

EPKINLY® (epcoritamab-bysp) Approved by U.S. FDA for Patients with Relapsed or Refractory (R/R) Follicular Lymphoma (FL)

Company Announcement

- Approval based on results from Phase 1/2 EPCORE® NHL-1 study, which demonstrated durable, clinically meaningful treatment responses in patients with challenging-to-treat R/R FL
- EPKINLY offers an off-the-shelf, T-cell engaging treatment option that enables treatment across practice settings to address high clinical need
- EPKINLY is the first and only bispecific antibody approved in the U.S. to treat both relapsed or refractory (R/R) follicular lymphoma (FL) and R/R diffuse large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy

COPENHAGEN, Denmark; June 27, 2024 – [Genmab A/S](#) (Nasdaq: **GMAB)** today announced that the U.S. Food and Drug Administration (FDA) has approved EPKINLY® (epcoritamab-bysp) for the treatment of adults with relapsed or refractory (R/R) follicular lymphoma (FL) after two or more lines of systemic therapy. With this approval, EPKINLY is the first and only T-cell engaging bispecific antibody administered subcutaneously approved in the U.S. to treat this patient population. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial(s).

FL is the second most common form of non-Hodgkin's lymphoma (NHL), accounting for 20-30 percent of all NHL cases.ⁱ About 15,000 people develop FL each year in the U.S.ⁱⁱ FL is considered incurable with current standard of care therapies and patients often relapse.^{iii,iv} With each subsequent line of therapy, patients receiving currently available treatments may experience shorter durability of response.^v

“Patients with relapsed or refractory follicular lymphoma face significant treatment challenges, especially in third-line settings where there is currently no clear standard of care treatment,” said Jeff Sharman, MD, Disease Chair, Hematology Research, Sarah Cannon Research Institute (SCRI) at Willamette Valley Cancer Institute in Eugene, Oregon. “This approval and the durable responses observed in the follicular lymphoma cohort of the EPCORE NHL-1 clinical trial, which reflected a real-world patient population, including patients with difficult-to-treat follicular lymphoma, demonstrate the potential of EPKINLY for patients who face limited therapeutic options post-relapse.”

The approval is based on results from the phase 1/2 EPCORE® NHL-1 clinical trial, which evaluated the safety and preliminary efficacy of EPKINLY in 127 adult patients with R/R FL who previously received a median of three lines of therapy and with 70% having double refractory disease. The results showed an overall response rate (ORR) of 82% and a complete response (CR) rate of 60%, including 67% of patients achieving minimal residual disease (MRD) negativity. Additionally, more than half of patients who responded to treatment in the study remained responsive to treatment at the time of data analysis (i.e., at a median follow-up of 14.8 months, median duration of response (DoR) was not reached). The study included prespecified subgroups representing patients with challenging-to-treat FL, including patients who were refractory to both anti-CD20 therapy and an alkylating agent, patients who were refractory to last prior treatment, and patients whose disease progressed within two years of first-line immunochemotherapy (POD24). These results were recently published in the [Lancet Haematology](#).

Common treatment-emergent adverse events (TEAEs) (≥20%) from the FL cohort of the trial were injection site reaction, cytokine release syndrome (CRS), COVID-19, fatigue, upper respiratory tract infection, musculoskeletal pain, rash, diarrhea, fever, cough, and headache. For patients who received EPKINLY at the recommended 3 step-up dosage schedule, CRS was primarily low grade (40% Grade 1, 9% Grade 2). There were no grade 3 CRS events observed. The prescribing information has a Boxed Warning for serious or life-threatening CRS and immune effector cell-associated neurotoxicity syndrome (ICANS).

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Warnings and precautions include infections, cytopenias, and embryo-fetal toxicity. Please see additional Important Safety Information below.

“With this approval, patients whose follicular lymphoma has relapsed or is refractory to at least two or more lines of systemic therapy, now have the option to be treated with EPKINLY, which has demonstrated durable responses without mandatory hospitalization using a 3 step-up dosage regimen in this patient population in clinical trials,” said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab. “In just over a year, EPKINLY has received a second indication in the U.S., making it the first and only bispecific antibody approved to treat patients with diffuse large B-cell lymphoma and follicular lymphoma after two or more lines of systemic therapy. The approved indications, along with the ongoing clinical development program, underscore the potential of epcoritamab to become a core therapy across B-cell malignancies.”

