Genmab Showcases Data From Comprehensive Epcoritamab Development Program in Patients Across B-Cell Lymphomas at European Hematology Association (EHA) Annual Meeting 2023

Media Release

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- **Results from phase 1/2 EPCORE™ NHL-2 trial investigating epcoritamab in combination with rituximab-lenalidomide (R2) showed a 98 percent overall response rate (ORR), 87 percent complete metabolic response (CMR) in patients with relapsed or refractory (R/R) follicular lymphoma (FL)**
- **Results from the EPCORE™ NHL-1 expansion cohort, including longer follow-up in challenging-to-treat large B-cell lymphoma (LBCL) patients, also presented**
- **First patients dosed in phase 3 EPCORE™ DLBCL-2 and phase 2 EPCORE™ DLBCL-3 trials demonstrates ongoing commitment to further evaluating epcoritamab**

Genmab A/S (Nasdaq: GMAB) today announced data from its ongoing phase 1/2 EPCORE™ NHL-2 trial investigating epcoritamab, a T-cell engaging bispecific antibody administered subcutaneously, in combination with rituximab-lenalidomide (R2) showed an overall response rate (ORR) of 98 percent and complete metabolic response (CMR) of 87 percent in response evaluable patients (n=104) with relapsed or refractory (R/R) follicular lymphoma (FL). These preliminary results will be presented today during an oral presentation at the 2023 European Hematology Association (EHA) Congress, being held in Frankfurt, Germany and virtually, June 8-11, 2023 (Abstract #S222). Epcoritamab is being co-developed by Genmab and AbbVie (NYSE: ABBV) as part of the companies' oncology collaboration.

Additional findings from the study observed consistent ORR and CMR across high-risk subgroups, including a 98 percent ORR and a 75 percent CMR in patients whose disease progressed within 24 months (POD24, n=40), a 95 percent ORR and 75.7 percent CMR in patients who were double refractory (refractory to both an anti-CD20 and an alkylating agent, n=37), a 100 percent ORR and 83.8 percent CMR in patients who were primary refractory (no response or relapse within six months after first-line treatment, n=37), and a 96 percent ORR and 80.9 percent CMR in patients refractory to prior anti-CD20 treatment (n=47). Median time to any response and CMR was 1.4 months. Estimated nine-month progression-free survival was 85 percent.

“Follicular lymphoma is a challenging cancer where disease progression within two years of initial treatment with chemoimmunotherapy, known as POD24, occurs in approximately 20 percent of patients and is a strong predictor of poor outcomes. Currently, there is no standard treatment approach for patients with high-risk, relapsed or refractory follicular lymphoma, including POD24,” said Anna Sureda, MD, PhD, Head of the Hematology Department and Hematopoietic Stem Cell Transplant Programme, Institut Català d'Oncologia, IDIBELL, Universitat de Barcelona, L’Hospitalet de Llobregat, Barcelona, Spain. “The results being presented today are encouraging and warrant further evaluation of epcoritamab in combination with R2 in this patient population to determine if this combination could potentially be offered as a treatment option for patients in need of alternative therapeutic options.”

Among the 111 patients in the safety analysis, the most common treatment emergent adverse events (TEAE) were neutropenia (57 percent) and cytokine release syndrome (CRS) (48 percent), injection-site reactions (41 percent), and fatigue (36 percent). CRS events were mostly low grade (G1-2, 46 percent; G3, 2 percent) and mostly occurred following the first full dose (cycle 1, day 15). All events resolved and none led to treatment discontinuation. Immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in two patients (G1, G2) and resolved. Results from this study were also presented at this year’s American Society of Clinical Oncology (ASCO) Meeting on June 6, 2023.

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"Together with AbbVie, through our comprehensive clinical development program, we remain committed to evaluating epcoritamab, alone or in combination with other therapies, as a potential treatment option across a variety of people affected by hematologic cancers," said Dr. Judith Klimovsky, Executive Vice President and Chief Development Officer of Genmab. "The data being presented at EHA demonstrate our shared commitment to develop epcoritamab as a potential core therapy for B-cell malignancies."

Additional Data Evaluating Epcoritamab
A poster presentation (Abstract #1118) at EHA featured updated results from the EPCORE NHL-1 large B-cell lymphoma (LBCL) expansion cohort, including longer follow-up (median follow up was 20 months) in challenging-to-treat, relapsed or refractory CD20+ LBCL patients. Of the 157 patients with R/R LBCL, including diffuse large B-cell lymphoma (DLBCL) and high grade B-cell lymphoma (HGBCL) (n=148), Primary mediastinal large B-cell lymphoma (PMBCL [n=4]), and FL (n=5), 36 remain on treatment. Results from the trial showed an overall response (OR) of 63.1 percent and complete response (CR) of 39.5 percent in patients with R/R LBCL and a 61.9 percent OR and 39.6 percent CR in patients with R/R DLBCL. The median overall survival (OS) was 18.5 months for LBCL patients and 19.4 months for DLBCL patients. The median duration of CR in both patient populations was 20.8 months. OS was not reached among complete responders in both patient populations.

