Odronextamab ASH Presentations Underscore Impressive Potential in Earlier Lines of Treatment and Additional Types of Lymphoma

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Odronextamab monotherapy led to complete responses in all patients with previously untreated follicular lymphoma evaluable for efficacy, per initial results from the safety lead-in portion of the confirmatory Phase 3 OLYMPIA-1 trial

Primary analysis from an expansion cohort of the ELM-1 trial highlighted continued efficacy and durability in diffuse large B-cell lymphoma patients whose disease had progressed after CAR-T therapy

First results from the ELM-2 trial in marginal zone lymphoma demonstrated high complete response rate in patients with relapsed/refractory disease

TARRYTOWN, N.Y., Dec. 09, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced new and updated data for odronextamab were presented at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego, CA. The presentations, including two orals, showcase the depth and breadth of the odronextamab clinical development program, with twelve abstracts spanning several B-cell non-Hodgkin lymphoma (B-NHL) subtypes across earlier lines of treatment.

OLYMPIA-1 Part 1 Results Showcased Compelling Potential in Previously Untreated Follicular Lymphoma (FL)
The ongoing Phase 3 OLYMPIA-1 confirmatory trial consists of a non-randomized safety run-in (Part 1) followed by a randomized efficacy portion (Part 2) evaluating odronextamab monotherapy versus rituximab plus standard-of-care chemotherapies.

In Part 1 (N=13), odronextamab led to complete responses (CR) in all 12 patients evaluable for efficacy at week 12. Historical clinical trial data indicate that the standard-of-care regimen R-Chemo was associated with an objective response rate (ORR) of 89% and 67% CR rate.[1] Among the 13 patients evaluable for safety, none experienced a dose-limiting toxicity (DLT). The most common treatment-emergent adverse events (TEAEs) were cytokine release syndrome (CRS; 62%), diarrhea (46%) and rash (39%). All cases of CRS were Grade 1. Infections occurred in 39% of patients, and 15% experienced a Grade 3 infection. Grade ≥3 TEAEs occurred in 46% of patients, which included one patient who discontinued early due to elevated liver enzymes. There were no reports of tumor lysis syndrome (TLS) or immune effector cell associated neurotoxicity syndrome (ICANS).

“The OLYMPIA-1 Phase 3 trial is designed to explore a novel, chemotherapy-free, fixed duration treatment that is being studied in the outpatient setting in patients with previously untreated follicular lymphoma,” said Elizabeth Brém, Associate Clinical Professor, Division of Hematology/Oncology at UC Irvine. “These compelling, initial data show the paradigm-changing potential of odronextamab in previously untreated patients and reinforce the remarkable complete response rates odronextamab demonstrated in late-line follicular lymphoma. We look forward to seeing the results of the Part 2 portion, which offers the first head-to-head evaluation of odronextamab monotherapy compared to standard-of-care chemo-immunotherapies.”

Durable Responses Shown in Diffuse Large B-Cell Lymphoma (DLBCL) that has Progressed After CAR-T Therapy
The primary analysis from an expansion cohort of the ELM-1 trial, which evaluated patients with DLBCL who progressed after CAR-T therapy, were presented in an oral session. Among 60 patients – with a median duration of treatment of 12 weeks (range <1 to 154 weeks) and a median duration of follow-up of 16 months – results assessed by independent central review showed:

- **48% ORR, with 32% achieving a CR**. These responses were observed across patients with high-risk features, including those that were refractory to their last therapy, double refractory, or refractory prior to CAR-T.
- **Among all patients,** there was a 15-month median duration of response (DoR) (95% confidence interval [CI]: 3 months to not estimable [NE]), 5-month median progression-free survival (PFS) (95% CI: 3 to 5 months), and a 10-month median overall survival (OS) (95% CI: 5 to 16 months).
- **Among CR patients,** medians were not reached in terms of PFS (95% CI: 9 months to NE) and OS (95% CI: 15 months to NE).

All patients experienced TEAEs, including 77% who experienced Grade ≥3 TEAEs. CRS occurred in 48% of patients (25% were Grade 1 and 23% were Grade 2). Infections occurred in 50% of patients, and 20% experienced a Grade ≥3 infection, including one treatment-related death due to COVID-19 pneumonia. No TLS or ICANS cases were reported.

“Studies show that half of patients receiving CAR-T therapies relapse within six months, and up to 35% of patients do not go on to receive subsequent treatments, highlighting the critical unmet need in diffuse large B-cell lymphoma progressing after CAR-T,” said Matthew Matasar, M.D., MS, Chief of Blood Disorders at Rutgers Cancer Institute and RWJBarnabas Health. “ELM-1 is one of the only trials that has prospectively evaluated the efficacy and safety of a CD20xCD3 bispecific antibody in patients with relapsed or

refractory large B-cell lymphoma progressing after CAR-T therapy. It is encouraging to see these outcomes with odronextamab in a patient population that to date has had an incredibly poor prognosis and limited treatment options."

