# Investigational Epcoritamab (DuoBody® CD3xCD20) Monotherapy Achieves High Overall and Complete Response Rates in Clinical Trial of Patients With Relapsed or Refractory (R/R) Chronic Lymphocytic Leukemia (CLL) in Preliminary Analysis

## Media Release

**COPENHAGEN, Denmark; December 8, 2024**

- **Preliminary analyses from the EPCORE® CLL-1 trial demonstrates overall response rate (ORR) of 61 percent and complete response (CR) rate of 39 percent in heavily pretreated patients with relapsed or refractory (R/R) chronic lymphocytic leukemia (CLL) who received epcoritamab monotherapy**
- **In the study, 75 percent of evaluable responders achieved undetectable minimal residual disease (MRD), indicating no detectable disease following treatment with epcoritamab**
- **The data were selected as part of the 2024 American Society of Hematology's (ASH's) Annual Meeting Press Program in the *Diagnosing and Treating Blood Cancers and "Almost Cancers"* briefing**

**Genmab A/S (Nasdaq: GMAB)** today announced results from the Phase 1b/2 EPCORE® CLL-1 clinical trial evaluating epcoritamab (Abstract #883), a T-cell engaging bispecific antibody administered subcutaneously, demonstrated an overall response rate (ORR) of 61 percent and a complete response (CR) rate of 39 percent in difficult-to-treat adult patients with relapsed or refractory (R/R) chronic lymphocytic leukemia (CLL) treated with epcoritamab monotherapy. These results, from the monotherapy expansion (EXP) cohort (n=23) of the trial, along with the first safety data from the optimization (OPT) cohort, were presented at the 66th Annual Meeting and Exposition of the American Society of Hematology (ASH), during the ASH Annual Meeting Press Program. The data will be presented during an oral session on December 9, 2024.

In the EXP cohort, the median time to response was two (2.0) months and the median time to CR was 5.6 months. Among all patients in the cohort, median progression-free survival (PFS) was 12.8 months and median overall survival (OS) was not reached (median follow-up was 22.8 months). An estimated 65 percent of patients were alive at 15 months. Among 12 responders evaluable for minimal residual disease (MRD) by next-generation sequencing in peripheral blood, nine patients (75 percent) had undetectable MRD.

The most frequent non-hematologic treatment-emergent adverse events (TEAEs) in the EXP cohort were cytokine release syndrome (CRS; 96 percent), diarrhea (48 percent), peripheral edema (48 percent), fatigue (43 percent), and injection-site reaction (43 percent). Cytopenias were common (anemia, 65 percent; thrombocytopenia, 65 percent; neutropenia, 48 percent); however, most patients had baseline anemia and thrombocytopenia, suggesting that these events were largely disease-related. Three cases of immune effector cell-associated neurotoxicity syndrome (ICANS) were reported (one Grade 1; two Grade 2), and there was one clinical tumor lysis syndrome (CTLS) case (Grade 2). These cases did not lead to treatment discontinuation. Four fatal TEAEs occurred - two cases of pneumonia, one case of sepsis and one case of squamous cell carcinoma of the skin.

The EXP cohort followed a 2-step step-up dose regimen, and CRS was manageable and primarily low grade (9 percent Grade 1, 70 percent Grade 2, 17 percent Grade 3). In the first data from the separate OPT cohort, which followed a 3-step step-up dose regimen, CRS severity was substantially reduced with only low-grade events (71 percent Grade 1, 12 percent Grade 2). In both cohorts, CRS events primarily occurred following the first full dose, and none led to treatment discontinuation. No ICANS or CTLS cases were reported in the OPT cohort.

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"These EPCORE CLL-1 data are encouraging, especially as the majority of patients were heavily pre-treated with at least four lines of therapy," said Alexey Danilov, MD, PhD, Marianne and Gerhard Pinkus, Professor and Director of Early Clinical Therapeutics and Associate Director of the Toni Stephenson Lymphoma Center, Department of Hematology and Hematopoietic Cell Transplantation, City of Hope. "Despite progress in treating chronic lymphocytic leukemia, there remains a tremendous need for additional therapeutic options for high-risk patients whose disease has progressed following standard chemoimmunotherapy and targeted therapies."

