Pfizer Logo

U.S. FDA Approves PADCEV® plus Keytruda® for Certain Patients with Bladder Cancer

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- *PADCEV plus Keytruda is the first and only approved perioperative treatment regimen that can significantly improve survival over current standard of care (surgery alone) in cisplatin-ineligible patients with muscle-invasive bladder cancer*
- *Approval is based on unprecedented data from the pivotal Phase 3 EV-303 trial showing a 60% reduction in the risk of disease recurrence, progression or death and a 50% reduction in the risk of death compared to surgery alone*
- *Represents the first and only ADC and PD-1 inhibitor regimen for this patient population and a potential new standard of care*

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 (ADC), in combination with the PD-1 inhibitor Keytruda® (pembrolizumab) or Keytruda QLEX™ (pembrolizumab and berahyaluronidase alfa-pmph), as neoadjuvant treatment and then continued after cystectomy (surgery) as adjuvant treatment for adult patients with muscle-invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy.[i] The approval of this perioperative (before and after surgery) treatment was based on results from the pivotal Phase 3 EV-303 clinical trial (also known as KEYNOTE-905), which were presented during a Presidential Symposium at the European Society of Medical Oncology (ESMO) Congress 2025.

Dr. Matthew Galsky, Lillian and Howard Stratton Professor of Medicine, Director of Genitourinary Medical Oncology, Mount Sinai Tisch Cancer Center, and EV-303 Investigator
"Enfortumab vedotin plus pembrolizumab is poised to address a critical unmet need. Half of patients with MIBC may experience cancer recurrence even after having their bladder removed, and many of these patients are ineligible to receive cisplatin. This approval, based on striking event-free and overall survival benefits, may represent an important practice-changing advance for these patients who've had no new options in decades."

Jeff Legos, PhD, MBA, Chief Oncology Officer, Pfizer
"Today's approval, granted months earlier than anticipated, ushers in a new era of treatment for cisplatin-ineligible patients with MIBC who have long been underserved by existing treatments. PADCEV plus pembrolizumab is the first and only FDA-approved perioperative treatment regimen to demonstrate a meaningful survival advantage compared to surgery alone, positioning it to reshape the treatment landscape and bring new hope to patients and families."

In the EV-303 study, perioperative treatment with PADCEV plus pembrolizumab resulted in a 60% reduction in the risk of tumor recurrence, progression or death compared to surgery alone, meeting the primary endpoint of

event-free survival (EFS) (Hazard Ratio [HR]=0.40; 95% confidence interval [CI]: 0.28-0.57; p<0.0001).The probability of remaining event free was 74.7% for patients who received the combination and 39.4% for patients treated with surgery only. The estimated median EFS has not yet been reached for the combination arm versus 15.7 months for the surgery arm. Data from the key secondary endpoint of overall survival (OS) showed that perioperative treatment with PADCEV plus pembrolizumab also resulted in a 50% reduction in the risk of death as compared to surgery alone (HR=0.50; 95% CI: 0.33-0.74; p=0.0002). The probability of survival at two years was 79.7% for patients who received the combination relative to 63.1% for patients treated with surgery only. The estimated median OS has not yet been reached for the combination arm versus 41.7 months for the surgery arm.[ii]

Moitreyee Chatterjee-Kishore, PhD, MBA, Head of Oncology Development, Astellas
"Building on the combination's established role in locally advanced or metastatic urothelial cancer where it is has become standard of care in the U.S., PADCEV plus pembrolizumab now has the potential to redefine care in an earlier disease setting as the only antibody-drug conjugate and PD-1 inhibitor regimen for cisplatin-ineligible patients with MIBC. The approval underscores our unwavering commitment to expanding the reach of this innovative combination to more eligible patients with bladder cancer."

The safety results in EV-303 were consistent with those previously reported for this combination, and there were no new safety signals. The most common (?20%) adverse reactions, including laboratory abnormalities, in patients treated with PADCEV plus intravenous pembrolizumab were increased glucose, decreased hemoglobin, increased aspartate aminotransferase, rash, increased alanine aminotransferase, fatigue, pruritus, increased creatinine, decreased sodium, decreased lymphocytes, peripheral neuropathy, increased potassium, alopecia, dysgeusia, diarrhea, decreased appetite, constipation, nausea, decreased phosphate, urinary tract infection, dry eye, and decreased weight. Grade ? 3 AEs due to any cause occurred in 71.3% of patients treated in the combination arm and 45.9% of patients who were in the surgery arm.[ii]

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

Perioperative PADCEV plus pembrolizumab is also being evaluated in cisplatin-eligible patients with MIBC in the EV-304 Phase 3 clinical trial (also known as KEYNOTE-B15).

