Linvoseltamab (BCMAxCD3) Initial Pivotal Phase 2 Data Show Clinically Meaningful Responses in Patients with Heavily Pre-treated Multiple Myeloma

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As presented at ASH, recommended 200 mg dose of linvoseltamab demonstrated a 64% response rate, with 45% achieving a very good partial response or better; responses may further improve with longer follow-up

Trial enrolled patients with particularly high disease burden, with 37% having bone marrow plasma cells ≥50% and the median soluble BCMA being 0.43 mg/L

Data represent initial efficacy results from first 58 patients in ongoing Phase 2 trial, which is now fully enrolled at the recommended dose

TARRYTOWN, N.Y., Dec. 12, 2022 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive initial data from a pivotal Phase 2 expansion cohort evaluating investigational linvoseltamab (formerly REGN5458) at the 200 mg dose recommended for further development in patients with heavily pre-treated, relapsed/refractory (R/R) multiple myeloma. The results were part of a broader presentation of new and updated data from a Phase 1/2 trial and were shared at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition in New Orleans, LA. Linvoseltamab is an investigational bispecific antibody designed to bridge B-cell maturation antigen (BCMA) on multiple myeloma cells with CD3-expressing T cells to facilitate local T-cell activation and cancer-cell killing.

"The need for innovative medicines is critical for patients with multiple myeloma who inevitably face a downward spiral of relapses, reduced responses to subsequent therapies, and increasingly shorter remissions," said Naresh Bumma, M.D., Hematologist and Assistant Professor in the Division of Hematology at Ohio State University, and a trial investigator. "At the recommended 200 mg dose in a pivotal Phase 2 trial, linvoseltamab demonstrated early, deep and durable responses in patients living with multiple myeloma who had been on at least three prior therapies, including those with higher risk and high disease burden. These clinically meaningful outcomes at 12 weeks reinforce the positive linvoseltamab results seen in the Phase 1 dose escalation portion, and we look forward to seeing data from more patients and longer follow-up."

As presented at ASH, out of 252 patients treated in the Phase 1/2 trial, 81% of patients were triple-refractory to existing therapeutic options, including an immunomodulatory drug, a proteasome inhibitor and an anti-CD38 antibody. Additionally, 37% had bone marrow plasma cells ≥50%, and the median soluble BCMA was 0.43 mg/L, representing a patient population with a higher disease burden than those enrolled in similar trials. Of the 87 patients in the 200 mg cohort, 58 were evaluated for efficacy. With a median follow-up of 3 months (range: 0 to 30 months), efficacy results were as follows:

- **64% objective response rate (ORR)**, with 45% achieving a very good partial response or better, as determined by an independent review committee. Based on earlier results, responses may increase with longer follow-up.
- **Median time to response was <1 month** (range: <1 to 5 months).
- **79% probability of maintaining a response at 6 months** (95% confidence interval: 50% to 92%), per Kaplan-Meier estimates.

Among the 87 patients treated in the 200 mg cohort assessed for safety, adverse events (AEs) occurred in 95% of patients, with 66% being ≥Grade 3. The most common AEs occurring in ≥20% of patients were cytokine release syndrome (CRS; 37%), fatigue (32%), anemia (28%), diarrhea, cough, headache (23% each) and neutropenia (20%). Discontinuations due to an AE occurred in 6% of patients. When CRS occurred, in 32 out of 87 patients, 23 of those patients experienced Grade 1, 8 experienced Grade 2, there was 1 transient Grade 3 case, and none were ≥Grade 4.

Among the overall patient population across different dose levels (n=252), the median time to first CRS onset was 11 hours (range: 0-47 hours) and all cases resolved, with a median time to resolution of 15 hours (range: 0-377 hours). Deaths due to AEs in the overall population were reported in 14 patients, including sepsis/bacterial infection (n=6), COVID-19 (n=4) or other causes (n=4). None of the deaths were considered related to treatment per the treating physician.

Linvoseltamab is currently under clinical development and its safety and efficacy have not been fully evaluated by any regulatory authority.

Investor Webcast Information
Regeneron will host a conference call and simultaneous webcast to share updates on the company's hematology portfolio on Wednesday, December 14 at 8:30 AM ET. A link to the webcast may be accessed from the 'Investors and Media' page of Regeneron's website at http://investor.regeneron.com/events.cfm. To participate via telephone, please register in advance at this link. Upon registration, all telephone participants will receive a confirmation email detailing how to join the conference call,

including the dial-in number along with a unique passcode and registrant ID that can be used to access the call. A replay of the conference call and webcast will be archived on the company's website for at least 30 days.

About the Phase 1/2 Trial
The ongoing, open-label, multicenter Phase 1/2 dose-escalation and dose-expansion trial is investigating linvoseltamab in patients with R/R multiple myeloma. Among the 252 patients enrolled, all have received at least three prior lines of therapy or are double refractory. Patients were administered linvoseltamab via a step-up dosing strategy designed to mitigate CRS.

The Phase 1 dose-escalation portion of the trial, which is now complete, primarily assessed safety, tolerability and dose-limiting toxicities of linvoseltamab and was comprised of 9 dose-levels. The fully-enrolled Phase 2 dose expansion portion of the trial is further assessing the safety and anti-tumor activity of linvoseltamab, with a primary objective of ORR. Key secondary objectives include duration of response, progression free survival, rate of minimal residual disease negative status and overall survival.

About Multiple Myeloma
Multiple myeloma is the second most common blood cancer with approximately 34,470 and 176,404 new diagnoses in the U.S. and the world, respectively, in 2022. It is characterized by the proliferation of cancerous plasma cells (multiple myeloma cells) that crowd out healthy blood cells in the bone marrow, infiltrate other tissues and cause potentially life-threatening organ injury. Multiple myeloma is not curable despite treatment advances, and while current treatments are able to slow the progression of the cancer, most patients will ultimately experience cancer progression and require additional therapies. In addition, patients are at increased risk of frequent infections, bone problems, reduced kidney function and anemia.

About Regeneron in Hematology
At Regeneron, we're applying more than three decades of biology expertise with our proprietary *VelociSuite*® technologies to develop medicines for patients with diverse blood cancers and rare blood disorders.

Our blood cancer research is focused on bispecific antibodies that are being investigated both as monotherapies and in combination with each other and emerging therapeutic modalities. Together, they provide us with unique combinatorial flexibility to develop customized and potentially synergistic cancer treatments.

Our research and collaborations to develop potential treatments for rare blood disorders include explorations in antibody medicine, gene editing and gene-knockout technologies, as well as investigational RNA-approaches focused on depleting abnormal proteins or blocking disease-causing cellular signaling.

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
Regeneron 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 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 linvoseltamab (a BCMAxCD3 bispecific antibody); 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

linvoseltamab); 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 linvoseltamab for the treatment of patients with heavily pre-treated, relapsed/refractory multiple myeloma; safety issues resulting from the administration of Regeneron's Products and Regeneron's Product Candidates (such as linvoseltamab) 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 (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, 2021 and its Form 10-Q for the quarterly period ended September 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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Note: An update has been made to the subhead to match the information contained in the body of the release on December 21.