Press Release

European Medicines Agency Validates Type II Variation Application for PADCEV™ (enfortumab vedotin) with KEYTRUDA™ (pembrolizumab) for Certain Patients with Muscle-Invasive Bladder Cancer

TOKYO, December 1, 2025 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced that the European Medicines Agency (EMA) validated for review a Type II variation application for PADCEV™ (enfortumab vedotin), a Nectin-4 directed antibody-drug conjugate, in combination with KEYTRUDA™ (pembrolizumab), a PD-1 inhibitor, as neoadjuvant treatment (before surgery), and then continued after radical cystectomy (surgery) as adjuvant treatment (after surgery), for adults with muscle-invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy.

The Type II variation application is based on results from the Phase 3 EV-303 clinical trial (also known as KEYNOTE-905). The study found that in this patient population, the combination led to a 60% reduction in risk of tumor recurrence, progression, or death and a 50% reduction in risk of death.[1] The safety results in EV-303 were consistent with those previously reported for the combination, and no new safety signals were identified.[1,2]

In Europe, bladder cancer is diagnosed in over 224,000 people annually, with MIBC accounting for a significant proportion of cases.[3] MIBC represents approximately 30% of all bladder cancer cases globally.[4] The standard treatment for patients with MIBC is neoadjuvant cisplatin-based chemotherapy followed by surgery.[5] However, up to half of patients with MIBC are not eligible to receive cisplatin and face limited treatment options, typically undergoing surgery without any systemic treatment.[6]

The EMA's Committee for Medicinal Products for Human Use (CHMP) and subsequently the European Commission (EC) are expected to share their opinion and decision on the Type II variation application calendar year 2026.

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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.[7] 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).[7]

Enfortumab vedotin in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph is approved as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment, for the treatment of adult patients with muscle invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy.

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 European Union, the combination is approved for the treatment of adult patients with la/mUC who are eligible for platinum-containing chemotherapy. Enfortumab vedotin is also approved as a single agent for the treatment of adult patients with la/mUC who have previously received a PD-1/PD-L1 inhibitor and platinum-containing chemotherapy or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

About the EV-303/KEYNOTE-905 Trial

The EV-303 trial (also known as KEYNOTE-905) is an ongoing, open-label, randomized, three-arm, controlled, Phase 3 study evaluating neoadjuvant and adjuvant enfortumab vedotin in combination with pembrolizumab or neoadjuvant and adjuvant pembrolizumab versus surgery alone in patients with MIBC who are either not eligible for or declined cisplatin-based chemotherapy. Patients were randomized to receive either neoadjuvant and adjuvant pembrolizumab (arm A), surgery alone (arm B) or neoadjuvant and adjuvant enfortumab vedotin in combination with pembrolizumab (arm C).

The primary endpoint of this trial is EFS between arm C and arm B, defined as the time from randomization to the first occurrence of any of the following events: progression of disease that precludes radical cystectomy (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 as assessed by imaging and/or biopsy or death due to any cause. Key secondary endpoints include OS and pCR rate between arm C and arm B, as well as EFS, OS and pCR rate between arm A and arm B.

For more information on the global EV-303 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 Merck Collaboration

Seagen and Astellas previously entered a clinical collaboration agreement with Merck to evaluate the combination of Seagen's and Astellas' PADCEV (enfortumab vedotin) and Merck's KEYTRUDA (pembrolizumab) in patients with muscle-invasive bladder cancer (MIBC) who are not eligible for or declined cisplatin-based chemotherapy. Pfizer Inc. successfully completed its acquisition of Seagen on December 14, 2023. KEYTRUDA is a registered trademark of Merck Sharp & Dohme Corp., 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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