Two Data Analyses from Clinical Trials Show Epcoritamab (DuoBody® CD3xCD20) Induces Durable, Complete Responses as Monotherapy and Combination Treatment in Patients With Diffuse Large B-Cell Lymphoma (DLBCL)

Media Release

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- **Results from Arm 1 of the EPCORE® NHL-2 trial show treatment with epcoritamab combination led to an overall response rate (ORR) of 100 percent and a complete response (CR) rate of 87 percent in high-risk patients with previously untreated diffuse large B-cell lymphoma (DLBCL)**
- **Extended follow-up data from EPCORE® NHL-1 trial demonstrates durability of responses and long-term safety of epcoritamab monotherapy for patients with challenging-to-treat relapsed/refractory (R/R) DLBCL**
- **Both analyses were presented at the 66th Annual Meeting and Exposition of the American Society of Hematology (ASH)**

Genmab A/S (Nasdaq: GMAB) today announced new long-term results from two ongoing clinical trials evaluating epcoritamab, a T-cell engaging bispecific antibody administered subcutaneously, in adult patients with diffuse large B-cell lymphoma (DLBCL). Results from Arm 1 of the Phase 1b/2 EPCORE® NHL-2 trial (NCT04663347), evaluating fixed-duration epcoritamab in combination with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), demonstrated an overall response rate (ORR) of 100 percent and a complete response (CR) rate of 87 percent in high-risk patients (n=46) with previously untreated DLBCL. Among complete responders, 83 percent remained in remission after two years. Separately, results from the Phase 2 EPCORE® NHL-1 trial (NCT03625037), evaluating epcoritamab monotherapy in challenging-to-treat adult patients (n=157) with relapsed or refractory (R/R) large B-cell lymphoma (LBCL; including 148 patients with R/R DLBCL), showed that among the 41 percent of patients who achieved a CR, an estimated 52 percent were still responding at three years (median CR duration: 36.1 months). Both analyses were presented at the 66th Annual Meeting and Exposition of the American Society of Hematology (ASH).

“The unprecedented durability of response seen in these data reinforce the potential of epcoritamab to become a core therapy for the treatment of multiple B-cell malignancies to benefit more patients,” said Dr. Judith Klimovsky, Executive Vice President and Chief Development Officer of Genmab. “These results support our ongoing Phase 3 trials for epcoritamab, including as an investigational first-line combination therapy in patients with previously untreated diffuse large B-cell lymphoma.”

EPCORE® NHL-2 Results in First-Line DLBCL (Abstract #581)
The EPCORE NHL-2 trial enrolled 46 patients considered to have high-risk DLBCL, identified by International Prognostic Index (IPI) scores of 3 to 5, a range associated with poor long-term outcomes. The IPI is a key tool used by oncologists to predict the prognosis of aggressive B-cell lymphomas.[i] At screening, 35 percent of patients (n=16) had bulky disease (>10 cm) and 21 percent (n=6) of evaluable patients (n=28) had double-hit/triple-hit LBCL based on gene rearrangements identified by central analysis.

- With a median follow-up of 27.4 months (range, 0.8-33.9), 87 percent of patients remained alive at two years and 74 percent were progression free.
- At two years, a minimal residual disease (MRD) analysis showed MRD negativity was achieved in 91 percent of evaluable patients (30/33), indicating no detectable disease.
- Epcoritamab in combination with R-CHOP is being studied further in the ongoing, randomized, Phase 3 EPCORE DLBCL-2 trial (NCT05578976).

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"More first-line treatment options for diffuse large B-cell lymphoma are needed, especially for patients with aggressive disease prognostic markers that may impact the efficacy of current standard first-line therapies," said Lorenzo Falchi, MD, Lymphoma Specialist, Department of Medicine, Memorial Sloan Kettering Cancer Center.[ii] "Relapse rates with the R-CHOP treatment regimen can reach 50 percent, so the durable responses observed in the study suggest significant potential for this first-line epcoritamab-based combination."

The most common treatment-emergent adverse events (TEAEs) were neutropenia (70 percent), anemia (69 percent), cytokine release syndrome (CRS; 60 percent), fatigue (49 percent), nausea (47 percent), pyrexia (42 percent), and injection-site reaction (40 percent). Four patients (9 percent) discontinued epcoritamab due to TEAEs; fatal TEAEs occurred in two patients (COVID-19 and septic shock). CRS events were mostly low grade (45 percent Grade 1, 11 percent Grade 2, 4 percent Grade 3) and mainly occurred after the first full dose. All CRS cases resolved, and none led to discontinuation. Immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in two patients (one Grade 1; one Grade 2) and resolved in a median of 2.5 days without leading to discontinuation.

