients. One patient discontinued treatment due to increased alanine aminotransferase and aspartate aminotransferase. No dose-limiting toxicities or treatment-related deaths have been observed as of data cutoff. These early efficacy and safety data support further dose expansions, and a separate Phase 1/2 trial is ongoing to investigate an antibody-drug conjugate format of REGN5093 (REGN5093-M114).

The potential uses of ubamatamab, Libtayo, REGN5093 and REGN5093-M114 described above are investigational, and their safety and efficacy have not been evaluated by any regulatory authority.

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 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 approximately one in five of all original, FDA-approved or authorized fully human monoclonal antibodies. This

includes REGEN-COV® (casirivimab and imdevimab), Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza® (evinacumab-dgnb) and Inmazeb™ (atoltivimab, maftivimab and odesivimab-ebgn).

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 for nearly 35 years by physician-scientists, our 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 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 additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

Regeneron Forward-Looking Statements and Use of Digital Media

This press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, 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 ubamatamab (a MUC16xCD3 bispecific antibody), REGN5093 (a METxMET bispecific antibody), and Regeneron's other investigational bispecific antibodies discussed or referenced in this press release (as monotherapy or in combination with Libtayo® (cemiplimab), as applicable); 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; 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 ubamatamab for the treatment of recurrent ovarian cancer and REGN5093 for the treatment of MET-altered advanced non-small cell lung cancer; safety issues resulting from the administration of Regeneron's Products (such as Libtayo) and Regeneron's Product Candidates (such as ubamatamab, REGN5093, and Regeneron's other investigational bispecific antibodies discussed or referenced in this press release) 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, Bayer, and Teva Pharmaceutical Industries Ltd. (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, Dupixent® (dupilumab), and Praluent® (alirocumab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2021 and its Form 10-Q for the quarterly period ended June 30, 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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