ASTRAZENECA'S IMFINZI™ (DURVALUMAB) RECEIVES US FDA ACCELERATED APPROVAL FOR PREVIOUSLY TREATED PATIENTS WITH ADVANCED BLADDER CANCER

Approval granted regardless of PD-L1 status, based on tumor response rate and duration of response

IMFINZI is the cornerstone in an extensive Immuno-Oncology program across multiple cancer types and stages of disease

(WILMINGTON, Del., May 1, 2017) – AstraZeneca and its global biologics research and development arm, MedImmune, today announced that the US Food and Drug Administration (FDA) has granted accelerated approval to IMFINZI™ (durvalumab). IMFINZI is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or whose disease has progressed within 12 months of receiving platinum-containing chemotherapy before (neoadjuvant) or after (adjuvant) surgery. IMFINZI is approved under the FDA's accelerated approval pathway, based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Pascal Soriot, Chief Executive Officer of AstraZeneca, said: "We are excited to offer IMFINZI as a breakthrough therapy for patients with locally-advanced or metastatic bladder cancer. IMFINZI is the cornerstone of our extensive Immuno-Oncology program, in development across many tumor types, as monotherapy and in combination. This first approval for IMFINZI is an important milestone in our return to growth and brings us another step closer to our goal of redefining the way cancer is treated."

IMFINZI is also under investigation in the Phase III DANUBE trial as first-line treatment in urothelial carcinoma as monotherapy and in combination with tremelimumab.

Nicholas J. Vogelzang, MD, FACP, FASCO, Clinical Professor at the University of Nevada School of Medicine; SWOG GU Vice Chair; US Oncology Research GU Chair; Comprehensive Cancer Centers of Nevada, said: "The usual course of treatment for patients with advanced bladder cancer begins with a standard platinum-containing chemotherapy. Patients who have disease progression during or following chemotherapy are left with few other treatment options. The approval of IMFINZI to treat this population of select patients signifies hope for those who are currently suffering, or may find themselves with limited options in the future."

The recommended dose of IMFINZI is 10 mg/kg body weight administered as an intravenous infusion over 60 minutes every two weeks until disease progression or unacceptable toxicity.

The accelerated FDA approval of IMFINZI, a human monoclonal antibody that blocks PD-L1, is based on data from Study 1108. This Phase I/II trial evaluated the safety and efficacy of IMFINZI in patients with locally advanced or metastatic urothelial carcinoma of the bladder. Patients had progressed while on or after a platinum-containing chemotherapy, including those who progressed within 12 months of receiving therapy in a neoadjuvant or adjuvant setting.

In the trial, IMFINZI demonstrated rapid and durable responses, with an objective response rate (ORR) of 17.0% (95% confidence interval [CI]: 11.9; 23.3) in all evaluable patients, regardless of PD-L1 status, and 26.3% (95% CI: 17.8; 36.4) in patients with PD-L1 high-expressing tumors (as determined by the VENTANA PD-L1 (SP263) Assay, Ventana Medical Systems Inc., a member of the Roche Group). PD-L1 high was defined as ≥25% of tumor cells (TC) or tumor-infiltrating immune cells (IC) expressing membrane PD-L1 if ICs involved >1% of the tumor area, or TC≥25% or IC=100% if ICs involved ≤1% of the tumor area. Additionally, approximately 14.3% of all evaluable patients achieved partial response and 2.7% achieved complete response. Of patients who had received only neoadjuvant or adjuvant therapy prior to trial entry, 24% (n=9) responded. Based on a secondary endpoint in this single-arm trial, median time to response was six weeks. Among the total 31 responding patients, 14 patients (45%) had ongoing responses of six months or longer and five patients (16%) had ongoing responses of 12 months or longer.

Efficacy results for Study 1 (bladder cancer cohort of Study 1108)

	All Patients (N=182)	**PD-L1 High (N=95)**	**PD-L1 Low/Negative (N=73)**	**PD-L1 Not Evaluable (N=14)**
Objective Response Rate (ORR) by BICR*, n (%) (95% confidence interval [CI])	31 (17.0%) (11.9; 23.3)	25 (26.3%) (17.8; 36.4)	3 (4.1%) (0.9; 11.5)	3 (21.4%) (4.7; 50.8)
Complete Response (CR)	5	3	1	1
Partial Response (PR)	26	22	2	2
Median Duration of Response (DoR), months (range)	Not reached (0.9+; 19.9+)	Not reached (0.9+; 19.9+)	12.3 (1.9+; 12.3)	Not reached (2.3+; 2.6+)
*BICR=Blinded Independent Central Review + Denotes a censored value				