The most common TEAEs of any grade (G) were CRS (51 percent), neutropenia (24 percent), pyrexia (24 percent), fatigue (23 percent), nausea (22 percent), and diarrhea (21 percent). Nine patients (6 percent) had G1–2 ICANS, and one patient had a G5 ICANS with confounding factors.

Demonstrating the company's commitment to evaluating the potential of epcoritamab in earlier lines of therapy, the first patients have been dosed in the phase 3 EPCORE DLBCL-2 (NCT: 05578976) and phase 2 EPCORE DLBCL-3 (NCT: 05660967) trials, designed to evaluate the safety and efficacy of epcoritamab as first-line treatment in adult and elderly patients with newly diagnosed DLBCL, respectively. The safety and efficacy of epcoritamab for first-line treatment in DLBCL has not been established.

About the EPCORE NHL-2 Study
EPCORE NHL-2 is a phase 1b/2, open-label, multinational, interventional trial to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics/biomarkers, immunogenicity, and preliminary efficacy of epcoritamab in combination with other standard of care agents in patients with B-cell non-Hodgkin lymphoma, including FL. In arms 2a and 2b of the EPCORE NHL-2 trial, 111 patients with R/R CD20+ FL received subcutaneous epcoritamab 48mg + R2 for 12 cycles (28 days each). Epcoritamab was dosed once weekly in cycles 1–3, once every two weeks in cycles 4–9, and once every four weeks in cycles ≥10 (2a) or once weekly in cycles 1–2 and once every four weeks in cycles ≥3 (2b) for ≤2 years.

Baseline characteristics included 58 percent of patients who had Follicular Lymphoma International Prognostic Index (FLIPI) 3–5, 60 percent who had stage IV disease, and 57 percent who had received only one prior line of treatment. Most had received alkylating agents (92 percent) or anthracyclines (63 percent); two had received prior CAR T therapy. The data being presented at EHA represent a pooled analyses from arms 2a and 2b of the EPCORE NHL-2 trial evaluating epcoritamab in combination with R2 in patients with R/R FL.

About Follicular Lymphoma (FL)
FL is typically an indolent (or slow growing) form of non-Hodgkin's lymphoma (NHL) that arises from B-lymphocytes.[i] FL is the second most common form of NHL overall, accounting for 20-30 percent of all NHL cases, and represents 10-20 percent of all lymphomas in the western world.[ii,iii] Although FL is an indolent lymphoma, it is considered incurable with conventional therapy.[iv,v]

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About Large B-cell Lymphoma (LBCL)
LBCL 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. There are an estimated 150,000 new LBCL cases each year globally.[vi]

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 towards 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.[vii]

Epcoritamab-bysp (EPKINLY™) was recently approved in the United States and is indicated for the treatment of adult patients with relapsed or refractory 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).

In October 2022, a Marketing Authorization Application was submitted for epcoritamab for the treatment of patients with R/R DLBCL after two or more lines of systemic therapy, which was validated by the European Medicines Agency. Additionally, in December 2022, a Japan new drug application was submitted to the Ministry of Health, Labor and Welfare of Japan for epcoritamab for the treatment of patients with R/R LBCL after two or more lines of systemic therapy. Epcoritamab is not approved in the European Union and Japan. The companies will share commercial responsibilities in the U.S. and Japan, with AbbVie responsible for further global commercialization. AbbVie will continue to pursue regulatory submissions for epcoritamab across international markets excluding the U.S. and Japan throughout the year.

Genmab and AbbVie are continuing to evaluate the use of epcoritamab as a monotherapy, and in combination, across lines of therapy in a range of hematologic malignancies. This includes an ongoing phase 3, open-label, randomized trial evaluating epcoritamab as a monotherapy in patients with R/R DLBCL (NCT: 04628494), an ongoing phase 3, open-label, randomized trial evaluating epcoritamab in combination 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.

U.S. IMPORTANT SAFETY INFORMATION
BOXED WARNINGS

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving EPKINLY (epcoritamab-bysp). Initiate treatment with the EPKINLY step-up dosing schedule to reduce the incidence and severity of CRS. Withhold EPKINLY until CRS resolves or permanently discontinue based on severity.**

- **Immune effector cell–associated neurotoxicity syndrome (ICANS), including life-threatening and fatal reactions, can occur with EPKINLY. Monitor patients for neurological**

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signs or symptoms of ICANS during treatment. Withhold EPKINLY until ICANS resolves or permanently discontinue based on severity.

