Updated Odronextamab Data from Relapsed/Refractory Diffuse Large B-cell Lymphoma Pivotal Trial Showed Deep and Durable Responses and the Potential of ctDNA To Predict Long-term Outcomes

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Phase 2 primary analysis results presented in ASH oral session demonstrated a 52% objective response rate (ORR), with 31% achieving a complete response (CR)

Results from a Phase 1 expansion cohort showed a 48% ORR and 30% CR in patients who had progressed on CAR-T

Additional exploratory data from the Phase 2 trial presented in an oral session showed an association between circulating tumor DNA (ctDNA) negativity and progression-free survival

TARRYTOWN, N.Y., Dec. 10, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced new and updated data for odronextamab in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). The data from the pivotal Phase 2 trial (ELM-2) and Phase 1 trial (ELM-1) were shared in several presentations – including two orals – 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.

“Diffuse large B-cell lymphoma has a high risk of relapse, which is why it is so critical to demonstrate continued disease control over the long term. The totality of the odronextamab data at ASH reinforces its potential as a promising treatment option for patients with this aggressive blood cancer,” said Sabarish Ram Ayyappan, M.D., medical director of hematologic malignancies, City of Hope Atlanta, and a trial investigator. “The primary analysis from the pivotal trial of odronextamab demonstrated impressive response rates, including in certain high-risk subgroups. Furthermore, these responses were durable and consistent with those seen in a Phase 1 trial in patients who had previously progressed on CAR-T therapy, a population with a very poor prognosis.”

As presented in an oral session, the primary Phase 2 analysis was performed by independent central review (ICR) among 127 DLBCL patients treated with odronextamab when all had the opportunity for ≥36 weeks of follow-up. Results were as follows:

- **52% objective response rate (ORR)**, **with 31% achieving a complete response (CR)**.
- **Responses were observed across high-risk subgroups**, including those with International Prognosis Index (IPI) high-risk scores of 3 to 5, high-grade lymphoma that is double-hit and triple-hit, and transformed DLBCL.
- **Median duration of response (DoR) was 10 months** (95% confidence interval [CI]: 5 to 18 months), with a 30-month median duration of follow-up for efficacy evaluable patients (95% CI: 20 to 33 months). The median duration of CR was 18 months (95% CI: 10 months to not estimable [NE]).
- The most common adverse events (AE) in ≥30% patients were cytokine release syndrome (CRS; 55%), pyrexia (43%), anemia (39%) and neutropenia (31%).
- In 60 patients that received the recommended step-up regimen, 53% experienced CRS. All cases were resolved with supportive measures, with a median duration of 2 days (range: 1 to 7 days). Among these patients, 40% (n=24) had Grade 1 CRS, 12% (n=7) had Grade 2 CRS, and 2% (n=1) had Grade 3 CRS.
- No events of immune effector cell-associated neurotoxicity syndrome (ICANS) were reported.

An additional analysis from the Phase 1 trial demonstrated encouraging and durable antitumor activity with odronextamab in heavily pretreated patients who had progressed after CAR-T therapy. Median duration of exposure was 11 weeks (range: <1 to 122 weeks) among 46 treated patients. Results among 44 efficacy-evaluable patients, including 73% who were CAR-T refractory, as assessed by ICR showed:

- **48% ORR, with 30% achieving a CR.** Notably, 8 patients converted from a partial response to a CR over the study period.
- **Both median DoR and median duration of CR were not reached** (95% CI: 2 to NE) with a 5-month median duration of follow-up (95% CI: 3 to 9 months).
- The most common AEs in ≥30% of patients were CRS (52%), anemia, pyrexia and fatigue (each 34%). All CRS events were resolved, with a median time to resolution of 2 days (range: 1 to 8 days). Among these patients, 27% (n=12) had Grade 1 CRS and 25% (n=11) had Grade 2 CRS.

In a separate oral presentation on an exploratory analysis from the Phase 2 trial, data showed a positive association between minimal residual disease (MRD) status, as measured by circulating tumor DNA (ctDNA), and progression-free survival (PFS). Among 70 R/R DLBCL and 65 R/R follicular lymphoma (FL) patients assessed, nearly all were MRD-positive at baseline. Notably, those who were MRD-negative at time of the first response assessment (Cycle 4, Day 15) had significantly longer PFS than those who remained MRD-positive (DLBCL Hazard Ratio [HR]: 0.27, 95% CI: 0.12 to 0.61; FL HR: 0.26, 95% CI: 0.1 to 0.66).

“Our research is among the first to analyze circulating tumor DNA in a pivotal trial in relapsed/refractory stages of diffuse large B-cell lymphoma and follicular lymphoma,” said Jon E. Arnason, M.D., hematologist and oncologist, Beth Israel Deaconess Medical Center, and a trial investigator. “These

findings strengthen the body of evidence supporting the importance of minimal residual disease status as a monitoring tool in the course of managing patients with lymphoma. As the data for circulating tumor DNA continues to grow, these insights may help inform future response-directed treatment paradigms."

Odronextamab is currently under regulatory review for the treatment of R/R DLBCL and R/R FL by the U.S. Food and Drug Administration (FDA), 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 for DLBCL and FL by the FDA. In the European Union, odronextamab has been granted Orphan Drug Designation in DLBCL and FL by the EMA.

The potential use of odronextamab in R/R DLBCL and R/R FL 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, overall survival, 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 Diffuse Large B-cell Lymphoma (DLBCL)
DLBCL is one of the most common subtypes of B-NHL. In the U.S., it is estimated that approximately 31,000 people will be diagnosed with DLBCL in 2023. Globally, there are an estimated 163,000 DLBCL cases each year. DLBCL is an aggressive cancer with up to 50% of patients with advanced stage disease progressing after first-line treatment (e.g., relapsing or becoming refractory to treatment). For patients with relapsed/refractory DLBCL, treatment options are limited, and prognosis is poor.

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 diffuse large B-cell lymphoma and relapsed/refractory follicular 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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