Patients should be monitored for immune-mediated adverse reactions including pneumonitis, hepatitis, colitis, endocrinopathies (including adrenal insufficiency, hypophysitis, or Type 1 diabetes mellitus), nephritis, rash, thrombocytopenic purpura, infection, infusion-related reactions, or embryo-fetal toxicity. Serious adverse reactions occurred in 46% of patients. The most frequent serious adverse reactions (>2%) were acute kidney injury (4.9%), urinary tract infection (4.4%), musculoskeletal pain (4.4%), liver injury (3.3%), general physical

health deterioration (3.3%), sepsis, abdominal pain, and pyrexia/tumor associated fever (2.7% each). Eight patients (4.4%) who were treated with IMFINZI experienced Grade 5 adverse events of cardiorespiratory arrest, general physical health deterioration, sepsis, ileus, pneumonitis, or immune-mediated hepatitis. Three additional patients were experiencing infection and disease progression at the time of death. IMFINZI was discontinued for adverse reactions in 3.3% of patients.

Clinical trials have demonstrated that patients with PD-L1 high-expressing tumors have a higher likelihood of response through blockade of the PD-1/PD-L1 pathway. PD-L1 expression testing may be a useful tool to help guide physicians in their treatment decisions, but it is not required for use of IMFINZI.

AstraZeneca strives to ensure that appropriate patients and their oncologists have access to IMFINZI and relevant support resources. These include educational resources, an Oncology Nurse Educator program and financial assistance programs. Additionally, AstraZeneca has launched Lighthouse, a program that provides support to patients during any immune-mediated adverse events they may encounter during treatment, through medically trained Lighthouse Advocates. The program aims to make patients' treatment experience as comfortable as possible.

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI™ (durvalumab).

Monitor patients for clinical signs and symptoms of immune-mediated pneumonitis, hepatitis, colitis or diarrhea, endocrinopathies, nephritis, rash or dermatitis, and other immune-mediated adverse reactions. Please refer to the full Prescribing Information for important dose management information specific to adverse reactions.

Immune-Mediated Pneumonitis
In the combined safety database (n=1414), immune-mediated pneumonitis occurred in 32 patients (2.3%), including 1 fatal case (0.1%) and 6 Grade 3–4 cases (0.4%). In Study 1 (n=182), 1 patient (0.5%) died from immune-mediated pneumonitis. Monitor patients for signs and symptoms of pneumonitis and evaluate with radiographic imaging when suspected. Administer corticosteroids for ≥Grade 2 pneumonitis. Withhold IMFINZI for Grade 2 pneumonitis; permanently discontinue for Grade 3–4 pneumonitis.

Immune-Mediated Hepatitis
In the combined safety database (n=1414), immune-mediated hepatitis occurred in 16 patients (1.1%), including 1 fatal case (<0.1%) and 9 Grade 3 cases (0.6%). Grade 3–4 elevations in ALT occurred in 40/1342 patients (3.0%), AST in 58/1336 patients (4.3%), and total bilirubin in 37/1341 patients (2.8%). In Study 1 (n=182), 1 patient (0.5%) died from immune-mediated hepatitis, and 2 patients (1.1%) experienced immune-mediated hepatitis, including 1 Grade 3 case (0.5%). Monitor patients for abnormal liver tests in each cycle during treatment with IMFINZI. Administer corticosteroids and withhold IMFINZI for Grade 2–3 ALT or AST >3–5X ULN or ≤8X ULN or total bilirubin >1.5–3X ULN or ≤5X ULN.

Permanently discontinue IMFINZI in patients with Grade 3 ALT or AST >8X ULN or total bilirubin >5X ULN, or in patients with concurrent ALT or AST >3X ULN and total bilirubin >2X ULN with no other cause.

Immune-Mediated Colitis

In the combined safety database (n=1414), immune-mediated colitis or diarrhea occurred in 18 patients (1.3%), including 1 Grade 4 case (<0.1%) and 4 Grade 3 cases (0.3%). In Study 1 (n=182), 23 patients (12.6%) experienced colitis or diarrhea, including 2 Grade 3–4 cases (1.1%). Monitor patients for signs and symptoms of colitis or diarrhea. Administer corticosteroids for ≥Grade 2 colitis or diarrhea. Withhold IMFINZI for Grade 2 colitis or diarrhea; permanently discontinue for Grade 3–4 colitis or diarrhea.

