Press Release

China's National Medical Products Administration (NMPA) Approves PADCEV™ (enfortumab vedotin) for Treatment of Locally Advanced or Metastatic Urothelial Cancer

- Approval based on the global EV-301 and China EV-203 trials, where enfortumab vedotin signficantly improved overall survival (OS) and objective response rate (ORR) respectively in patients following prior treatment with platinum-based chemotherapy and PD-1/L1 inhibitors[1,2]

- Enfortumab vedotin will provide a much needed new treatment option for patients with locally advanced or metastatic urothelial cancer in China

TOKYO, August 20, 2024 – Astellas Pharma Inc. (TSE:4503, President and CEO: Naoki Okamura, "Astellas") today announced that the Center for Drug Evaluation (CDE) of China's National Medical Products Administration (NMPA) has approved PADCEV™ (enfortumab vedotin) for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC) after prior treatment with platinum-containing chemotherapy and programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitors.

Urothelial cancer is a debilitating and often aggressive cancer that affects both the lower urinary tract (bladder and urethra) and upper urinary tract (ureter and renal pelvis).[3,4,5] Over 92,000 people were diagnosed with bladder cancer in China in 2022, and approximately 41,000 deaths were reported as a result of the disease.[6] Survival rates are particularly poor with locally advanced or metastatic urothelial cancer, driving the urgent need for new therapies that extend patients' lives.

Professor Guo Jun, Principal Investigator, EV-203 trial and Director of the Department of Melanoma and Urological Oncology, Beijing Cancer Hospital, China
"On August 13, 2024, the NMPA officially approved the use of enfortumab vedotin for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (la/mUC) after prior treatment with platinum-containing chemotherapy and PD-1/PD-L1 inhibitors. This approval, based on a global Phase 3 registration study as well as a bridging study in Chinese patients, is a milestone event where patients will now have access to this new antibody-drug conjugate (ADC) treatment in China."

Professor Dingwei Ye, Academic Leader, Department of Urology and Principal Expert, Urological Oncology MDT Management, Fudan University-Affiliated Cancer Hospital, China
“Enfortumab vedotin will benefit patients in our country, bringing a new treatment to those with locally advanced or metastatic urothelial carcinoma (la/mUC) who have previously received platinum-containing chemotherapy and PD-1/PD-L1 inhibitors.”

Professor Zhisong He, Deputy Director, Institute of Urology, Peking University First Hospital, China
"Enfortumab vedotin is an ADC that is directed against Nectin-4. The approval of the EV-203 indication expands doctors’ treatment choices."

Ahsan Arozullah, M.D., M.P.H., Senior Vice President, Head of Oncology Development, Astellas
“We remain committed to driving scientific progress that leads to meaningful changes in the course of cancer across the globe. The approval of enfortumab vedotin by the CDE provides patients in China with another treatment option for locally advanced or metastatic urothelial cancer, providing hope of better outcomes for those affected by this condition.”

The CDE’s approval of enfortumab vedotin is supported by data from the global EV-301 and China EV-203 trials. EV-203 serves as a bridging trial to EV-301, a Phase 3 randomized trial that has supported global registrations of enfortumab vedotin. EV-203 (NCT04995419) is a single-arm, open-label, multicenter Phase 2 trial of enfortumab vedotin in Chinese patients with la/mUC who previously received a PD-1/PD-L1 inhibitor and platinum-based chemotherapy.[1] Results showed that EV-203 met its primary endpoint, demonstrating statistical significance in ORR for patients treated with enfortumab vedotin alone compared to historical controls (37.5% [n/N=15/40; 95% CI: 22.7–54.2]), as confirmed by the independent review committee.[1] The efficacy and pharmacokinetic data from the trial are consistent with global data, with safety findings demonstrating that the majority of treatment related adverse events were grade 1–2.[1]

