Astellas and Seagen Announce Positive Topline Results from Second Cohort of Patients in Phase 2 Pivotal Trial of PADCEV® (enfortumab vedotin-ejfv) in Advanced Urothelial Cancer

- Durable Responses Observed in Patients Who Had Previously Received Immunotherapy but Were Ineligible for Cisplatin in Locally Advanced or Metastatic Setting -

TOKYO and BOTHELL, Wash. -- October 12, 2020 -- Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and Seagen Inc. (Nasdaq:SGEN) today announced positive topline results from the second cohort of patients in the pivotal phase 2 single-arm clinical trial known as EV-201. The cohort is evaluating the antibody-drug conjugate PADCEV® (enfortumab vedotin-ejfv) for patients with locally advanced or metastatic urothelial cancer who have been previously treated with a PD-1/L1 inhibitor and have not received a platinum-containing chemotherapy and are ineligible for cisplatin. Results showed a 52 percent objective response rate (ORR) [95% Confidence Interval (CI): 40.8, 62.4] per blinded independent central review and a median duration of response of 10.9 months. The most frequently reported treatment-related adverse events Grade 3 or greater that occurred in more than 5 percent of patients were: neutropenia, rash, fatigue, increased lipase, diarrhea, decreased appetite, anemia and hyperglycemia. Data from cohort 2 of the trial will be submitted for presentation at an upcoming scientific congress and will be discussed with regulatory authorities.

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.[1, 2] The U.S. Food and Drug Administration (FDA) granted accelerated approval to PADCEV in 2019 based on results from the first cohort in this trial, which included patients whose disease had progressed during or following platinum-based chemotherapy and a PD-1/L1 inhibitor.

"Advanced urothelial cancer in patients who have received immunotherapy and are ineligible for cisplatin is a particularly difficult disease to treat," said Arjun Balar, M.D., Associate Professor of Medicine, Director Genitourinary Medical Oncology Program, NYU Laura and Isaac Perlmutter Cancer Center, NYU Langone Health and an investigator for the trial. "Typically, these patients are frail, suffer from multiple comorbidities beyond their urothelial cancer and are not able to tolerate additional treatment beyond immunotherapy, leading many to discontinue therapy altogether."

"We are committed to developing new treatments for patients with hard-to-treat cancers, such as those with locally advanced or metastatic urothelial cancer that has progressed following treatment with a PD-1 or PD-L1 inhibitor and who are ineligible for cisplatin therapy," said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Oncology Therapeutic Area Head, Astellas. "We look forward to discussing these data with regulatory authorities including the FDA."

"This is the first trial to report objective responses in patients with advanced urothelial cancer who had previously received immunotherapy but were ineligible for cisplatin in this setting due to inadequate kidney function or other conditions," said Roger Dansey, M.D., Chief Medical Officer at Seagen. "These promising new data from EV-201 may support a regulatory application to extend use of PADCEV in U.S. patients whose cancer has progressed after immunotherapy and who are ineligible for cisplatin."

Urothelial cancer is the most common type of bladder cancer (90 percent of cases), and can also be found in the urothelial cells that line the renal pelvis (where urine collects inside the kidney), ureter (tube that connects the kidneys to the bladder) and urethra.[3] Globally, approximately 580,000 people will be diagnosed with bladder cancer in 2020, and bladder cancer will be attributed to approximately 210,000 deaths worldwide.[4]

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.[5] 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.

For more information about the EV-201 clinical trial, please visit clinicaltrials.gov.

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.[1]

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.[1,2] 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).[2] PADCEV is co-developed by Astellas and Seagen.

PADCEV Important Safety Information

Warnings and Precautions

- **Hyperglycemia** occurred in patients treated with PADCEV, including death and diabetic ketoacidosis (DKA), 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.

- **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), bullous dermatitis, exfoliative dermatitis, 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 for skin reactions. Consider appropriate treatment, such as topical corticosteroids and antihistamines for skin reactions, as clinically indicated. For severe (Grade 3) skin reactions, withhold PADCEV until improvement or resolution and administer appropriate medical treatment. Permanently discontinue PADCEV in patients that develop Grade 4 or recurrent Grade 3 skin reactions.

- **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 are co-developing PADCEV (enfortumab vedotin-ejfv) under a collaboration that was entered into in 2007 and expanded in 2009.

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 submission of data from cohort 2 of the EV-201 trial for presentation at an upcoming scientific congress; intended regulatory actions, including the potential submission of a regulatory application to extend the use of PADCEV in U.S. patients or plans to discuss data from cohort 2 of the EV-201 trial with regulatory authorities; and the therapeutic potential of PADCEV, including its efficacy, safety and therapeutic uses. 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 that the data from cohort 2 of the EV-201 trial may not be selected for presentation at scientific congresses; the possibility of delays in the submission of any regulatory application to extend the use of PADCEV in U.S. patients; that the results from cohort 2 of the EV-201 trial may not be enough to support any approvals by regulatory authorities; that any product labeling that is approved may be narrower or less desirable than anticipated; the risk of adverse events or safety signals; and the possibility that adverse regulatory actions may occur. 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 June 30, 2020 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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[1] PADCEV [package insert]. Northbrook, IL: Astellas, Inc.
[2] Challita-Eid P, Satpayev D, Yang P, et al. Enfortumab Vedotin Antibody-Drug Conjugate Targeting Nectin-4 Is a Highly Potent Therapeutic Agent in Multiple Preclinical Cancer Models. Cancer Res 2016;76(10):3003-13.
[3] American Society of Clinical Oncology. Bladder cancer: introduction (10-2017). https://www.cancer.net/cancertypes/bladder-cancer/introduction. Accessed 05-09-2019.
[4] International Agency for Research on Cancer. Cancer Tomorrow: Bladder. http://gco.iarc.fr/tomorrow. Accessed 07-31-2020.
[5] ClinicalTrials.gov Identifier: NCT03219333. A Study of Enfortumab Vedotin for Patients With Locally Advanced or Metastatic Urothelial Bladder Cancer (EV-201). https://clinicaltrials.gov/ct2/show/NCT03219333. Accessed on 08-03-2020.