Linvoseltamab in Combination with Carfilzomib or Bortezomib Shows Promising Initial Results in Earlier Lines of Treatment for Relapsed/Refractory Multiple Myeloma

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First results to be presented in two ASCO oral presentations

Data in both combinations demonstrate high response rates

TARRYTOWN, N.Y., May 22, 2025 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced initial results from two cohorts of the Phase 1b LINKER-MM2 trial evaluating linvoseltamab in combination with two different proteasome inhibitors (PI) – carfilzomib or bortezomib – in patients with relapsed/refractory (R/R) multiple myeloma (MM). The trial included patients who had progressed after at least two lines of therapy and were either double-class refractory (immunomodulatory drug [IMiD] and PI) or triple-class exposed (IMiD, PI and anti-CD38 monoclonal antibody). The data will be featured in two oral presentations at the American Society of Clinical Oncology (ASCO) 2025 Annual Meeting on Monday, June 2 at 8:00 AM CDT.

“In clinical trials, treatment with linvoseltamab monotherapy in later-line settings generated impressive response rates, warranting investigation in earlier lines as well as in combination with other cancer therapies,” said Salomon Manier, M.D., Ph.D., Professor of Hematology at Lille University Hospital in France. “While early, these compelling results for linvoseltamab combination therapy demonstrated high rates of clinical activity, even amongst those with previous exposure to the proteasome inhibitors evaluated in the cohorts. We look forward to seeing these results mature to see if these benefits can be maintained.”

Linvoseltamab combined with carfilzomib showed strong responses in R/R MM
All treated patients (n=23) had previous exposure to PIs and more than half (n=12) were refractory to at least one PI. Moreover, 48% had baseline soft tissue plasmacytomas, and 39% were over 75 years old, representing a patient population with high-risk features. Of the 21 patients evaluable for efficacy, 11 patients received linvoseltamab 100 mg, and five patients each received linvoseltamab 150 mg or 200 mg prior to initiation of carfilzomib.

With a median follow-up of 15 months, efficacy results across all dose levels showed a 90% objective response rate (ORR; 19 of 21 patients), with 76% (16 of 21 patients) achieving a complete response (CR). At 12 months, the estimated probability of maintaining a response was 87% (n=19; 95% confidence interval [CI]: 56% to 97%) and being progression-free was 83% (n=21; 95% CI: 55% to 94%). A registrational, randomized Phase 3 trial investigating this combination against standard-of-care in the same setting is planned.

Among the 23 patients evaluable for safety, the most common treatment emergent adverse events (TEAEs; >50%) of any grade and Grade ≥3 were neutropenia (65% and 56.5%), cytokine release syndrome (CRS; 61% and 0%), diarrhea (52% and 4%) and thrombocytopenia (52% and 30%). Infections occurred in 91% of patients (Grade ≥3: 43.5%, including one fatality). Serious adverse events (SAEs) occurred in 83% of patients. One dose-limiting toxicity (DLT) of Grade 4 thrombocytopenia during tumor lysis syndrome was observed in the 100 mg dose level, and one Grade 1 immune effector cell-associated neurotoxicity syndrome (ICANS) was observed in the 150 mg dose level.

Additional linvoseltamab combination with bortezomib showed promising clinical activity in R/R MM
Among enrolled patients (n=24), 6 received linvoseltamab at 100 mg and 18 at 200 mg before initiating bortezomib. More than half were refractory to PIs, including 58% to carfilzomib and 13% to bortezomib. Of the 20 patients evaluable for efficacy and with a median duration of follow-up of 9 months, results across dose levels showed an 85% ORR (17 of 20 patients), with 50% (10 of 20 patients) achieving a CR.

The most common TEAEs (>50%) of any grade and Grade ≥3 were CRS (58% and 0%), neutropenia (54% and 50%) and thrombocytopenia (54% and 37.5%). Four patients experienced ICANS (one Grade 1 and three Grade 2). Infections occurred in 75% of patients (Grade ≥3: 38%). SAEs occurred in 83% of patients. Two patients died due to adverse events: one due to pneumonia deemed related to treatment and occurring prior to initiation of bortezomib, and another due to COVID-19 deemed unrelated to treatment. One DLT of Grade 3 cytomegalovirus reactivation was observed in the 200 mg dose level.

The uses of linvoseltamab in combination with either carfilzomib or bortezomib in patients with R/R MM are investigational and have not been approved by any regulatory authority.

