Astellas and Seagen Announce Updated Results from Two Trials of PADCEV® (enfortumab vedotin-ejfv) in Patients with Locally Advanced or Metastatic Urothelial Cancer Not Eligible for Cisplatin Chemotherapy

- Durable Responses Observed in Second Cohort of Patients in Pivotal EV-201 Trial of PADCEV and in Initial First-Line Cohort of the EV-103 Trial Evaluating PADCEV in Combination with KEYTRUDA® (pembrolizumab) -

- Data to be Presented in Virtual Scientific Program of the 2021 American Society of Clinical Oncology Annual Meeting -

TOKYO & BOTHELL, Wash. – May 19, 2021 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and Seagen Inc**.** (Nasdaq:SGEN) today announced updated results from two clinical trials examining PADCEV® (enfortumab vedotin-ejfv) alone (EV-201 Cohort 2) and PADCEV in combination with Merck's (known as MSD outside the United States and Canada) KEYTRUDA® (pembrolizumab) (EV-103 Cohort A) in patients with locally advanced or metastatic urothelial cancer who are not able to receive cisplatin chemotherapy.

"EV-201 Cohort 2 is the first study to report objective responses in patients with advanced urothelial cancer that progressed following immunotherapy and who have medical conditions that prevent them from receiving cisplatin chemotherapy," said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Oncology Therapeutic Area Head, Astellas. "The analysis that will be presented at ASCO showed that after a median follow-up of 16 months, many patients continued to benefit from PADCEV – an important finding for these patients, who have very limited treatment options."

"EV-103 is the first clinical trial to combine the antibody-drug conjugate PADCEV with Merck's anti-PD-1 therapy KEYTRUDA in patients newly diagnosed with locally advanced or metastatic urothelial cancer," said Roger Dansey, M.D., Chief Medical Officer, Seagen. "The updated data from EV-103 Cohort A, with two years of follow-up, build upon findings from the initial analysis, showing continued durability for this platinum-free combination."

***Enfortumab vedotin in cisplatin-ineligible patients with locally advanced or metastatic urothelial cancer who received prior PD-1/PD-L1 inhibitors: An updated analysis of EV-201 Cohort 2* (Abstract 4524)**

Patients in Cohort 2 of EV-201 received prior treatment with an immunotherapy but had not received a platinum-containing chemotherapy in the locally advanced or metastatic setting and were ineligible for cisplatin chemotherapy.

With a median follow-up of 16 months, 51 percent of patients who received PADCEV had a confirmed objective response [95% Confidence Interval (CI): 39.8, 61.3] per blinded independent central review (the primary endpoint), with 22 percent of patients experiencing a complete response (CR). Median duration of response (DOR) was 13.8 months [95% CI: 6.4, not reached]. Patients lived a median of 6.7 months

without cancer progression [progression-free survival (PFS) (95% CI: 5.0-8.3)] and had a median overall survival (OS) of 16.1 months (95% CI: 11.3, 24.1).

The most common all-grade treatment-related adverse events (TRAEs) were alopecia (51%), peripheral sensory neuropathy (49%) and fatigue (34%), and the most common Grade 3 or greater TRAEs were neutropenia (9%), maculopapular rash (8%) and fatigue (7%). Grade 3 or greater TRAEs of special interest included skin reactions (17%), peripheral neuropathy (8%) and hyperglycemia (6%). Four deaths were previously reported as treatment-related by investigators in patients age 75 years and older with multiple comorbidities.

The U.S. Food and Drug Administration (FDA) recently granted Priority Review to a supplemental application for PADCEV based on the primary analysis from EV-201 Cohort 2, which was published this month in *The Lancet Oncology*.

Study EV-103: Update on durability results and long-term outcome of enfortumab vedotin + pembrolizumab in first-line locally advanced or metastatic urothelial carcinoma (la/mUC) (**Abstract 4528)**

In the dose-escalation cohort and expansion Cohort A in EV-103, patients were treated with a combination of PADCEV and the anti-PD-1 therapy KEYTRUDA as a first-line treatment for locally advanced or metastatic disease. Participants were ineligible for cisplatin-based chemotherapy, had no prior systemic treatment for locally advanced or metastatic disease, and did not receive adjuvant/neoadjuvant platinum-based therapy within 12 months prior to enrollment.

The primary outcome measure in this analysis was safety. With a median follow-up of 24.9 months, the longer-term analysis demonstrated a safety profile generally consistent with previous findings, with no new safety signals observed. The most common TRAEs were peripheral sensory neuropathy (55.6%), fatigue (51.1%) and alopecia (48.9%), and the most common Grade 3 or greater TRAEs were increased lipase (17.8%), maculopapular rash (11.1%) and fatigue (11.1%). Grade 3 or greater TRAEs of interest included skin reactions (20%), hyperglycemia (8.9%) and peripheral neuropathy (4.4%). There was one death previously reported as possibly related to study treatment (multiple organ dysfunction syndrome).

