

## Genmab and Seagen Present Data from Tisotumab Vedotin (TIVDAK®) Clinical Development Program and Additional Cervical Cancer Research at ASCO 2022 Annual Meeting

### Media Release

Copenhagen, Denmark, June 6, 2022

- **Interim results of tisotumab vedotin plus pembrolizumab from Phase 1b/2 innovaTV 205 trial, showing 41% objective response rate in first-line patients with recurrent or metastatic cervical cancer (r/mCC), to be presented in an oral session**
- **Additional poster presentations to include debut of web-based tool for identifying geographical areas across the country in high need of cervical cancer intervention**

[Genmab A/S](#) (Nasdaq: GMAB) and [Seagen Inc.](#) (Nasdaq: SGEN) today announced interim data from the innovaTV 205 trial, which included data evaluating tisotumab vedotin (TIVDAK®) in combination with pembrolizumab (Cohort E) in patients with recurrent or metastatic cervical cancer (r/mCC) who have not received prior systemic therapy, with a confirmed objective response rate (ORR) of 41% (95% Confidence Interval [CI]: 24% to 59%) and median durability of response that was not reached within almost 19 months of median follow up. Data were presented during an oral session at the American Society of Clinical Oncology (ASCO) 2022 Annual Meeting on June 6.

“These data showed encouraging and durable anti-tumor activity and provide rationale for the continued development of tisotumab vedotin (TV) in front-line recurrent or metastatic cervical cancer, including its potential use as part of triplet or quadruplet combination therapy,” said Domenica Lorusso, M.D., Ph.D., a gynecologic oncologist working at the Gynaecology Oncology Unit of Policlinico Gemelli IRCCS of Rome and an investigator of the innovaTV 205 clinical trial. “These early results from multiple expansion cohorts of innovaTV 205 support our continued efforts to investigate TV as part of combination therapy to further improve treatment response and durability for this group of patients with high unmet need.”

Dose expansion Cohort E enrolled 33 patients with recurrent or metastatic cervical cancer who had not received any prior systemic therapy. At the time of data cutoff, the confirmed ORR among 32 evaluable patients was 41% (95% Confidence Interval [CI], range 24% to 59%), with 16% of patients (n=5) achieving complete responses and 25% of patients (n=8) achieving partial responses. Median duration of response (DOR) was not reached. Median progression-free survival (PFS) was 5.3 months (95% CI: 4.0 to 12.2).

Building on data presented at the European Society for Medical Oncology (ESMO) Congress 2021, additional longer-term follow-up data from Cohorts D (tisotumab vedotin in combination with carboplatin in previously untreated patients) and Cohort F (tisotumab vedotin in combination with pembrolizumab in previously treated patients) of the innovaTV 205 trial were also included in the ASCO 2022 oral presentation.

In Cohort E, the most common treatment-emergent adverse events (TEAEs) were alopecia (61%), diarrhea (55%), epistaxis (49%), conjunctivitis (45%), and nausea (46%). Prespecified adverse events (AEs) of interest (grade 1-2/grade ≥3) with tisotumab vedotin included ocular (58%/9%), peripheral neuropathy (49%/3%), and bleeding (61%/6%).

Tisotumab vedotin in combination with pembrolizumab across lines of treatment (Cohorts E/F), and with carboplatin (Cohort D) in first-line, demonstrated a tolerable and manageable safety profile. Across all three cohorts, no new safety signals were reported outside of known adverse events associated with the individual agents.

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Tisotumab vedotin is approved for treatment of patients with previously treated recurrent or metastatic cervical cancer in the US and is commercialized under the tradename TIVDAK. See TIVDAK U.S. Important Safety Information, including Boxed Warning, below.

“With Genmab, we will continue to investigate tisotumab vedotin in combination with other therapies because there is still an unmet need for more effective first-line treatment for advanced cervical cancer patients,” said Marjorie Green, M.D., Senior Vice President and Head of Late-Stage Development, Seagen. “We’re also researching innovative new tools to help increase awareness of the disparities and unmet needs that cervical cancer patients experience in order to better support this community in the future.”

