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U.S. FDA Approves PADCEV® plus Keytruda® as Neoadjuvant and Adjuvant Treatment for Muscle-Invasive Bladder Cancer Regardless of Cisplatin Eligibility

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- *First and only treatment regimen for adults with MIBC, regardless of cisplatin eligibility, representing a platinum-free potential standard of care*
- *Broadened approval supported by Phase 3 EV-304 data showing a nearly 50% reduction in the risk of tumor recurrence, progression or death, and a 35% reduction in the risk of death, versus standard of care in cisplatin-eligible patients*

NEW YORK & TOKYO--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) and Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced that the U.S. Food and Drug Administration (FDA) has approved PADCEV® (enfortumab vedotin-ejfv), a Nectin-4 directed antibody-drug conjugate, plus the PD-1 inhibitor, Keytruda® (pembrolizumab) or Keytruda QLEX™ (pembrolizumab and berahyaluronidase alfa-pmph) as neoadjuvant and adjuvant (before and after surgery) treatment for adult patients with muscle-invasive bladder cancer regardless of cisplatin eligibility[i]. This now marks the first platinum-free regimen approved for adult patients with MIBC, regardless of cisplatin eligibility.

The approval was based on results from the pivotal Phase 3 EV-304 clinical trial (also known as KEYNOTE-B15), which were presented at the 2026 American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU). This expanded indication builds on the November 2025 U.S. FDA approval of the combination for use as neoadjuvant and adjuvant treatment in cisplatin-ineligible adult patients with MIBC, based on results from the EV-303 Phase 3 clinical trial (also known as KEYNOTE-905) that were published in the *New England Journal of Medicine.*

Christopher Hoimes, DO, Director of the Bladder Cancer Program and Center for Cancer Immunotherapy at Duke Cancer Institute, and an EV-304 Principal Investigator
"For muscle-invasive bladder cancer, a comprehensive treatment approach is important; the neoadjuvant phase can help shrink the tumor and target undetectable cancer cells early before surgery, while the adjuvant phase can be critical in eliminating residual, undetectable cancer cells following surgery. These data from EV-304 and this approval show that by delivering this regimen across both the neoadjuvant and adjuvant phases, without platinum-based chemotherapy, we can significantly reduce the risk of recurrence and improve overall survival — offering a potential new standard of care for adult patients with muscle-invasive bladder cancer."

Aamir Malik, Executive Vice President, Chief U.S. Commercial Officer, Pfizer
"Today's approval marks a historic turning point for the treatment of muscle-invasive bladder cancer, providing adult patients with the first approved platinum-free combination regimen shown to significantly improve survival over the current standard of care – regardless of cisplatin-eligibility. PADCEV plus pembrolizumab has

established itself as the standard of care for first line therapy of advanced stages of bladder cancer, and we're thrilled to be able to provide this community a much-needed new treatment option in an earlier, potentially curative-intent setting."

Moitreyee Chatterjee-Kishore, PhD, MBA, Head of Oncology Development, Astellas
"The approval of neoadjuvant and adjuvant PADCEV plus pembrolizumab expands the established impact of this combination and represents a critical leap forward in how muscle-invasive bladder cancer can be treated. By delivering a clinically meaningful survival benefit, with profound event-free survival and pathological complete response rates, this regimen is the first platinum-free treatment option in nearly 25 years to outperform standard of care chemotherapy, offering new hope to patients living with this disease."