As previously reported, results demonstrated an objective response rate of 73.3 percent (95% CI: 58.1, 85.4) per investigator assessment, with 15.6 percent of patients experiencing a CR. The median PFS was 12.3 months (95% CI: 8.0, not reached). With longer-term follow-up, the study showed a median DOR of 25.6 months (95% CI: 8.3, not reached) and median OS of 26.1 months (95% CI: 15.7, not reached).

The FDA granted Breakthrough Therapy designation last year for the PADCEV and KEYTRUDA combination for patients with unresectable locally advanced or metastatic urothelial cancer who are unable to receive cisplatin-based chemotherapy in the first-line setting.

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.[1] Globally, approximately 573,000 new cases of bladder cancer and more than 212,000 deaths are reported annually.[2]

About the EV-201 Trial

The EV-201 trial (NCT03219333) is a single-arm, dual-cohort, 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.[1] 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.

About the EV-103 Trial

EV-103 (NCT03288545) is an ongoing, multi-cohort, open-label, multicenter phase 1b/2 trial of PADCEV alone or in combination, evaluating safety, tolerability and efficacy in muscle invasive urothelial cancer, and in locally advanced or metastatic urothelial cancer in first- or second-line settings.

The dose-escalation cohort and expansion Cohort A include locally advanced or metastatic urothelial cancer patients who are ineligible for cisplatin-based chemotherapy. Patients were dosed in a 21-day cycle, receiving an intravenous (IV) infusion of enfortumab vedotin on Days 1 and 8 and pembrolizumab on Day 1. At the time of the initial analysis, 45 patients (5 from the dose-escalation cohort and 40 from the dose-expansion Cohort A) with locally advanced and/or metastatic urothelial cancer had been treated with enfortumab vedotin (1.25 mg/kg) plus pembrolizumab in the first-line setting.

The primary outcome measure of the cohorts included in this analysis is safety. Key secondary objectives related to efficacy include objective response rate, disease control rate, duration of response, progression-free survival and overall survival.

Additional enrolling cohorts in the EV-103 study include:

- PADCEV as monotherapy or in combination with pembrolizumab in a first-line setting for locally advanced or metastatic disease, in patients ineligible for cisplatin-based chemotherapy (Cohort K)
- PADCEV as a monotherapy in muscle-invasive disease (Cohort L)

About PADCEV® (enfortumab vedotin-ejfv)

PADCEV was approved by the U.S. Food and Drug Administration (FDA) in December 2019 and is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a platinum-containing chemotherapy before (neoadjuvant) or after (adjuvant) surgery or in a locally advanced or metastatic setting. PADCEV was approved under the FDA's Accelerated Approval Program based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[3]

PADCEV 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.[3,4] Nonclinical data suggest the anticancer activity of PADCEV 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] PADCEV is co-developed by Astellas and Seagen.

PADCEV (enfortumab vedotin-ejfv) U.S. Important Safety Information

Warnings and Precautions

Skin reactions: Severe cutaneous adverse reactions, including fatal cases of Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN), occurred in patients treated with PADCEV. SJS and TEN occurred predominantly during the first cycle of treatment but may occur later.

Skin reactions occurred in 54% of the 310 patients treated with PADCEV in clinical trials. Twenty-six percent (26%) of patients had maculopapular rash and 30% had pruritus. Grade 3-4 skin reactions occurred in 10% of patients and included symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), dermatitis bullous, dermatitis exfoliative, and palmar-plantar erythrodysesthesia. In one clinical trial, the median time to onset of severe skin reactions was 0.8 months (range: 0.2 to 5.3). Of the patients who experienced rash, 65% had complete resolution and 22% had partial improvement. Monitor patients closely throughout treatment for skin reactions. Consider topical corticosteroids and antihistamines as clinically indicated. Withhold PADCEV and consider referral for specialized care for severe (Grade 3) skin reactions, suspected SJS, or TEN. Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.

Hyperglycemia occurred in patients treated with PADCEV, including death and diabetic ketoacidosis, in those with and without pre-existing diabetes mellitus. The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C. In one clinical trial, 8% of patients developed Grade 3-4 hyperglycemia. Patients with baseline hemoglobin A1C ≥8% were excluded. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. If blood glucose is elevated (>250 mg/dL), withhold PADCEV.

Peripheral neuropathy (PN), predominantly sensory, occurred in 49% of the 310 patients treated with PADCEV in clinical trials; 2% experienced Grade 3 reactions. In one clinical trial, peripheral neuropathy occurred in patients treated with PADCEV with or without preexisting peripheral neuropathy. The median time to onset of Grade ≥2 was 3.8 months (range: 0.6 to 9.2). Neuropathy led to treatment discontinuation in 6% of patients. At the time of their last evaluation, 19% had complete resolution, and 26% had partial improvement. Monitor patients for symptoms of new or worsening peripheral neuropathy and consider dose interruption or dose reduction of PADCEV when peripheral neuropathy occurs. Permanently discontinue PADCEV in patients that develop Grade ≥3 peripheral neuropathy.

Ocular disorders occurred in 46% of the 310 patients treated with PADCEV. The majority of these events involved the cornea and included keratitis, blurred vision, limbal stem cell deficiency and other events associated with dry eyes. Dry eye symptoms occurred in 36% of patients, and blurred vision occurred in 14% of patients, during treatment with PADCEV. The median time to onset to symptomatic ocular disorder was 1.9 months (range: 0.3 to 6.2). Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve. Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam. Consider dose interruption or dose reduction of PADCEV for symptomatic ocular disorders.