One highlight of real-world studies presented is a poster discussion on the [Cervical Cancer Geographical Burden Analyzer](#). This is an open access, web-based, interactive tool to visualize geographical areas in the US where cervical cancer education or healthcare resource needs are high.

“The Cervical Cancer Geographical Burden Analyzer has potential to help expand understanding of cervical cancer disease burden across different communities,” said Tara Castellano, M.D., Gynecologic Oncologist at Louisiana State University’s Department of Gynecologic Oncology and lead investigator for research and development of the Cervical Cancer Geographical Disease Burden Analyzer. “This tool may be particularly useful for researchers, policy makers, and advocacy groups to inform allocation of healthcare resources.”

Additional updates from the tisotumab vedotin clinical development program were presented at the ASCO 2022 Annual Meeting, including trial-in-progress overviews for innovaTV 205/ENGOT-cx8/GOG-3024 evaluating first-line tisotumab vedotin in combination with pembrolizumab, carboplatin and bevacizumab in first-line r/mCC; and for innovaTV 207 Part D evaluating tisotumab vedotin in combination with pembrolizumab and platinum in squamous cell carcinoma of the head and neck (HNSCC) and squamous cell non-small cell lung cancer (sqNSCLC).

“The collective data presented for tisotumab vedotin at the ASCO 2022 Annual Meeting are reflective of our commitment to investigating this therapy across treatment lines and in combination with other therapies,” said Jan van de Winkel, Ph. D., Chief Executive Officer, Genmab. “With Seagen, we are continuing to advance clinical trials in order to explore future treatment options for recurrent or metastatic cervical cancer patients.”

### About the innovaTV 205 Trial

The innovaTV 205 trial (also known as ENGOT-cx8/GOG-3024) is a Phase 1b/2 open-label, multi-center trial of tisotumab vedotin monotherapy and in combination with bevacizumab, pembrolizumab, or carboplatin in patients with recurrent or metastatic cervical cancer. The study consists of two parts: dose escalation (Cohorts A, B, and C) and dose expansion (Cohorts D, E, F, G and H). Patients enrolled in the dose escalation cohorts have progressed during or after standard of care therapy or are intolerant or ineligible to receive standard of care treatments. The primary objective is to identify and establish the maximum tolerated dose and Recommended Phase 2 Dose (RP2D) of tisotumab vedotin as combination therapy. Within the dose expansion cohorts, patients with recurrent or metastatic cervical cancer who have not previously received prior systemic therapy are treated in Cohorts D, E and H, with patients who have progressed on or after standard of care treatments evaluated in Cohorts F and G. For more information about the innovaTV 205 clinical trial and the study collaborators, please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (Identifier: NCT03786081).

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### **About Tisotumab Vedotin**

Tisotumab vedotin-tftv (TIVDAK®) is an antibody-drug conjugate (ADC) composed of Genmab's human monoclonal antibody directed to tissue factor (TF) and Seagen'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 suggests 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.

In September 2021, the U.S. Food and Drug Administration granted accelerated approval for tisotumab vedotin-tftv (TIVDAK) in adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. TIVDAK is the first and only approved ADC for the treatment of these patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. The ongoing clinical trial innovaTV 301, an open-label, randomized, global trial, is intended as the confirmatory trial for use in verifying and describing the clinical benefit and as support for US and global regulatory applications.

