Press Release

Astellas Submits New Drug Application for Enfortumab Vedotin in Japan

Enfortumab vedotin to be reviewed by Ministry of Health, Labour and Welfare for patients with locally advanced or metastatic urothelial cancer that has progressed after anti-cancer medication

TOKYO, March 11, 2021 - Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced the submission of a New Drug Application (NDA) to Japan's Ministry of Health, Labour and Welfare (MHLW) for enfortumab vedotin for the treatment of patients with locally advanced or metastatic urothelial cancer that has progressed after anti-cancer medication. If approved, enfortumab vedotin would be the first antibody-drug conjugate (ADC) available in Japan for people living with this form of urothelial cancer.

The submission is based on two global clinical trials with sites in Japan. The Phase 3 EV-301 trial evaluated enfortumab vedotin versus chemotherapy in adult patients with locally advanced or metastatic urothelial cancer who were previously treated with platinum-based chemotherapy and a PD-1/L1 inhibitor. The Phase 2 EV-201 trial evaluated enfortumab vedotin in patients with locally advanced or metastatic urothelial cancer who have been previously treated with a PD-1/L1 inhibitor, including those who have also been treated with a platinum-containing chemotherapy (cohort 1) and those who have not received a platinum-containing chemotherapy and who are ineligible for cisplatin (cohort 2).[1,2]

Enfortumab vedotin met the primary endpoints of overall survival (EV-301) and confirmed objective response rate per blinded independent central review (EV-201).[3,4,5]

“More than 24,000 people in Japan are diagnosed with urothelial cancer each year. For those whose cancer progresses despite treatment with chemotherapy and immunotherapy, there is no standard treatment option currently,” said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Oncology Therapeutic Area Head, Astellas. “Based on data from two global clinical trials, and following the Ministry of Health, Labour and Welfare’s review, enfortumab vedotin may offer a new option for these patients.”

About Urothelial Cancer

Urothelial cancer is the most common type of bladder cancer (90 percent of cases), and can also be found in the renal pelvis (where urine collects inside the kidney), ureter (tube that connects the kidneys to the bladder) and urethra.[6] Globally, approximately 549,000 new cases of bladder cancer and 200,000 deaths are reported annually.[7] In Japan, it is estimated that 24,300 patients are diagnosed with this form of cancer and 9,500 deaths are reported annually.[8]

Locally advanced and metastatic urothelial cancer is an aggressive disease that is associated with poor survival and high healthcare costs.[9] Five-year relative survival rates for metastatic disease are estimated to be approximately 7 percent.[10]

About the EV-301 Trial
The EV-301 trial (NCT03474107) is a global, multicenter, open-label, randomized phase 3 trial designed to evaluate enfortumab vedotin versus physician's choice of chemotherapy (docetaxel, paclitaxel or vinflunine) in approximately 600 patients with locally advanced or metastatic urothelial cancer who were previously treated with a PD-1 or PD-L1 inhibitor and platinum-based therapies.[1] The primary endpoint is overall survival of participants treated with enfortumab vedotin compared to those treated with chemotherapy. Secondary endpoints include progression-free survival, duration of response, and overall response rate, as well as assessment of safety/tolerability and quality-of-life parameters. Results of the EV-301 trial were published in the *New England Journal of Medicine*.

About the EV-201 Trial
The EV-201 trial (NCT03219333) is a single-arm, pivotal phase 2 clinical trial of enfortumab vedotin for patients with locally advanced or metastatic urothelial cancer who have been previously treated with a PD-1 or PD-L1 inhibitor, including those who have also been treated with a platinum-containing chemotherapy (cohort 1) and those who have not received a platinum-containing chemotherapy in this setting and who are ineligible for cisplatin (cohort 2). The trial enrolled 128 patients in cohort 1 and 91 patients in cohort 2 at multiple centers internationally.[2] The primary endpoint is confirmed objective response rate per blinded independent central review. Secondary endpoints include assessments of duration of response, disease control rate, progression-free survival, overall survival, safety and tolerability. Results of the first cohort from the EV-201 trial were published in *The Journal of Clinical Oncology* and results from the second cohort were presented at the 2021 American Society of Clinical Oncology Genitourinary Cancer Symposium.

About Enfortumab Vedotin
Enfortumab vedotin is an antibody-drug conjugate (ADC) that is directed against Nectin-4, a protein located on the surface of cells and highly expressed in bladder cancer.[11,12] 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).[11]

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

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.

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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