Cytokine Release Syndrome (CRS)

- EPKINLY can cause CRS, including serious or life-threatening reactions. CRS occurred in 51 percent of patients at the recommended dose in the clinical trial (37 percent grade 1, 17 percent grade 2, and 2.5 percent grade 3). Recurrent CRS occurred in 16 percent of patients. Of all the CRS events, most (92 percent) occurred during cycle 1. In cycle 1, 9 percent of CRS events occurred after the 0.16 mg dose (cycle 1, day 1), 16 percent after the 0.8 mg dose (cycle 1, day 8), 61 percent after the 48 mg dose (cycle 1, day 15), and 6 percent after the 48 mg dose (cycle 1, day 22). The median time to onset of CRS from the most recently administered EPKINLY dose across all doses was 24 hours (range, 0-10 days). The median time to onset after the first full 48 mg dose was 21 hours (range, 0-7 days). CRS resolved in 98 percent of patients; the median duration of CRS events was 2 days (range, 1-27 days).
- Signs and symptoms of CRS can include pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia. Concurrent neurological adverse reactions associated with CRS occurred in 2.5 percent of patients and included headache, confusional state, tremors, dizziness, and ataxia.
- Initiate EPKINLY according to the step-up dosing schedule. Administer pretreatment medications to reduce the risk of CRS and monitor patients for potential CRS. Following administration of the first 48 mg dose, patients should be hospitalized for 24 hours. At the first signs or symptoms of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines, and administer supportive care as appropriate. Withhold or discontinue EPKINLY based on the severity of CRS.
- Patients who experience CRS (or other adverse reactions that impair consciousness) should be evaluated and advised not to drive and to refrain from operating heavy or potentially dangerous machinery until resolution.

Immune Effector Cell–Associated Neurotoxicity Syndrome (ICANS)

- EPKINLY can cause life-threatening and fatal ICANS. ICANS occurred in 6 percent (10/157) of patients in the clinical trial (4.5 percent grade 1, 1.3 percent grade 2, 0.6 percent fatal: 1 event). Of the 10 ICANS events, 9 occurred in cycle 1 of treatment. The median time to onset was 16.5 days (range, 8-141 days) from the start of treatment. Relative to the most recent administration, the median time to onset was 3 days (range, 1-13 days). The median duration of ICANS was 4 days (range, 0-8 days), with ICANS resolving in 90 percent of patients with supportive care.
- Signs and symptoms of ICANS can include confusional state, lethargy, tremors, dysgraphia, aphasia, and nonconvulsive status epilepticus. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.
- Monitor for potential ICANS. At the first signs or symptoms of ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or discontinue EPKINLY per recommendations and consider further management per current practice guidelines.
- Patients who experience signs or symptoms of ICANS or any other adverse reactions that impair cognition or consciousness should be evaluated, including potential neurology evaluation, and patients at increased risk should be advised not to drive and to refrain from operating heavy or potentially dangerous machinery until resolution.

Infections

- EPKINLY can cause serious and fatal infections. In the clinical trial, serious infections, including opportunistic infections, were reported in 15 percent of patients treated with EPKINLY at the recommended dose (14 percent grade 3 or 4, 1.3 percent fatal). The most common grade 3 or

greater infections were sepsis, COVID-19, urinary tract infection, pneumonia, and upper respiratory tract infection.
- Monitor patients for signs and symptoms of infection prior to and during treatment with EPKINLY and treat appropriately. Avoid administration of EPKINLY in patients with active infections.
- Prior to starting EPKINLY, provide *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis and consider prophylaxis against herpes virus.
- Withhold or consider permanent discontinuation of EPKINLY based on severity.

Cytopenias
- EPKINLY can cause serious or severe cytopenias, including neutropenia, anemia, and thrombocytopenia. Among patients who received the recommended dose in the clinical trial, grade 3 or 4 events occurred in 32 percent (decreased neutrophils), 12 percent (decreased hemoglobin), and 12 percent (decreased platelets). Febrile neutropenia occurred in 2.5 percent.
- Monitor complete blood counts throughout treatment. Based on severity of cytopenias, temporarily withhold or permanently discontinue EPKINLY. Consider prophylactic granulocyte colony-stimulating factor administration as applicable.

Embryo-Fetal Toxicity
- EPKINLY may cause fetal harm. Advise pregnant women of the potential risk to the fetus. Verify pregnancy status in females of reproductive potential prior to initiating EPKINLY. Advise females of reproductive potential to use effective contraception during treatment with EPKINLY and for 4 months after the last dose.

Adverse Reactions
- The most common (≥20 percent) adverse reactions were CRS, fatigue, musculoskeletal pain, injection site reactions, pyrexia, abdominal pain, nausea, and diarrhea. The most common grade 3 to 4 laboratory abnormalities (≥10 percent) were decreased lymphocyte count, decreased neutrophil count, decreased white blood cell count, decreased hemoglobin, and decreased platelets.

Lactation
- Advise women not to breastfeed during treatment and for 4 months after the last dose of EPKINLY.

Please see the full **Prescribing Information** and **Medication Guide**, including Boxed 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.

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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.

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