Use of epcoritamab + R-CHOP in first-line DLBCL is not approved in the U.S. or in the EU or in any other territory. The safety and efficacy of epcoritamab for use as a combination therapy in DLBCL have not been established.

EPCORE® NHL-1 Results in Third-Line LBCL (Abstract #4480)
Three-year follow-up results from the Phase 2 EPCORE® NHL-1 trial evaluated epcoritamab monotherapy in 157 patients with R/R LBCL and demonstrated that epcoritamab continues to deliver durable responses in challenging-to-treat patients.

- The ORR was 59 percent, and the CR rate was 41 percent. Median duration of response was 20.8 months (95 percent CI, 13.0-32.0) and median duration of CR was 36.1 months (95 percent CI, 20.2 to not reached [NR]).
- 52 percent of patients who experienced a CR were still responding at three years (median CR duration: 36.1 months).
- Of the 119 patients who were MRD-evaluable, 54 (45 percent) achieved MRD-negativity. In a cycle 3-day 1 landmark analysis, 3-year PFS rates were 52 percent among MRD-negative patients and 18 percent among MRD-positive patients.

The most common TEAEs were CRS (51 percent; 32 percent Grade 1, 16 percent Grade 2, 3 percent Grade 3), fatigue (25 percent), and pyrexia (25 percent); CRS rates remained unchanged since prior reports. Fatal TEAEs were reported in 20 patients; 10 patients had Grade 5 COVID-19 (including COVID-19 pneumonia). Seventy-three percent of patients treated with epcoritamab for two or more years did not experience a Grade 3 or higher infection after two years (median follow-up after 2 years, 12.3 months). Incidence of Grade 3 or higher cytopenias was highest (27 percent) during the first eight weeks of treatment and rates were within 0-13 percent in subsequent 12-week time periods up to week 144. Immunoglobulin G levels decreased by a median of approximately 20 percent after the start of epcoritamab treatment (baseline median, 540.0 mg/dL) and remained stable over time.

About Diffuse Large B-Cell Lymphoma (DLBCL)
DLBCL is the most common type of non-Hodgkin's lymphoma (NHL) worldwide, accounting for approximately 25-30 percent of all NHL cases.[iii,iv] In the U.S., there are approximately 25,000 new cases of DLBCL diagnosed each year.[v] DLBCL can arise in lymph nodes as well as in organs outside of the lymphatic system, occurs more commonly in the elderly and is slightly more prevalent in men.[vi,vii] DLBCL

is a fast-growing type of NHL, a cancer that develops in the lymphatic system and affects B-cell lymphocytes, a type of white blood cell. For many people living with DLBCL, their cancer either relapses, which means it may return after treatment, or becomes refractory, meaning it does not respond to treatment. Although new therapies have become available, treatment management can remain a challenge. [viii,ix]

About the EPCORE® NHL-2 Trial
EPCORE® NHL-2 is a Phase 1b/2 open-label interventional trial to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics/biomarkers, immunogenicity, and preliminary efficacy of epcoritamab as a monotherapy and in combination with other standard of care agents in patients with B-cell non-Hodgkin's lymphoma (B-NHL). The trial consists of two parts: Part 1 (Dose Escalation) and Part 2 (Dose Expansion). The primary objective of Part 1 is safety, and the primary goal of Part 2 is preliminary efficacy. The primary endpoint was overall response rate (ORR) based on best overall response per Lugano criteria. MRD negativity was assessed as a secondary endpoint.

Arm 1 of the trial is epcoritamab plus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL). More information on this trial can be found at https://www.clinicaltrials.gov/ (NCT: 04663347).

About the EPCORE® NHL-1 Trial
EPCORE® NHL-1 is an open-label, multicohort, single-arm, Phase 1/2 trial of epcoritamab in participants with relapsed or refractory large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL). The trial was conducted at 88 sites across 15 countries and consisted of three parts: a Phase 1 first-in-human, dose escalation part; a Phase 2a expansion part; and a Phase 2a dose optimization part. More information on this trial can be found at https://www.clinicaltrials.gov/ (NCT: 03625037).

About 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.[x]

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 investigator's 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 (R^2) in patients with R/R FL (NCT05409066), a trial evaluating epcoritamab in combination with rituximab and lenalidomide (R^2) compared to chemoimmunotherapy in patients with previously untreated FL (NCT06191744), and a trial

evaluating epcoritamab in combination with lenalidomide 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 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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[ii] Dr. Falchi has financial interests related to Genmab and AbbVie.
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