Investigational Tisotumab Vedotin Phase 2 Data Demonstrates Encouraging Antitumor Activity in Patients with Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma (HNSCC)

Media Release

COPENHAGEN, Denmark; June 3, 2024

- **Results from innovaTV207 evaluating tisotumab vedotin, showing 32.5% confirmed objective response rate in patients with recurrent or metastatic HNSCC, presented in a rapid oral session at 2024 ASCO® Annual Meeting**
- **HNSCC is the sixth most common cancer worldwide, with incidence rates expected to increase 30% by 2030**[i]

Genmab A/S (Nasdaq: GMAB) announced today that data from the Phase 2 innovaTV 207 trial (NCT03485209) Part C (n=40), investigating tisotumab vedotin, an antibody-drug conjugate directed to tissue factor, demonstrated encouraging antitumor activity as a monotherapy in patients with head and neck squamous cell carcinoma (HNSCC) who experienced disease progression on or after first-line therapy. The study showed 32.5% of patients achieved a confirmed objective response rate (cORR), one patient experienced a complete response (CR) and 12 achieved a partial response (PR). These results were presented in a rapid oral session today at the 2024 ASCO Annual Meeting, being held in Chicago, Illinois, May 31 – June 4, 2024.

In the HNSCC cohort of innovaTV 207 Part C (n=40), median duration of response (DOR) was 5.6 months and median time-to-response (TTR) was 1.4 months. All patients were required to have received a platinum-based regimen in the recurrent or metastatic setting or have persistent disease following platinum-based chemoradiation and a checkpoint inhibitor (CPI), if eligible. The study also showed that among patients with no more than one or two lines of therapy in the recurrent or metastatic setting (n=25), 40% had achieved a cORR at the time of data cut-off.

“Most patients with recurrent or metastatic head and neck squamous cell carcinoma experience disease progression despite the use of platinum-based therapy and immunotherapy, and treatment options are limited,” said Dr. Judith Klimovsky, Executive Vice President and Chief Development Officer of Genmab, “These updated results underscore the importance of our ongoing work with our partner to advance the clinical development program for tisotumab vedotin and investigate potential treatment options for pretreated patients living with unmet needs.”

The safety findings were consistent with previous tisotumab vedotin trials, and no new safety signals were observed. Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 67.5% of patients, and the most common were peripheral neuropathy events (40%). Adverse events of special interest (of any grade) were prespecified for ocular, peripheral neuropathy, and bleeding events, and occurred in 52.5%, 47.5%, and 40% patients, respectively.

As of December 2023, 40 patients with recurrent or metastatic HNSCC were treated with tisotumab vedotin monotherapy (1.7 mg/kg intravenously, once every two weeks). In this cohort, 32 (80%) received prior platinum-based therapy, 19 (47.5%) received at least two prior lines of systemic therapy (median: 2; range: 1-3), 40 (100%) received prior CPI, 23 (57.5%) received prior taxane, and 27 (67.5%) received prior cetuximab. The primary sites at diagnosis were oropharynx (n=16), larynx (n=13), and oral cavity (n=9).

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About the innovaTV 207 Trial
The innovaTV 207 trial (NCT03485209) is an open-label, global, Phase 2, multicohort, multicenter study evaluating tisotumab vedotin monotherapy or in combination for advanced solid tumors. In Part C, patients with recurrent or metastatic HNSCC received tisotumab vedotin monotherapy (1.7 mg/kg IV once every two weeks). All patients were required to have received a platinum-based regimen, either in the recurrent/metastatic setting, or to have persistent disease following platinum-based chemoradiation and a checkpoint inhibitor, if eligible. The primary endpoint of the trial is confirmed objective response rate (cORR) per RECIST 1.1 per investigator, defined as the proportion of patients who achieve a confirmed complete or partial response. Selected secondary endpoints include duration of response (DOR), time-to-response (TTR), and safety. For more information about the phase 2 innovaTV 207 clinical trial of tisotumab vedotin, please visit www.clinicaltrials.gov.

About Tisotumab Vedotin
Tisotumab vedotin 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-tftv 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-tftv also mediates antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity.

Tisotumab vedotin (TIVDAK®) has received full approval by the U.S. FDA for the treatment of adult patients with recurrent or metastatic cervical cancer (r/mCC) with disease progression on or after chemotherapy. Tisotumab vedotin in HNSCC is not approved in any country, including the U.S. and the EU. The safety and efficacy of tisotumab vedotin has not been established for these investigational uses.

Virtual mid- to late-stage pipeline update at ASCO 2024
On Monday, June 3, at 9:00 AM CDT (10:00 AM EDT/4:00 PM CEST), Genmab will host a review of data presented at ASCO from its mid- to late-stage pipeline. The event will be virtual and webcast live. Details, including the webcast link and registration will be available on www.genmab.com. This meeting is not an official program of the ASCO Annual Meeting.

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.

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About the Pfizer and Genmab Collaboration
Tisotumab vedotin is co-owned by Genmab and Pfizer, under an agreement in which the companies share costs and profits for the product on a 50:50 basis.

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i Johnson, Daniel E., et al. "Head and Neck Squamous Cell Carcinoma." Nature Reviews Disease Primers, Nature Publishing Group, 26 Nov. 2020, https://www.nature.com/articles/s41572-020-00224-3#Fig2.