Compelling Efficacy Highlighted in Marginal Zone Lymphoma (MZL) in Heavily Pretreated Patients
Another oral presentation featured data from a cohort of heavily pretreated patients with relapsed/refractory (R/R) MZL, a setting with no approved treatment options. In the potentially pivotal ELM-2 trial, 42 patients were enrolled, of which 35 patients were evaluable for efficacy. At a median duration of follow-up of 11 months, results showed:

- **77% ORR, with all responders achieving a CR,** per investigator assessment.
- **Medians were not reached** in terms of DoR (95% CI: 12 months to NE), duration of CR (95% CI: 12 months to NE), PFS (95% CI: 15 months to NE) and OS (95% CI: NE to NE).

Among 42 patients evaluated for safety, the most common TEAEs (≥15%) were CRS (55%; all were Grade 1 or 2), infusion-related reaction (36%), pyrexia (36%) and neutropenia (31%). Grade ≥3 TEAEs occurred in 83% of patients and included neutropenia and increased levels of alanine aminotransferase and aspartate aminotransferase. Infections occurred in 69% of patients, and 24% experienced a Grade ≥3 infection. Four patients (10%) discontinued treatment due to TEAEs.

Odronextamab is approved in the European Union as Ordspono™ to treat R/R FL or DLBCL after two or more lines of systemic therapy but its safety and efficacy have not been fully evaluated by any other regulatory authority. For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu. The U.S. regulatory resubmission for odronextamab in R/R FL after two or more lines of systemic therapy is expected to be submitted in the first half of 2025. The potential use of odronextamab in R/R MZL is investigational and has not been approved by any regulatory authority.

About B-Cell Non-Hodgkin Lymphomas (B-NHL)
B-NHL is the most common lymphoma in the United States and has several different subtypes including FL, DLBCL and MZL. FL and MZL are slow-growing subtypes, and both are incurable. It is estimated that approximately 120,000 FL cases are diagnosed annually worldwide, while MZL is estimated to be 5 to 10% of NHLs. DLBCL is an aggressive subtype, with up to 50% of high-risk patients experiencing progression after first-line treatment. It is estimated that approximately 163,000 DLBCL cases are diagnosed annually worldwide.

About the Odronextamab Clinical Trial Program
Odronextamab is a 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. It is being investigated in a broad clinical program spanning several trials.

ELM-1 is an ongoing, open-label, multicenter Phase 1 trial to investigate the safety and tolerability of odronextamab in patients with CD20+ B-cell malignancies previously treated with CD20-directed antibody therapy, including a cohort of patients who had progressed after CAR-T therapy.

ELM-2 is an ongoing, open-label, multicenter Phase 2 trial investigating odronextamab across five independent disease-specific cohorts, including DLBCL, FL, mantle cell lymphoma, MZL and other subtypes of B-NHL. The primary endpoint is ORR according to the Lugano Classification as assessed by IRC, and secondary endpoints include CR, PFS, OS and DoR.

OLYMPIA is a broad Phase 3 clinical trial program investigating odronextamab in earlier lines of therapy and other B-NHLs and includes:

- OLYMPIA-1 evaluating odronextamab against rituximab plus standard-of-care chemotherapies in FL.
- OLYMPIA-2 evaluating odronextamab plus chemotherapy against rituximab plus standard-of-care chemotherapies in FL.
- OLYMPIA-3 evaluating odronextamab plus chemotherapy against rituximab plus standard-of-care chemotherapies in previously untreated DLBCL.
- OLYMPIA-4 evaluating odronextamab compared to an investigator's choice of standard-of-care regimens in previously treated aggressive B-NHL.
- OLYMPIA-5 evaluating odronextamab plus lenalidomide against rituximab plus lenalidomide in FL and MZL.

Regeneron is also investigating additional odronextamab combination therapies in R/R aggressive B-NHL. These include the ATHENA-1 trial evaluating odronextamab in combination with a costimulatory CD22xCD28 bispecific antibody (REGN5837) and the CLIO-1 trial evaluating odronextamab in combination with Regeneron's PD-1 inhibitor Libtayo ® (cemiplimab).

These potential uses described in the OLYMPIA, ATHENA-1 and CLIO-1 trials are investigational, and their safety and efficacy have not been evaluated by any regulatory authority. For more information, visit the Regeneron clinical trials website or contact via clinicaltrials@regeneron.com or +1 844-734-6643.

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.

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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 the various clinical programs discussed or referenced in this press release evaluating odronextamab as a monotherapy or a combination therapy; 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 follicular lymphoma in the United States based on the anticipated U.S. Food and Drug Administration regulatory resubmission as well as the other potential indications discussed or referenced in this press release; 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 (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 (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 September 30, 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

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[1] Morschhauser F, Fowler NH, Feugier P, et al. Rituximab plus lenalidomide in advanced untreated follicular lymphoma. *N Engl J Med*. 379, 934-947 (2018).

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Source: Regeneron Pharmaceuticals, Inc.