REGENERON

Updated Linvoseltamab Data Showcase Continued Deepening of Responses in Patients with Heavily Pre-Treated Multiple Myeloma

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At 14-months median follow-up in the pivotal trial, 50% of patients achieved a complete response or better and a 71% overall response rate, as presented in an EHA oral presentation and simultaneously published in the *Journal of Clinical Oncology*

Also presented at EHA, a retrospective study of patient outcomes that compared investigational linvoseltamab to real-world standard-of-care treatment in clinical practice

TARRYTOWN, N.Y., June 16, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that 14-month median follow-up data from the pivotal Phase 1/2 LINKER-MM1 trial of linvoseltamab in patients with relapsed/refractory (R/R) multiple myeloma (MM) were shared during an oral presentation at the European Hematology Association (EHA) Congress 2024 and published in the *Journal of Clinical Oncology*. These longer-term results show a deepening of responses following the 11-month median follow-up data presented at the American Association for Cancer Research Annual Meeting in April. 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 T-cell activation and cancer-cell killing.

“Previous results from LINKER-MM1 have demonstrated that linvoseltamab has compelling efficacy characterized by deep and durable responses. With 14-months of median follow-up, 50% of patients achieved a complete response or better, despite their cancer being refractory to or relapsing on standard therapies,” said Suzanne Lentzsch, MD, PhD, Director of the Multiple Myeloma and Amyloidosis Program at Columbia University. “Additionally, a study using US-based electronic health record data to indirectly compare linvoseltamab to real-world standard-of-care treatment also support the overall body of evidence for this investigational medicine in heavily pretreated multiple myeloma. Collectively, these presentations underscore the exciting potential of linvoseltamab as we await decisions from regulatory authorities.”

The 14-month median follow-up LINKER-MM1 data for linvoseltamab among patients treated at the 200 mg dose (N=117) reinforce the durability and increasing depth of response shown in previous data cuts. Per the presentation and publication, results showed:

- **71% objective response rate (ORR)**, **with 50% of patients achieving a complete response (CR) or better** and 63% achieving a very good partial response (VGPR) or better, as determined by an independent review committee.
- **Median duration of response (DoR) of 29 months for all responders, while median DoR was not reached for those who achieved a CR or better**. In analyses that were not pre-specified, there was an 81% and 95% estimated probability of maintaining a response at 12 months after achieving a partial response or better among all patients and those who achieved a CR or better, respectively.
- **Median progression-free survival (PFS) was not reached**. There was a 70% estimated probability of being progression free at 12 months among all patients; the estimated probability was 96% among those who achieved a CR or better, per an analysis that was not pre-specified.
- **Median overall survival (OS) of 31 months** for all patients (95% CI: 22 months to NE). In analyses that were not pre-specified, the median OS was not reached for patients who achieved a CR or better, and there was a 75% and 100% estimated probability of survival at 12 months among all patients and those who achieved a CR or better, respectively.
- **High rates of CRs or better in prespecified subgroups,** including 55% (17 of 31 patients) among those aged 75 years or older, 48% (22 of 46 patients) among those with high cytogenetic risk, 45% (9 of 20 patients) among Black or African American patients, and 28% (10 of 36 patients) among those with plasmacytomas (including extramedullary and paramedullary).

Safety data at the 14-month median follow-up was generally consistent with those at the 11-month median follow-up. Cytokine release syndrome (CRS) was the most commonly occurring treatment-emergent adverse event (TEAE) and was observed in 46% of patients; 35% were Grade 1, 10% were Grade 2 and one case (1%) was Grade 3. Adjudicated immune effector cell-associated neurotoxicity syndrome (ICANS) events of any grade occurred in 8% of patients, including three cases that were Grade 3 and no cases that were ≥Grade 4. Infections occurred in 74% of patients – including 36% that were Grade 3 or 4 – and decreased in frequency and severity after 6 months. The most common Grade 3 or 4 TEAEs (≥20%) were neutropenia (42%) and anemia (31%). Six deaths considered due to TEAEs by investigators occurred on treatment or within 30 days of the last treatment dose; five were due to infection, and one was due to renal failure.

