Ordspono™ (odronextamab) Approved in the European Union for the Treatment of Relapsed/Refractory Follicular Lymphoma and Diffuse Large B-cell Lymphoma

August 26, 2024 at 7:00 AM EDT

Approval of Ordspono is based on data demonstrating robust and durable responses in both relapsed/refractory follicular lymphoma and diffuse large B-cell lymphoma, including in the post-CAR-T setting

Ordspono is Regeneron's first approved bispecific antibody and will provide an off-the-shelf option that can be administered in the out-patient setting, with hope for complete remission

TARRYTOWN, N.Y., Aug. 26, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that the European Commission (EC) has approved Ordspono™ (odronextamab) to treat adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) or R/R diffuse large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy. This marks the first regulatory approval of Ordspono in the world for these patients. Ordspono is a bispecific antibody that acts by linking the lymphoma cell to a killer T cell.

"The EC approval of Ordspono is a meaningful advancement for EU patients and their physicians as a new option to treat both indolent and aggressive lymphomas," said Stefano Luminari, M.D., Professor of Oncology at the University of Modena and Reggio Emilia, hematologist at the Hematology Unit of Arcispedale Sant Maria Nuova in Reggio Emilia, and a trial investigator. "In clinical trials, Ordspono demonstrated remarkable complete response rates in follicular lymphoma, as well as compelling efficacy results in diffuse large B-cell lymphoma, including in the post-CAR-T setting. Physicians, especially in the community setting, will have an off-the-shelf option that can be administered out-patient – offering the chance for complete remission."

The approval is based on results from the Phase 1 ELM-1 and pivotal Phase 2 ELM-2 trials, which demonstrated robust, durable response rates in adults with R/R FL or R/R DLBCL:

- In R/R FL, results from ELM-2 (N=128) as assessed by an independent review committee (IRC) showed an objective response rate (ORR) of 80%, with 73% achieving a complete response (CR). Among complete responders, the median duration of response (DoR) was 25 months (95% confidence interval [CI]: 20 months to not estimable [NE]).
- In R/R DLBCL,
  - results from ELM-2 (N=127) in patients who were CAR-T therapy naive, as assessed by an IRC showed 52% ORR, with 31% achieving a CR. Among complete responders the median DoR was 18 months (95% CI: 10 months to NE).
  - results from ELM-1 (N=60) in patients who had progressed after CAR-T therapy, as assessed by an IRC showed 48% ORR, with 32% achieving a CR. Among responders (n=29), the median DoR was 15 months (95% CI: 3 months to NE).

The most common adverse reactions were cytokine release syndrome (CRS; 54%), neutropenia (41%), pyrexia (39%), anemia (38%), thrombocytopenia (27%), diarrhea (24%) and COVID-19 (22%). The most common serious adverse reactions were CRS (14%), pneumonia (9%), COVID-19 (9%) and pyrexia (6%). Ordspono can cause serious or fatal infections, and CRS, which may be serious or life-threatening.

"Ordspono marks the first approval from our bispecific antibody platform, which we hope will increasingly contribute to our growing portfolio of practice-changing medicines for oncology and other diseases," said George D. Yancopoulos, M.D., Ph.D., Board co-Chair, President and Chief Scientific Officer of Regeneron. "Building upon this approval, we are excited about our OLYMPIA program, which includes multiple Phase 3 trials investigating Ordspono as a monotherapy and in various combinations, in earlier lines of therapy. We're also excited to be advancing our broader pipeline of CD3 and other bispecific therapies, both to additional hematologic cancers such as myeloma, as well as to solid tumors."

About FL and DLBCL
FL and DLBCL are the two most common subtypes of B-cell non-Hodgkin lymphoma (B-NHL). While FL is a slow-growing subtype, it is an incurable disease, and most patients will relapse after initial treatment. DLBCL is an aggressive subtype, with up to 50% of high-risk patients experiencing progression after first-line treatment. It is estimated that approximately 120,000 FL cases and 163,000 DLBCL cases are diagnosed annually worldwide. In Europe, it is estimated that approximately 15,000 FL cases and 31,000 DLBCL cases are diagnosed each year.

About the Ordspono (odronextamab) Clinical Trial Program
Ordspono 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. Ordspono as monotherapy is indicated for the treatment of adult patients with R/R FL or R/R DLBCL, after two or more lines of systemic therapy. For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu in due course.

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, marginal zone lymphoma 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, progression-free survival, overall survival and DoR.

Regeneron is conducting a broad Phase 3 development program, known as OLYMPIA, investigating odronextamab in earlier lines of therapy and other B-NHLs. In addition, Regeneron is investigating odronextamab in combination with a costimulatory bispecific antibody, REGN5837 (CD22xCD28), and Regeneron's PD-1 inhibitor cemiplimab for R/R aggressive B-NHL through the ATHENA-1 and CLIO-1 studies, respectively. These potential uses 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 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.

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 Ordspono™ (odronextamab) to treat adult patients with relapsed or refractory ("R/R") follicular lymphoma or R/R diffuse large B-cell lymphoma; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products (such as Ordspono) and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on any of the foregoing; 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 odronextamab in combination with REGN5837 (CD22xCD28 costimulatory bispecific antibody) or cemiplimab (PD-1 inhibitor) for R/R aggressive B-cell non-Hodgkin lymphoma and other Regeneron's Product Candidates discussed or referenced in this press release; 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 (such as Ordspono) 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), 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, 2023 and its Form 10-Q for the quarterly period ended June 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 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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Source: Regeneron Pharmaceuticals, Inc.