Genmab Announces New Data from Phase 1b/2 EPCORE® CLL-1 Highlighting Potential of Epcoritamab as Monotherapy and in Combination for Patients with Richter Transformation (RT)

Media Release

COPENHAGEN, Denmark; December 8, 2025

- **Two-year epcoritamab monotherapy data demonstrate high complete response and encouraging survival rates in patients with Richter transformation (RT), highlighting its potential as a treatment option for those unsuitable for chemotherapy**
- **Additional early data show promising efficacy of epcoritamab combination regimens in patients with RT**
- **Results underscore the potential of epcoritamab as a versatile therapy for a broad range of B-cell malignancies**

Genmab A/S (Nasdaq: GMAB) today announced new and updated data from three arms of the ongoing Phase 1b/2 EPCORE® CLL-1 trial (NCT04623541) evaluating the efficacy and safety of epcoritamab-bysp, a T-cell engaging bispecific antibody administered subcutaneously, as a monotherapy and in combination for the treatment of patients with Richter transformation (RT), a rare complication in which chronic lymphocytic leukemia (CLL) evolves into an aggressive lymphoma, most often diffuse large B-cell lymphoma (DLBCL). The results were presented today in two oral presentations (abstracts 1015 and 1017) at the 67th Annual Meeting and Exposition of the American Society of Hematology (ASH), in Orlando, Florida.

EPCORE® CLL-1, Arm 2A (Epcoritamab Monotherapy)
In Arm 2A of the trial, patients with RT (n=42) received epcoritamab monotherapy in the first-line setting or in second- or later-line settings, with a median follow-up of 22.9 months. In the first-line setting (n=21), patients achieved an overall response rate (ORR) of 57%, with 52% experiencing a complete response (CR). The median overall survival (OS) was 27.5 months, progression-free survival (PFS) was 8.5 months, and the median duration of response (DOR) and duration of complete response (DOCR) were not reached. Among RT patients who received epcoritamab monotherapy in second- or third-line settings (n=21), ORR was 38% and the CR rate was 29%. The median DOR was 6.6 months, median PFS was 2.9 months, and median OS was 9.8 months. The results from Arm 2A have been simultaneously published in *The Lancet Haematology*.

“Patients with Richter transformation, an aggressive form of lymphoma, have limited treatment options and face a poor prognosis,” said Arnon Kater, M.D., Ph.D., Department of Hematology, Amsterdam UMC. “The response and survival rates observed in this trial evaluating epcoritamab as a monotherapy treatment are encouraging, especially as a potential option for patients with Richter transformation.”

In this arm, cytokine release syndrome (CRS) occurred in 86% of patients (79% with Grade 1/2), immune effector cell-associated neurotoxicity syndrome (ICANS) in 12% of patients (all Grade 1/2), and clinical tumor lysis syndrome (CTLS) in 5%. Most CRS events occurred after the first full dose and resolved within a median of three days in 97% of patients.

EPCORE® CLL-1, Arm 2B (Epcoritamab Lenalidomide Combination)
In Arm 2B, previously-treated patients with RT (n=11) ineligible to receive chemoimmunotherapy who had two or less prior lines of therapy received epcoritamab in combination with lenalidomide. With a median follow-up of 16.7 months, the ORR was 82% and the CR rate was 73%. The median OS at nine months was not reached, and the median PFS was 5.7 months. The estimated median DOR and DOCR were not reached.

Genmab Announces New Data from Phase 1b/2 EPCORE® CLL-1 Highlighting Potential of Epcoritamab as Monotherapy and in Combination for Patients with Richter Transformation (RT)

In this arm of the trial, CRS events were primarily low grade and resolved in 10 patients, with a median time to resolution of four days. One patient discontinued due to CRS. ICANS occurred in two patients (Grade 1/2) and resolved in a median of 2.5 days. There was one treatment-related Grade 5 event.

“With no standard of care for patients with Richter transformation, clinicians are in need of new, therapeutic options with the potential for patients to achieve and maintain remissions,” said Philip A. Thompson, MB, MS, Peter MacCallum Cancer Center Melbourne, Australia. “These first results from the combination arms of the EPCORE CLL-1 study demonstrate the potential of epcoritamab combination regimens as potential therapeutic options for those living with Richter transformation.”

EPCORE® CLL-1, Arm 2C (Epcoritamab R-CHOP Combination)
In Arm 2C, previously untreated patients with RT (n=30) received epcoritamab in combination with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). With a median follow-up of 13.6 months, the ORR was 77% and the CR rate was 63%. The median OS was 16.4 months and the median PFS was 16.0 months. The estimated median DOR and median DOCR were not reached.

