Preliminary Analysis of Data Evaluating Investigational Epcoritamab (DuoBody® CD3xCD20) Combination Demonstrates 95% Overall Response Rate in Patients with Previously Untreated Follicular Lymphoma

Media Release

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- **Preliminary analysis of data from the EPCORE™ NHL-2 study demonstrates patients with previously untreated follicular lymphoma (FL) who received epcoritamab in combination with rituximab-lenalidomide (R^2) experienced a 95% overall response rate (ORR)**
- **Results from the optimization cohort of the EPCORE™ NHL- 1 study show that mitigation strategies led to a clinically significant reduction in rate of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) in patients with relapsed/refractory (R/R) FL treated with epcoritamab**

Genmab A/S (Nasdaq: GMAB) today announced new efficacy and safety data from two ongoing Phase 1/2 clinical trials evaluating epcoritamab, a T-cell engaging bispecific antibody administered subcutaneously, in adult patients with certain types of follicular lymphoma (FL). A preliminary analysis of data from the EPCORE™ NHL-2 study (NCT04663347), evaluating epcoritamab in combination with rituximab-lenalidomide (R^2), demonstrated an overall response rate (ORR) of 95% and complete response rate (CRR) of 85% in patients with previously untreated FL. The safety and efficacy for this use have not been established. The data were shared during a rapid oral presentation (Abstract #7014) at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting, being held in Chicago, IL and virtually, May 31-June 4, 2024.

Separately, new data from the cycle 1 optimization part (C1 OPT) of the EPCORE™ NHL-1 study (NCT03625037), evaluating epcoritamab in patients with relapsed/refractory (R/R) FL, showed that following additional mitigation strategies, cytokine release syndrome (CRS) (any grade) was reported in 49 percent of patients vs. 66 percent of patients (any grade) in the pivotal cohort. Additionally, there were no Grade 3 or higher CRS events and no reported immune effector cell-associated neurotoxicity syndrome (ICANS). CRS and ICANS are adverse reactions, which can be serious and/or life threatening. Patients need to be monitored and carefully managed per current practice guidelines. These results (Abstract #7015) were selected to be a part of Best of ASCO® (July 19-20 in Boston, MA), which features the most impactful research from the 2024 ASCO Annual Meeting.

FL is the second most common form of non-Hodgkin's lymphoma (NHL), accounting for 20-30 percent of all NHL cases.[i] About 15,000 people develop FL each year in the U.S.[ii] FL is considered incurable with current standard of care therapies and patients often relapse.[iii,iv] With each subsequent line of therapy, patients receiving currently available treatments may experience shorter durability of remission.[v]

"Follicular lymphoma is considered incurable and patients at all stages of disease need innovative treatment options. Our data at this year's ASCO suggest that epcoritamab can potentially provide promising overall and complete responses for patients with follicular lymphoma, whether previously untreated or post-relapse. Importantly, we've also focused on reducing incidence of CRS and ICANS through optimizing dosing safety of epcoritamab for patients with relapsed/refractory disease," said Judith Klimovsky, Executive Vice President & Chief Development Officer, Genmab. "These data reflect our efforts, alongside our partner AbbVie, to continue the development of epcoritamab as a potential core therapy across B-cell malignancies."

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EPCORE™ NHL-2 Results in First-Line FL (Abstract #7014)
The EPCORE NHL-2 study analysis included results from two arms of the study. Arm 6 evaluated epcoritamab in combination with R2 in patients with previously untreated FL (n=41). With a median follow-up of 21.1 months, additional findings from this arm showed durable responses, with an estimated 89 percent of patients remaining progression free and 93 percent of patients who had achieved a CR remaining in CR at 18 months.

“The results from this preliminary analysis of epcoritamab in combination with rituximab-lenalidomide as a first-line, chemotherapy-free treatment for patients with FL are encouraging and support the continued evaluation of epcoritamab in this patient population,” said Joshua Brody, MD, Director, Lymphoma Immunotherapy Program Icahn School of Medicine at Mount Sinai Hess Center for Science and Medicine.

The most common treatment-emergent adverse events (TEAEs) in these first-line patients were COVID-19 (63 percent), CRS (56 percent) and neutropenia (56 percent). All CRS events were low grade (41 percent Grade 1 and 15 percent Grade 2) and resolved. Most CRS events occurred after patients received their first full dose of epcoritamab, and none led to treatment discontinuation. Two fatal TEAEs occurred due to COVID-19 pneumonia and septic shock.

The EPCORE NHL-2 study results also included the first data disclosure from arm 7, which evaluated epcoritamab administered every 8 weeks for patients with first- or second-line FL in CR or partial response (PR) following standard-of-care treatment (n=20). Median follow-up was 19.7 months. An estimated 90 percent of patients remained alive at 21 months. Notably, 100 percent of patients who entered the arm with a PR converted to a CR (n=8).

