Latest Odronextamab Data in Relapsed/Refractory Follicular Lymphoma Showed Compelling Responses and Overall Maintenance of Patient-Reported Outcomes

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Updated results presented at ASH demonstrated an 80% objective response rate and a 73% complete response (CR), with a 23-month median duration of response and 24-month median duration of CR

Oral presentation showcased overall maintenance of patient-reported outcomes from baseline to 50 weeks during investigational odronextamab treatment, complementing the overall efficacy and safety profile in this heavily pretreated and highly refractory patient population

TARRYTOWN, N.Y., Dec. 10, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive data for odronextamab in patients with relapsed/refractory (R/R) follicular lymphoma (FL) from a pivotal Phase 2 trial (ELM-2). These data – which include updated efficacy, safety and patient-reported outcomes (PROs) – were presented at the 65th American Society of Hematology (ASH) Annual Meeting and Exposition from December 9 to 12 in San Diego, CA. Odronextamab is an investigational CD20xCD3 bispecific antibody designed to bridge CD20 on cancer cells with CD3-expressing T cells to facilitate local T-cell activation and cancer-cell killing.

“The odronextamab data presented at ASH in patients with relapsed/refractory follicular lymphoma showcase a strong profile across measures of efficacy, safety and health-related quality of life,” said Benoît Tessoulin, M.D., Ph.D., Nantes University Hospital, Nantes; CRCI^{2}NA, Nantes University, Nantes, France, and a trial investigator. “As clinicians, our focus must remain patients’ wellbeing, along with favorable outcomes. For odronextamab, it is particularly encouraging to see the unprecedented clinical results complemented by patient-reported outcomes that show quality of life and functional measures are maintained overall. These presentations underscore the potential role of odronextamab as a future medicine that treats relapsed/refractory follicular lymphoma and may allow patients to maintain health-related quality of life during the course of their therapy.”

As shared at ASH, longer-term data from the Phase 2 odronextamab trial continued to confirm high rates of durable responses in patients with R/R FL. At a prespecified interim analysis that occurred when the first 80 patients had ≥12 months of follow-up, results among 128 patients that were assessed by independent central review (ICR) demonstrated:

- **80% objective response rate (ORR), with 73% achieving a complete response (CR).**
- **Median duration of response (DoR) was 23 months** (95% confidence interval [CI]: 17 months to not estimable [NE]) **and median duration of CR was 24 months** (95% CI: 18 months to NE) with a 18-month median duration of follow-up for efficacy evaluable patients (95% CI: 15 to 28 months).
- **Median progression-free survival (PFS) in complete responders was 28 months** (95% CI: 20 months to NE) and 21 months for all patients (95% CI: 17 to 28 months).
- **Median overall survival (OS) was not reached** (95% CI: 32 months to NE).
- The most common adverse events (AE) occurring in ≥30% of patients were cytokine release syndrome (CRS; 56%), neutropenia (48%), pyrexia (36%), anemia (34%), COVID-19 (31%) and infusion-related reactions (31%).
- In 60 patients that received the recommended step-up regimen, 57% experienced CRS. All cases were resolved with supportive measures, with a median duration of 2 days (range: 1 to 10 days). Among these patients, 45% (n=27) had Grade 1 CRS, 10% (n=6) had Grade 2 CRS, and 2% (n=1) had Grade 3 CRS.
- There was one Grade 2 immune effector cell-associated neurotoxicity syndrome event reported, which was not associated with CRS.

As presented during an oral session at ASH, patients with R/R FL treated with odronextamab in the ELM-2 trial completed three validated questionnaires aimed at measuring health-related quality of life (HRQoL), functioning and symptoms. Pre-specified analyses were conducted across six scales. Overall, patients reported generally good HRQoL, functioning and low symptom burden at baseline as assessed across several scales. Key findings through Week 50 showed:

- **Overall maintenance of moderate to high levels of functioning and HRQoL without detriments to patient-reported symptoms** based on an analysis of changes in PRO scores from baseline over time, as measured by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) scores.
- **Median time to definitive deterioration in physical function and lymphoma-specific symptoms was not reached** (per EORTC QLQ-30 and Functional Assessment of Cancer Therapy Lymphoma subscale, respectively). In an individual patient-level analysis, more patients reported maintenance or clinically meaningful improvement in physical functioning and lymphoma-specific symptoms than deterioration at each assessment.

Odronextamab is currently under regulatory review for the treatment of R/R FL and diffuse large B-cell lymphoma (DLBCL) by the U.S. Food and Drug Administration, with a target action date of March 31, 2024, as well as by the European Medicines Agency (EMA). In the U.S., odronextamab has been granted Fast Track Designation by the FDA. In the European Union, odronextamab has been granted Orphan Drug Designation by the EMA.

The potential use of odronextamab in R/R FL and R/R DLBCL is currently under clinical development, and the 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 Thursday, 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 Odronextamab Clinical Program
ELM-1 is an ongoing, open-label, multicenter Phase 1 trial to investigate the safety and tolerability of odronextamab in patients with CD20-positive B-cell malignancies previously treated with CD20-directed antibody therapy. The trial includes an expansion cohort evaluating DLBCL patients who had progressed on CAR-T therapy.

ELM-2 is an ongoing, open-label, multicenter pivotal Phase 2 trial investigating odronextamab in 375 patients across five independent disease-specific cohorts, including DLBCL, FL, mantle cell lymphoma, marginal zone lymphoma and other subtypes of B-cell non-Hodgkin lymphoma (B-NHL). The primary endpoint of ELM-2 is ORR according to the Lugano Classification, and secondary endpoints include CR, PFS, OS, DoR, disease control rate, safety and quality of life.

Regeneron has initiated a broad Phase 3 development program to investigate odronextamab in earlier lines of therapy and other B-NHLs, representing one of the largest clinical programs in lymphoma.

About Follicular Lymphoma (FL)
One of the most common subtypes of B-NHL, FL is a slow-growing (indolent) form of B-NHL, with most cases diagnosed in advanced stages. Although median survival ranges from 8 to 15 years in advanced FL, current therapeutic options are not curative, and most patients relapse within five years, regardless of the regimen. In the U.S., it is estimated that approximately 13,100 people will be diagnosed with FL in 2023. In some cases, FL can transform into DLBCL, at which point it is often treated in the same way as DLBCL.

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, and 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 (NASDAQ: REGN) 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 numerous FDA-approved treatments and product candidates in development, almost all of which were homegrown in our laboratories. Regeneron's medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, hematologic conditions, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its 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 Regeneron, please visit www.regeneron.com or follow Regeneron on LinkedIn.

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 odronextamab; 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 odronextamab for the treatment of relapsed/refractory follicular lymphoma and relapsed/refractory diffuse large B-cell lymphoma; 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 odronextamab); 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 (such as odronextamab) 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 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 September 30, 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 (https://investor.regeneron.com) and its LinkedIn page (https://www.linkedin.com/company/regeneron-pharmaceuticals).

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