“People living with follicular lymphoma are in need of additional options when their cancer returns,” said Lee Greenberger, Ph.D., Chief Scientific Officer at The Leukemia & Lymphoma Society. “Today’s approval is welcome news for patients, as it provides another tool in the physician arsenal for this difficult-to-treat form of cancer.”

NCCN® Clinical Practice Guidelines

The National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for “B-Cell Lymphomas” were recently updated ([Version 2.2024](#)) to add EPKINLY as a Category 2A, preferred recommendation for third-line and subsequent therapy for patients with FL. This recommendation is based on uniform NCCN consensus that the intervention is appropriate.^{vi}

About the EPCORE® NHL-1 Trial

EPCORE® NHL-1 is an open-label, multi-center safety and preliminary efficacy trial of epcoritamab that consists of three parts: a dose escalation part; an expansion part; and an optimization part. The trial was designed to evaluate subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin’s lymphoma (B-NHL), including FL. In the expansion part, additional patients were enrolled to further explore the safety and efficacy of epcoritamab in three cohorts of patients with different types of relapsed/refractory B-NHLs who have limited therapeutic options. The expansion part generated pivotal data from patients with FL and DLBCL. The optimization part evaluated additional CRS mitigation strategies during cycle 1. The primary endpoint of the expansion part was overall response rate as assessed by an Independent Review Committee. Secondary efficacy endpoints included duration of response, complete response rate, duration of complete response, progression-free survival, and time to response as determined by the Lugano criteria. Overall survival, time to next therapy, and rate of minimal residual disease negativity were also evaluated as secondary efficacy endpoints. The primary endpoint of the optimization part was the rate of \geq Grade 2 CRS events and all grade CRS events from first dose of epcoritamab through 7 days following administration of the second full dose of epcoritamab.

About Follicular Lymphoma (FL)

FL is typically an indolent (or slow-growing) form of non-Hodgkin’s lymphoma (NHL) that arises from B-lymphocytes.^{vii} Although FL is an indolent lymphoma, it is considered incurable with conventional therapy and patients who achieve remission also often experience relapse.^{iii,iv,viii} Additionally, with each relapse the remission and time to next treatment is shorter.^{ix,x}

About EPKINLY® (epcoritamab-bysp)

EPKINLY is a prescription medicine used to treat adults with certain types of diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma, or follicular lymphoma (FL) that has come back or that did not respond to previous treatment after receiving 2 or more treatments. EPKINLY is approved based

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on patient response data. Studies are ongoing to confirm the clinical benefit of EPKINLY. It is not known if EPKINLY is safe and effective in children.

Epcoritamab is an IgG1-bispecific antibody created using Genmab's proprietary DuoBody® technology and administered subcutaneously. Genmab's DuoBody-CD3 technology is designed to direct cytotoxic T cells selectively to elicit an immune response toward target cell types. Epcoritamab is designed to simultaneously bind to CD3 on T cells and CD20 on B cells and induces T-cell-mediated killing of CD20+ cells.^{xi}

Epcoritamab (approved under the brand name EPKINLY in the U.S. and Japan, and TEPKINLY in the EU) has received regulatory approval in certain lymphoma indications in several territories. Epcoritamab is being co-developed by Genmab and AbbVie as part of the companies' oncology collaboration. The companies will share commercial responsibilities in the U.S. and Japan, with AbbVie responsible for further global commercialization.

Genmab and AbbVie continue to evaluate the use of epcoritamab as a monotherapy, and in combination, across lines of therapy in a range of hematologic malignancies. This includes four ongoing Phase 3, open-label, randomized trials including a trial evaluating epcoritamab as a monotherapy in patients with R/R DLBCL compared to investigators choice chemotherapy ([NCT04628494](#)), a trial evaluating epcoritamab in combination with R-CHOP in adult participants with newly diagnosed DLBCL ([NCT05578976](#)), a trial evaluating epcoritamab in combination with rituximab and lenalidomide (R2) in patients with R/R FL ([NCT05409066](#)), and a trial evaluating epcoritamab in combination with rituximab and lenalidomide (R2) compared to chemoimmunotherapy in patients with previously untreated FL ([NCT06191744](#)). The safety and efficacy of epcoritamab has not been established for these investigational uses. Please visit www.clinicaltrials.gov for more information.

