

Press Release

European Commission Expands PADCEV™ (enfortumab vedotin) Plus Keytruda® (pembrolizumab) Approval to Adults with Resectable Muscle-Invasive Bladder Cancer Regardless of Cisplatin Eligibility

- *Expanded indication provides an approved perioperative treatment option for adult patients with resectable MIBC in the European Union -*
- *Approval is based on Phase 3 EV-304 results demonstrating statistically significant improvements in Event-Free Survival and Overall Survival compared with neoadjuvant gemcitabine and cisplatin chemotherapy in cisplatin-eligible adults with MIBC -*

TOKYO, 23 October, 2026 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, “Astellas”) today announced that the European Commission (EC) has granted Marketing Authorization for PADCEV™ (enfortumab vedotin), in combination with Keytruda® (pembrolizumab), as neoadjuvant treatment (before surgery) and then continued after radical cystectomy as adjuvant treatment (after surgery), for adults with resectable muscle-invasive bladder cancer (MIBC) in the European Union (EU), regardless of cisplatin eligibility.

The approval is based on results from the Phase 3 EV-304 clinical trial (KEYNOTE-B15)¹ and expands the existing EU indication for cisplatin-ineligible adults established through EV-303 (KEYNOTE-905). The combination is now approved for adults with resectable MIBC, regardless of cisplatin eligibility.

Matthew D. Galsky, M.D., Mount Sinai Tisch Cancer Center, Icahn School of Medicine at Mount Sinai, New York, and an EV-304 Principal Investigator

“For cisplatin-eligible patients with resectable muscle-invasive bladder cancer, neoadjuvant cisplatin-based chemotherapy has been an established treatment approach for many years. With this approval, physicians now have a regimen option shown to significantly reduce the risk of recurrence and improve overall survival, without cisplatin-based chemotherapy, providing greater flexibility when planning care for appropriate patients.”

MIBC is an advanced, aggressive form of bladder cancer associated with substantial risk of recurrence and disease progression, even though patients are treated with curative intent.^{2,3} For cisplatin-eligible adults with resectable MIBC, neoadjuvant cisplatin-based chemotherapy followed by radical cystectomy has been a standard

treatment approach; however, recurrence remains a significant challenge, with just under half of patients experiencing disease recurrence within five years.²

In EV-304, neoadjuvant enfortumab vedotin plus pembrolizumab followed by continued adjuvant treatment after radical cystectomy significantly improved Event-Free Survival (EFS) and Overall Survival (OS) compared with neoadjuvant gemcitabine and cisplatin chemotherapy in cisplatin-eligible adults with MIBC. The combination reduced the risk of tumor recurrence, progression, or death by 47% (Hazard Ratio (HR) 0.53; CI, 95%, 0.41–0.70; 1-sided p<0.0001) and reduced the risk of death by 35% (HR 0.65; 95% CI, 0.48-0.89; 1-sided p=0.0029).¹ The combination also demonstrated a pathological complete response (pCR) rate of 55.8% compared with 32.5% with neoadjuvant chemotherapy at the time of surgery (estimated difference 23.4%; 95% CI 16.7-29.8; 1-sided p<0.0001).¹

Moitreyee Chatterjee-Kishore, Ph.D., MBA, Executive Vice President and Head of Oncology Development, Astellas

“The EV-304 results demonstrate the potential to change the treatment trajectory for people with resectable muscle-invasive bladder cancer by bringing an effective perioperative approach into an earlier stage of disease. This approval, together with the existing indication for cisplatin-ineligible adults, enables a consistent treatment approach with enfortumab vedotin plus pembrolizumab for adults with resectable muscle-invasive bladder cancer in the EU and reinforces our commitment to advancing care across urothelial cancer.”

The safety profile in EV-304 was consistent with the known profiles of the individual medicines, and no new safety signals were observed.¹ Grade ≥3 adverse events due to any cause occurred in 75.7% of patients treated with perioperative enfortumab vedotin plus pembrolizumab compared to 67.2% of patients treated with neoadjuvant chemotherapy.¹

Astellas is working closely with regulatory authorities and health technology assessment bodies across the European Union to support patient access following approval.