About the EV-303/KEYNOTE-905 Trial
The EV-303 trial (also known as KEYNOTE-905) is an ongoing, open-label, randomized, three-arm, controlled, Phase 3 study evaluating neoadjuvant and adjuvant PADCEV in combination with pembrolizumab or neoadjuvant and adjuvant pembrolizumab versus surgery alone in patients with MIBC who are either not eligible for or declined cisplatin-based chemotherapy. Patients were randomized to receive either neoadjuvant and adjuvant pembrolizumab (arm A), surgery alone (arm B) or neoadjuvant and adjuvant PADCEV in combination with pembrolizumab (arm C).[iii]

The primary endpoint of this trial is EFS between arm C and arm B, defined as time from randomization to the first of: disease progression preventing curative surgery, failure to undergo surgery for participants with muscle invasive residual disease, incomplete surgical resection, local or distant recurrence after surgery, or death.[i] Key secondary endpoints include OS and pCR rate between arm C and arm B, as well as EFS, OS and pCR rate between arm A and arm B.[viii]

For more information on the global EV-303 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.[iv,v] MIBC represents approximately 30% of all bladder cancer cases.[vi] The standard treatment for patients with MIBC is neoadjuvant cisplatin-based chemotherapy followed by surgery, which has been shown to prolong survival.[vii] However, up to half of patients who are diagnosed with MIBC are not eligible to receive cisplatin and face limited treatment options, typically undergoing surgery without any systemic treatment.[viii] Of those who do undergo bladder surgery, one third are cisplatin-ineligible.

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.[ix] 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 is also approved for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC) in the United States, Japan and a number of other countries around the world. In the European Union, the combination is approved for the treatment of adult patients with la/mUC who are eligible for platinum-containing chemotherapy. 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]

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) who are ineligible for cisplatin-containing chemotherapy.

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 (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 61% (all grades) of the 167 patients treated with PADCEV in combination with intravenous pembrolizumab for the treatment of MIBC in clinical trials. The majority of skin reactions that occurred included rash and maculo-papular rash. Grade 3-4 skin reactions occurred in 10% of patients (Grade 3: 9%, Grade 4: 1.2%), including rash, maculo-papular rash, toxic skin eruption, dermatitis exfoliative generalized, erythema, exfoliative rash, skin toxicity, toxic epidermal necrolysis, and toxic erythema of chemotherapy. A fatal reaction of toxic epidermal necrolysis occurred in one patient (0.6%). The median time to onset of severe skin reactions was 0.6 months (range: 0.2 to 8.8 months). Skin reactions led to discontinuation of PADCEV in 10% of patients. Of the patients who experienced a skin reaction and had data regarding resolution (n=102), 83% had complete resolution and 17% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 29% (5/17) 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 locally advanced or 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 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 diabetic ketoacidosis 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, 4.2% of the 167 patients had pneumonitis/ILD of any grade. All events were Grade 1-2. The median time to onset of any grade pneumonitis/ILD was 2.5 months (range: 1.9 to 9.7 months).

When PADCEV was given in combination with intravenous pembrolizumab for the treatment of locally advanced or 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 two 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, 39% of the 167 patients had PN of any grade, 12% had Grade 2 neuropathy, and 3% had Grade 3 neuropathy. The median time to onset of Grade ?2 PN was 4.7 months (range: 0.2 to 11 months). Of the patients who experienced neuropathy and had data regarding resolution (n=65), 32% had complete resolution, and 68% of patients had residual neuropathy at last evaluation. Of the patients with residual neuropathy at last evaluation, 27% (12/44) had Grade ?2 neuropathy.

When PADCEV was given in combination with intravenous pembrolizumab for the treatment of locally advanced or 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 $\geq$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:** increased glucose, decreased hemoglobin, increased aspartate aminotransferase (AST), rash, increased alanine aminotransferase (ALT), fatigue, pruritus, increased creatinine, decreased sodium, decreased lymphocytes, peripheral neuropathy, increased potassium, alopecia, dysgeusia, diarrhea, decreased appetite, constipation, nausea, decreased phosphate, urinary tract infection, dry eye, and decreased weight.
- **PADCEV in combination with intravenous pembrolizumab for the treatment of locally advanced or mUC:** increased AST, increased creatinine, rash, increased glucose, peripheral neuropathy, 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, urinary tract infection, and decreased platelets.

