Press Release

China's National Medical Products Administration (NMPA) Approves PADCEV™ in combination with KEYTRUDA® (pembrolizumab) for the Treatment of Advanced Bladder Cancer

- First regimen to be approved in China to demonstrate superiority to platinum-containing chemotherapy for the treatment of locally advanced or metastatic urothelial cancer, the standard of care for nearly 40 years[1]

- NMPA approval based on the global Phase 3 EV-302 trial (also known as KEYNOTE-A39) where the treatment combination significantly improved overall survival and progression-free survival outcomes[1]

TOKYO, January 8, 2025 – Astellas Pharma Inc. (TSE:4503, President and CEO: Naoki Okamura, "Astellas") today announced that China's National Medical Products Administration (NMPA) has approved PADCEV™ (enfortumab vedotin) in combination with KEYTRUDA® (pembrolizumab) for adult patients with locally advanced or metastatic urothelial cancer (la/mUC). The treatment combination will provide a new therapeutic option to patients with la/mUC in China and offer an alternative to platinum-containing chemotherapy, the standard of care for nearly 40 years.[1]

Bladder cancer leads to significant morbidity and mortality across China. Over 92,000 people were diagnosed with bladder cancer in 2022, and approximately 41,000 deaths were reported as a result of the disease.[2] Urothelial cancer, which accounts for 90% of all bladder cancers, is a debilitating and frequently aggressive cancer.[3] When the disease is diagnosed at a late stage, survival rates are often extremely poor, driving the urgent need for new treatment strategies that can extend patients' lives.

Professor Guo Jun, Lead Primary Investigator of the EV-302 trial in China, Director of the Department of Urologic Oncology and Melanoma/Sarcoma, Beijing Cancer Hospital, China, Vice Chairman and Chief-Secretary of the Chinese Society of Clinical Oncology (CSCO):
"The NMPA approval of enfortumab vedotin in combination with pembrolizumab is the first non-platinum treatment for Chinese patients with advanced urothelial cancer that can be used in the first-line setting. The results of the EV-302 study demonstrate that this combination nearly doubled median overall survival (OS), and increased median progression-free survival (PFS), overall response rate and complete

response rate compared to platinum-based chemotherapy. These results were seen in a broad population of patients with locally advanced or metastatic urothelial cancer, regardless of patients' biomarker status, cisplatin eligibility or liver metastasis. I believe that this new treatment regimen will change the clinical treatment landscape of urothelial carcinoma in China and bring hope of longer survival to more Chinese patients with advanced urothelial carcinoma."

Professor Huang Jian, Lead Primary Investigator of the EV-302 Study in China, Chairman of the Urology Subcommittee of the Chinese Medical Association, Department of Urology at Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China:
"The current first-line treatment strategy for advanced urothelial carcinoma in China is platinum-based chemotherapy, with very limited clinical options available. The approval of enfortumab vedotin in combination with pembrolizumab represents the first treatment regimen in the past 20-30 years that has shown superiority over platinum-based chemotherapy in the entire population. We hope that this combination could become the future standard of care treatment."

Ahsan Arozullah, M.D., M.P.H., Senior Vice President, Head of Oncology Development, Astellas:
"We are delighted that the NMPA has recognized the benefits that enfortumab vedotin has offered to patients with previously treated locally advanced or metastatic urothelial cancer in China following its approval in August 2024. This latest approval in combination with pembrolizumab marks another step forward in our mission to bring new, innovative treatment strategies to patients in China. We look forward to making a significant impact on patients' lives, helping to slow disease progression and give them precious more time."

The NMPA's approval of enfortumab vedotin in combination with pembrolizumab is supported by the results from the Phase 3 EV-302 clinical trial (also known as KEYNOTE-A39). The trial demonstrated that the treatment combination improved median overall survival (OS) and median progression-free survival (PFS) with statistically significant and clinically meaningful results in patients with previously untreated la/mUC compared to platinum-containing chemotherapy. A median OS of 31.5 months (95% CI: 25.4-NR) was achieved with the treatment combination compared to 16.1 months (95% CI: 13.9-18.3) with platinum-containing chemotherapy, representing a 53% reduction in risk of death (Hazard Ratio [HR]=0.47; 95% Confidence Interval [CI]: 0.38-0.58; P<0.00001). A median PFS of 12.5 months (95% CI: 10.4-16.6) was reported with the treatment combination compared to 6.3 months (95% CI: 6.2-6.5) with platinum-containing chemotherapy, representing a 55% reduction in the risk of cancer progression or death (HR=0.45; 95% CI: (0.38-0.54); P<0.00001). The safety results were consistent with those previously reported with this treatment combination, and no new safety issues were identified.[1]

Astellas has already reflected the impact from this latest approval from the NMPA in China in its financial forecast for the current fiscal year ending March 31, 2025.