In arm 7, the most common TEAEs were COVID-19 (70 percent) and CRS (55 percent). Only one CRS event (Grade 1) occurred during Q8W maintenance dosing. All other CRS events were during cycle 1 (C1) step-up dosing, as expected for these patients who had not previously received epcoritamab. One fatal TEAE occurred related to respiratory failure caused by post-acute COVID syndrome.

EPCORE™ NHL-1 Data in Later-line FL (Abstract #7015)
In this C1 optimization cohort in patients with R/R FL, patients received epcoritamab in 3 step-up doses (0.16, 0.8, and 3 mg), along with dexamethasone prophylaxis and hydration recommendations followed by full 48-mg doses until disease progression or unacceptable toxicity. There was no mandatory hospitalization. With a median follow-up of 5.7 months, CRS rate was 49% (Grade 1 40%, Grade 2 9%), primarily occurring during cycle 1, and all events resolved. CRS was adequately identified in the outpatient setting and appropriately treated. There were no ICANS events.

These findings show that mitigation measures implemented early in the epcoritamab treatment cycle may lead to substantial improvements in the incidence and severity of CRS and ICANS. Further, among the 81 response-evaluable patients in the cohort, ORR was 91 percent and CR rate was 68 percent, suggesting that the additional CRS mitigation did not impact efficacy.

On February 26, 2024, the U.S. Food and Drug Administration (FDA) granted Priority Review for the supplemental Biologics License Application (sBLA) for epcoritamab-bysp for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) after two or more lines of systemic therapy. Use of epcoritamab in FL 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 FL have not been established.

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About the EPCORE™ NHL-2 Trial
EPCORE™ NHL-2 is a phase 1b/2, open-label, multinational, interventional trial to evaluate the safety, and preliminary efficacy of epcoritamab in combination with standard of care agents in patients with B-cell non-Hodgkin's lymphoma, including FL, and across multiple lines of therapy. The trial consists of two parts – Part 1 (dose escalation) and Part 2 (dose expansion) – and 10 different treatment arms. The primary objective of Part 1 is safety, and it includes arm 1-5 and arm 10. Part 2 includes all 10 arms (arm 1-10) with the objective of preliminary efficacy. However, the primary objective of arm 7 is safety. More information on this trial be found at https://www.clinicaltrials.gov/ (NCT: 04663347).

About the EPCORE™ NHL-1 Trial
EPCORE™ NHL-1 is an open-label, multi-center safety and preliminary efficacy trial of epcoritamab that consists of three parts: a dose escalation part; an expansion part; and an optimization part. The trial was designed to evaluate subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma (B-NHL), including FL. In the expansion part, additional patients were enrolled to further explore the safety and efficacy of epcoritamab in three cohorts of patients with different types of relapsed/refractory B-NHLs who have limited therapeutic options and generated pivotal data for patients with FL and diffuse large B-cell lymphoma (DLBCL). The optimization part evaluated additional cytokine release syndrome (CRS) mitigation strategies during cycle 1. The primary endpoint of the expansion part was ORR as assessed by an IRC. Secondary efficacy endpoints included duration of response, complete response rate, duration of complete response, progression-free survival, and time to response as determined by the Lugano criteria. Overall survival, time to next therapy, and rate of minimal residual disease negativity were also evaluated as secondary efficacy endpoints. The primary endpoint of the optimization part was the rate of ≥ Grade 2 CRS events and all grade CRS events from first dose of epcoritamab through 7 days following administration of the second full dose of epcoritamab.

About Follicular Lymphoma (FL)
FL is typically an indolent (or slow-growing) form of non-Hodgkin's lymphoma (NHL) that arises from B-lymphocytes.[vi] 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.[i,vii] Although FL is an indolent lymphoma, it is considered incurable with conventional therapy and patients who achieve remission also often experience relapse.[iii,iv,viii] Additionally, with each relapse the remission and time to next treatment is shorter[ix], adding increased cost to the health system and negatively impacting the patient's quality of life.[x]

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.[xi]

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. Use of epcoritamab in FL is not approved in the U.S. or in the EU or in any other territory. 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.

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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 including a trial evaluating epcoritamab as a monotherapy in patients with R/R DLBCL compared to investigators choice chemotherapy (NCT: 04628494), a trial evaluating epcoritamab in combination with R-CHOP in adult participants with newly diagnosed DLBCL (NCT: 05578976), a trial evaluating epcoritamab in combination with rituximab and lenalidomide (R2) in patients with R/R FL (NCT: 05409066), and a trial evaluating epcoritamab in combination with R2 compared to chemoimmunotherapy in patients with previously untreated FL (NCT: 06191744). The safety and efficacy of epcoritamab has not been established for these investigational uses. Please visit 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.

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 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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