- **PADCEV as a single agent:** increased glucose, increased AST, decreased lymphocytes, increased creatinine, rash, fatigue, peripheral neuropathy, 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-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%) serious adverse reactions were urinary tract infection (3.6%) and hematuria (2.4%). **Fatal adverse reactions** occurred in 1.2% of patients including myasthenia gravis and toxic epidermal necrolysis (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 adverse reactions (?1%) leading to discontinuation of PADCEV were rash (4.8%), peripheral neuropathy (2.4%), and diarrhea, dysgeusia, fatigue, pruritus, and toxic epidermal necrolysis (1.2% each). **Adverse reactions leading to dose interruption** of PADCEV occurred in 29% of patients. The most common adverse reactions (?2%) leading to dose interruption of PADCEV were rash (8%), neutropenia (3.6%), and hyperglycemia (3%), and fatigue and peripheral neuropathy (2.4% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 13% of patients. The most common adverse reactions (?1%) leading to dose reduction of PADCEV were rash (4.8%), pruritus (1.8%), and peripheral neuropathy, increased alanine aminotransferase, increased aspartate aminotransferase, decreased appetite, fatigue, neutropenia, and decreased weight (1.2% each). Seven (4.2%) patients did not receive surgery due to adverse reactions. The **adverse reactions that led to cancellation of surgery** were acute myocardial infarction, bile duct cancer, colon cancer, respiratory distress, urinary tract infection and deaths due to myasthenia gravis and toxic epidermal necrolysis (0.6% each). Of the 146 patients who received neoadjuvant treatment with PADCEV in combination with intravenous pembrolizumab and underwent RC, 6 (4.1%) patients experienced delay of surgery due to adverse reactions.
- **Adjuvant phase**: Of the 149 patients who underwent surgery, 100 patients received adjuvant treatment with PADCEV in combination with intravenous pembrolizumab. Of the 49 patients who did not receive adjuvant treatment, discontinuation of treatment with PADCEV in combination with intravenous pembrolizumab prior to the adjuvant phase was due to an adverse event in 21 patients. **Serious adverse reactions** occurred in 43% of patients receiving PADCEV in combination with pembrolizumab. The most frequent (?2%) serious adverse reactions were urinary tract infection (8%), acute kidney injury and pyelonephritis (5% each), urosepsis (4%), and hypokalemia, intestinal obstruction, and sepsis (2% each). **Fatal adverse reactions** occurred in 7% of patients, including urosepsis, hemorrhage intracranial, death, myocardial infarction, multiple organ dysfunction syndrome, and pneumonia pseudomonal (1% each). **Adverse reactions leading to discontinuation** of PADCEV occurred in 26% of patients. The most common adverse reactions (?2%) leading to discontinuation of PADCEV were peripheral neuropathy (5%) and rash (4%). **Adverse reactions leading to dose interruption** of PADCEV occurred in 36% of patients. The most common adverse reactions (?2%) leading to dose interruption of PADCEV were rash (6%), diarrhea and urinary tract infection (5% each), fatigue (4%), pruritus (3%), and peripheral neuropathy and pyelonephritis (2% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 7% of patients. The most common adverse reactions (?2%) leading to dose reduction of PADCEV was weight decreased (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 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 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 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-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.

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, 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 previously entered a clinical collaboration agreement with Merck to evaluate the combination of Seagen's and Astellas' PADCEV® (enfortumab vedotin) and Merck's Keytruda® (pembrolizumab) in patients with muscle-invasive bladder cancer (MIBC) who are not eligible for or declined 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).

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.

Pfizer Disclosure Notice
The information contained in this release is as of November 21, 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 or pembrolizumab and berahyaluronidase alfa-pmph in cisplatin-ineligible patients with muscle-invasive bladder cancer, including their potential benefits and an approval in the U.S. for the combination as a neoadjuvant treatment and then continued after cystectomy as adjuvant treatment for adult patients with muscle-invasive bladder cancer who are ineligible for cisplatin-containing chemotherapy 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; risks associated with interim 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 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, 2024, 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.

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Pfizer Contacts:
PfizerMediaRelations@Pfizer.com

For Investors
IR@pfizer.com

Astellas Contacts:
Corporate.Communications@us.astellas.com

Corporate Communications
+1-847-686-1813

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