Pfizer Logo

Pfizer and Astellas' PADCEV® (enfortumab vedotin-ejfv) plus KEYTRUDA® (pembrolizumab) Shows Long-Term Efficacy in First-Line Treatment of Locally Advanced or Metastatic Urothelial Cancer (la/mUC)

Monday, February 10, 2025 - 05:00pm

- *Enfortumab vedotin plus pembrolizumab continues to demonstrate superior efficacy versus chemotherapy in a broad population, reinforcing the combination as standard of care in first-line treatment of la/mUC*
- *At nearly 30 months of follow-up in the Phase 3 EV-302 trial, the combination doubled median overall survival and progression-free survival compared to chemotherapy, with no new safety signals identified*

NEW YORK & TOKYO--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) and Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced additional follow-up results from the Phase 3 EV-302 clinical trial (also known as KEYNOTE-A39) evaluating the efficacy and safety of PADCEV ® (enfortumab vedotin-ejfv), a Nectin-4 directed antibody-drug conjugate, plus KEYTRUDA® (pembrolizumab), a PD-1 inhibitor, in patients with previously untreated locally advanced or metastatic urothelial cancer (la/mUC). The results showed a sustained overall survival (OS) and progression-free survival (PFS) benefit consistent with the findings of the primary analysis after an additional 12 months of follow-up (median follow-up of 29.1 months).[1,2] These data will be presented during a rapid oral session (Abstract 664) at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) 2025 in San Francisco, CA, on February 14 at 4:10pm PT.

Thomas Powles, M.R.C.P., M.D., Professor of Genitourinary Oncology at Queen Mary University of London; Director, Barts Cancer Center, London; EV-302 Primary Investigator

"These latest findings from the EV-302 trial reaffirm the primary results, which demonstrated survival improvements for patients treated with enfortumab vedotin and pembrolizumab that were previously unprecedented in locally advanced or metastatic urothelial cancer. These data show that the potential survival benefit has become even more robust with extended follow up and further solidify the combination as standard of care."

Results showed enfortumab vedotin plus pembrolizumab reduced the risk of death by 49% versus chemotherapy (hazard ratio [HR] = 0.51, 95% confidence interval [CI], 0.43-0.61). The median OS was 33.8 months for the combination versus 15.9 months for chemotherapy. The OS benefit was observed in all prespecified subgroups, including cisplatin eligible and ineligible subgroups. Enfortumab vedotin plus pembrolizumab also reduced the risk of disease progression or death by 52% versus chemotherapy (HR = 0.48, 95% CI, 0.41-0.57). The median PFS was 12.5 months for the combination versus 6.3 months for chemotherapy. The safety profile was consistent

with previous findings and no new safety concerns were identified.[1]

Please see Important Safety Information at the end of this press release, including **BOXED WARNING** for enfortumab vedotin.

In addition to longer follow-up data, an exploratory analysis evaluating treatment outcomes and safety profile in patients with confirmed complete response (cCR) will also be presented. Among patients evaluable for response, confirmed objective response rate (cORR) was 67.5% for enfortumab vedotin plus pembrolizumab compared to 44.2% for chemotherapy. Median duration of response (DOR) was 23.3 months (95% CI, 17.8-not estimable [NE]) for the combination and 7.0 months (95% CI, 6.2-9.0) for chemotherapy. A cCR was achieved in 30.4% of patients treated with enfortumab vedotin plus pembrolizumab and 14.5% of patients treated with chemotherapy. Median duration of cCR was not reached for the combination and 15.2 months (95% CI, 10.3-NE) for chemotherapy. In patients with cCR, grade ?3 treatment-related adverse events occurred in 61.7% of patients in the enfortumab vedotin plus pembrolizumab arm compared to 71.9% in the chemotherapy arm. There were no treatment-related deaths in the cCR subgroup.[1]

Roger Dansey, M.D.?, Chief Oncology Officer, Pfizer

“Patients with bladder cancer can face a poor prognosis, particularly in the advanced stages, and until recently had few available treatment options. The updated EV-302 results show sustained long-term efficacy in a broad population that includes both cisplatin eligible and ineligible patients and reinforce this combination’s ability to reshape the urothelial cancer treatment landscape.”

