EPKINLY™ (epcoritamab) Approved by Japan Ministry of Health, Labour and Welfare as the First Bispecific Antibody to Treat Adults Patients with Certain Types of Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL)

Media Release

- **Subcutaneous EPKINLY™ (epcoritamab) is the first and only bispecific antibody approved in Japan to treat adult patients with certain types of relapsed/refractory (R/R) large B-cell lymphoma (LBCL) after two or more lines of systemic therapy**
- **Approval based on results of EPCORE™ NHL-3 and EPCORE™ NHL-1 clinical trials, evaluating EPKINLY in patients with certain types of R/R LBCL**
- **LBCL is a common form of non-Hodgkin's lymphoma (NHL) and currently has limited treatment options, particularly in the R/R setting**

COPENHAGEN, Denmark; September 25, 2023 – Genmab A/S (Nasdaq: GMAB) announced today that the Japan Ministry of Health, Labour and Welfare has approved EPKINLY™ (epcoritamab) as the first and only T-cell engaging bispecific antibody treatment in Japan of adult patients with certain types of relapsed or refractory large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma (HGBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B), after two or more lines of systemic therapy. Epcoritamab is being co-developed by Genmab and AbbVie as part of the companies' oncology collaboration.

"Despite recent advances in the treatment of LBCL, the prognosis for patients with relapsed/refractory LBCL remains generally poor, and there is a need for additional treatment options for patients whose condition has worsened after multiple lines of treatment," said Koji Izutsu, MD, PhD, principal investigator of the phase 1/2 EPCORE NHL-3 trial in Japan and Head of the Hematology Department, National Cancer Center Hospital. "In the EPCORE NHL-3 trial, subcutaneous epcoritamab monotherapy demonstrated responses in a considerable number of patients with relapsed/refractory DLBCL, indicating that this approval is of great significance."

The approval of EPKINLY in Japan is based on the results from two open-label, multi-center studies designed to evaluate the safety and preliminary efficacy of EPKINLY monotherapy in patients with R/R LBCL. In the phase 1/2 EPCORE NHL-1 trial, 157 patients with relapsed or refractory LBCL demonstrated an overall response rate (ORR) of 63 percent ([95 percent confidence interval (CI): 55.0-70.6]) and a complete response (CR) rate of 39 percent (data cutoff: January 31, 2022). Of 157 patients treated with EPKINLY, 130 (82.8 percent) experienced treatment related side effects. The most common side effects (>15 percent) included cytokine release syndrome (49.7 percent), injection site reactions (19.7 percent), and neutropenia (17.8 percent).

In the phase 1/2 EPCORE NHL-3 trial, 36 patients with relapsed or refractory DLBCL after two or more lines of treatment demonstrated similar results with an ORR of 56 percent ([95 percent CI: 38.1-72.1]) and a CR rate of 44 percent (data cutoff: January 31, 2022). Of 36 patients treated with EPKINLY, 36 (100 percent) experienced treatment related side effects. The most common side effects (>15 percent) included cytokine release syndrome (83.3 percent), injection site reactions (58.3 percent), neutropenia (30.6 percent), lymphopenia (19.4 percent), decreased appetite (19.4 percent), thrombocytopenia (19.4 percent), and rash (19.4 percent).

"This approval marks an important milestone for patients in Japan with relapsed/refractory large B-cell lymphoma who are in need of alternative therapeutic options and who may now have access to EPKINLY, the first approved T-cell engaging bispecific antibody," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab. "We are working closely with AbbVie to deliver EPKINLY to patients in

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Japan as quickly as possible and we remain committed to continue evaluating epcoritamab as a potential core therapy across B-cell malignancies."

About the EPCORE™ NHL-3 Trial
EPCORE™ NHL-3 is an open-label, multi-center safety and preliminary efficacy trial of epcoritamab including a phase 1 first-in-human, dose escalation part; and a phase 2 expansion part. The trial was designed to evaluate subcutaneous epcoritamab in Japanese patients with relapsed, progressive or refractory mature B-NHL, including DLBCL. In the phase 2 expansion part, additional patients are treated with epcoritamab to further explore the safety and efficacy of epcoritamab in patients with R/R DLBCL and R/R FL who had limited therapeutic options.