Also shared at EHA was a retrospective study comparing outcomes of linvoseltamab 200 mg Phase 2 patients (N=105) in LINKER-MM1 at 14-months of median follow-up to those of real-world external control patients (N=101) who received standard-of-care (SOC) treatment in clinical practice (approximately 80 varied regimens). Patients receiving SOC treatment also met similar inclusion/exclusion criteria to the LINKER-MM1 trial. Comparing linvoseltamab to SOC treatment, the ORR was 70% versus 32% (odds ratio [OR] 5.4), median PFS was 20 months versus 3 months (hazard ratio [HR]: 0.23), and median OS was not reached versus 12 months (HR: 0.40).

In the U.S., linvoseltamab has been granted Fast Track Designation and was accepted for Priority Review for the treatment of R/R MM by the U.S. Food and Drug Administration with a target action date of August 22, 2024. Linvoseltamab is also under review for R/R MM by the European Medicines Association.

The Phase 3 confirmatory trial (LINKER-MM3) for linvoseltamab in patients with R/R MM is ongoing. Linvoseltamab is currently under clinical development, and its safety and efficacy have not been fully evaluated by any regulatory authority.

About Multiple Myeloma
As the second most common blood cancer, there are over 176,000 new cases of MM diagnosed globally, and 35,000 cases are diagnosed in the U.S. every year. In the U.S., there are approximately 8,000 people who have MM that has progressed after three lines of therapy, and 4,000 whose disease has progressed after four or more therapies. The disease is characterized by the proliferation of cancerous plasma cells (MM cells) that crowd out healthy blood cells in the bone marrow, infiltrate other tissues and cause potentially life-threatening organ injury. Despite treatment advances, MM is not curable and while current treatments are able to slow progression of the cancer, most patients will ultimately experience cancer progression and require additional therapies.

About the Linvoseltamab Phase 1/2 Trial and Clinical Development Program
The ongoing, open-label, multicenter Phase 1/2 dose-escalation and dose-expansion LINKER-MM1 trial is investigating linvoseltamab in 282 enrolled patients with relapsed/refractory MM. The Phase 1 dose-escalation portion of the trial – which is now complete – primarily assessed safety, tolerability and dose-limiting toxicities across nine dose levels of linvoseltamab and explored different administration regimens. The ongoing Phase 2 dose expansion portion is assessing the safety and anti-tumor activity of linvoseltamab, with the primary endpoint of ORR. Key secondary endpoints include DoR, PFS, rate of minimum residual disease (MRD) negative status and OS.

Eligibility in the Phase 2 portion requires patients to have received at least three prior lines of therapy or have triple-class refractory MM. Linvoseltamab is administered with an initial step-up dosing regimen followed by the full 200 mg dose administered weekly. At week 16, all patients transition to every two-week dosing. A response-adapted regimen further enables patients to shift to every four-week dosing if they achieve a VGPR or better and have completed at least 24 weeks of therapy. The regimen requires a total of two 24-hour hospitalizations for safety monitoring.

The broader linvoseltamab clinical development program includes additional trials in earlier lines of therapy and stages of disease that are planned or underway. They include a Phase 1/2 trial in first-line MM, a Phase 2 trial in high-risk smoldering MM, and a Phase 2 trial in monoclonal gammopathy of undetermined significance. A Phase 1 trial of linvoseltamab in combination with a Regeneron CD38xCD28 costimulatory bispecific in MM is also planned. For more information, visit the Regeneron clinical trials website, or contact via clinicaltrials@regeneron.com or 844-734-6643.

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 various combinations 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, and investigational RNA-approaches focused on depleting abnormal proteins or blocking disease-causing cellular signaling.

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.

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 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 any potential regulatory approval of linvoseltamab for the treatment of relapsed/refractory multiple myeloma ("R/R MM") by the U.S. Food and Drug Administration (the "FDA") (including the timing of enrollment of patients in the Phase 3 confirmatory trial for linvoseltamab in patients with R/R MM referenced in this press release (the "R/R MM Confirmatory Trial"), whether any beneficial regulatory designations previously granted by the FDA and referenced in this press release will positively impact the timing for potential FDA approval, and whether any such approval will be obtained by the FDA's target action date referenced in this press release) or the European Medicines Agency; 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 (such as the R/R MM Confirmatory Trial), on any of the foregoing or any potential regulatory approval of Regeneron's Products and Regeneron's Product Candidates (such as linvoseltamab); 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 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).

Contacts:

Media Relations
Tammy Allen
Tel: +1 914-306-2698
tammy.allen@regeneron.com

Investor Relations
Vesna Tosic
Tel: +1 914-847-5443
vesna.tosic@regeneron.com

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