



## Pivotal Odronextamab (CD20xCD3) Phase 2 Data in Patients with Relapsed/Refractory Diffuse Large B-cell Lymphoma Debut at ASH

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**49% objective response rate (ORR) in heavily pre-treated patients who were naïve to prior CAR-T, with 31% achieving a complete response (CR)**

**Even in patients who received prior CAR-T, 48% ORR and 32% CR observed in a dose expansion cohort from a Phase 1 trial**

**Data will form the basis of regulatory submissions planned for 2023**

TARRYTOWN, N.Y., Dec. 11, 2022 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive new and updated data from a Phase 1 and pivotal Phase 2 trial (ELM-1 and ELM-2) evaluating investigational odronextamab in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). These included first data from a Phase 2 cohort of patients naïve to prior CAR-T therapy (CAR-T naïve), as well as updated data from a dose expansion cohort of a Phase 1 trial in patients who had progressed on CAR-T therapy (post-CAR-T). The results were presented in an oral session at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition in New Orleans, LA, and will form the basis of planned submissions to regulatory authorities in 2023, including to the U.S. Food and Drug Administration (FDA). Odronextamab is an investigational bispecific antibody designed to bridge CD20 on cancer cells with CD3-expressing T cells to facilitate local T-cell activation and cancer-cell killing.

"People with diffuse large B-cell lymphoma face a disease that often relapses and becomes more aggressive each time it returns, leaving doctors with a shrinking set of treatment options," said Won Seog Kim, M.D., Ph.D., Samsung Medical Center and Division of Hematology-Oncology at Sungkyunkwan University, in Seoul, South Korea, and trial investigator. "The Phase 1 and pivotal Phase 2 odronextamab data demonstrated deep and durable responses that were consistent in patients who progress after CAR-T therapy, which is important as they have particularly difficult-to-treat disease and no effective treatment options. Coupled with its overall safety profile, these clinically important results reinforce the potential of odronextamab to treat this aggressive blood cancer."

At ASH, efficacy in R/R DLBCL was presented from 130 CAR-T naïve patients in a Phase 2 cohort (includes those with an opportunity for assessment at 12 weeks; median follow-up: 21 months, range: 3 to 30 months) and 31 CAR-T experienced patients in a dose expansion cohort of a Phase 1 trial (median follow-up: 24 months, range: 3 to 38.5 months). All patients had received at least two prior therapies, including a CD20 antibody and alkylating agent. Patients were treated with a step-up regimen of odronextamab in the first cycle to help mitigate the risk of cytokine release syndrome (CRS) before receiving the full dose of 160 mg. The step-up regimen was modified part way through the trial to further mitigate CRS. Results as assessed by independent central review were as follows:

- **Among CAR-T naïve patients, a 49% objective response rate (ORR), with 31% achieving a complete response (CR).** The median duration of complete response (mDOCR) was 18 months (95% confidence interval [CI]: 10 months to not evaluable [NE]).
- **Among post-CAR-T patients, a 48% ORR, with 32% achieving a CR.** The mDOCR was not reached (95% CI: 2 months to NE).

Among 140 patients in the Phase 2 cohort assessed for safety, adverse events (AE) occurred in 99% of patients, with 79% being  $\geq$ Grade 3. The most common AEs occurring in  $\geq$ 20% of patients were CRS (55%), anemia (42%), pyrexia (39%), neutropenia (28%) and hypokalemia (20%). Discontinuations due to an AE occurred in 10% of patients, and there were 5 deaths due to pneumonia (n=3), COVID-19 (n=1) and pseudomonal sepsis (n=1) where the relationship to odronextamab treatment could not be excluded.

CRS was the most common AE, of which 64% of cases were mild (Grade 1) and all resolved within a median time of 2 days (range: 1-133 days). There were no Grade 4 or 5 CRS cases, and the incidence of Grade 2 or higher cases was reduced with the modified step-up regimen when compared to the original (original regimen n=67 vs. step-up regimen n=73; Grade 2: 18% vs. 14%, Grade 3: 7.5% vs. 1%).

Based on these data, the OLYMPIA Phase 3 development program investigating odronextamab in earlier stages of the disease is in the process of being initiated. In the U.S., odronextamab has been granted Fast Track Designation for DLBCL by the FDA. In the European Union, Orphan Drug Designation was granted for DLBCL by the European Medicines Agency. Odronextamab is currently under clinical development and its 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 Wednesday, 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 Trials

ELM-2 is an ongoing, open-label, multicenter Phase 2 trial investigating odronextamab in more than 500 patients across five independent disease-specific cohorts, including DLBCL, follicular lymphoma, mantle cell lymphoma, marginal zone lymphoma and other subtypes of B-cell non-Hodgkin lymphoma (B-NHL). The primary endpoint is ORR according to the Lugano Classification, and secondary endpoints include CR, progression free survival, overall survival, duration of response, disease control rate, safety and quality of life.

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. Subcutaneous administration is being evaluated in two disease specific cohorts.

## About Diffuse Large B-cell Lymphoma (DLBCL)

One of the most common subtypes of B-NHL, DLBCL is an aggressive form of B-NHL 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*<sup>®</sup> 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](mailto:clinicaltrials@regeneron.com) or 844-734-6643) or visit our clinical trials [website](#).

## 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 nearly 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<sup>®</sup>, which is conducting one of the largest genetics sequencing efforts in the world.

For more information, please visit [www.Regeneron.com](http://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 impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of 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 (a CD20xCD3 bispecific antibody); 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 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 patients with relapsed/refractory diffuse large B-cell lymphoma; 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 (including those discussed or referenced in this press release) may be replicated in other studies and/or lead to advancement of product candidates to clinical trials or therapeutic applications; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; 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; 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 or collaboration agreement, including Regeneron's agreements with Sanofi and Bayer (or their respective affiliated companies, as applicable), to be cancelled or terminated; 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<sup>®</sup> (afibercept) Injection, Praluent<sup>®</sup> (alirocumab), and REGEN-COV<sup>®</sup> (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, 2021 and its Form 10-Q for the quarterly period ended September 30, 2022. 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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