In the study, 56 percent of the patients had primary refractory disease and 81 percent of patients were refractory to their last therapy. The median number of prior therapies was three (range: 2 to 8), with 44 percent of patients receiving two prior therapies, 25 percent receiving three prior therapies, and 31 percent receiving four or more prior therapies. Nineteen percent had prior autologous stem cell transplantation (ASCT), no one had prior chimeric antigen receptor (CAR) T-cell therapy.

About the EPCORE™ NHL-1 Trial
EPCORE™ NHL-1 is an open-label, multi-center safety and preliminary efficacy trial of epcoritamab that includes a phase 1 first-in-human, dose escalation part; a phase 2a expansion part; and a dose optimization part. The trial was designed to evaluate subcutaneous epcoritamab in patients with relapsed, progressive or refractory CD20+ mature B-cell NHL, including large B-cell lymphoma (LBCL) and DLBCL.[iii] Data from the dose escalation part of the study, which determined the recommended phase 2 dose, were published in September 2021.[iv] In the phase 2 expansion part, additional patients were treated with epcoritamab to further explore the safety and efficacy of epcoritamab in three cohorts of patients with different types of relapsed/refractory B-cell NHLs who had limited therapeutic options.[iii]

The primary endpoint of the phase 2 expansion part was overall response rate as assessed by an independent review committee. Secondary efficacy endpoints included duration of response, complete response rate, progression-free survival, overall survival, time to response, time to next therapy, and rate of minimal residual disease negativity.

About Large B-cell Lymphoma (LBCL)
LBCL is a type of non-Hodgkin's lymphoma (NHL), a cancer that develops in the lymphatic system, and includes several disease types such as DLBCL, HGBCL, and PMBCL, which are classified as fast-growing, aggressive lymphomas. The total number of patients with NHL, which accounts for more than 90 percent of malignant lymphoma in Japan, is estimated to be approximately 124,000, and DLBCL is reported to account for approximately 30 to 40 percent of NHL.[i,ii,iii]

About Follicular Lymphoma (FL)
FL is the second most frequent B-cell lymphoma after DLBCL, and accounts for 10 to 20 percent of NHL. Grade 3B disease, which is reported to account for 5 to 10 percent of FL, is treated according to aggressive lymphoma.[iv,v]

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 towards target cell types. EPKINLY is designed to

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simultaneously bind to CD3 on T cells and CD20 on B cells and induces T-cell mediated killing of CD20+ cells.[vi]

Epcoritamab-bysp (EPKINLY™) was approved in the United States in May 2023 and is indicated for the treatment of adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS), including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma (HGBL) after two or more lines of systemic therapy. This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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 three ongoing phase 3, open-label, randomized trials including a trial evaluating epcoritamab as a monotherapy in patients with R/R DLBCL (NCT: 04628494) compared to investigators choice chemotherapy, a phase 3, trial evaluating epcoritamab in combination with R-CHOP in adult participants with newly diagnosed DLBCL (NCT: 05578976), and a phase 3, open-label clinical trial evaluating epcoritamab in combination in patients with R/R follicular lymphoma (FL) (NCT: 05409066). Epcoritamab is not approved to treat newly diagnosed patients with DLBCL or FL. The safety and efficacy of epcoritamab has not been established for these investigational uses. Please visit 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). CRS is common during treatment with EPKINLY and can be serious or life-threatening. Tell your healthcare provider or get medical help right away if you develop symptoms of CRS, including fever of 100.4°F (38°C) or higher, dizziness or lightheadedness, trouble breathing, chills, fast heartbeat, feeling anxious, headache, confusion, shaking (tremors), or problems with balance and movement, such as trouble walking.**

  Due to the risk of CRS, you will receive EPKINLY on a "step-up" dosing schedule. The step-up dosing schedule is when you receive smaller "step-up" doses of EPKINLY on day 1 and day 8 of your first cycle of treatment (cycle 1). You will receive your first full dose of EPKINLY on day 15 of cycle 1. If your dose of EPKINLY is delayed for any reason, you may need to repeat the step-up dosing schedule. Before each dose in cycle 1, you will receive medicines to help reduce your risk of CRS. Your healthcare provider will decide if you need to receive medicine to help reduce your risk of CRS with future cycles.