EPKINLY® (epcoritamab-bysp) U.S. IMPORTANT SAFETY INFORMATION

Important Warnings—EPKINLY can cause serious side effects, including:

- **Cytokine release syndrome (CRS)**, which is common during treatment with EPKINLY and can be serious or life-threatening. To help reduce your risk of CRS, you will receive EPKINLY on a step-up dosing schedule (when you receive 2 or 3 smaller step-up doses of EPKINLY before your first full dose during your first cycle of treatment), and you may also receive other medicines before and for 3 days after receiving EPKINLY. If your dose of EPKINLY is delayed for any reason, you may need to repeat the step-up dosing schedule.
- **Neurologic problems** that can be life-threatening and lead to death. Neurologic problems may happen days or weeks after you receive EPKINLY.

People with DLBCL or high-grade B-cell lymphoma should be hospitalized for 24 hours after receiving their first full dose of EPKINLY on day 15 of cycle 1 due to the risk of CRS and neurologic problems.

Tell your healthcare provider or get medical help right away if you develop a fever of 100.4°F (38°C) or higher; dizziness or lightheadedness; trouble breathing; chills; fast heartbeat; feeling anxious; headache; confusion; shaking (tremors); problems with balance and movement, such as trouble walking; trouble speaking or writing; confusion and disorientation; drowsiness, tiredness or lack of energy; muscle weakness; seizures; or memory loss. **These may be symptoms of CRS or neurologic problems.** If you have any symptoms that impair consciousness, **do not** drive or use heavy machinery or do other dangerous activities until your symptoms go away.

EPKINLY can cause other serious side effects, including:

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- **Infections** that may lead to death. Your healthcare provider will check you for signs and symptoms of infection before and during treatment and treat you as needed if you develop an infection. You should receive medicines from your healthcare provider before you start treatment to help prevent infection. Tell your healthcare provider right away if you develop any symptoms of infection during treatment, including fever of 100.4°F (38°C) or higher, cough, chest pain, tiredness, shortness of breath, painful rash, sore throat, pain during urination, or feeling weak or generally unwell.
- **Low blood cell counts**, which can be serious or severe. Your healthcare provider will check your blood cell counts during treatment. EPKINLY may cause low blood cell counts, including low white blood cells (neutropenia), which can increase your risk for infection; low red blood cells (anemia), which can cause tiredness and shortness of breath; and low platelets (thrombocytopenia), which can cause bruising or bleeding problems.

Your healthcare provider will monitor you for symptoms of CRS, neurologic problems, infections, and low blood cell counts during treatment with EPKINLY. Your healthcare provider may temporarily stop or completely stop treatment with EPKINLY if you develop certain side effects.

Before you receive EPKINLY, tell your healthcare provider about all your medical conditions, including if you have an infection, are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed. If you receive EPKINLY while pregnant, it may harm your unborn baby. **If you are a female who can become pregnant**, your healthcare provider should do a pregnancy test before you start treatment with EPKINLY and you should use effective birth control (contraception) during treatment and for 4 months after your last dose of EPKINLY. Tell your healthcare provider if you become pregnant or think that you may be pregnant during treatment with EPKINLY. Do not breastfeed during treatment with EPKINLY and for 4 months after your last dose of EPKINLY.

In DLBCL or high-grade B-cell lymphoma, the most common side effects of EPKINLY include CRS, tiredness, muscle and bone pain, injection site reactions, fever, stomach-area (abdominal) pain, nausea, and diarrhea. **The most common severe abnormal laboratory test results** include decreased white blood cells, decreased red blood cells, and decreased platelets.