Astellas has already reflected the impact of the EC approval in its financial forecast for the current fiscal year ending March 31, 2027.

About PADCEV (enfortumab vedotin)

PADCEV (enfortumab vedotin) is a first-in-class antibody-drug conjugate (ADC) that is directed against Nectin-4, a protein located on the surface of cells and highly expressed in bladder cancer.⁴ Nonclinical data suggest the anticancer activity of enfortumab vedotin is due to its binding to Nectin-4-expressing cells, followed by the internalization and release of the anti-tumor agent monomethyl auristatin E (MMAE) into the cell, which result in the cell not reproducing (cell cycle arrest) and in programmed cell death (apoptosis).⁴

Enfortumab vedotin in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph is also approved as neoadjuvant treatment and then continued after radical cystectomy as adjuvant treatment for adult patients with muscle-invasive bladder cancer (MIBC) regardless of eligibility for cisplatin-containing chemotherapy in the United States.

Additionally, enfortumab vedotin plus pembrolizumab is approved for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC) regardless of cisplatin eligibility in the United States, Japan, and a number of other countries around the world. In the EU, the combination is approved for the treatment of adult patients with unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy.

About the EV-304/KEYNOTE-B15 Trial

The EV-304 trial is an ongoing, open-label, randomized, controlled, Phase 3 study evaluating neoadjuvant and adjuvant enfortumab vedotin in combination with pembrolizumab versus neoadjuvant chemotherapy (gemcitabine and cisplatin) in patients with MIBC who are eligible for cisplatin-based chemotherapy. Patients were randomized to receive either neoadjuvant and adjuvant (before and after surgery) enfortumab vedotin in combination with pembrolizumab (arm A) or neoadjuvant chemotherapy (arm B). Curative-intent surgery (cystectomy) was performed in both arms. Enfortumab vedotin in combination with pembrolizumab was administered as a planned total of 9 cycles of enfortumab vedotin and 17 cycles of pembrolizumab, split before and after surgery.

The primary endpoint of this trial is EFS, defined as the time from randomization to the first occurrence of any of the following events: progression of disease that precludes RC or failure to undergo RC in participants with residual disease, gross residual disease left behind at the time of surgery, local or distant recurrence based on BICR or death due to any cause. Key secondary endpoints include OS and pCR rate.

For more information on the global EV-304 trial, go to clinicaltrials.gov.

About Astellas

Astellas is a global life sciences company committed to turning innovative science into VALUE for patients. We provide transformative therapies in disease areas that include oncology, ophthalmology, urology, immunology and women's health. Through our research and development programs, we are pioneering new healthcare solutions for diseases with high unmet medical need. Learn more at www.astellas.com.

About the Pfizer, Astellas and MSD Collaboration

Seagen and Astellas previously entered a clinical collaboration agreement with MSD to evaluate the combination of Seagen and Astellas' PADCEV (enfortumab vedotin) and MSD's KEYTRUDA (pembrolizumab) in patients with urothelial cancer. Pfizer Inc. successfully completed its acquisition of Seagen on December 14, 2023. KEYTRUDA is a registered trademark of MSD, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (known as MSD outside of the United States and Canada).

Cautionary Notes

In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future

performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties. Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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References

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2. Squires P, *et al.* Treatment Patterns, Disease Recurrence, and Overall Survival in Patients With Muscle-Invasive Bladder Cancer After Radical Cystectomy: A Population-Level Claims-Based Analysis. *Clin Genitourin Cancer.* 2026;24(1):102466.
3. Bladder Cancer Awareness Network. What is Muscle Invasive Bladder Cancer? Available at: <https://bcn.org/what-is-muscle-invasive-bladder-cancer/>. Date Accessed: October 2026.
4. Challita-Eid PM., *et al.* Enfortumab vedotin antibody-drug conjugate targeting nectin-4 is a highly potent therapeutic agent in multiple preclinical cancer models. *Cancer Res.* 2016;76(10):3003-13.