TIVDAK® (tisotumab vedotin) Approved by Japan Ministry of Health, Labour and Welfare for the Treatment of Advanced or Recurrent Cervical Cancer that has Progressed on or after Chemotherapy

Media Release

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- **TIVDAK® is the first and only antibody-drug conjugate (ADC) approved for patients with advanced or recurrent cervical cancer in Japan**
- **Approval is based on results from the global Phase 3 innovaTV 301 trial, in which TIVDAK demonstrated superior overall survival compared to chemotherapy**
- **Rising cervical cancer incidence and mortality rates in Japan signify need for new treatment options**

Genmab A/S (Nasdaq: GMAB) today announced that the Japan Ministry of Health, Labour and Welfare has approved TIVDAK® (tisotumab vedotin) for the treatment of advanced or recurrent cervical cancer that has progressed on or after cancer chemotherapy. TIVDAK is the first and only ADC to be approved for people living with cervical cancer in Japan.

In recent years, cervical cancer incidence and mortality rates have increased in Japan, particularly among women under age 50.[i,ii,iii] Moreover, patients with recurrent or metastatic cervical cancer whose disease has progressed after first-line therapy have limited treatment options.

“Patients with advanced or recurrent cervical cancer, in general, have a poor prognosis. The advent of new treatment options, especially for second-line or later treatment, is much needed,” said Aikou Okamoto, M.D., Ph.D., Chief Professor, Department of Obstetrics and Gynecology at The Jikei University School of Medicine. “Cervical cancer treatment has advanced in recent years, but it is very meaningful that the approval of tisotumab vedotin as an ADC has increased the number of treatment options with a new mechanism of action that is expected to prolong overall survival. This is good news for patients and healthcare professionals.”

The approval is based on data from the randomized, open-label, global Phase 3 innovaTV 301 clinical trial 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 included 502 patients, 101 of which were Japanese. 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.

Adverse drug reactions occurred in 219 (87.6%) of 250 patients (including 50 Japanese patients) treated with TIVDAK. The most common (≥20%) adverse reactions included conjunctivitis (n=76; 30.4%), nausea (n=73; 29.2%), peripheral sensory neuropathy (n=67; 26.8%), alopecia (n=61; 24.4%), and epistaxis (n=57; 22.8%), at the data cutoff date of July 24, 2023.

“As a company, we understand the urgent need for patients with advanced cervical cancer whose disease has progressed,” said Judith Klimovsky, M.D., Executive Vice President and Chief Development Officer of Genmab. “This approval marks an important step forward in transforming the treatment paradigm in Japan, ultimately bringing new hope and possibility to patients and their loved ones.”

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 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 Japan and all other regions globally, outside the United States and China. In these regions, Pfizer partners with Genmab and Zai Lab, respectively, on commercialization.

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] Cancer Statistics Cervix, National Cancer Center, Cancer Information Service, ganjoho.jp/reg_stat/statistics/stat/cancer/17_cervix_uteri.html#anchor1. Accessed 14 Feb. 2025.
[ii] Trends in Cancer Incidence and Mortality Rates, World Health Organization, gco.iarc.fr/overtime/en. Accessed 14 Feb. 2025.
[iii] For Correct Understanding of Cervical Cancer and HPV Vaccine, Japan Society of Obstetrics and Gynecology, www.jsog.or.jp/citizen/5765/. Accessed 14 Feb. 2025.