Ahsan Arozullah, M.D., M.P.H., Senior Vice President, Head of Oncology Development, Astellas

“The combination of enfortumab vedotin and pembrolizumab was the first approval to offer an alternative to platinum-containing chemotherapy, which had been the standard of care for first-line locally advanced or metastatic urothelial cancer for decades. We are delighted that the additional follow-up results of the EV-302 trial show a durable benefit. These data represent yet another milestone in our long-standing commitment to helping patients around the world live longer and healthier lives.”

Enfortumab vedotin plus pembrolizumab is approved for the treatment of adult patients with la/mUC in the United States, the European Union, Japan and a number of other countries around the world. Enfortumab vedotin is also approved as a single agent for the treatment of adult patients with la/mUC who have previously received a PD-1/PD-L1 inhibitor and platinum-containing chemotherapy or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.[3]

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About EV-302

The EV-302 trial is an open-label, randomized, controlled Phase 3 study, evaluating enfortumab vedotin in combination with pembrolizumab versus platinum-containing chemotherapy in patients with previously untreated la/mUC. The study enrolled 886 patients with previously untreated la/mUC who were eligible for cisplatin- or carboplatin-containing chemotherapy regardless of PD-L1 status. Patients were randomized to receive either enfortumab vedotin in combination with pembrolizumab or platinum-containing chemotherapy. The dual primary endpoints of this trial are OS and PFS per RECIST v1.1 by blinded independent central review (BICR). Select secondary endpoints include ORR per RECIST v1.1 by BICR, DOR per RECIST v1.1 by BICR, and safety.[4]

The EV-302 trial is part of an extensive clinical program evaluating this combination in multiple stages of urothelial cancer and other solid tumors. Primary results from the EV-302 study were presented at the European Society for Medical Oncology (ESMO) Congress in October 2023.

About PADCEV® (enfortumab vedotin-ejfv)

PADCEV ® (enfortumab vedotin-ejfv) 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.[5] 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).[3]

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

BOXED WARNING: SERIOUS SKIN REACTIONS

- PADCEV can cause severe and fatal cutaneous adverse reactions including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), which occurred predominantly during the first cycle of treatment, but may occur later.
- Closely monitor patients for skin reactions.
- Immediately withhold PADCEV and consider referral for specialized care for suspected SJS or TEN or severe skin reactions.
- Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.

Indication

PADCEV® , in combination with pembrolizumab, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC).

PADCEV, as a single agent, is indicated for the treatment of adult patients with locally advanced or mUC who:

- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Skin reactions Severe cutaneous adverse reactions, including fatal cases of SJS or 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 70% (all grades) of the 564 patients treated with PADCEV in combination with pembrolizumab in clinical trials. When PADCEV was given in combination with pembrolizumab, the incidence of skin reactions, including severe events, occurred at a higher rate compared to PADCEV as a single agent. The majority of the skin reactions that occurred with combination therapy included maculo-papular rash, macular rash and papular rash. Grade 3-4 skin reactions occurred in 17% of patients (Grade 3: 16%, Grade 4: 1%), including maculo-papular rash, bullous dermatitis, dermatitis, exfoliative dermatitis, pemphigoid, rash, erythematous rash, macular rash, and papular rash. A fatal reaction of bullous dermatitis occurred in one patient

(0.2%). The median time to onset of severe skin reactions was 1.7 months (range: 0.1 to 17.2 months). Skin reactions led to discontinuation of PADCEV in 6% of patients.

Skin reactions occurred in 58% (all grades) of the 720 patients treated with PADCEV as a single agent in clinical trials. Twenty-three percent (23%) of patients had maculo-papular rash and 34% had pruritus. Grade 3-4 skin reactions occurred in 14% of patients, including maculo-papular rash, erythematous rash, rash or drug eruption, symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia. The median time to onset of severe skin reactions was 0.6 months (range: 0.1 to 8 months). Among patients experiencing a skin reaction leading to dose interruption who then restarted PADCEV (n=75), 24% of patients restarting at the same dose and 24% of patients restarting at a reduced dose experienced recurrent severe skin reactions. Skin reactions led to discontinuation of PADCEV in 3.1% of patients.

Monitor patients closely throughout treatment for skin reactions. Consider topical corticosteroids and antihistamines, as clinically indicated. For persistent or recurrent Grade 2 skin reactions, consider withholding PADCEV until Grade ?1. Withhold PADCEV and refer for specialized care for suspected SJS, TEN or for Grade 3 skin reactions. Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.

Hyperglycemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without pre-existing diabetes mellitus, treated with PADCEV. Patients with baseline hemoglobin A1C ?8% were excluded from clinical trials. In clinical trials of PADCEV as a single agent, 17% of the 720 patients treated with PADCEV developed hyperglycemia of any grade; 7% of patients developed Grade 3-4 hyperglycemia (Grade 3: 6.5%, Grade 4: 0.6%). Fatal events of hyperglycemia and DKA occurred in one patient each (0.1%). The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C. The median time to onset of hyperglycemia was 0.5 months (range: 0 to 20 months). Hyperglycemia led to discontinuation of PADCEV in 0.7% of patients. Five percent (5%) of patients required initiation of insulin therapy for treatment of hyperglycemia. Of the patients who initiated insulin therapy for treatment of hyperglycemia, 66% (23/35) discontinued insulin at the time of last evaluation. 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.

Pneumonitis/Interstitial Lung Disease (ILD) Severe, life-threatening or fatal pneumonitis/ILD occurred in patients treated with PADCEV. When PADCEV was given in combination with pembrolizumab, 10% of the 564 patients treated with combination therapy had pneumonitis/ILD of any grade and 4% had Grade 3-4. A fatal event of pneumonitis/ILD occurred in two patients (0.4%). The incidence of pneumonitis/ILD, including severe events, occurred at a higher rate when PADCEV was given in combination with pembrolizumab compared to PADCEV as a single agent. The median time to onset of any grade pneumonitis/ILD was 4 months (range: 0.3 to 26 months).

In clinical trials of PADCEV as a single agent, 3% of the 720 patients treated with PADCEV had pneumonitis/ILD of any grade and 0.8% had Grade 3-4. The median time to onset of any grade pneumonitis/ILD was 2.9 months (range: 0.6 to 6 months).

Monitor patients for signs and symptoms indicative of pneumonitis/ILD such as hypoxia, cough, dyspnea or interstitial infiltrates on radiologic exams. Evaluate and exclude infectious, neoplastic and other causes for such signs and symptoms through appropriate investigations. Withhold PADCEV for patients who develop Grade 2 pneumonitis/ILD and consider dose reduction. Permanently discontinue PADCEV in all patients with Grade 3 or 4 pneumonitis/ILD.

Peripheral neuropathy (PN) When PADCEV was given in combination with pembrolizumab, 67% of the 564 patients treated with combination therapy had PN of any grade, 36% had Grade 2 neuropathy, and 7% had Grade 3 neuropathy. The incidence of PN occurred at a higher rate when PADCEV was given in combination with pembrolizumab compared to PADCEV as a single agent. The median time to onset of Grade ?2 PN was 6 months (range: 0.3 to 25 months).

PN occurred in 53% of the 720 patients treated with PADCEV as a single agent in clinical trials including 38% with sensory neuropathy, 8% with muscular weakness and 7% with motor neuropathy. Thirty percent of patients experienced Grade 2 reactions and 5% experienced Grade 3-4 reactions. PN occurred in patients treated with PADCEV with or without preexisting PN. The median time to onset of Grade ?2 PN was 4.9 months (range: 0.1 to 20 months). Neuropathy led to treatment discontinuation in 6% of patients.

Monitor patients for symptoms of new or worsening PN and consider dose interruption or dose reduction of PADCEV when PN occurs. Permanently discontinue PADCEV in patients who develop Grade ?3 PN.

Ocular disorders were reported in 40% of the 384 patients treated with PADCEV as a single agent in clinical trials in which ophthalmologic exams were scheduled. The majority of these events involved the cornea and included events associated with dry eye such as keratitis, blurred vision, increased lacrimation, conjunctivitis, limbal stem cell deficiency, and keratopathy. Dry eye symptoms occurred in 30% of patients, and blurred vision occurred in 10% of patients, during treatment with PADCEV. The median time to onset to symptomatic ocular disorder was 1.7 months (range: 0 to 30.6 months). 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 720 patients treated with PADCEV as a single agent in clinical trials, 1% of patients experienced skin and soft tissue reactions, including 0.3% who experienced Grade 3-4 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. Two patients (0.3%) 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

Most common adverse reactions, including laboratory abnormalities(?20%) (PADCEV in combination with pembrolizumab) Increased aspartate aminotransferase (AST), increased creatinine, rash, increased glucose, PN, increased lipase, decreased lymphocytes, increased alanine aminotransferase (ALT), decreased hemoglobin, fatigue, decreased sodium, decreased phosphate, decreased albumin, pruritus, diarrhea, alopecia, decreased weight, decreased appetite, increased urate, decreased neutrophils, decreased potassium, dry eye, nausea, constipation, increased potassium, dysgeusia, urinary tract infection and decreased platelets.