Infusion site extravasation: Skin and soft tissue reactions secondary to extravasation have been observed after administration of PADCEV. Of the 310 patients, 1.3% of patients experienced skin and soft tissue reactions. Reactions may be delayed. Erythema, swelling, increased temperature, and pain worsened until 2-7 days after extravasation and resolved within 1-4 weeks of peak. One percent (1%) of patients developed extravasation reactions with secondary cellulitis, bullae, or exfoliation. Ensure adequate venous access prior to starting PADCEV and monitor for possible extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions.

Embryo-fetal toxicity: PADCEV can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during PADCEV treatment and for 2 months after the last dose. Advise male patients with

female partners of reproductive potential to use effective contraception during treatment with PADCEV and for 4 months after the last dose.

Adverse Reactions

Serious adverse reactions occurred in 46% of patients treated with PADCEV. The most common serious adverse reactions (≥3%) were urinary tract infection (6%), cellulitis (5%), febrile neutropenia (4%), diarrhea (4%), sepsis (3%), acute kidney injury (3%), dyspnea (3%), and rash (3%). Fatal adverse reactions occurred in 3.2% of patients, including acute respiratory failure, aspiration pneumonia, cardiac disorder, and sepsis (each 0.8%).

Adverse reactions leading to discontinuation occurred in 16% of patients; the most common adverse reaction leading to discontinuation was peripheral neuropathy (6%). Adverse reactions leading to dose interruption occurred in 64% of patients; the most common adverse reactions leading to dose interruption were peripheral neuropathy (18%), rash (9%) and fatigue (6%). Adverse reactions leading to dose reduction occurred in 34% of patients; the most common adverse reactions leading to dose reduction were peripheral neuropathy (12%), rash (6%) and fatigue (4%).

The most common adverse reactions (≥20%) were fatigue (56%), peripheral neuropathy (56%), decreased appetite (52%), rash (52%), alopecia (50%), nausea (45%), dysgeusia (42%), diarrhea (42%), dry eye (40%), pruritus (26%) and dry skin (26%). The most common Grade ≥3 adverse reactions (≥5%) were rash (13%), diarrhea (6%) and fatigue (6%).

Lab Abnormalities

In one clinical trial, Grade 3-4 laboratory abnormalities reported in ≥5% were: lymphocytes decreased (10%), hemoglobin decreased (10%), phosphate decreased (10%), lipase increased (9%), sodium decreased (8%), glucose increased (8%), urate increased (7%), neutrophils decreased (5%).

Drug Interactions

Effects of other drugs on PADCEV Concomitant use with a strong CYP3A4 inhibitor may increase free MMAE exposure, which may increase the incidence or severity of PADCEV toxicities. Closely monitor patients for signs of toxicity when PADCEV is given concomitantly with strong CYP3A4 inhibitors.
Specific Populations

Lactation Advise lactating women not to breastfeed during treatment with PADCEV and for at least 3 weeks after the last dose.

Hepatic impairment Avoid the use of PADCEV in patients with moderate or severe hepatic impairment.

For more information, please see the full Prescribing Information for PADCEV here.

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 Seagen

Seagen Inc. is a global biotechnology company that discovers, develops and commercializes transformative cancer medicines to make a meaningful difference in people's lives. Seagen is headquartered in the Seattle, Washington area, and has locations in California, Canada, Switzerland and the European Union. For more information on our marketed products and robust pipeline, visit www.seagen.com and follow @SeagenGlobal on Twitter.

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 the Astellas, Seagen and Merck Collaboration

Astellas and Seagen entered a clinical collaboration agreement with Merck to evaluate the combination of Seagen's and Astellas' PADCEV® (enfortumab vedotin-ejfv) and Merck'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., Kenilworth, NJ, USA.

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.

Seagen Forward Looking Statements

Certain statements made in this press release are forward looking, such as those, among others, relating to the therapeutic potential of PADCEV, including its efficacy, safety and therapeutic uses, the potential approval by the FDA of the sBLA submission based on the results of cohort 2 of the EV-201 clinical trial and the potential for approval of PADCEV and KEYTRUDA in combination for patients with unresectable locally advanced or metastatic urothelial cancer who are unable to receive cisplatin-based

chemotherapy in the first-line setting. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include, without limitation, the possibility that the sBLA submission based on the EV-201 second cohort clinical trial may not be ultimately approved by the FDA in a timely manner or at all; that, even if the PADCEV label is expanded based on the results of the second cohort of the EV-201 clinical trial, the product labeling may not be as broad or desirable as requested or anticipated; and that setbacks in the development and commercialization of PADCEV could occur as a result of the difficulty and uncertainty of pharmaceutical product development, the risk of adverse events or safety signals, adverse regulatory actions or other factors. More information about the risks and uncertainties faced by Seagen is contained under the caption "Risk Factors" included in the company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 filed with the Securities and Exchange Commission. Seagen disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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