- **Neurologic problems. EPKINLY can cause serious neurologic problems that can be life-threatening and lead to death. Neurologic problems may happen days or weeks after you receive EPKINLY. Your healthcare provider may refer you to a healthcare provider who specializes in neurologic problems. Tell your healthcare provider right away if you develop any symptoms of neurologic problems, including trouble speaking or writing, confusion and disorientation, drowsiness, tiredness or lack of energy, muscle weakness, shaking (tremors), seizures, or memory loss.**

Due to the risk of CRS and neurologic problems, you should be hospitalized for 24 hours after receiving your first full dose of EPKINLY on day 15 of cycle 1. Your healthcare provider will

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monitor you for symptoms of CRS and neurologic problems during treatment with EPKINLY, as well as other side effects, and treat you if needed. Your healthcare provider may temporarily stop or completely stop your treatment with EPKINLY if you develop CRS, neurologic problems, or any other side effects that are severe.

Do not drive or use heavy or potentially dangerous machinery if you develop dizziness, confusion, tremors, drowsiness, or any other symptoms that impair consciousness until your symptoms go away. These may be symptoms of CRS or neurologic problems.

EPKINLY can also cause other serious side effects, including:

- **Infections. EPKINLY can cause serious infections that may lead to death. Your healthcare provider will check you for symptoms of infection before and during treatment. 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. Low blood cell counts are common during treatment with EPKINLY and 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 cell counts (neutropenia), which can increase your risk for infection; low red blood cell counts (anemia), which can cause tiredness and shortness of breath; and low platelet counts (thrombocytopenia), which can cause bruising or bleeding problems.**

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 of your medical conditions, including if you:

- **have an infection.**
- **are pregnant or plan to become pregnant. EPKINLY may harm your unborn baby. Females who are able to become pregnant: Your healthcare provider should do a pregnancy test before you start treatment with EPKINLY. 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.**
- **are breastfeeding or plan to breastfeed. It is not known if EPKINLY passes into your breast milk. Do not breastfeed during treatment with EPKINLY and for 4 months after your last dose of EPKINLY.**

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

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.

These are not all the possible side effects of EPKINLY. Call your doctor for medical advice about side effects.

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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 the Full Prescribing Information and Medication Guide, including Important Warnings.

About Genmab
Genmab is an international biotechnology company with a core purpose guiding its unstoppable team to strive towards improving the lives of patients through innovative and differentiated antibody therapeutics. For more than 20 years, its passionate, innovative and collaborative team has invented next-generation antibody technology platforms and leveraged translational research and data sciences, which has resulted in a proprietary pipeline including bispecific T-cell engagers, next-generation immune checkpoint modulators, effector function enhanced antibodies and antibody-drug conjugates. To help develop and deliver novel antibody therapies to patients, Genmab has formed 20+ strategic partnerships with biotechnology and pharmaceutical companies. 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 locations in Utrecht, the Netherlands, Princeton, New Jersey, U.S. and Tokyo, Japan. For more information, please visit Genmab.com and follow us on Twitter.com/Genmab.

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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 pre-clinical 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] Patient Survey in 2020 (MHLW), https://www.mhlw.go.jp/toukei/list/10-20.html (as of August 3, 2023)
[ii] Saito et al, Japanese Journal of Clinical Oncology 2020 Jan 24; 50(1), 96-97. DOI: 10.1093/jjco/hyz202
[iii] Ghielmini et al, 2013; Annals of Oncology. 2013 Mar;24(3):561-76. DOI: 10.1093/annonc/mds517
[iv] Practical Guidelines for Hematological Malignancies 2018, Japanese Society of Hematology
[v] Barraclough et al, British Journal of Haematolgy, 2021 Oct; 195(1):15-24, DOI: 10.1111/bjh.17404

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[vi] Engelberts PJ, Hiemstra IH, de Jong B, 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.