Most common adverse reactions, including laboratory abnormalities (?20%) (PADCEV monotherapy) Increased glucose, increased AST, decreased lymphocytes, increased creatinine, rash, fatigue, PN, decreased albumin, decreased hemoglobin, alopecia, decreased appetite, decreased neutrophils, decreased sodium, increased ALT, decreased phosphate, diarrhea, nausea, pruritus, increased urate, dry eye, dysgeusia, constipation, increased lipase, decreased weight, decreased platelets, abdominal pain, dry skin.

EV-302 Study: 440 patients with previously untreated la/mUC (PADCEV in combination with pembrolizumab)

Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with pembrolizumab. The most common serious adverse reactions (?2%) were rash (6%), acute kidney injury (5%), pneumonitis/ILD (4.5%), urinary tract infection (3.6%), diarrhea (3.2%), pneumonia (2.3%), pyrexia (2%), and hyperglycemia (2%). **Fatal adverse reactions** occurred in 3.9% of patients treated with PADCEV in combination with pembrolizumab including acute respiratory failure (0.7%), pneumonia (0.5%), and pneumonitis/ILD (0.2%).

Adverse reactions leading to discontinuation of PADCEV occurred in 35% of patients. **The most common adverse reactions (?2%) leading to discontinuation** of PADCEV were PN (15%), rash (4.1%) and pneumonitis/ILD (2.3%). Adverse reactions leading to dose interruption of PADCEV occurred in 73% of patients. **The most common adverse reactions (?2%) leading to dose interruption** of PADCEV were PN (22%), rash (16%), COVID-19 (10%), diarrhea (5%), pneumonitis/ILD (4.8%), fatigue (3.9%), hyperglycemia (3.6%), increased ALT (3%) and pruritus (2.5%). Adverse reactions leading to dose reduction of PADCEV occurred in 42% of patients. **The most common adverse reactions (?2%) leading to dose reduction** of PADCEV were rash (16%), PN (13%) and fatigue (2.7%).

EV-103 Study: 121 patients with previously untreated la/mUC who were not eligible for cisplatin-containing chemotherapy (PADCEV in combination with pembrolizumab)

Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with pembrolizumab; the most common (?2%) were acute kidney injury (7%), urinary tract infection (7%), urosepsis (5%), sepsis (3.3%), pneumonia (3.3%), hematuria (3.3%), pneumonitis/ILD (3.3%), urinary retention (2.5%), diarrhea (2.5%), myasthenia gravis (2.5%), myositis (2.5%), anemia (2.5%), and hypotension (2.5%). **Fatal adverse reactions** occurred in 5% of patients treated with PADCEV in combination with pembrolizumab, including sepsis (1.6%), bullous dermatitis (0.8%), myasthenia gravis (0.8%), and pneumonitis/ILD (0.8%). **Adverse reactions leading to discontinuation** of PADCEV occurred in 36% of patients; the most common (? 2%)were PN (20%) and rash (6%). **Adverse reactions leading to dose interruption** of PADCEV occurred in 69% of patients; the most common (?2%)were PN (18%), rash (12%), increased lipase (6%), pneumonitis/ILD (6%), diarrhea (4.1%), acute kidney injury (3.3%), increased ALT (3.3%), fatigue (3.3%), neutropenia (3.3%), urinary tract infection (3.3%), increased amylase (2.5%), anemia (2.5%), COVID-19 (2.5%), hyperglycemia (2.5%), and hypotension (2.5%). **Adverse reactions leading to dose reduction** of PADCEV occurred in 45% of patients; the most common (?2%) were PN (17%), rash (12%), fatigue (5%), neutropenia (5%), and diarrhea (4.1%).

EV-301 Study: 296 patients previously treated with a PD-1/L1 inhibitor and platinum-based chemotherapy (PADCEV monotherapy)

Serious adverse reactions occurred in 47% of patients treated with PADCEV; the most common (?2%) were urinary tract infection, acute kidney injury (7% each), and pneumonia (5%). **Fatal adverse reactions** occurred in 3% of patients, including multiorgan dysfunction (1%), hepatic dysfunction, septic shock, hyperglycemia, pneumonitis/ILD, and pelvic abscess (0.3% each). **Adverse reactions leading to discontinuation** occurred in

17% of patients; the most common (?2%) were PN (5%) and rash (4%). **Adverse reactions leading to dose interruption** occurred in 61% of patients; the most common (?4%) were PN (23%), rash (11%), and fatigue (9%). **Adverse reactions leading to dose reduction** occurred in 34% of patients; the most common (?2%) were PN (10%), rash (8%), decreased appetite, and fatigue (3% each).