In follicular lymphoma the most common side effects of EPKINLY include injection site reactions, CRS, COVID-19, tiredness, upper respiratory tract infections, muscle and bone pain, rash, diarrhea, fever, cough, and headache. **The most common severe abnormal laboratory test results** include decreased white blood cells and decreased red blood cells.

These are not all of the possible side effects of EPKINLY. Call your doctor for medical advice about side effects. You are encouraged to report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch or to Genmab US, Inc. at 1-855-4GENMAB (1-855-443-6622).

Please see [Medication Guide](#), including Important Warnings.

Helping Patients Access Care

Genmab strives to positively impact the lives of patients when our medicines reach the people who need them. We understand the impact that cancer can have, and we offer support throughout the treatment journey. **MyNavCare Patient Support by Genmab™** is available to patients in the U.S. who have been prescribed EPKINLY. **MyNavCare** offers resources and services, from financial information to ongoing patient support, to help eligible patients access their Genmab medication. **MyNavCare** provides helpful information for patients, care partners and the healthcare providers who serve those patients throughout their treatment journey. Patients, care partners and healthcare providers interested in learning more about **MyNavCare** can visit www.MyNavCare.com or call 1-866-NAV-CAR1 (1-866-628-2271).

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About Genmab

Genmab is an international biotechnology company with a core purpose of guiding its unstoppable team to strive toward improving the lives of patients with innovative and differentiated antibody therapeutics. For 25 years, its passionate, innovative and collaborative team has invented next-generation antibody technology platforms and leveraged translational, quantitative and data sciences, resulting in a proprietary pipeline including bispecific T-cell engagers, antibody-drug conjugates, next-generation immune checkpoint modulators and effector function-enhanced antibodies. By 2030, Genmab's vision is to transform the lives of people with cancer and other serious diseases with knock-your-socks-off (KYSO[®]) antibody medicines.

Established in 1999, Genmab is headquartered in Copenhagen, Denmark, with international presence across North America, Europe and Asia Pacific. For more information, please visit Genmab.com and follow us on [LinkedIn](#) and [X](#).

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ⁱ Ma S. Risk factors of follicular lymphoma. *Expert Opin Med Diagn*. 2012;6:3232333. doi: 10.1517/17530059.2012.686996.

ⁱⁱ Leukemia & Lymphoma Society. <https://www.lls.org/research/follicular-lymphoma-fl>. Accessed March 2024.

ⁱⁱⁱ Link BK, et al. Second-Line and Subsequent Therapy and Outcomes for Follicular Lymphoma in the United States: Data From the Observational National LymphoCare Study. *Br J Haematol* 2019;184(4):660-663.

^{iv} Ren J, et al. Economic Burden and Treatment Patterns for Patients With Diffuse Large B-Cell Lymphoma and Follicular Lymphoma in the USA. *J Comp Eff Res* 2019;8(6):393-402.

^v Ghione P, Palomba ML, Ghesquieres H, et al. Treatment patterns and outcomes in relapsed/refractory follicular lymphoma: results from the international SCHOLAR-5 study. *Haematologica*. 2023;108(3):822-832. doi: 10.3324/haematol.2022.281421.

^{vi} National Comprehensive Cancer Network "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines); B-Cell Lymphomas." Version 2.2024 published April 30, 2024.

^{vii} Lymphoma Research Foundation official website. <https://lymphoma.org/aboutlymphoma/nhl/fl/>. Accessed February 2024.

^{viii} Lymphoma Research Foundation official website. <https://lymphoma.org/understanding-lymphoma/aboutlymphoma/nhl/follicular-lymphoma/relapsedfl/>. Accessed February 2024.

^{ix} Rivas-Delgado, A., Magnano, L., Moreno-Velázquez, et al. Response duration and survival shorten after each relapse in patients with follicular lymphoma treated in the rituximab era. *Br J Haematol*. 2018;184(5):753-759. doi:10.1111/bjh.15708

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^x Kuruvilla J, Ewara EM, Elia-Pacitti J, et al. Estimating the Burden of Illness of Relapsed Follicular Lymphoma and Marginal Zone Lymphoma in Ontario, Canada. *Curr Oncol.* 2023;30(5):4663-4676. doi:10.3390/curroncol30050352

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