### **Indication**

TIVDAK is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

### **Important Safety Information**

#### **BOXED WARNING: OCULAR TOXICITY**

**TIVDAK caused changes in the corneal epithelium and conjunctiva resulting in changes in vision, including severe vision loss, and corneal ulceration. Conduct an ophthalmic exam at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care before, during, and after infusion. Withhold TIVDAK until improvement and resume, reduce the dose, or permanently discontinue, based on severity.**

### **Warnings and Precautions**

**Ocular Adverse Reactions** occurred in 60% of patients with cervical cancer treated with TIVDAK across clinical trials. The most common were conjunctival adverse reactions (40%), dry eye (29%), corneal adverse reactions (21%), and blepharitis (8%). Grade 3 ocular adverse reactions occurred in 3.8 % of patients, including severe ulcerative keratitis in 3.2% of patients. One patient experienced ulcerative keratitis with perforation requiring corneal transplantation. Cases of symblepharon were reported in patients with other tumor types treated with TIVDAK at the recommended dose. In innovaTV 204, 4% of patients experienced visual acuity changes to 20/50 or worse including 1% of patients who experienced a visual acuity change to 20/200. Of the patients who experienced decreased visual acuity to 20/50 or worse, 75% resolved, including the patient who experienced decreased visual acuity to 20/200.

Refer patients to an eye care provider for an ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care to reduce the risk of ocular adverse reactions. Promptly refer patients to an eye care provider for any new or

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worsening ocular signs and symptoms. Withhold dose, reduce the dose, or permanently discontinue TIVDAK based on the severity of the adverse reaction.

**Peripheral Neuropathy (PN)** occurred in 42% of cervical cancer patients treated with TIVDAK across clinical trials; 8% of patients experienced Grade 3 PN. PN adverse reactions included peripheral neuropathy (20%), peripheral sensory neuropathy (11%), peripheral sensorimotor neuropathy (5%), motor neuropathy (3%), muscular weakness (3%), and demyelinating peripheral polyneuropathy (1%). One patient with another tumor type treated with TIVDAK at the recommended dose developed Guillain-Barre syndrome. Monitor patients for signs and symptoms of neuropathy. For new or worsening PN, withhold, dose reduce, or permanently discontinue TIVDAK based on the severity of PN.

**Hemorrhage** occurred in 62% of cervical cancer patients treated with TIVDAK across clinical trials. The most common all grade hemorrhage adverse reactions were epistaxis (44%), hematuria (10%), and vaginal hemorrhage (10%). Grade 3 hemorrhage occurred in 5% of patients. Monitor patients for signs and symptoms of hemorrhage. For patients experiencing pulmonary or CNS hemorrhage, permanently discontinue TIVDAK. For Grade  $\geq 2$  hemorrhage in any other location, withhold until bleeding has resolved, blood hemoglobin is stable, there is no bleeding diathesis that could increase the risk of continuing therapy, and there is no anatomical or pathologic condition that can increase the risk of hemorrhage recurrence. After resolution, either resume treatment or permanently discontinue TIVDAK.

**Pneumonitis:** Severe, life-threatening, or fatal pneumonitis can occur in patients treated with antibody-drug conjugates containing vedotin, including TIVDAK. Among patients with cervical cancer treated with TIVDAK across clinical trials, 2 patients (1.3%) experienced pneumonitis, including 1 patient who had a fatal outcome.

Monitor patients for pulmonary symptoms of pneumonitis. Infectious, neoplastic, and other causes for symptoms should be excluded through appropriate investigations.

Withhold TIVDAK for patients who develop persistent or recurrent Grade 2 pneumonitis and consider dose reduction. Permanently discontinue TIVDAK in all patients with Grade 3 or 4 pneumonitis.

**Embryo-Fetal Toxicity:** TIVDAK can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TIVDAK and for 2 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TIVDAK and for 4 months after the last dose.

### Adverse Reactions

In the innovaTV 204 clinical trial (n=101), serious adverse reactions occurred in 43% of patients; the most common ( $\geq 3\%$ ) were ileus (6%), hemorrhage (5%), pneumonia (4%), PN, sepsis, constipation, and pyrexia (each 3%). Fatal adverse reactions occurred in 4% of patients who received TIVDAK, including septic shock, pneumonitis, sudden death, and multisystem organ failure (each 1%).

