



## TIVDAK® (tisotumab vedotin-tftv) Receives U.S. FDA Approval to Treat Recurrent or Metastatic Cervical Cancer

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### Company Announcement

- Full approval based on global Phase 3 study demonstrating overall survival benefit of TIVDAK compared to chemotherapy
- TIVDAK is the first antibody-drug conjugate in this patient population to have positive overall survival data

**COPENHAGEN, Denmark; April 30, 2024** – [Genmab A/S](#) (Nasdaq: **GMAB**) and [Pfizer Inc.](#) (NYSE: **PFE**) announced today the U.S. Food and Drug Administration (FDA) has approved the supplemental Biologics License Application (sBLA) for TIVDAK® (tisotumab vedotin-tftv) for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. This FDA action converts the September 2021 accelerated approval of TIVDAK to a full approval. TIVDAK is the first antibody-drug conjugate (ADC) with demonstrated overall survival data to be granted full FDA approval in this patient population.

The approval is based on results from the global, randomized, Phase 3 innovaTV 301 clinical trial ([NCT04697628](#)), in which TIVDAK met its primary endpoint of overall survival (OS) in patients with previously treated recurrent or metastatic cervical cancer compared to chemotherapy. Secondary endpoints of progression-free survival (PFS) and a confirmed objective response rate (ORR) were also met. In October 2023, results from the innovaTV 301 study were initially [disclosed](#) during the Presidential Symposium at the European Society of Medical Oncology (ESMO) Congress.

"As a treating physician, it is encouraging to see overall survival data among these patients and a manageable safety profile with tisotumab vedotin," said Brian Slomovitz, M.D., Director of Gynecologic Oncology and Co-Chair of the Cancer Research Committee at Mount Sinai Medical Center, Miami Beach. "Treatment options for patients with advanced or recurrent cervical cancer are limited. The five-year survival rate for patients who have metastatic disease at diagnosis is less than 20% in the U.S.<sup>i</sup> There is a high unmet need for more treatment options that have demonstrated survival benefit in the contemporary treatment landscape. The approval of tisotumab vedotin brings us a step closer to fulfilling that need."

The innovaTV 301 study met its primary endpoint of OS, demonstrating a 30% reduction in the risk of death compared with chemotherapy (Hazard ratio [HR]: 0.70 [95% CI: 0.54, 0.89], two-sided p=0.0038<sup>ii</sup>). Median OS for patients treated with TIVDAK was 11.5 months [95% CI: 9.8-14.9] versus chemotherapy 9.5 months [95% CI: 7.9-10.7].

"The full FDA approval of TIVDAK represents a significant achievement for women with recurrent and metastatic cervical cancer, reinforcing TIVDAK as a treatment option that has proven to extend survival in patients whose disease has advanced after initial treatments," said Jan van de Winkel, Ph.D., Chief Executive Officer of Genmab. "This milestone underscores the importance of our ongoing clinical development program to assess the full potential of tisotumab vedotin as a treatment option in other indications."

"Recurrent or metastatic cervical cancer is a particularly devastating and mostly incurable disease, and patients are in need of survival-extending treatment options," said Chris Boshoff, M.D., Ph.D., Chief Oncology Officer, Executive Vice President at Pfizer. "Today's full approval by the FDA reinforces the important role of TIVDAK for these patients, as the first antibody-drug conjugate with statistically significant prolonged overall survival data."

The safety profile of TIVDAK in innovaTV 301 was consistent with its known safety profile as presented in the U.S. prescribing information which includes a **BOXED WARNING for Ocular Toxicity**. No new safety issues were identified. The most common (≥25%) adverse reactions, including laboratory abnormalities, in patients receiving TIVDAK were hemoglobin decreased (41%), peripheral neuropathy (38%), conjunctival adverse reactions (37%), aspartate aminotransferase increased (34%), nausea (33%), alanine aminotransferase increased (30%), fatigue (28%), sodium decreased (27%), epistaxis (26%), and constipation (25%).

The sBLA application received a Priority Review Designation, which is granted by the U.S. FDA to medicines that may offer significant advances in treatment or may provide a treatment where no adequate therapy exists.<sup>iii</sup> TIVDAK was granted accelerated approval in the U.S. by the FDA in September 2021, based on tumor response and durability of response from the innovaTV 204 pivotal Phase 2 single-arm clinical trial evaluating TIVDAK as a monotherapy in patients with previously treated recurrent or metastatic cervical cancer.