In the EV-304 clinical trial, patients were randomized to receive surgery with neoadjuvant and adjuvant PADCEV plus pembrolizumab or surgery with neoadjuvant chemotherapy. PADCEV plus pembrolizumab was administered as a planned total of 9 cycles of PADCEV and 17 cycles of pembrolizumab split before and after surgery.[ii] PADCEV plus pembrolizumab demonstrated:

- A 47% reduction in the risk of tumor recurrence, progression or death compared to patients treated with standard of care neoadjuvant gemcitabine and cisplatin (Hazard Ratio (HR) of 0.53; 95% Confidence Interval (CI), 0.41–0.70; 1-sided p<0.0001). [ii]
- An estimated 79.4% of patients were event-free at two years, compared with 66.2% treated with standard of care. [ii]
- A 35% reduction in the risk of death compared to neoadjuvant chemotherapy (HR of 0.65; 95% CI, 0.48-0.89; 1-sided p=0.0029). [ii]
- A pathological complete response (pCR) rate of 55.8% compared with 32.5% with chemotherapy at the time of surgery (estimated difference 23.4%; 95% CI 16.7-29.8; 1-sided p<0.0001). [ii]
- A safety profile consistent with prior experience with this combination, and no new identifiable safety signals. Grade ?3 adverse events (AEs) due to any cause occurred in 75.7% of patients treated with neoadjuvant and adjuvant PADCEV plus pembrolizumab compared to 67.2% of patients treated with neoadjuvant chemotherapy. [ii]

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

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About the EV-304/KEYNOTE-B15 Trial
The EV-304 trial is an ongoing, open-label, randomized, controlled, Phase 3 study evaluating neoadjuvant and adjuvant enfortumab vedotin in combination with pembrolizumab versus neoadjuvant chemotherapy (gemcitabine and cisplatin) in patients with MIBC who are eligible for cisplatin-based chemotherapy. Patients were randomized to receive either neoadjuvant and adjuvant (before and after surgery) enfortumab vedotin in combination with pembrolizumab (arm A) or neoadjuvant gemcitabine-cisplatin chemotherapy (arm B). Curative-intent surgery (cystectomy) was performed in both arms. Enfortumab vedotin in combination with pembrolizumab was administered as a planned total of 9 cycles of enfortumab vedotin and 17 cycles of pembrolizumab split before and after surgery.[ii]

The primary endpoint of this trial is EFS, defined as the time from randomization to the first occurrence of any of the following events: progression of disease that precludes radical cystectomy (RC) or failure to undergo RC in participants with residual disease, gross residual disease left behind at the time of surgery, local or distant recurrence based on blinded independent central review (BICR) or death due to any cause. Key secondary endpoints include OS and pCR rate.[iii]

For more information on the global EV-304 trial, go to clinicaltrials.gov.

About Muscle-Invasive Bladder Cancer
Bladder cancer is the ninth most common cancer worldwide, diagnosed in more than 614,000 people each year globally, including an estimated 85,000 people in the U.S.[iii,iv] MIBC represents approximately 30% of all bladder cancer cases.[v] The standard treatment for patients with MIBC is neoadjuvant cisplatin-based chemotherapy followed by surgery.[vi] Even after undergoing surgery to have their bladder removed, approximately half of patients with MIBC experience disease recurrence.[vii]

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.[viii] 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).[i]

PADCEV plus pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph is approved for the treatment of adult patients with MIBC in the United States and for cisplatin-ineligible patients with MIBC in the European Union.

PADCEV plus pembrolizumab is also approved for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC) in the United States, the European Union, Japan and a number of other countries around the world. PADCEV 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.[i]

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

BOXED WARNING: SERIOUS SKIN REACTIONS

- **PADCEV (enfortumab vedotin-ejfv) 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.**

INDICATIONS

PADCEV, in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment, is indicated for the treatment of adult patients with muscle invasive bladder cancer (MIBC).

PADCEV, in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC).

