Pfizer Logo

PADCEV® (enfortumab vedotin-ejfv) with KEYTRUDA® (pembrolizumab) Approved by FDA as the First and Only ADC Plus PD-1 to Treat Advanced Bladder Cancer

Friday, December 15, 2023 - 05:00pm

– PADCEV plus pembrolizumab approved based on groundbreaking EV-302 trial –

– Confirmatory trial found PADCEV plus pembrolizumab nearly doubled median overall survival compared to standard of care platinum-based chemotherapy –

NEW YORK & TOKYO--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) and Astellas Pharma Inc. (TSE:4503, President and CEO: Naoki Okamura, "Astellas")today announced that on December 15, 2023 the U.S. Food and Drug Administration (FDA) has approved PADCEV® (enfortumab vedotin-ejfv, an antibody-drug conjugate [ADC]) with KEYTRUDA® (pembrolizumab, a PD-1 inhibitor) for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC). This combination is the first approved to offer an alternative to platinum-containing chemotherapy, the current standard of care in first-line la/mUC.

The approval is based on results from the Phase 3 EV-302 clinical trial (also known as KEYNOTE-A39), which demonstrated the combination nearly doubled median overall survival (OS) and median progression-free survival (PFS) in patients with previously untreated la/mUC compared to platinum-containing chemotherapy. Findings from EV-302 were presented at the European Society for Medical Oncology (ESMO) Congress 2023. EV-302 also serves as the confirmatory trial for the U.S. accelerated approval of this combination for adult patients with la/mUC who are not eligible to receive cisplatin-containing chemotherapy (approved in April 2023) and expands the labeled indication to include patients who are eligible to receive cisplatin chemotherapy. EV-302 is also serving as the basis for global submissions.

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

“In the Phase 3 EV-302 study, the combination of PADCEV and pembrolizumab demonstrated survival benefit for patients with advanced bladder cancer, nearly doubling median OS and median PFS compared with chemotherapy. We hope the approval of this combination will transform the standard of care for advanced bladder cancer and give patients more time with their loved ones.”

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

“Today’s FDA approval represents a paradigm change in the treatment of advanced bladder cancer and provides hope to the thousands of Americans impacted by this aggressive disease. This achievement is notable, as it is the first regimen approved in advanced urothelial cancer that has demonstrated superiority to platinum chemotherapy, the gold standard of care for decades.”

The EV-302 study met its dual primary endpoints of OS and PFS compared to platinum-containing chemotherapy. Treatment with the combination resulted in a median OS of 31.5 months (95% CI: 25.4-NR) compared to 16.1 months (95% CI: 13.9-18.3) with chemotherapy, representing a 53% reduction in risk of death (Hazard Ratio [HR]=0.47; 95% Confidence Interval [CI]: 0.38-0.58; P<0.00001). The median PFS of 12.5 months (95% CI: 10.4-16.6) with the combination compared to 6.3 months (95% CI: 6.2-6.5) with chemotherapy represents a 55% reduction in the risk of cancer progression or death (HR=0.45; 95% CI: (0.38-0.54); P<0.00001). Consistent OS and PFS results were observed across pre-defined subgroups, including cisplatin eligibility and PD-L1 expression level. Cisplatin eligible and ineligible subgroups (n=244 and 198, respectively) saw a 47% and 57% reduced risk of death, respectively, and a 52% and 57% reduced risk of progression or death, respectively. PD-L1 and high PD-L1 expression subgroups (n=184 and 254, respectively) saw a 56% and 51% reduced risk of death, respectively, and a 50% and 58% reduced risk of progression or death, respectively.

The most common (?20%) all-grade adverse events (AEs), including laboratory abnormalities, related to treatment with enfortumab vedotin and pembrolizumab were increased aspartate aminotransferase, increased creatinine, rash, increased glucose, peripheral neuropathy, increased lipase, decreased lymphocytes, increased alanine aminotransferase, 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. The safety results in EV-302 are consistent with those previously reported with this combination in EV-103 in cisplatin-ineligible patients with la/mUC. No new safety issues were identified.

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

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

“Advanced bladder cancer is a common cause of cancer-related death. The overall survival benefit seen in the EV-302 trial demonstrates the potential for PADCEV in combination with pembrolizumab to impact first-line treatment of patients with locally advanced or metastatic urothelial carcinoma. In my opinion, this is a meaningful advancement over platinum-based chemotherapy in the systemic treatment of these patients.”