Immune-Mediated Endocrinopathies

- Immune-mediated thyroid disorders, adrenal insufficiency, type 1 diabetes mellitus and hypophysitis/hypopituitarism have occurred with IMFINZI. Monitor patients for clinical signs and symptoms of endocrinopathies. For Grade 2–4 endocrinopathies (except hypothyroidism) withhold dose until clinically stable and offer symptomatic management for hyperthyroidism. For Grade 2–4 hypothyroidism, initiate thyroid hormone replacement as needed
- Thyroid disorders—In the combined safety database (n=1414), immune-mediated hypothyroidism and hyperthyroidism occurred in 136 patients (9.6%) and 81 patients (5.7%), respectively. Thyroiditis occurred in 10 patients (0.7%), including 1 Grade 3 case (<0.1%) in a patient who had a myocardial infarction. In 9 patients with thyroiditis, transient hyperthyroidism preceded hypothyroidism. In Study 1 (n=182), Grade 1–2 hypothyroidism or thyroiditis occurred in 10 patients (5.5%). Grade 1–2 hyperthyroidism or thyroiditis leading to hyperthyroidism occurred in 9 patients (4.9%). Monitor patients for abnormal thyroid function tests prior to and periodically during treatment
- Immune-mediated adrenal insufficiency—In the combined safety database (n=1414), immune-mediated adrenal insufficiency occurred in 13 patients (0.9%), including 2 Grade 3 cases (0.1%). In Study 1 (n=182), Grade 1 adrenal insufficiency occurred in 1 patient (0.5%). Administer corticosteroids and hormone replacement as clinically indicated
- Type 1 diabetes mellitus—In the combined safety database (n=1414), new onset type 1 diabetes mellitus without an alternative etiology occurred in 1 patient (<0.1%). For type 1 diabetes mellitus, initiate insulin as indicated and withhold IMFINZI until clinically stable
- Hypophysitis—In the combined safety database (n=1414), hypopituitarism leading to adrenal insufficiency and diabetes insipidus occurred in 1 patient (<0.1%). Administer corticosteroids and hormone replacement as clinically indicated

Other Immune-Mediated Adverse Reactions

- IMFINZI has caused immune-mediated rash. Other immune-related adverse reactions, including aseptic meningitis, hemolytic anemia, immune thrombocytopenic purpura, myocarditis, myositis, nephritis, and ocular inflammatory toxicity including uveitis and keratitis, have occurred in ≤1.0% of patients treated with IMFINZI

- Immune-mediated rash or dermatitis—In the combined safety database (n=1414), immune-mediated rash or dermatitis occurred in 220 patients (15.6%) and 4 patients (0.3%) developed vitiligo. In Study 1 (n=182), 20 patients (11.0%) developed rash, including 1 Grade 3 case (0.5%). Patients should be monitored for signs and symptoms of rash or dermatitis. Administer corticosteroids if indicated. Withhold IMFINZI for Grade 3 rash or dermatitis or Grade 2 rash or dermatitis lasting >1 week. Permanently discontinue IMFINZI in patients with Grade 4 rash or dermatitis
- Immune thrombocytopenic purpura—In the combined safety database (n=1414), 1 fatal case (<0.1%) of immune thrombocytopenic purpura occurred. Monitor patients for signs and symptoms of immune thrombocytopenic purpura
- Nephritis—In the combined safety database (n=1414), immune-mediated nephritis occurred in 3 patients (0.2%), including 2 Grade 3 cases (0.1%). Monitor patients for abnormal renal function tests prior to and during each cycle of IMFINZI. Administer corticosteroids for ≥Grade 2 nephritis (creatinine >1.5X ULN). Withhold IMFINZI for Grade 2 nephritis; permanently discontinue for ≥Grade 3 nephritis (creatinine >3X ULN)

Infection
Severe infections, including sepsis, necrotizing fasciitis, and osteomyelitis, occurred in patients receiving IMFINZI. In the combined safety database (n=1414), infections occurred in 531 patients (37.6%). In Study 1 (n=182), infections occurred in 54 patients (29.7%). 11 patients (6.0%) experienced Grade 3–4 infection and 5 patients (2.7%) were experiencing infection at the time of death. 8 patients (4.4%) experienced urinary tract infection, the most common ≥Grade 3 infection. Monitor patients for signs and symptoms of infection and treat with anti-infectives for suspected or confirmed infections. Withhold IMFINZI for ≥Grade 3 infection.

Infusion-Related Reactions
In the combined safety database (n=1414), severe infusion-related reactions occurred in 26 patients (1.8%). In Study 1 (n=182), infusion-related reactions occurred in 3 patients (1.6%). There were 5 Grade 3 (0.4%) and no Grade 4 or 5 reactions. Patients should be monitored for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1–2 infusion-related reactions and permanently discontinue for Grade 3–4 infusion-related reactions.

Embryo-Fetal Toxicity
Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. There are no data on the use of IMFINZI in pregnant women. Advise pregnant women of the potential risk to a fetus and advise women of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of IMFINZI.