PADCEV, as a single agent, is indicated for the treatment of adult patients with la/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 65% (all grades) of the 570 patients treated with PADCEV in combination with intravenous pembrolizumab for the treatment of MIBC in clinical trials. The majority of the skin reactions that occurred with combination therapy included rash and maculo-papular rash. Grade 3-4 skin reactions occurred in 13% of patients (Grade 3: 12%, Grade 4: 1.1%), including maculo-papular rash, rash, SJS, dermatitis, exfoliative generalized dermatitis, toxic skin eruption, acute generalized exanthematous pustulosis, bullous dermatitis, erythema, macular rash, and pruritic rash. A fatal reaction of TEN occurred in one patient (0.2%). The median time to onset of severe skin reactions was 0.6 months (range: 0.1 to 24 months). Skin reactions led to discontinuation of PADCEV in 8% of patients. Of the patients who experienced a skin reaction and had data regarding resolution (n=367), 87% had complete resolution and 13% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 31% (15/49) had Grade ?2 skin reactions.

Skin reactions occurred in 70% (all grades) of the 564 patients treated with PADCEV in combination with intravenous pembrolizumab for the treatment of la/mUC in clinical trials. The majority of skin reactions that occurred 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. Of the patients who experienced a skin reaction and had data regarding resolution (n=391), 59% had complete resolution and 41% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 27% (43/159) had Grade ?2 skin reactions.

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. Of the patients who experienced a skin reaction and had data regarding resolution (n=328), 58% had complete resolution and 42% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 39% (53/137) had Grade ?2 skin reactions.

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 preexisting 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 by 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 intravenous pembrolizumab for the treatment of MIBC, 7% of the 570 patients treated with combination therapy had pneumonitis/ILD of any grade and 1.8% had Grade 3-4. The median time to onset of any grade pneumonitis/ILD was 3.2 months (range: 0.7 to 13 months).

When PADCEV was given in combination with intravenous pembrolizumab for the treatment of la/mUC, 10% of the 564 patients had pneumonitis/ILD of any grade and 4% had Grade 3-4. A fatal event of pneumonitis/ILD occurred in 2 patients (0.4%). 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 intravenous pembrolizumab for the treatment of MIBC, 42% of the 570 patients treated with combination therapy had PN of any grade, 14% had Grade 2 neuropathy, and 3% had Grade 3 neuropathy. The median time to onset of Grade ?2 PN was 4.9 months (range: 0.2 to 23 months). Of the patients who experienced neuropathy and had data regarding resolution (n=239), 41% had complete resolution, and 59% of patients had residual neuropathy at last evaluation. Of the patients with residual neuropathy at last evaluation, 30% (42/142) had Grade ?2 neuropathy.

When PADCEV was given in combination with intravenous pembrolizumab for the treatment of la/mUC, 67% of the 564 patients had PN of any grade, 36% had Grade 2 neuropathy, and 7% had Grade 3 neuropathy. The median time to onset of Grade ?2 PN was 6 months (range: 0.3 to 25 months). Of the patients who experienced neuropathy and had data regarding resolution (n=373), 13% had complete resolution, and 87% of patients had

residual neuropathy at last evaluation. Of the patients with residual neuropathy at last evaluation, 45% (146/326) had Grade ?2 neuropathy.

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. Of the patients who experienced neuropathy who had data regarding resolution (n=296), 11% had complete resolution, and 89% had residual neuropathy at the time of their last evaluation. Of the patients with residual neuropathy at last evaluation, 50% (132/262) had Grade ?2 neuropathy.

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 intravenous pembrolizumab for the treatment of MIBC:** decreased hemoglobin, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), rash, increased creatinine, decreased lymphocytes, fatigue, pruritus, decreased sodium, PN, increased potassium, diarrhea, alopecia, dysgeusia, decreased appetite, nausea, constipation, urinary tract infection (UTI), dry eye, increased glucose, decreased weight, decreased potassium, hyperglycemia, decreased phosphate, and decreased neutrophils.

- **PADCEV in combination with intravenous pembrolizumab for the treatment of la/mUC:** increased AST, increased creatinine, rash, increased glucose, PN, increased lipase, decreased lymphocytes, increased 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, UTI, and decreased platelets.
- **PADCEV as a single agent:** 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, and dry skin.