"Today marks a great day for patients, especially adults battling advanced cervical cancer," said Tamika Felder, cervical cancer patient advocate and Founder and Chief Visionary Officer, Cervivor, Inc. "This full approval opens up new treatment paths for this patient community who have long faced limited options."

### About Cervical Cancer

Cervical cancer remains a disease with high unmet need despite advances in effective vaccination and screening practices to prevent and diagnose pre-/early-stage cancers for curative treatment. Recurrent and/or metastatic cervical cancer is a particularly devastating and mostly incurable disease; up to 15% of adults with cervical cancer present with metastatic disease at diagnosis<sup>iv,v</sup> and, for adults diagnosed at earlier stages who receive treatment, up to 61%<sup>vi</sup> will experience disease recurrence. It was estimated that in 2023, more than 13,960 new cases of invasive cervical cancer were diagnosed in the U.S. and 4,310 adults would die from the disease.<sup>vii</sup>

### About the innovaTV 301 Trial

The innovaTV 301 trial (NCT04697628) is a global, 1:1 randomized, open-label Phase 3 trial evaluating TIVDAK® (tisotumab vedotin-tftv) 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](http://www.clinicaltrials.gov).

#### **About TIVDAK<sup>®</sup> (tisotumab vedotin-tftv)**

TIVDAK (tisotumab vedotin-tftv) 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.

#### **About Genmab**

Genmab is an international biotechnology company with a core purpose guiding its unstoppable team to strive towards improving the lives of patients through 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, next-generation immune checkpoint modulators, effector function enhanced antibodies, and antibody-drug conjugates. To help develop and deliver novel antibody therapies to patients, Genmab has formed 20+ strategic partnerships with biotechnology and pharmaceutical companies. By 2030, Genmab's vision is to transform the lives of people with cancer and other serious diseases with knock-your-socks-off (KYSO<sup>®</sup>) antibody medicines.

Established in 1999, 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](http://Genmab.com) and follow us on [LinkedIn](#) and [X](#).

#### **About Pfizer Oncology**

At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes game-changing mechanisms of action to attack cancer from multiple angles, including antibody-drug conjugates (ADCs), small molecules, bispecific antibodies and other immunotherapy biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to extend and improve patients' lives.

#### **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.

#### **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](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 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<sup>®</sup>; the Y-shaped Genmab logo<sup>®</sup>; Genmab in combination with the Y-shaped Genmab logo<sup>®</sup>; HuMax<sup>®</sup>; DuoBody<sup>®</sup>; HexaBody<sup>®</sup>; DuoHexaBody<sup>®</sup> and HexElect<sup>®</sup>. Tivdak<sup>®</sup> is a trademark of Pfizer Inc.

#### **Pfizer Disclosure Notice**

The information contained in this release is as of April 29, 2024. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

*This release contains forward-looking information about Pfizer Oncology and TIVDAK<sup>®</sup> (tisotumab vedotin-tftv), including its potential benefits and its ongoing clinical development program, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of TIVDAK; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in particular jurisdictions for TIVDAK; whether and when any applications that may be pending or filed for TIVDAK may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether TIVDAK will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of TIVDAK; whether the collaboration between Pfizer and Genmab will be successful; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.*

*A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2023 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).*

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<sup>i</sup> Cervical Cancer: Statistics. American Society of Clinical Oncology (ASCO). September 2023. <https://www.cancer.net/cancer-types/cervical-cancer/statistics>

<sup>ii</sup> The threshold for statistical significance is 0.0226 (two-sided).

<sup>iii</sup> Priority Review. U.S. Food and Drug Administration. January 4, 2018. <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review>

<sup>iv</sup> National Cancer Institute. SEER Cancer Stat Facts: Cervical Cancer. 2023. <https://seer.cancer.gov/statfacts/html/cervix.html>

<sup>v</sup> 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.

<sup>vi</sup> 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.

<sup>vii</sup> Key Statistics for Cervical Cancer. American Cancer Society. Atlanta, GA. 2023. <https://www.cancer.org/cancer/types/cervical-cancer/about/key-statistics.html>

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