Nursing Mothers
There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for adverse reactions in breastfed infants from IMFINZI, advise a lactating woman not to breastfeed during treatment and for at least 3 months after the last dose.

Most Common Adverse Reactions

- The most common adverse reactions (≥15%) were fatigue (39%), musculoskeletal pain (24%), constipation (21%), decreased appetite (19%), nausea (16%), peripheral edema (15%), and urinary tract infection (15%). The most common Grade 3 or 4 adverse reactions (≥3%) were fatigue, urinary tract infection, musculoskeletal pain, abdominal pain, dehydration, and general physical health deterioration
- Adverse reactions leading to discontinuation of IMFINZI occurred in 3.3% of patients. Serious adverse reactions occurred in 46% of patients. The most frequent serious adverse reactions (>2%) were acute kidney injury (4.9%), urinary tract infection (4.4%), musculoskeletal pain (4.4%), liver injury (3.3%), general physical health deterioration (3.3%), sepsis, abdominal pain, and pyrexia/tumor associated fever (2.7% each)

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

Please see complete Prescribing Information including Patient Information.

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NOTES TO EDITORS

About IMFINZI™ (durvalumab)
IMFINZI™ (durvalumab, previously known as MEDI4736) is a human monoclonal antibody directed against PD-L1, which blocks the interaction of PD-L1 with PD-1 and CD80.

Durvalumab is also being tested in the first-line treatment of patients with unresectable and metastatic bladder cancer as a monotherapy and in combination with tremelimumab, a checkpoint inhibitor that targets CTLA-4, as part of the DANUBE Phase III trial, which had the last patient commenced dosingduring the first quarter of 2017 (global trial, excluding China). Additional clinical trials are ongoing to investigate durvalumab as monotherapy or in combination with tremelimumab in multiple solid tumors and blood cancers.

About bladder cancer
Urothelial bladder cancers arise from the epithelium of the bladder and are the sixth most common form of cancer in the US. It is estimated that in 2017, approximately 79,000 Americans will be diagnosed with bladder cancer, and almost 17,000 will die from this disease. Metastatic bladder cancer remains an area of unmet medical need with five-year overall survival rates of approximately 5%.

The tumor microenvironment of urothelial carcinoma (UC) significantly impairs lymphocyte function, helping the cancer to evade immune detection by exploiting inhibitory checkpoint pathways, such as PD-L1/PD-1. PD-L1 is widely expressed in tumor and immune cells in UC patients and helps tumors to evade detection from the immune system through binding to the PD-1 receptor on cytotoxic T lymphocytes.

About AstraZeneca's approach to Immuno-Oncology (IO)
Immuno-Oncology (IO) is a therapeutic approach designed to stimulate the body's immune system to attack tumors. At AstraZeneca and MedImmune, our biologics research and development arm, our IO portfolio is anchored by immunotherapies that have been designed to overcome anti-tumor immune suppression. We believe that IO-based therapies will offer the potential for life-changing cancer treatments for the vast majority of patients.

We are pursuing a comprehensive clinical trial program that includes durvalumab (anti-PD-L1) as monotherapy and in combination with tremelimumab (anti-CTLA-4) in multiple tumor types, stages of disease, and lines of therapy, using the PD-L1 biomarker as a decision-making tool to define the best potential treatment path for a patient. In addition, the ability to combine our IO portfolio with small, targeted molecules from across our oncology pipeline, and with those of our research partners, may provide new treatment options across a broad range of tumors.

About AstraZeneca in Oncology
AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With at least six new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advance New Oncology as one of AstraZeneca's five Growth Platforms focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy as illustrated by our majority investment in Acerta Pharma in hematology.

By harnessing the power of four scientific platforms – Immuno-Oncology, Tumor Drivers and Resistance, DNA Damage Response and Antibody Drug Conjugates – and by championing the development of personalized combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

About MedImmune
MedImmune is the global biologics research and development arm of AstraZeneca, a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialization of small molecule and biologic prescription medicines. MedImmune is pioneering innovative research and exploring novel pathways across Oncology; Respiratory, Cardiovascular & Metabolic Diseases; and Infection and Vaccines. The MedImmune headquarters is located in Gaithersburg, Md., one of AstraZeneca's three global R&D centers, with additional sites in Cambridge, UK, and Mountain View, Ca. For more information, please visit www.medimmune.com.

About AstraZeneca
AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines, primarily for the treatment of diseases in three main therapy areas – Oncology, Cardiovascular & Metabolic Diseases and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. AstraZeneca operates in over 100 countries and

its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca-us.com and follow us on Twitter @AstraZenecaUS.

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