Astellas and Seattle Genetics Announce PADCEV® (enfortumab vedotin-ejfv) Significantly Improved Overall Survival in Phase 3 Trial in Previously Treated Locally Advanced or Metastatic Urothelial Cancer

- Trial Stopped Early Due to Positive Results at Planned Interim Analysis -

- Data Intended to Support Global Registrations and Convert Accelerated to Regular Approval in U.S. -

TOKYO and BOTHELL, Wash. -- September 18, 2020 -- Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and Seattle Genetics, Inc. (Nasdaq:SGEN) today announced that a phase 3 trial of PADCEV® (enfortumab vedotin-ejfv) met its primary endpoint of overall survival compared to chemotherapy. The results were reviewed by an independent Data Monitoring Committee following a planned interim analysis. The global EV-301 clinical trial compared PADCEV to 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.

In the trial, PADCEV significantly improved overall survival (OS), with a 30 percent reduction in risk of death (Hazard Ratio [HR]=0.70; [95% Confidence Interval (CI): 0.56, 0.89]; p=0.001). PADCEV also significantly improved progression-free survival (PFS), a secondary endpoint, with a 39 percent reduction in risk of disease progression or death (HR=0.61 [95% CI: 0.50, 0.75]; p<0.00001).

For patients in the PADCEV arm of the trial, adverse events were consistent with those listed in the U.S. Prescribing Information, with rash, hyperglycemia, decreased neutrophil count, fatigue, anemia and decreased appetite as the most frequent Grade 3 or greater adverse event(s) occurring in more than 5 percent of patients. Data from EV-301 will be submitted for presentation at an upcoming scientific congress. Patients in the chemotherapy arm of the trial will be offered the opportunity to receive PADCEV.

The results will be submitted to the U.S. Food and Drug Administration (FDA) as the confirmatory trial following the drug's accelerated approval in 2019. EV-301 is also intended to support global registrations.

"EV-301 is the first randomized trial to show overall survival results compared to chemotherapy in patients with locally advanced or metastatic urothelial cancer who previously have received platinum-based treatment and a PD-1 or PD-L1 inhibitor, and we are encouraged by the potential this may have in helping patients who have otherwise limited alternatives," said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Oncology Therapeutic Area Head, Astellas. "We look forward to discussing these results with global health authorities."

"These survival results from the confirmatory trial for PADCEV are welcome news for patients whose cancer has progressed after platinum-based chemotherapy and immunotherapy," said Roger Dansey, M.D., Chief Medical Officer at Seattle Genetics. "We continue to explore PADCEV's activity across the spectrum of urothelial cancer including its potential for use in earlier lines of therapy."

Globally, approximately 580,000 people will be diagnosed with bladder cancer in 2020.[1] Urothelial cancer accounts for 90 percent of all bladder cancers 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.[2]

Approximately 80 percent of people do not respond to PD-1 or PD-L1 inhibitors after a platinum-containing therapy has failed as an initial treatment for advanced disease.[3]

About the EV-301 Trial
The EV-301 trial (NCT03474107) is a global, multicenter, open-label, randomized phase 3 trial designed to evaluate PADCEV 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. The primary endpoint is overall survival of participants treated with PADCEV 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.

For more information about the EV-301 clinical trial, please visit www.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.[4]

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.[4,5] 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 Seattle Genetics.

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 Seattle Genetics
Seattle Genetics, Inc. is a global biotechnology company that discovers, develops and commercializes transformative medicines targeting cancer to make a meaningful difference in people's lives. The company is headquartered in the Seattle, Washington area, with locations in California, Switzerland and the European Union. For more information on our robust pipeline, visit www.seattlegenetics.com and follow @SeattleGenetics on Twitter.

About the Astellas and Seattle Genetics Collaboration
Astellas and Seattle Genetics are co-developing PADCEV (enfortumab vedotin-ejfv) under a 50:50 worldwide development and commercialization 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.

Seattle Genetics 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 the EV-301 trial for presentation at an upcoming scientific congress; intended regulatory actions, including plans to submit the results of the EV-301 trial to the FDA as the confirmatory trial following the drug's accelerated approval in the U.S. and plans to discuss the results with global health authorities and seek global registrations; conduct of a comprehensive clinical development program for PADCEV, which includes exploring PADCEV's activity in other types of urothelial cancer and its potential for use in earlier lines of therapy; the therapeutic potential of PADCEV, including its efficacy, safety and therapeutic uses, and anticipated development activities, including ongoing and future clinical trials. 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 the EV-301 trial may not be selected for presentation at scientific congresses; the possibility of delays in the submission of results to the FDA; that the results from the EV-301 trial may not be enough to convert PADCEV's accelerated approval in the U.S. to regular approval or to support any other global registrations; that, even if PADCEV receives regular approval in the U.S. or any other global registrations, the product labeling may not be as broad or desirable as anticipated; the possibility that ongoing and subsequent clinical trials may fail to establish sufficient activity; 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 Seattle Genetics 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. Seattle Genetics 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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