EV-304 Study: Patients with cisplatin-eligible MIBC (PADCEV in combination with intravenous pembrolizumab)

- **Neoadjuvant phase:** Of a total of 403 patients, **serious adverse reactions** occurred in 27% of patients receiving PADCEV in combination with intravenous pembrolizumab; the most common (?1.5%) were rash (3.2%), pneumonitis/ILD (2.2%), and diarrhea (1.7%). **Fatal adverse reactions** occurred in 1.7% of patients, including multiple organ dysfunction syndrome (0.5%) and COVID-19 pneumonia, cardiac arrest, pneumonia, septic shock, and urosepsis (0.2% each). Additional fatal adverse reactions were reported in 2 patients in the post-surgery phase before adjuvant treatment started, including pneumonia and sepsis (1 patient each). **Adverse reactions leading to discontinuation** of PADCEV in the neoadjuvant phase occurred in 21% of patients; the most common (?1%) were PN (5%) and rash (3.5%). **Adverse reactions leading to dose interruption** of PADCEV in the neoadjuvant phase occurred in 35% of patients; the most common (?2%) were rash (10%), increased ALT (4%), neutropenia (3.7%), hyperglycemia (3%). **Adverse reactions leading to dose reduction** of PADCEV in the neoadjuvant phase occurred in 15% of patients; the most common (?1%) were rash (9%) and pruritus (2%). Of the 403 patients in the PADCEV in combination with intravenous pembrolizumab arm who received neoadjuvant treatment, thirteen (3.2%) patients did not receive surgery due to adverse reactions. The **adverse reactions that led to cancellation of surgery** were multiple organ dysfunction syndrome (0.5%) and adenocarcinoma of colon, COVID-19 pneumonia, cardiac arrest, chronic obstructive pulmonary disease, coronary artery disease, glomerulonephritis, immune-mediated lung disease, myocarditis, pneumonia, pneumonitis, and urosepsis (0.2% each). Of the 351 patients who received neoadjuvant treatment with PADCEV in combination with intravenous pembrolizumab and underwent radical cystectomy (RC), 26 (7%) patients experienced delay of surgery due to adverse reactions.
- **Adjuvant phase:** Of the 351 patients who underwent surgery, 225 patients received adjuvant treatment with PADCEV with or without intravenous pembrolizumab. Of the 126 patients who did not receive adjuvant PADCEV, discontinuation of PADCEV prior to the adjuvant phase was due to an adverse event in 65 patients. **Serious adverse reactions** occurred in 36% of patients receiving PADCEV; the most common (?1.5%) included UTI (8%), sepsis (2.2%), and diarrhea, hyperglycemia, pneumonitis/ILD, and urosepsis (1.8% each). **Fatal adverse reactions** occurred in 3.1% of patients and included cardiac arrest, death, duodenal ulcer perforation, acute pancreatitis, renal failure, small cell lung cancer, and toxic shock syndrome (0.4% each). **Adverse reactions leading to discontinuation** of PADCEV in the adjuvant phase occurred in 16% of patients; the most common (?1%) were rash (3.6%), PN (1.8%), and UTI (1.3%). **Adverse reactions leading to dose interruption** of PADCEV in the adjuvant phase occurred in 34% of patients; the most common (?2%) were diarrhea and UTI (5% each), rash (4%), and COVID-19 (2.7%). **Adverse reactions leading to dose reduction** of PADCEV in the adjuvant phase occurred in 5% of patients; the most common (>1%) included rash (1.3%).