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

For more information, please see the press release “Astellas and Seagen Announce China's National Medical Products Administration Accepts Biologics License Application for Enfortumab Vedotin in Certain Patients with Locally Advanced or Metastatic Urothelial Cancer” issued on March 9, 2023: https://www.astellas.com/en/news/27441

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About EV-203
The China EV-203 trial is a Phase 2, multicenter, single-arm bridging trial designed to evaluate the efficacy, safety, and pharmacokinetic performance of enfortumab vedotin as a treatment for patients in China. The trial enrolled a total of 40 patients with la/mUC who previously received a PD-1/PD-L1 inhibitor and platinum-based chemotherapy.[1]

The trial met the primary endpoint of confirmed objective response rate (ORR) by independent review committee, achieved by 37.5% of patients who received treatment with enfortumab vedotin (n/N=15/40, 95% CI: 22.7-54.2). Complete response was achieved in 1 (2.5%) patient and partial response in 14 (35.0%) patients.[1]

No new safety signals were identified during the trial. Most treatment-related adverse events reported with enfortumab vedotin were grade 1–2. Two patients discontinued treatment with enfortumab vedotin due to experiencing treatment-related adverse events (acute coronary syndrome and hyperglycemia/rash).[1]

For more information on the EV-203 trial (NCT04995419) go to https://clinicaltrials.gov.

About EV-301
The global EV-301 trial (NCT03474107) is a multicenter, open-label, randomized Phase 3 trial designed to evaluate enfortumab vedotin versus physician's choice of chemotherapy (docetaxel, paclitaxel or vinflunine) in 608 patients with locally advanced or metastatic urothelial cancer who were previously treated with a PD-1/PD-L1 inhibitor and platinum-containing therapies.[2] The primary endpoint was overall survival and secondary endpoints included progression-free survival, overall response rate, duration of response and disease control rate, as well as assessment of safety/tolerability and quality-of-life parameters.

Results from EV-301 showed that median overall survival was longer in the enfortumab vedotin group than in the chemotherapy group (12.88 vs. 8.97 months respectively; HR= 0.70; 95% CI: 0.56-0.89; p=0.001).[2] Progression-free survival was also longer in the enfortumab vedotin group than in the chemotherapy group (5.55 vs. 3.71 months respectively; HR=0.62; 95% CI: 0.51-0.75; P<0.001).[2] The incidence of treatment-related adverse events was similar in the two groups (93.9% in the enfortumab vedotin group and 91.8% in the chemotherapy group). The incidence of events of grade 3 or higher was also similar in the two groups (51.4% and 49.8%, respectively).[2] Results were published in the New England Journal of Medicine.

For more information on the EV-301 trial (NCT03474107) go to https://clinicaltrials.gov.

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.[5] Urothelial cancer accounts for 90% of all bladder cancers and can also be found in the renal pelvis, ureter, and urethra.[7,8] If bladder cancer has spread to surrounding organs or muscles, it is called locally advanced disease.[9] If the cancer has spread to other parts of the body, it is called metastatic disease.[10] Approximately 12% of cases are locally advanced or metastatic urothelial cancer at diagnosis.[11]

In China, the incidence rate of bladder cancer in 2022 ranked 11th among all cancers, with over 92,000 new cases diagnosed that year.[6] The five year prevalence of bladder cancer in China is estimated to be 2.5/100,000 cases, or 276,102 cases.[6] 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.[12]

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.[13,14] 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).[13]

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

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).

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.

About Astellas
Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into VALUE for patients. For more information, please visit our website at https://www.astellas.com/en.

About the Astellas and Pfizer Collaboration
Astellas and Pfizer are co-developing enfortumab vedotin under a 50:50 worldwide development and commercialization collaboration. In the United States, Astellas and Pfizer co-promote enfortumab vedotin under the brand name PADCEV® (enfortumab vedotin-ejfv). In the Americas outside the US, Pfizer holds responsibility for commercialization activities and regulatory filings. Outside of the Americas, Astellas holds responsibility for commercialization activities and regulatory filings.

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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