Genmab Announces Epcoritamab Added to National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for 'B-Cell Lymphomas'

Media Release

COPENHAGEN, Denmark; June 22, 2023 – Genmab A/S (Nasdaq: GMAB) today announced that epcoritamab, a T-cell engaging bispecific antibody, has been added to the National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for "B-cell Lymphomas" (Version 4.2023) for third-line and subsequent therapy for patients with diffuse large B-cell lymphoma (DLBCL), including patients with disease progression after transplant or chimeric antigen receptor (CAR) T-cell therapy and as a Category 2A, preferred regimen for patients with histologic transformation of indolent lymphomas to DLBCL and no intention to proceed to transplant, including patients with disease progression after transplant or CAR T-cell therapy. This recommendation is based on uniform NCCN consensus that the intervention is appropriate.[i] Epcoritamab is being co-developed by Genmab and AbbVie (NYSE: ABBV) as part of the companies' oncology collaboration.

Epcoritamab-bysp (EPKINLY™) was recently approved by the U.S. Food and Drug Administration (FDA) 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).

"The NCCN Guidelines are a resource for treating various types of cancer and providing healthcare providers with information for making informed treatment decisions," said Dr. Judith Klimovsky, Executive Vice President and Chief Development Officer of Genmab. "We are pleased that the NCCN has updated its Guidelines to include epcoritamab in a speedy manner."

About Diffuse Large B-cell Lymphoma (DLBCL)
DLBCL is the most common type of B-cell non-Hodgkin's lymphoma (B-NHL) worldwide, accounting for approximately 30 percent of all NHL cases and comprising an estimated 30,400 U.S. cases in 2022. 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.[ii, iii] 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.[iv,v]

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.[vi]

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,

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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 for the treatment of newly diagnosed DLBCL or R/R FL and 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 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.

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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

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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.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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.

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combination with the HexaBody logo®; DuoHexaBody® and HexElect®. EPCORE™ and EPKINLY™ are owned by AbbVie Biotechnology Ltd.

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[i] National Comprehensive Cancer Network "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines); B-Cell Lymphomas." Version 4.2023; published June 2, 2023.
[ii] Sehn LH, Salles G. *N Engl J Med.* 2021;384:842-858.
[iii] Kanas G, Ge W, Quek RGW, et al. *Leukemia & Lymphoma.* 2022;63(1):54-63.
[iv] Sehn LH, Salles G. *N Engl J Med.* 2021;384:842-858.
[v] Crump M, Neelapu SS, Farooq U, et al. *Blood.* 2017;130(16):1800-1808.
[vi] Engelberts 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