Adverse reactions leading to permanent discontinuation occurred in 13% of patients receiving TIVDAK; the most common ( $\geq 3\%$ ) were PN (5%) and corneal adverse reactions (4%). Adverse reactions leading to dose interruption occurred in 47% of patients; the most common ( $\geq 3\%$ ) were PN (8%), conjunctival adverse reactions (4%), and hemorrhage (4%). Adverse reactions leading to dose reduction occurred in 23% of patients; the most common ( $\geq 3\%$ ) were conjunctival adverse reactions (9%) and corneal adverse reactions (8%).

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The most common ( $\geq 25\%$ ) adverse reactions, including laboratory abnormalities, were hemoglobin decreased (52%), fatigue (50%), lymphocytes decreased (42%), nausea (41%), PN (39%), alopecia (39%), epistaxis (39%), conjunctival adverse reactions (37%), hemorrhage (32%), leukocytes decreased (30%), creatinine increased (29%), dry eye (29%), prothrombin international normalized ratio increased (26%), activated partial thromboplastin time prolonged (26%), diarrhea (25%), and rash (25%).

### Drug interactions

**Strong CYP3A4 Inhibitors:** Concomitant use with strong CYP3A4 inhibitors may increase unconjugated monomethyl auristatin E (MMAE) exposure, which may increase the risk of TIVDAK adverse reactions. Closely monitor patients for TIVDAK adverse reactions.

### Use in Specific Populations

**Moderate or Severe Hepatic Impairment:** MMAE exposure and adverse reactions are increased. Avoid use.

**Lactation:** Advise lactating women not to breastfeed during TIVDAK treatment and for at least 3 weeks after the last dose.

Please see full prescribing information, including **BOXED WARNING** for TIVDAK [here](#).

### About Genmab

Genmab is an international biotechnology company with a core purpose to improve the lives of people with cancer. For more than 20 years, Genmab's vision to transform cancer treatment has driven its passionate, innovative and collaborative teams to invent next-generation antibody technology platforms and leverage translational research and data sciences, fueling multiple differentiated cancer treatments that make an impact on people's lives. To develop and deliver novel therapies to patients, Genmab has formed 20+ strategic partnerships with biotechnology and pharmaceutical companies. Genmab's proprietary pipeline includes bispecific T-cell engagers, next-generation immune checkpoint modulators, effector function enhanced antibodies and antibody-drug conjugates.

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](https://www.genmab.com) and follow us on [Twitter.com/Genmab](https://twitter.com/Genmab).

### About Seagen

Seagen is a global biotechnology company that discovers, develops, and commercializes transformative cancer medicines to make a meaningful difference in people's lives. Seagen is headquartered in the Seattle, Washington area, and has locations in California, Canada, Switzerland, and the European Union. For more information on the company's marketed products and robust pipeline, visit [www.seagen.com](https://www.seagen.com) and follow [@SeagenGlobal](https://twitter.com/SeagenGlobal) on Twitter.

### About the Seagen and Genmab Collaboration

Tisotumab vedotin is being co-developed by Genmab and Seagen, under an agreement in which the companies share costs and profits for the product on a 50:50 basis.

### Genmab Forward-Looking Statements

*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*

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*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](http://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](http://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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### Seagen Forward-Looking Statements

*Certain statements made in this press release are forward looking, such as those, among others, relating to the therapeutic potential of tisotumab vedotin, its possible efficacy, safety and therapeutic uses, the referenced clinical trials, and the tisotumab vedotin development program, including the potential for development of tisotumab vedotin in a first-line treatment setting and/or as part of a combination therapy, as well as other planned clinical trial activities. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include the inability of tisotumab vedotin to show sufficient activity in ongoing or future trials, the risk of adverse events or safety signals, difficulties and delays in planned clinical trial initiations, enrollment and conduct or in obtaining data from clinical trials, in each case for a variety of reasons, including the difficulty and uncertainty of pharmaceutical product development, unexpected adverse events and/or adverse regulatory action, and the possibility that clinical results may fail to support continued development. More information about the risks and uncertainties faced by Seagen is contained under the caption "Risk Factors" included in the company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2022 filed with the Securities and Exchange Commission. Seagen disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.*

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