For more information, please see the press release "China's National Medical Products Administration Accepts Astellas and Pfizer's Supplemental Biologics

License Application for enfortumab vedotin with KEYTRUDA® (pembrolizumab) for First-Line Treatment of Advanced Bladder Cancer" issued on March 28, 2024: https://www.astellas.com/en/news/28961

About Bladder and Urothelial Cancer

Urothelial cancer, or bladder cancer, begins in the urothelial cells, which line the urethra, bladder, ureters, renal pelvis, and some other organs.[4] Urothelial cancer accounts for 90% of all bladder cancers and can also be found in the renal pelvis, ureter, and urethra.[3,5,6] If bladder cancer has spread to surrounding organs or muscles, it is called locally advanced disease.[7] If the cancer has spread to other parts of the body, it is called metastatic disease.[8] Approximately 12% of cases are locally advanced or metastatic urothelial cancer at diagnosis.[9]

In China, the incidence rate of bladder cancer in 2022 ranked 11th among all cancers, with over 92,000 new cases diagnosed that year.[2] The five year prevalence of bladder cancer in China is estimated to be 2.5/100,000 cases, or 276,102 cases.[2] Continuous treatment and surveillance makes bladder cancer one of the most expensive cancer types over the lifetime of a patient, and the costliest cancer when compared to other malignancies.[10]

About EV-302

EV-302 is an ongoing, open-label, randomized, controlled Phase 3 trial, evaluating enfortumab vedotin in combination with pembrolizumab versus platinum-containing chemotherapy in patients with previously untreated la/mUC. The trial enrolled 886 patients with previously untreated la/mUC who were eligible for cisplatin- or carboplatin-containing chemotherapy regardless of PD-L1 status. Patients were randomized to receive either enfortumab vedotin in combination with pembrolizumab or platinum-containing chemotherapy. The dual primary endpoints of this trial are OS and PFS per RECIST v1.1 by blinded independent central review (BICR). Select secondary endpoints include ORR per RECIST v1.1 by BICR, DOR per RECIST v1.1 by BICR, and safety.[1]

The most common (≥3%) Grade 3 or higher adverse events related to treatment with enfortumab vedotin and pembrolizumab were maculo-papular rash, hyperglycemia, neutropenia, peripheral sensory neuropathy, diarrhea, and anemia. The safety results in EV-302 are generally consistent with the known safety events previously reported with each agent alone, and with the safety profile of this combination in EV-103 in cisplatin-ineligible patients with la/mUC. No new safety issues were identified.[1]

The EV-302 trial is part of an extensive clinical program evaluating this combination in multiple stages of urothelial cancer and other solid tumors. Findings from EV-302 were presented at the 2023 European Society for Medical Oncology (ESMO) Congress and were published in the *New England Journal of Medicine*.[1]

For more information on the EV-302 trial (NCT04223856) go to https://clinicaltrials.gov.

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.[11] 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).[12]

PADCEV is indicated in China as monotherapy for the treatment of adult patients with locally advanced or metastatic urothelial cancer after prior treatment with platinum-containing chemotherapy and programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitors, and in combination with KEYTRUDA® (pembrolizumab) for adult patients with locally advanced or metastatic urothelial cancer.

Ongoing Investigational Trials

EV-302 (NCT04223856) is an open-label, randomized, controlled Phase 3 trial, evaluating enfortumab vedotin in combination with pembrolizumab versus platinum-containing chemotherapy in patients with previously untreated locally advanced or metastatic urothelial cancer (la/mUC) who were eligible for cisplatin- or carboplatin-containing chemotherapy regardless of PD-L1 status.

EV-103 (NCT03288545) is an ongoing, multi-cohort, open-label, multicenter Phase 1b/2 trial investigating enfortumab vedotin alone or in combination with pembrolizumab and/or chemotherapy in first- or second-line settings in patients with la/mUC and in patients with muscle-invasive bladder cancer (MIBC).

EV-203 (NCT04995419) is a Phase 2, multicenter, single-arm bridging trial in China designed to evaluate the efficacy, safety, and pharmacokinetic performance of enfortumab vedotin as treatment for patients in China. A total of 40 patients were enrolled in the trial.

Enfortumab vedotin in combination with pembrolizumab is being investigated in an extensive program in multiple stages of urothelial cancer, including two Phase 3 clinical trials in MIBC in EV-304 (NCT04700124, also known as KEYNOTE-B15) and EV-303 (NCT03924895, also known as KEYNOTE-905). The use of enfortumab vedotin in combination with pembrolizumab in second-line urothelial cancer and MIBC has not been proven safe or effective.

EV-104 (NCT05014139) is a Phase 1 trial exploring enfortumab vedotin in patients with non-muscle invasive bladder cancer (NMIBC). The trial is being conducted in two-parts, assessing dose escalation and dose expansion with enfortumab vedotin when administered intravesically as a monotherapy.

EV-202 (NCT04225117) is an ongoing, multi-cohort, open-label, multicenter Phase 2 trial investigating enfortumab vedotin alone in patients with previously treated advanced solid tumors. This trial also has a cohort that is investigating enfortumab vedotin in combination with pembrolizumab in patients with previously untreated recurrent / metastatic head and neck squamous cell carcinoma.

Important Safety Information

For Important Safety Information for enfortumab vedotin please see the full Summary of Product Characteristics at: https://www.ema.europa.eu/en/documents/product-information/padcev-epar-product-information_en.pdf

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 Astellas, Pfizer and MSD Collaboration

Astellas and Pfizer have a clinical collaboration agreement with MSD to evaluate the combination of Astellas' and Pfizer's PADCEV™ (enfortumab vedotin) and MSD's KEYTRUDA® (pembrolizumab) in patients with previously untreated metastatic urothelial cancer. 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).

Astellas 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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