Linvoseltamab is approved in the European Union as Lynozyfic™ for adults to treat R/R MM that has progressed after at least three prior therapies (including a PI, an IMiD and an anti-CD38 monoclonal antibody) and that has demonstrated progression on

the last therapy. For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu. In the U.S., the FDA accepted for review the Biologics License Application for linvoseltamab in adults with R/R MM with a target action date of July 10, 2025.

About Multiple Myeloma
As the second most common blood cancer, there are over 187,000 new cases of MM diagnosed globally every year, with more than 36,000 diagnosed and 12,000 deaths anticipated in the U.S. in 2025. In the U.S., there are approximately 8,000 people who have MM that has progressed after three lines of therapy. 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 LINKER-MM2
LINKER-MM2 is a Phase 1b, open-label clinical trial evaluating linvoseltamab in combination with other cancer treatments in patients with R/R MM. Combination treatments include standard-of-care and novel therapies such as IMiD, PIs, anti-CD38 antibodies, checkpoint inhibitors, and a gamma secretase inhibitor. The primary endpoints are incidence of DLTs (dose-finding portion only) and incidence and severity of TEAEs. Secondary endpoints include ORR, DoR and progression-free survival.

In the carfilzomib cohort, linvoseltamab is administered first with an initial step-up dosing regimen followed by at least two full doses (100, 150 or 200 mg) before initiation of carfilzomib (56 mg/m²). In the bortezomib cohort, the same initial step-up process is followed but linvoseltamab is administered with at least one full dose (100 or 200 mg) before initiation of bortezomib (1.3 mg/m²).

About the Linvoseltamab Clinical Development Program
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.

Linvoseltamab is being investigated in a broad clinical development program exploring its use as a monotherapy as well as in combination regimens across different lines of therapy in MM, including earlier lines of treatment, as well as plasma cell precursor disorders.

In addition to LINKER-MM2, trials include:

- LINKER-MM1: Phase 1/2 dose-escalation and dose-expansion trial evaluating the safety, tolerability, dose-limiting toxicities and anti-tumor activity of linvoseltamab monotherapy in R/R MM
- LINKER-MM3: Phase 3 confirmatory trial evaluating linvoseltamab monotherapy compared to the combination of elotuzumab, pomalidomide and dexamethasone in R/R MM
- Phase 1 trial evaluating linvoseltamab in combination with a Regeneron CD38xCD28 costimulatory bispecific in R/R MM
- LINKER-MM4: Phase 1/2 trial evaluating linvoseltamab monotherapy in newly diagnosed MM
- LINKER-SMM1: Phase 2 trial evaluating linvoseltamab monotherapy in high-risk smoldering MM
- LINKER-MGUS1: Phase 2 dose-ranging trial evaluating linvoseltamab monotherapy in high-risk monoclonal gammopathy of unknown significance and non-high-risk SMM
- LINKER-AL2: Phase 1/2 trial evaluating linvoseltamab monotherapy in R/R systemic light chain amyloidosis

For more information on Regeneron's clinical trials in blood cancer, visit the 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'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 a substantial proportion of all original, FDA-approved fully human monoclonal antibodies. This includes Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza® (evinacumab-dgnb), Inmazeb® (atoltivimab, maftivimab and odesivimab-ebgn) and Veopoz® (pozelimab-bbfg). In addition,

REGEN-COV® (casirivimab and imdevimab) had been authorized by the FDA during the COVID-19 pandemic until 2024.

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 in combination with carfilzomib or bortezomib in patients with relapsed/refractory ("R/R") multiple myeloma ("MM"); the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products, including linvoseltamab as a monotherapy (such as for the treatment of R/R MM in the United States based on the Biologics License Application referenced in this press release) and in combination with carfilzomib or bortezomib or other combination regimens discussed or referenced in this press release across different lines of therapy in MM and plasma cell precursor disorders; 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 in combination with the above-referenced agents); 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 and risks associated with tariffs and other trade restrictions; safety issues resulting from the administration of Regeneron's Products and Regeneron's Product Candidates (such as linvoseltamab in combination with the above-referenced agents) 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 or copay assistance for Regeneron's Products from third-party payors and other third parties, including private payor 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 payors and other third parties and new policies and procedures adopted by such payors and other third parties; changes in laws, regulations, and policies affecting the healthcare industry; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates (including biosimilar versions of Regeneron's Products); 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 on Regeneron's business; and risks associated with 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), 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), 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, 2024 and its Form 10-Q for the quarterly period ended March 31, 2025. 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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