TIVDAK® (tisotumab vedotin) Approved by European Commission for Previously Treated Recurrent or Metastatic Cervical Cancer

Media Release

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- **TIVDAK® is the first and only antibody-drug conjugate (ADC) approved to treat recurrent or metastatic cervical cancer with disease progression on or after systemic therapy**
- **In the global Phase 3 innovaTV 301 clinical trial TIVDAK demonstrated superior overall survival compared to chemotherapy**
- **TIVDAK is approved for the treatment of recurrent or metastatic cervical cancer in the European Union, United States and Japan**

Genmab A/S (Nasdaq: GMAB) announced today that the European Commission (EC) has granted marketing authorization for TIVDAK® (tisotumab vedotin), an antibody-drug conjugate (ADC), as monotherapy treatment for adult patients with recurrent or metastatic cervical cancer with disease progression on or after systemic therapy. TIVDAK is the first and only ADC to be granted European Union (EU) marketing authorization for people living with recurrent or metastatic cervical cancer.

Despite progress in cervical cancer prevention and early detection, there remains a high need for new treatment options, particularly in advanced forms of the disease. In fact, cervical cancer is the fourth most common cause of cancer death among women globally.[i] In the European Union, cervical cancer is the 11th most frequently occurring cancer among women.[ii] Up to 15% of adults with cervical cancer present with metastatic disease at diagnosis[iii,iv] and, for those diagnosed at earlier stages who receive treatment, up to 61%[v] will experience disease recurrence. For these patients, the prognosis can be poor.[vi]

“Recurrent or metastatic cervical cancer is a devastating disease, and patients can face a difficult treatment journey with limited options,” said Ignace Vergote, M.D., Ph.D., University Hospitals Leuven, co-founder of European Network of Gynaecological Oncological Trial groups (ENGOT), and lead investigator on the innovaTV 301 clinical trial. “In clinical trials, TIVDAK demonstrated a superior overall survival benefit and manageable safety profile compared to chemotherapy, supporting its position to become a potential new standard of care in this setting with a novel mechanism of action. This approval is an important step forward in the treatment landscape for advanced cervical cancer.”

The approval is supported by data from the global, randomized, Phase 3 innovaTV 301 trial (NCT04697628) that evaluated the efficacy and safety of TIVDAK compared to chemotherapy in patients with advanced or recurrent cervical cancer who were previously treated with chemotherapy. The trial met its primary endpoint of overall survival (OS), demonstrating a 30% reduction in risk of death (HR: 0.70 [95% CI: 0.54-0.89], two-sided p=0.0038) compared to chemotherapy. Median OS was 11.5 months [95% CI: 9.8-14.9] among patients treated with TIVDAK compared to 9.5 months [95% CI: 7.9-10.7] for patients who received chemotherapy. Secondary endpoints of progression-free survival (PFS) and confirmed objective response rate (ORR) were also met, further validating its clinical benefit. PFS results were statistically significant, with TIVDAK demonstrating a 33% reduction in the risk of disease progression compared with chemotherapy (HR: 0.67 [95% CI, 0.54-0.82], p<0.0001). Data from the innovaTV 204 (NCT03438396) pivotal Phase 2 single-arm clinical trial evaluating TIVDAK as monotherapy in patients with previously treated recurrent or metastatic cervical cancer was also included in the marketing authorization application (MAA).

The most common (≥25%) adverse reactions, including laboratory abnormalities, in patients receiving tisotumab vedotin were peripheral neuropathy (39%), nausea (37%), epistaxis (33%), conjunctivitis (32%), alopecia (31%), anaemia (27%), and diarrhoea (25%).

"We recognize the urgent need to accelerate science and innovate new treatment options for gynecologic cancers, including cervical cancer," said Brad Bailey, Executive Vice President and Chief Commercial Officer of Genmab. "The European Commission approval of TIVDAK marks a milestone in our work to transform the treatment paradigm and help improve outcomes for patients. As the first medicine that Genmab will bring to patients in Europe independently, we're committed to bringing this important option to as many patients in Europe with previously treated recurrent or metastatic cervical cancer as possible."