EV-201, Cohort 2 Study: 89 patients previously treated with a PD-1/L1 inhibitor and not eligible for cisplatin-based chemotherapy (PADCEV monotherapy)

Serious adverse reactions occurred in 39% of patients treated with PADCEV; the most common (?3%) were pneumonia, sepsis, and diarrhea (5% each). **Fatal adverse reactions** occurred in 8% of patients, including acute kidney injury (2.2%), metabolic acidosis, sepsis, multiorgan dysfunction, pneumonia, and pneumonitis/ILD (1.1% each). **Adverse reactions leading to discontinuation** occurred in 20% of patients; the most common (?2%) was PN (7%). **Adverse reactions leading to dose interruption** occurred in 60% of patients; the most common (?3%) were PN (19%), rash (9%), fatigue (8%), diarrhea (5%), increased AST, and hyperglycemia (3% each). **Adverse reactions leading to dose reduction** occurred in 49% of patients; the most common (?3%) were PN (19%), rash (11%), and fatigue (7%).

DRUG INTERACTIONS

Effects of other drugs on PADCEV (*Dual P-gp and Strong CYP3A4 Inhibitors*)

Concomitant use with dual P-gp and strong CYP3A4 inhibitors may increase unconjugated monomethyl auristatin E exposure, which may increase the incidence or severity of PADCEV toxicities. Closely monitor patients for signs of toxicity when PADCEV is given concomitantly with dual P-gp and strong CYP3A4 inhibitors.

SPECIFIC POPULATIONS

Lactation Advise lactating women not to breastfeed during treatment with PADCEV and for 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 U.S. full Prescribing Information including BOXED WARNING for PADCEV here .

About Pfizer Oncology

At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and bispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world’s most common cancers, including breast cancer, genitourinary cancer, hematology-oncology, and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

About Astellas

Astellas is a global life sciences company committed to turning innovative science into VALUE for patients. We provide transformative therapies in disease areas that include oncology, ophthalmology, urology, immunology and women's health. Through our research and development programs, we are pioneering new healthcare

solutions for diseases with high unmet medical need. Learn more at www.astellas.com.

About the Pfizer, Astellas and Merck Collaboration

Seagen and Astellas 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. Pfizer Inc. successfully completed its acquisition of Seagen on December 14, 2023. KEYTRUDA is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (known as MSD outside of the United States and Canada).

Pfizer Disclosure Notice

The information contained in this release is as of February 10, 2025. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer Oncology and PADCEV® (enfortumab vedotin-ejfv) in combination with pembrolizumab in patients with previously untreated locally advanced or metastatic urothelial cancer, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risk and uncertainties include, among other things, uncertainties regarding the commercial success of PADCEV; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any applications may be filed in particular jurisdictions for any potential indication for PADCEV with pembrolizumab or as a single agent; whether and when any such applications that may be pending or filed for PADCEV with pembrolizumab or as a single agent may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether PADCEV with pembrolizumab or as a single agent will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of PADCEV with pembrolizumab or as a single agent; whether the collaboration between Pfizer, Astellas and Merck will be successful; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com .

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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References

[1] Powels T, et al. EV-302: Updated analysis from the phase 3 global study of enfortumab vedotin in combination with pembrolizumab (EV+P) vs chemotherapy (chemo) in previously untreated locally advanced or metastatic urothelial carcinoma (la/mUC). *J Clin Oncol* 43, 2025 (suppl 5; abstr 664)
[2] Powels T, Valderrama BP, Gupta S, et al. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. *N Engl J Med* 2024;390:875-888.
[3] PADCEV [package insert]. Northbrook, IL: Astellas Pharma US, Inc.
[4] National Cancer Institute. Enfortumab Vedotin and Pembrolizumab vs Chemotherapy Alone in Untreated Locally Advanced or Metastatic Urothelial Cancer (EV-302). ClinicalTrials.gov identifier: NCT04223856. Published January 6, 2020. Updated September 27, 2024. Accessed January 6, 2025. https://clinicaltrials.gov/study/NCT04223856?tab=results#results-overview.
[5] Challita-Eid PM, 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.

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