



Genmab and Seagen Announce FDA Accelerated Approval for TIVDAK™ (tisotumab vedotin-tftv) in Previously Treated Recurrent or Metastatic Cervical Cancer

September 20, 2021

- **TIVDAK is a First-in-Class Antibody-Drug Conjugate Directed to Tissue Factor, a Protein Expressed on Cervical Cancer Cells**
- **New Monotherapy Approved for Use in a Cancer with Limited Treatment Options**

COPENHAGEN, Denmark, and BOTHELL, Wash.; September 20, 2021 – [Genmab A/S](#) (Nasdaq: GMAB) and [Seagen Inc.](#) (Nasdaq: SGEN) today announced that the U.S. Food and Drug Administration (FDA) has granted accelerated approval to TIVDAK™ (tisotumab vedotin-tftv), the first and only approved antibody-drug conjugate (ADC) for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. TIVDAK is approved under the FDA's Accelerated Approval Program based on tumor response and the durability of the response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.¹

"Once recurrent or metastatic cervical cancer progresses, there is a need for more options for these patients," said Robert L. Coleman, M.D., Chief Scientific Officer, US Oncology Research and lead investigator of the innovaTV 204 clinical trial. "This is an important development for patients with recurrent or metastatic cervical cancer."

In the innovaTV 204 clinical trial, TIVDAK was evaluated in 101 patients with recurrent or metastatic cervical cancer who had received no more than two prior systemic regimens in the recurrent or metastatic setting, including at least one prior platinum-based chemotherapy regimen. Results from the trial showed a 24 percent confirmed objective response rate (ORR) (95% CI; 15.9-33.3), as assessed by an independent review committee (IRC) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria. The median duration of response (DOR) was 8.3 months (95% CI; 4.2 to not reached).

The prescribing information for TIVDAK includes a **BOXED WARNING** for ocular toxicity, and Warnings for peripheral neuropathy, hemorrhage, pneumonitis, and embryo-fetal toxicity. The most common (≥25%) adverse reactions, including laboratory abnormalities, were hemoglobin decreased (52%), fatigue (50%), lymphocytes decreased (42%), nausea (41%), peripheral neuropathy (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%). Please see Important Safety Information below.¹

"We are thrilled to see this new treatment approved by the FDA. We are grateful to have another option for this devastating disease," said Tamika Felder, Founder, Cervivor.

"TIVDAK's approval as a monotherapy in the U.S. is an important milestone for women with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy, as they are in need of a new treatment option and we look forward to making it available to them," said Jan van de Winkel, Ph.D., Chief Executive Officer, Genmab. "The journey towards the approval of TIVDAK started nearly two decades ago with innovative research by scientists at Genmab and Seagen and reflects on our purpose of making an impact in the lives of cancer patients and their families. Today's announcement marks Genmab's evolution into a fully integrated biotechnology company and we would like to thank patients, caregivers, investigators and our collaborators for their participation in our clinical studies."

"We are pleased with the accelerated approval of TIVDAK, Seagen's third FDA-approved antibody-drug conjugate, and fourth approved medicine. Our mission at Seagen is to develop medicines that make a difference for people impacted by cancer," said Roger Dansey, M.D., Chief Medical Officer, Seagen.

The Biologics License Application (BLA) for TIVDAK was submitted in February 2021 and accepted with Priority Review in April 2021. The submission was based on the results of the innovaTV 204 trial.

The FDA's Accelerated Approval Program allows for approval of a medicine based on a surrogate endpoint that is reasonably likely to predict clinical benefit, if the medicine fills an unmet medical need for a serious condition. A global, randomized phase 3 clinical trial (innovaTV 301) is underway and is also intended to support global registrations.

About Cervical Cancer

It is estimated that in 2021, more than 14,480 new cases of invasive cervical cancer will be diagnosed in the U.S., and 4,290 women will die from the disease.² Cervical cancer remains one of the leading causes of cancer death in women globally, with over 311,000 women dying of the disease in 2018.³

About the innovaTV 204 Trial

The innovaTV 204 trial (NCT03438396/GOG-3023/ENGOT-cx6) is an open-label, multicenter, single-arm Phase 2 trial that evaluated tisotumab vedotin in 101 patients with recurrent or metastatic cervical cancer who had received no more than two prior systemic regimens in the recurrent or metastatic setting, including at least one prior platinum-based chemotherapy regimen. Patients were excluded if they had active ocular surface disease, any prior episode of cicatricial conjunctivitis or Stevens-Johnson syndrome, Grade ≥2 peripheral neuropathy or known coagulation defects leading to an increased risk of bleeding. The main efficacy outcome measures were confirmed ORR per RECIST v1.1 as assessed by an IRC and DOR.¹

The study was conducted by Genmab in collaboration with Seagen, European Network of Gynaecological Oncological Trial Groups (ENGOT) and the GOG Foundation, Inc. (GOG). For more information about the phase 2 [innovaTV 204](#) clinical trial and other clinical trials with tisotumab vedotin, please visit www.clinicaltrials.gov.

About TIVDAK (tisotumab vedotin-tftv)

TIVDAK (tisotumab vedotin-tftv) is an 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 TIVDAK 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, TIVDAK also mediates antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity.¹

TIVDAK (tisotumab vedotin-tftv) for injection, for intravenous use, 40 mg 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. 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 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-Barré 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 ≥ 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 indicative 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

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%).

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 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 our marketed products and robust pipeline, visit 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.

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Genmab Forward Looking Statements

This Company Announcement 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 Company Announcement 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.

Genmab A/S and/or its subsidiaries own the following trademarks: Genmab®; the Y-shaped Genmab logo®; Genmab in combination with the Y-shaped Genmab logo. TIVDAK™ and the TIVDAK logo are trademarks owned by Seagen Inc.

Seagen Forward Looking Statements

Certain of the statements made in this press release are forward looking, such as those, among others, relating to the continued FDA approval of TIVDAK (tisotumab vedotin-tftv) for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy; the conduct of an ongoing randomized phase 3 clinical trial (innovaTV 301) intended to verify the clinical benefit of TIVDAK and support global registrations; and the therapeutic potential of TIVDAK, including its efficacy, safety and therapeutic uses. 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 possibility that innovaTV 301 and subsequent clinical trials may fail to establish sufficient efficacy; that adverse events or safety signals may occur; that utilization and adoption of TIVDAK by prescribing physicians may be limited by the availability and extent of reimbursement and other factors; and that adverse regulatory actions may occur. 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 June 30, 2021 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.

References

1 TIVDAK [package insert]. Bothell, WA: Seagen, Inc.

2 Cancer Stat Facts: Cervical Cancer. National Cancer Institute website. <https://seer.cancer.gov/statfacts/html/cervix.html>. Accessed September 16, 2021.

3 Bray F, Ferlay J, Soerjomataram I, et al. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2018;0: 1-31.

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Attachment

- [200921_CA62_innovaTV 204 Approval](#)