Today has marked a significant paradigm shift in the way we think about Stage III non-small cell lung cancer (NSCLC). AstraZeneca presented the results from the Phase III PACIFIC clinical trial at the World Conference on Lung Cancer, showing that IMFINZI® (durvalumab) reduced the risk of death by 32% compared to placebo (HR 0.68, 99.73% CI 0.47-0.997; p=0.0025) in patients with unresectable Stage III NSCLC whose disease had not progressed following concurrent platinum-based chemotherapy and radiation therapy (CRT). This was a first planned analysis of overall survival; the study is still ongoing. Updated data from the PACIFIC trial demonstrated that IMFINZI improved progression-free survival (PFS) by 11.6 months versus placebo (17.2 months for IMFINZI arm [n=476; 95% CI 13.1-23.9] vs 5.6 months for placebo arm [n=237; 95% CI 4.6-7.7]; HR 0.51; 95% CI 0.41-0.63).

Please find the press release pasted below and linked here.

IMFINZI is the first and only approved medicine to demonstrate survival benefit in this setting – marking a significant change in the treatment paradigm. The results strongly support IMFINZI as a standard of care for patients with unresectable Stage III NSCLC whose disease has not progressed following CRT. These results bring new hope to patients in a setting where there has been limited advancements for patients in over a decade.

We recognize that your partnership is critical to communicating this hopeful news to the cancer community by bridging the knowledge gap regarding Stage III disease. There may be patient misperceptions regarding the difference between Stage III and Stage IV NSCLC – and potentially both considered a fatal disease. However, these different stages of disease are distinct, and correspond with different long-term survival rates. Additionally, according to a study published in 2017, 28% of patients who had unresectable Stage III NSCLC did not receive any chemotherapy or radiation. While any lung cancer diagnosis is certainly frightening, we hope that the PACIFIC data demonstrate the advancement of treatment options and shifts in the standard of care that should give patients hope.

To help facilitate the conversations with your constituents, we wanted to share the following resources, which we hope you will find helpful:

1. An overview of Stage III non-small cell lung cancer
2. An infographic explaining the stages of non-small cell lung cancer
3. A blog post explaining various clinical trial endpoints
4. An infographic outlining the role of IMFINZI in unresectable Stage III non-small cell lung cancer
5. An infographic outlining key Immuno-Oncology clinical trials in AstraZeneca's pipeline

To learn more, please visit https://www.imfinzihcp.com.

IMFINZI® (durvalumab) is the first immunotherapy to demonstrate significant overall survival benefit in unresectable, Stage III lung cancer
September 25, 2018

IMFINZI reduced the risk of death by nearly one-third compared to placebo in the Phase III PACIFIC trial

Updated data reaffirm unprecedented improvement in progression-free survival of more than 11 months

AstraZeneca and MedImmune, its global biologics research and development arm, have presented data on overall survival (OS) in the Phase III PACIFIC trial of IMFINZI® (durvalumab) during the Presidential Symposium of the IASLC 19th World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer in Toronto, Canada. Results were published simultaneously in the *New England Journal of Medicine*.

Results from the Phase III PACIFIC trial in patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease had not progressed following chemoradiation showed that IMFINZI significantly improved OS, the second primary endpoint of the trial, compared to placebo regardless of PD-L1 expression, reducing the risk of death by 32% (HR 0.68, 99.73% CI 0.47-0.997; p=0.0025). See data table below.

Sean Bohen, Executive Vice President, Global Medicines Development and Chief Medical Officer, said: “These data establish IMFINZI as the first immunotherapy to demonstrate an overall survival benefit for patients with unresectable, Stage III non-small cell lung cancer following chemoradiation therapy. Today’s announcement brings new hope to patients in a setting where survival rates have not changed in decades.”

Scott J. Antonia, MD, Ph.D., chair of the Thoracic Oncology Department at Moffitt Cancer Center in Tampa, Florida, USA and principal investigator in the PACIFIC trial said: “The five-year survival rate in this setting has historically been around 15% after concurrent chemoradiation therapy. The significant survival benefit observed using the PACIFIC regimen provides confidence and clear rationale for a new standard of care.”

Summary of primary endpoints:

	IMFINZI (n=476)	**Placebo (n=237)**
OS (primary endpoint)[1]		
Number of deaths (%)	183 (38.4%)	116 (48.9%)
Hazard ratio (99.73% CI)[2,3]	0.68 (0.47, 0.997)	
p-value[2-4]	0.0025	
Median in months (95% CI)	NR[5] (34.7, NR)	28.7 (22.9, NR)
PFS (primary endpoint)[1,6]		
Number (%) of patients with event	243 (51.1%)	173 (73.0%)
Hazard ratio (95% CI)[2,7]	0.51 (0.41, 0.63)	
Median in months (95% CI)	17.2 (13.1, 23.9)	5.6 (4.6, 7.7)

[1]The data cut-off date for first-planned OS analysis and updated PFS analysis was March 22, 2018.