Additional data from the EXP cohort showed high response rates in patients with high-risk factors treated with epcoritamab, including TP53 aberrations, IGHV-unmutated disease and double-exposed disease – prognostic markers that are associated with disease progression and decreased survival.[i,ii,iii] In patients with TP53 aberrations (n=15), the ORR was 67 percent with a CR of 33 percent. Among patients with IGHV-unmutated disease (n=16), the ORR was 63 percent, and the CR was 44 percent. In double-refractory patients, the ORR was 53 percent, and the CR was 37 percent.

All patients in the trial had prior chemoimmunotherapy, and most patients had previously received targeted therapies such as BTK and BCL2 inhibitors (double-exposed) and had high-risk disease characteristics.

"Chronic lymphocytic leukemia is incurable, and patients often need a variety of treatments throughout their lifetime, especially if their disease has high-risk prognostic factors, has relapsed or has become refractory to the current standard-of-care, including targeted therapies," said Dr. Judith Klimovsky, Executive Vice President & Chief Development Officer, Genmab. "These early data show the potential therapeutic applicability of epcoritamab in relapsed or refractory chronic lymphocytic leukemia, and further reinforce the potential of epcoritamab as a core therapy for the treatment of B-cell malignancies."

Use of epcoritamab in CLL is not approved in the U.S. or in the EU or in any other territory. The safety and efficacy of epcoritamab for use in CLL have not been established.

**About Chronic Lymphocytic Leukemia (CLL)**
Chronic lymphocytic leukemia (CLL) is the most prevalent type of leukemia, affecting over 200,000 people in the United States alone.[iv] Chronic lymphocytic leukemia can be classified as either slow growing (indolent) or fast growing (aggressive).[v] CLL is incurable, and many patients will likely relapse and progress on frontline therapies.[vi] Most patients will experience consecutive episodes of disease progression and will require several lines of treatment in their lifetime.[vii,viii]

**About the EPCORE® CLL-1 Trial**
EPCORE® CLL-1 is a Phase 1b/2, open-label, multi-center trial to evaluate the safety and preliminary efficacy of epcoritamab as a monotherapy and in combination with standard of care agents in patients with difficult-to-treat relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL), R/R small lymphocytic lymphoma (SLL) and Richter's Syndrome (RS). The trial consists of two parts: a dose-escalation phase (Phase 1b) and an expansion phase (Phase 2). Patients with RS are only included in the expansion phase. The primary objective of Phase 1b is to determine the recommended Phase 2 dose and the maximum tolerated dose as well as establish the safety profile of epcoritamab monotherapy and epcoritamab plus venetoclax in participants with R/R CLL. The purpose of Phase 2 is to assess and evaluate the preliminary efficacy, safety and tolerability profiles of epcoritamab monotherapy and epcoritamab plus venetoclax for patients with R/R CLL and SLL. Additionally, epcoritamab monotherapy and combination therapy will be evaluated in patients with RS to assess their efficacy, safety and

tolerability profiles. More information on this trial can be found at https://www.clinicaltrials.gov/ (NCT: 04623541).

**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.[ix]

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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*This Media Release contains forward looking statements. The words "believe," "expect," "anticipate," "intend" and "plan" and similar expressions identify forward looking statements. Actual results or performance may differ materially from any future results or performance expressed or implied by such statements. The important factors that could cause our actual results or performance to differ materially include, among others, risks associated with preclinical and clinical development of products, uncertainties related to the outcome and conduct of clinical trials including unforeseen safety issues, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products or technologies obsolete, and other factors. For a further discussion of these risks, please refer to the risk management sections in Genmab's most recent financial reports, which are available on www.genmab.com and the risk factors included in Genmab's most recent Annual Report on Form 20-F and other filings with the U.S. Securities and Exchange Commission (SEC), 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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