Andrea Maddox-Smith, CEO, Bladder Cancer Advocacy Network (BCAN)

“Despite advances in the treatment of advanced bladder cancer, there remains a need for therapies that extend patients’ lives. Our network is thrilled that the FDA has approved a new treatment option, and we are excited about the hope it will provide to members of the bladder cancer patient community.”

About EV-302

The EV-302 trial is an open-label, randomized, controlled Phase 3 study, evaluating enfortumab vedotin in combination with pembrolizumab versus 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 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 objective response rate (ORR) and duration of response (DOR) per RECIST v1.1 by BICR, and safety.

About Bladder and Urothelial Cancer

- Urothelial cancer, or bladder cancer, begins in the urothelial cells, which line the urethra, bladder, ureters, renal pelvis, and some other organs.[i]
- If bladder cancer has spread to surrounding organs or muscles, it is called locally advanced disease. If the cancer has spread to other parts of the body, it is called metastatic disease. [ii]
- Globally, approximately 573,000 new cases of bladder cancer and 212,000 deaths are reported annually.[iii]
- It is estimated that approximately 82,290 people in the U.S. will be diagnosed with bladder cancer in 2023. [iv]
- Urothelial cancer accounts for 90% of all bladder cancers and can also be found in the renal pelvis, ureter, and urethra. [ii]
- Approximately 12% of cases are locally advanced or metastatic urothelial cancer at diagnosis.[v]

Ongoing Investigational Trials

The EV-302 trial (NCT04223856) is an open-label, randomized, controlled Phase 3 study, evaluating the impact of treatment with enfortumab vedotin in combination with pembrolizumab versus chemotherapy in patients with previously untreated locally advanced or metastatic urothelial cancer (la/mUC) who were eligible for cisplatin- or carboplatin-containing chemotherapy regardless of PD-L1 status.

The EV-103 trial (NCT03288545) is an ongoing, multi-cohort, open-label, multicenter Phase 1b/2 study investigating enfortumab vedotin alone or in combination with pembrolizumab and/or chemotherapy in first- or second-line settings in patients with la/mUC and in patients with muscle-invasive bladder cancer (MIBC).

Enfortumab vedotin in combination with pembrolizumab is being investigated in an extensive program in multiple stages of urothelial cancer, including two Phase 3 clinical trials in MIBC in EV-304 (NCT04700124, also known as KEYNOTE-B15) and EV-303 (NCT03924895, also known as KEYNOTE-905). The use of enfortumab vedotin in combination with pembrolizumab in MIBC has not been proven safe or effective.

The EV-202 trial (NCT04225117) is an ongoing, multi-cohort, open-label, multicenter Phase 2 study investigating enfortumab vedotin alone in patients with previously treated advanced solid tumors. This study also has a cohort that is investigating enfortumab vedotin in combination with pembrolizumab in patients with previously untreated recurrent/ metastatic head and neck squamous cell carcinoma.

About PADCEV® (enfortumab vedotin-ejfv)

PADCEV (enfortumab vedotin-ejfv) is a first-in-class antibody-drug conjugate (ADC) that is directed to Nectin-4, a protein located on the surface of cells and highly expressed in bladder cancer.[vi] 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).[vii]

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 game-changing mechanisms of action to attack cancer from multiple angles, including antibody-drug conjugates (ADCs), small molecules, bispecifics and other immunotherapies. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer and hematologic malignancies, as well as melanoma, gastrointestinal, gynecological and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to extend and improve patients' lives.

About Astellas

Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into VALUE for patients. For more information, please visit our website at https://www.astellas.com/en.

About 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. As previously announced, 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.

Pfizer Disclosure Notice

The information contained in this release is as of December 15, 2023. 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, an antibody-drug conjugate [ADC]) and KEYTRUDA® (pembrolizumab, a PD-1 inhibitor), including its potential benefits, and an approval in the U.S. of PADCEV with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC) and ongoing investigational trials for

PADCEV with pembrolizumab, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of PADCEV with pembrolizumab; 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 drug applications may be filed in particular jurisdictions for PADCEV with pembrolizumab; whether and when any applications that may be pending or filed for PADCEV with pembrolizumab 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 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; 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, 2022 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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