In this arm, CRS events were primarily low Grade (Grade 1, 7; Grade 2, 8; Grade 3, 2) and median time to resolution was 2.0 days. No patients discontinued due to CRS. ICANS occurred in four patients (Grade 1, 3; Grade 3, 1); three cases resolved in a median of one day, and one was ongoing at time of death. There were three treatment-related Grade 5 events.

“The results from these trials demonstrate the potential of epcoritamab as a monotherapy, and in combination, in patients with Richter transformation, a rare, often fatal, transformation of chronic lymphocytic leukemia into an aggressive lymphoma, mostly diffuse large B-cell lymphoma,” said Dr. Judith Klimovsky, Executive Vice President and Chief Development Officer of Genmab. “We are deeply committed to exploring epcoritamab as a potential core therapy across a range of B-cell malignancies, both as an initial treatment and as a later line of therapy.”

The safety and efficacy of epcoritamab have not been established for these investigational uses.

In all three study arms, safety was consistent with the known profiles of each agent. In Arm 2A, the most common treatment-emergent adverse events (TEAEs) were infection (74%), anemia (50%), thrombocytopenia (48%), neutropenia (45%), diarrhea (36%), and fatigue (31%). Four patients (10%) discontinued treatment due to a TEAE, and three (7%) experienced fatal events, none considered related to study treatment. In Arm 2B, common TEAEs were CRS (100%), neutropenia (82%), thrombocytopenia (73%), anemia and hypokalemia (45% each). Grade ≥3 TEAEs occurred in all patients, serious TEAEs in 10/11, and epcoritamab-related discontinuations and fatal TEAEs in one patient each. In Arm 2C, common TEAEs were CRS (56%), anemia (60%), neutropenia (73%), thrombocytopenia (46%), diarrhea (33%), and febrile neutropenia (30%). Grade ≥3 TEAEs occurred in 27 (90%) patients and serious TEAEs in 25 (83%). TEAEs led to epcoritamab discontinuations in six (20%) patients and there were three fatal TEAEs (one epcoritamab related). CTLS was not reported in Arms 2B or 2C.

About Richter Transformation (RT)
Richter transformation (RT) is a rare but aggressive evolution of chronic lymphocytic leukemia (CLL), most often into CD20+ diffuse large B-cell lymphoma (DLBCL).[i] Prognosis of RT is poor, with complete remission rates of approximately 20% and median survival often less than one year following chemoimmunotherapy.[ii,iii]

Genmab Announces New Data from Phase 1b/2 EPCORE® CLL-1 Highlighting Potential of Epcoritamab as Monotherapy and in Combination for Patients with Richter Transformation (RT)

About the EPCORE® CLL-1 Trial
EPCORE® CLL-1 is a global, 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 transformation (RT). The trial consists of two parts: a dose-escalation phase (Phase 1b) and an expansion phase (Phase 2). Patients with RT are only included in the expansion phase. In patients with RT, epcoritamab monotherapy (Arm 2A) and combination therapy with lenalidomide (Arm 2B) or R-CHOP (Arm 2C) will be evaluated to assess their efficacy, safety and tolerability profiles.

More information on this trial can be found at 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.[iv]

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. Where approved, epcoritamab is a readily accessible therapy. 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 four ongoing Phase 3, open-label, randomized trials, among them 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 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.®

Genmab Announces New Data from Phase 1b/2 EPCORE® CLL-1 Highlighting Potential of Epcoritamab as Monotherapy and in Combination for Patients with Richter Transformation (RT)

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:
David Freundel, Senior Director, Global Communications & Corporate Affairs
T: +1 609 613 0504; E: dafr@genmab.com

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

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.

---

[i] National Cancer Institute: Richter transformation. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/richter-transformation Accessed November 2025.
[ii] Mac Manus MP, Rainer Bowie CA, Hoppe RT. What is the prognosis for patients who relapse after primary radiation therapy for early-stage low-grade follicular lymphoma? Int J Radiat Oncol Biol Phys. 1998 Sep 1;42(2):365-71. doi: 10.1016/s0360-3016(98)00233-8. PMID: 9788417.
[iii] Jain T, Heyman B. Updates on the Treatment of Richter's Syndrome, Including Novel Combination Approaches. Cancers (Basel). 2025 Mar 11;17(6):943. doi: 10.3390/cancers17060943. PMID: 40149279; PMCID: PMC11940134.
[iv] Engelberts PJ, et al. DuoBody-CD3xCD20 Induces Potent T-Cell-Mediated Killing of Malignant B Cells in Preclinical Models and Provides Opportunities for Subcutaneous Dosing. *EBioMedicine*. 2020;52:102625. doi: 10.1016/j.ebiom.2019.102625.