About the innovaTV 301 Trial
The innovaTV 301 trial (NCT04697628) is a global, 1:1 randomized, open-label Phase 3 trial evaluating tisotumab vedotin versus investigator's choice of single agent chemotherapy (topotecan, vinorelbine, gemcitabine, irinotecan or pemetrexed) in 502 patients with recurrent or metastatic cervical cancer who received one or two prior systemic regimens in the recurrent or metastatic setting.

Patients with recurrent or metastatic cervical cancer with squamous cell, adenocarcinoma or adenosquamous histology, and disease progression during or after treatment with chemotherapy doublet +/- bevacizumab and an anti-PD-(L)1 agent (if eligible) are included. The primary endpoint was overall survival. The main secondary outcomes were progression-free survival and objective response rate.

The study was conducted by Seagen, which was acquired by Pfizer in December 2023, in collaboration with Genmab, European Network of Gynaecological Oncological Trial Groups (ENGOT, study number ENGOT cx-12) and the Gynecologic Oncology Group (GOG) Foundation (study number GOG 3057), as well as other global gynecological oncology cooperative groups. For more information about the Phase 3 innovaTV 301 clinical trial and other clinical trials with tisotumab vedotin, please visit www.clinicaltrials.gov.

About Tisotumab Vedotin
Tisotumab vedotin (approved under the brand name TIVDAK® in the EU, U.S. and Japan) is an antibody-drug conjugate (ADC) composed of Genmab's human monoclonal antibody directed to tissue factor (TF) and Pfizer's ADC technology that utilizes a protease-cleavable linker that covalently attaches the microtubule-disrupting agent monomethyl auristatin E (MMAE) to the antibody. Nonclinical data suggest that the anticancer activity of tisotumab vedotin is due to the binding of the ADC to TF-expressing cancer cells, followed by internalization of the ADC-TF complex and release of MMAE via proteolytic cleavage. MMAE disrupts the microtubule network of actively dividing cells, leading to cell cycle arrest and apoptotic cell death. In vitro, tisotumab vedotin also mediates antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity.

About the Pfizer and Genmab Collaboration
Tisotumab vedotin is co-developed and co-commercialized globally by Genmab and Pfizer, under an agreement in which the companies share costs and profits.

With respect to the commercialization of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer, Genmab leads commercialization in Europe and all other regions globally, outside the United States and China. In these regions, Pfizer partners with Genmab and Zai Lab, respectively, on commercialization.

Pfizer is currently the marketing authorization holder (MAH) for tisotumab vedotin in the European Union. This responsibility is expected to transfer to Genmab in 2025.

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 more than 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.

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[i] Wu, Jie, and Qianyun Jin. "Global Burden of Cervical Cancer: Current Estimates, Temporal Trend and Future Projections Based on the Globocan 2022." Journal of the National Cancer Center, 23 Jan. 2025, www.sciencedirect.com/science/article/pii/S2667005425000134.

[ii] "Cervical Cancer Burden in EU-27 - Europa.Eu." Cancer Factsheets in EU-27 Countries, ECIS - European Cancer Information System, 17 Nov. 2021, https://ecis.jrc.ec.europa.eu/sites/default/files/2023-12/cervical_cancer_en-Nov_2021.pdf.

[iii] National Cancer Institute. SEER Cancer Stat Facts: Cervical Cancer. 2023. https://seer.cancer.gov/statfacts/html/cervix.html.

[iv] McLachlan J, Boussios S, Okines A, et al. The impact of systemic therapy beyond first-line treatment for advanced cervical cancer. Clin Oncol (R Coll Radiol). 2017;29(3):153-60.

[v] Pfaendler KS, Tewari KS. Changing paradigms in the systemic treatment of advanced cervical cancer. Am J Obstet Gynecol. 2016 Jan;214(1):22-30. doi: 10.1016/j.ajog.2015.07.022. Epub 2015 Jul 26. PMID: 26212178; PMCID: PMC5613936.

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