Updated Linvoseltamab (BCMAxCD3) Data from Pivotal Trial Demonstrates Early, Deep and Durable Responses in Patients with Heavily Pre-treated Multiple Myeloma

May 25, 2023 at 5:05 PM EDT

71% objective response rate, with 59% of patients achieving a very good partial response or better at the recommended 200 mg dose, per new data to be shared in an oral session at ASCO

Benefit also observed across prespecified subgroups, including patients with high disease burden and aggressive disease

Data from this trial to form the basis of planned regulatory submissions, starting with the FDA in 2023

TARRYTOWN, N.Y., May 25, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced updated data from two Phase 2 expansion dose cohorts evaluating investigational linvoseltamab (formerly REGN5458) in patients with heavily pre-treated, relapsed/refractory (R/R) multiple myeloma. The results will be shared in an oral session at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting and the LINKER-MM1 trial will form the basis of planned submissions to regulatory authorities, including to the U.S. Food and Drug Administration (FDA) later this year. Linvoseltamab is an investigational BCMAxCD3 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.

“Despite advances, new treatments are needed that drive meaningful and durable responses to help patients with relapsed and/or refractory multiple myeloma,” said Hans Lee, M.D., Associate Professor and Director, Multiple Myeloma Clinical Research at The University of Texas MD Anderson Cancer Center. “Treatment with linvoseltamab at the recommended 200 mg dose in the LINKER-MM1 trial demonstrated impressive efficacy, with rapid, deep and durable responses in patients with multiple myeloma that’s highly refractory to standard therapies. Moreover, less than half of patients experienced any grade cytokine release syndrome, which was mostly Grade 1, with some Grade 2 and a single Grade 3 case. This reinforces the potential of linvoseltamab as a promising treatment option.”

The new data to be presented at ASCO 2023 are from patients treated in the 50 mg (n=104) and 200 mg (n=117) cohorts of the Phase 1/2 trial. Initial results were presented at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition in December 2022. Among the 200 mg cohort, the median soluble BCMA (sBCMA) was 377 ng/mL, 22% had bone marrow plasma cells ≥50% and 36% had high-risk cytogenetics, representing a patient population with a high disease burden and poor prognosis. The primary endpoint was objective response rate (ORR) assessed by independent review committee, which will be available when the data are more mature. The secondary endpoints included ORR and other efficacy measures assessed by local investigator. With a median follow-up of 6 months, patients receiving the recommended 200 mg dose showed:

- **71% ORR**, per local investigator.
- **59% achieved a very good partial response (VGPR) or better, with 30% achieving a complete response (CR) or stringent complete response (sCR),** per local investigator. Based on earlier results, responses may deepen with longer follow-up.
- **Median time to onset of response was less than 1 month**.
- **84% and 79% probability of maintaining a response at 6 and 12 months**, respectively, per Kaplan-Meier estimates.
- **Median progression-free survival was not reached**.

Strong efficacy per ORR was consistently observed in the 200 mg cohort across multiple subgroups, even in high risk patients such as adults ≥75 years of age (n=31; 68%), patients with International Staging System (ISS) stage II and III disease (n=44 and 22; 73% and 59% respectively), patients with extramedullary plasmacytomas (defined as disease without bone association, n=16; 56%) as well as patients with baseline sBCMA ≥400 ng/mL (n=51; 55%). Additionally, among patients treated with 50 mg and 200 mg that achieved CR or sCR with available minimal residual disease (MRD) data, 54% were MRD negative at 10^{-5}.

No new safety signals were identified with longer follow-up in the Phase 1 or Phase 2 portions of the trial. Among all patients in the 200 mg cohort, 79% experienced Grade ≥3 adverse events (AE). Most commonly occurring AEs (in ≥20% of patients) were cytokine release syndrome (CRS; 45%), neutropenia, cough, fatigue and diarrhea (33% each), anemia (27%), arthralgia (26%), and headache (23%). Discontinuations due to an AE occurred in 16% of patients. Deaths due to treatment-emergent AEs, on-treatment or within 30 days post last dose, in the 200 mg cohort were reported in 6 patients. None of the deaths were considered related to treatment per the treating physician. Among the 200 mg cohort, the majority of CRS cases were mild or moderate, there was a single case of Grade 3 CRS, and no cases of ≥Grade 4 CRS. The median time to first CRS onset was 15 hours (range: 0-177 hours), with the median time to resolution within 1 day (17 hours; range: 1-144 hours). Among the 50 mg and

200 mg dose cohorts (n=221), there were 14 immune effector cell-associated neurotoxicity syndrome events (ICANS, 6% all Grades; 2% Grades 3-4).

“With these latest pivotal results, linvoseltamab demonstrated notable response rates, providing encouraging evidence for this bispecific antibody,” said L. Andres Sirulnik, M.D., Ph.D., Senior Vice President, Translational and Clinical Sciences, Hematology at Regeneron. “We designed linvoseltamab with patient needs at the center and are proud that it has provided benefit across the spectrum of relapsed refractory multiple myeloma patients, even those with hard-to-treat disease. We look forward to sharing these data with regulatory authorities with the goal of bringing this medicine to patients with heavily pre-treated multiple myeloma as soon as possible.”

Based on these data, the Phase 3 development program investigating linvoseltamab in earlier stages of the disease has been initiated. In the U.S., linvoseltamab has been granted Fast Track Designation for multiple myeloma by the FDA. Linvoseltamab is currently under clinical development, and its safety and efficacy have not been fully evaluated by any regulatory authority.

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 282 patients enrolled, all have received at least three prior lines of therapy or are triple refractory. Patients were administered linvoseltamab utilizing a step-up dosing regimen that was designed to help mitigate CRS.

The Phase 1 dose-escalation portion of the trial, which is now complete, primarily assessed safety, tolerability and dose-limiting toxicities across 9 dose levels of linvoseltamab exploring different administration regimens. 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. Globally, there were 176,404 new diagnoses in 2020 and 35,730 new diagnoses estimated for 2023 in the U.S. 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 fracture and pain, 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'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 or authorized fully human monoclonal antibodies. This includes REGEN-COV® (casirivimab and imdevimab), Dupixent® (dupilumab), Libtayo®, Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza® (evinacumab-dgnb) and Inmazeb® (atoltivimab, maftivimab and odesivimab-ebgn).

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 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 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 linvoseltamab for the treatment of relapsed/refractory multiple myeloma; 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 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, 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, 2022 and its Form 10-Q for the quarterly period ended March 31, 2023. 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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Source: Regeneron Pharmaceuticals, Inc.