EPKINLY® (epcoritamab) Approved by Japan Ministry of Health, Labour and Welfare for Additional Indication as a Treatment for Relapsed or Refractory Follicular Lymphoma

Media Release

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- **Approval based on results from two Phase 1/2 EPCORE® clinical trials, which demonstrated strong and durable efficacy in patients with relapsed or refractory (R/R) follicular lymphoma (FL) who had received two or more lines of systemic therapy**
- **EPKINLY is the first and only T-cell engaging bispecific antibody administered subcutaneously approved in Japan to treat both R/R FL and R/R large B-cell lymphomas, after two or more prior lines of therapy**
- **EPKINLY is the only bispecific antibody approved with a dual indication for the treatment of certain B-cell malignancies in the United States, European Union and Japan**

Genmab A/S (Nasdaq: GMAB) announced today that the Japan Ministry of Health, Labour and Welfare has approved EPKINLY® (epcoritamab) for the treatment of patients with relapsed or refractory (R/R) follicular lymphoma (FL; Grades 1 to 3A) who have received two or more prior lines of therapy. With this additional indication, EPKINLY is now the first and only T-cell engaging bispecific antibody administered subcutaneously to be approved in Japan to treat both R/R FL and R/R large B-cell lymphomas, including diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma and primary mediastinal large B-cell lymphoma, after two or more prior lines of therapy.

FL is typically an indolent (or slow growing) form of non-Hodgkin's lymphoma (NHL) that arises from B-lymphocytes and is the second most common form of NHL, accounting for 20-30 percent of all cases.[i] There are approximately 19,000 patients currently living with FL in Japan.[ii] FL is considered incurable with current standard of care therapies.[iii] Patients often relapse and, with each relapse, the remission and time to next treatment is shorter.[iv] Over time, transformation to DLBCL, an aggressive form of NHL associated with poor survival outcomes, can occur in more than 25 percent of FL patients.[v]

"In the treatment of follicular lymphoma, where options become limited with each relapse, there remains a high unmet need for third-line and subsequent therapies in the absence of a clear standard of care," said Dr. Koji Izutsu, Head of the Department of Hematology, National Cancer Center Hospital, who served as the principal investigator of the Japanese Phase 1/2 clinical trial (EPCORE NHL-3 trial). "The responses and tolerability demonstrated in this trial support the potential of epcoritamab to become an important option in future treatment strategies for relapsed/refractory follicular lymphoma."

The approval is based on results from the global Phase 1/2 EPCORE NHL-1 and the Japanese Phase 1/2 EPCORE NHL-3 clinical trials, which were open-label, multicenter studies to evaluate the safety and efficacy of EPKINLY as a monotherapy in patients with R/R mature B-cell non-Hodgkin's lymphoma, including FL. In the Japanese trial, a 2-step step-up dosing (SUD) regimen was used. In the global trial, two different dose escalation methods were used – 2-step and 3-step SUD regimens – to mitigate a common adverse reaction from T-cell engaging cancer treatments known as cytokine release syndrome (CRS).

EPCORE® NHL-1 Global Clinical Trial Results
Among the 128 evaluable patients with R/R FL in the EPCORE NHL-1 trial, the overall response rate (ORR) and the complete response (CR) rate were 82 percent (95 percent CI: 74.3-88.3) and 62.5 percent, respectively (data cut-off: April 21, 2023). Ninety-one patients were evaluable for a minimal residual disease (MRD) analysis, with 67 percent of patients achieving 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).

Among the patients who received EPKINLY with the 2-step SUD regimen (n=128), adverse events were observed in 119 patients (93 percent). The most common treatment-emergent adverse events (TEAEs) (≥20 percent) included CRS (66.4 percent) and injection site reactions (36.7 percent).

As part of a separate dose-optimization cohort in the trial, a 3-step SUD regimen was evaluated in 86 patients with FL (Grades 1 to 3A). Adverse events were observed in 78 patients (90.7 percent). The most common TEAEs included CRS (48.8 percent) and injection site reactions (26.7 percent).

EPCORE® NHL-3 Japanese Clinical Trial Results
Among the 21 evaluable patients with R/R FL in the Japanese trial, with a median follow up of 21.2 months, the ORR and the CR rate were 95.2 percent (95 percent CI: 76.2-99.9) and 76.2 percent, respectively. Additionally, 88.9 percent of patients achieved MRD negativity (n=18).

Among patients who received EPKINLY with the 2-step SUD regimen, the most common TEAEs included CRS (90.5 percent), injection site reactions (71.4 percent), rash (28.6 percent), neutropenia (28.6 percent), increased alanine aminotransferase (23.8 percent) and increased aspartate aminotransferase (23.8 percent).

“Patients living with relapsed or refractory follicular lymphoma in Japan deserve options, and we are proud that EPKINLY may help treat patients as their cancer returns or stops responding to other therapies,” said Dr. Judith Klimovsky, Executive Vice President and Chief Development Officer of Genmab. “Over the last year, EPKINLY has been approved in the U.S., the European Union (as TEPKINLY®) and Japan. With a dual indication in relapsed or refractory follicular lymphoma and diffuse large B-cell lymphoma after two or more prior therapies, we are committed to making epcoritamab available to patients in need and continuing its broad development as a potential core therapy across B-cell malignancies.”

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 (ORR) as assessed by an Independent Review Committee. Secondary efficacy endpoints included duration of response (DoR), complete response (CR) rate, duration of complete response (DoCR), progression-free survival (PFS), and time to response as determined by the Lugano criteria. Overall survival (OS), time to next therapy, and rate of minimal residual disease (MRD) negativity were also evaluated as secondary efficacy endpoints. The primary endpoint of the optimization part was the rate of ≥ 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 the EPCORE® NHL-3 Trial
EPCORE® NHL-3 is an open-label, multi-center safety and efficacy trial of epcoritamab that consists of a Phase 1 first-in-human dose escalation part and a Phase 2 expansion part. The Phase 2 expansion part evaluated subcutaneous administration of epcoritamab in Japanese patients with relapsed, progressive, or refractory mature B-cell NHL, including FL. The primary endpoint of the expansion part was ORR as assessed by IRC, and secondary efficacy endpoints included DOR, CR rate, DoCR, PFS, and time to response based on the Lugano criteria.

About EPKINLY® (epcoritamab)
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.[vi]

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. Both companies will pursue additional international regulatory approvals for the investigational R/R FL indication and additional approvals for the R/R DLBCL indication.

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 five 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 patients with newly diagnosed DLBCL (NCT05578976), a trial evaluating epcoritamab in combination with rituximab and lenalidomide (R2) in patients with R/R FL (NCT05409066), a trial evaluating epcoritamab in combination with rituximab and lenalidomide (R2) compared to chemoimmunotherapy in patients with previously untreated FL (NCT06191744), and a trial evaluating epcoritamab in combination with R2 compared to chemotherapy infusion in patients with R/R DLBCL (NCT06508658). The safety and efficacy of epcoritamab has not been established for these investigational uses. Please visit www.clinicaltrials.gov for more information.

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 more than 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.

Contact:
Caitlin Craparo, Senior Director, Commercialization Communications
T: +1 609 255 7397; E: cacr@genmab.com

Andrew Carlsen, Vice President, Head of Investor Relations
T: +45 3377 9558; E: acn@genmab.com

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which are available at www.sec.gov. Genmab does not undertake any obligation to update or revise forward looking statements in this Media Release nor to confirm such statements to reflect subsequent events or circumstances after the date made or in relation to actual results, unless required by law.

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Genmab A/S
Carl Jacobsens Vej 30
2500 Valby
Denmark

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