EV-303 Study: Patients with cisplatin-ineligible MIBC (PADCEV in combination with intravenous pembrolizumab)

- **Neoadjuvant phase:** Of a total of 167 patients, **serious adverse reactions** occurred in 27% of patients receiving PADCEV in combination with intravenous pembrolizumab; the most frequent (?2%) were UTI (3.6%) and hematuria (2.4%). **Fatal adverse reactions** occurred in 1.2% of patients including myasthenia gravis and TEN (0.6% each). Additional fatal adverse reactions were reported in 2.7% of patients in the post-surgery phase before adjuvant treatment started, including sepsis and intestinal obstruction (1.4% each). **Adverse reactions leading to discontinuation** of PADCEV occurred in 22% of patients; the most common (?1%) were rash (4.8%), PN (2.4%), and diarrhea, dysgeusia, fatigue, pruritus, and TEN (1.2% each). **Adverse reactions leading to dose interruption** of PADCEV occurred in 29% of patients; the most common (?2%) were rash (8%), neutropenia (3.6%), hyperglycemia (3%), and fatigue and PN (2.4% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 13% of patients; the most common (?1%) were rash (4.8%), pruritus (1.8%), and PN, increased ALT, increased AST, decreased appetite, fatigue, neutropenia, and decreased weight (1.2% each). Seven (4.2%) patients did not receive surgery due to adverse reactions. The **most commonadverse reactions that led to cancellation of surgery** were acute myocardial infarction, bile duct cancer, colon cancer, respiratory distress, UTI and deaths due to myasthenia gravis and TEN (0.6% each). Of the 146 patients who received neoadjuvant treatment with PADCEV in combination with intravenous pembrolizumab and underwent RC, six (4.1%) patients experienced delay of surgery due to adverse reactions.
- **Adjuvant phase:** Of the 146 patients who underwent surgery, 92 patients received adjuvant treatment with PADCEV with or without intravenous pembrolizumab. Of the 54 patients who did not receive adjuvant PADCEV, discontinuation of PADCEV prior to the adjuvant phase was due to an adverse event in 27 patients. **Serious adverse reactions** occurred in 43% of patients receiving PADCEV; the most frequent (?2%) were UTI (8%), acute kidney injury, pyelonephritis, and urosepsis (4.3% each), and hypokalemia, intestinal obstruction, and sepsis (2.2% each). **Fatal adverse reactions** occurred in 8% of patients, including urosepsis, hemorrhage intracranial, death, myocardial infarction, multiple organ dysfunction syndrome, and pneumonia pseudomonal (1.1% each). **Adverse reactions leading to discontinuation** of PADCEV occurred in 28% of patients; the most common (?2%) were PN (5%) and rash (4.3%). **Adverse reactions leading to dose interruption** of PADCEV occurred in 39% of patients; the most common (?2%) were rash (7%), diarrhea and UTI (5% each), fatigue (4.3%), pruritus (3.3%), and PN and pyelonephritis (2.2% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 8% of patients; the most common (?2%) was weight decreased (2.2%).

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

Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with intravenous pembrolizumab; the most common (?2%) were rash (6%), acute kidney injury (5%), pneumonitis/ILD (4.5%), UTI (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 intravenous 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 (? 2%) 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 (?2%) were rash (16%), PN (13%), and fatigue (2.7%).

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

Serious adverse reactions occurred in 47% of patients treated with PADCEV; the most common (?2%) were UTI, 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 (3%), and fatigue (3%).

EV-201, Cohort 2 Study: 89 patients previously treated with a PD-1/L1 inhibitor and not eligible for cisplatin-based chemotherapy for la/mUC (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 (3%), and hyperglycemia (3%). **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.

Please see full Prescribing Information, including **BOXED WARNING**.

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 multispecific 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, gastrointestinal 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 muscle-invasive bladder cancer (MIBC) who are eligible for cisplatin-based chemotherapy. 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 July 10, 2026. 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, PADCEV ® (enfortumab vedotin-ejfv) and an approval by the FDA for an expanded indication for PADCEV in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph as neoadjuvant and adjuvant (before and after surgery) treatment for adult patients with muscle-invasive bladder cancer regardless of cisplatin eligibility, 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 with regulatory authorities in particular jurisdictions for any potential indication for PADCEV with pembrolizumab (including the application filed with the FDA for the treatment of patients with muscle-invasive bladder cancer) or as a single agent; whether and when any 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; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; 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, 2025, 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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