[2]Stratified by sex, age, and smoking history.
[3]Confidence interval adjusted for interim analysis.
[4]Criteria for statistical significance at the interim analysis of OS was a p-value ≤ 0.00274 for OS (using Lan DeMets spending function approximating O'Brien Fleming boundary).
[5]Not Reached (NR).
[6]Assessed by Blinded Independent Central Review (BICR) according to RECIST v1.1.
[7]No formal statistical comparison was made because the study had achieved significance for PFS at the first planned interim analysis (data cutoff of Feb 13, 2017).

The safety and tolerability profile for IMFINZI was consistent with that reported at the time of the previous progression-free survival (PFS) analysis. IMFINZI can cause serious, potentially fatal adverse reactions. In the updated analysis, the most common adverse reactions (greater than or equal to 20% of patients) among patients on IMFINZI versus placebo were cough (35.2% vs 25.2%), fatigue (24.0% vs 20.5%), dyspnea (22.3% vs 23.9%) and radiation pneumonitis (20.2% vs 15.8%). 30.5% of patients experienced a grade 3 or 4 adverse event (AE) with IMFINZI vs 26.1% with placebo, and 15.4% of patients discontinued treatment due to AEs with IMFINZI vs 9.8% of patients on placebo.

IMFINZI is currently approved in the US for the treatment of patients with unresectable Stage III NSCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy, based on the PACIFIC trial. It is also approved in the EU, Canada, Switzerland, India, Japan and Brazil. Other global health authority reviews and submissions are ongoing.

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab).

IMFINZI can cause serious, potentially fatal adverse reactions including immune-mediated pneumonitis, hepatitis, colitis or diarrhea, endocrinopathies, nephritis, rash or dermatitis, other immune-mediated adverse reactions, infection, and infusion-related reactions. Please refer to the full Prescribing Information for important dosage modification and management information specific to adverse reactions.

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis, defined as requiring use of corticosteroids. Fatal cases have been reported. Monitor patients for signs and symptoms of pneumonitis and evaluate with radiographic imaging when suspected. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold IMFINZI for Grade 2 pneumonitis; permanently discontinue for Grade 3 or 4 pneumonitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, pneumonitis occurred in 5% of patients, including Grade 3 (0.8%), Grade 4 (<0.1%), and Grade 5 (0.3%) pneumonitis. Pneumonitis led to discontinuation of IMFINZI in 1.5% of the 1889 patients. In the PACIFIC study, the incidence of pneumonitis (including radiation pneumonitis) was 34%, including Grade 3 (3.4%) and Grade 5 (1.1%) pneumonitis in the

IMFINZI arm. In the PACIFIC study, pneumonitis led to discontinuation of IMFINZI in 6% of patients.

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis, defined as requiring use of corticosteroids. Fatal cases have been reported. Monitor patients for signs and symptoms of hepatitis during and after discontinuation of IMFINZI, including clinical chemistry monitoring. Administer corticosteroids for Grade 2 or higher elevations of ALT, AST, and/or total bilirubin. Withhold IMFINZI for ALT or AST greater than 3 but less than or equal to 8 times the ULN or total bilirubin greater than 1.5 but less than or equal to 5 times the ULN; permanently discontinue IMFINZI for ALT or AST greater than 8 times the ULN or total bilirubin greater than 5 times the ULN or concurrent ALT or AST greater than 3 times the ULN and total bilirubin greater than 2 times the ULN with no other cause.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hepatitis occurred in 12% of patients, including Grade 3 (4.4%), Grade 4 (0.4%), and Grade 5 (0.2%) hepatitis. Hepatitis led to discontinuation of IMFINZI in 0.7% of the 1889 patients.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis, defined as requiring use of corticosteroids. Administer corticosteroids for Grade 2 or greater colitis or diarrhea. Withhold IMFINZI for Grade 2 colitis or diarrhea; permanently discontinue for Grade 3 or 4 colitis or diarrhea.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, colitis or diarrhea occurred in 18% of patients, including Grade 3 (1.0%) and Grade 4 (0.1%) colitis. Diarrhea or colitis led to discontinuation of IMFINZI in 0.4% of the 1889 patients.

Immune-Mediated Endocrinopathies

IMFINZI can cause immune-mediated endocrinopathies, including thyroid disorders, adrenal insufficiency, type 1 diabetes mellitus, and hypophysitis/hypopituitarism. Monitor patients for clinical signs and symptoms of endocrinopathies.

- **Thyroid disorders**—Monitor thyroid function prior to and periodically during treatment. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated. Withhold IMFINZI for Grades 2–4 hyperthyroidism, until clinically stable. Continue IMFINZI for hypothyroidism. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hypothyroidism occurred in 11% of patients, while hyperthyroidism occurred in 7% of patients. Thyroiditis occurred in 0.9% of patients, including Grade 3 (<0.1%). Hypothyroidism was preceded by thyroiditis or hyperthyroidism in 25% of patients.
- **Adrenal insufficiency**—Administer corticosteroids as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher adrenal insufficiency. In clinical studies enrolling 1889 patients with various cancers

who received IMFINZI, adrenal insufficiency occurred in 0.7% of patients, including Grade 3 (<0.1%) adrenal insufficiency.

- **Type 1 diabetes mellitus**—Initiate treatment with insulin as clinically indicated. Withhold IMFINZI for Grades 2–4 type 1 diabetes mellitus, until clinically stable. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, type 1 diabetes mellitus occurred in <0.1% of patients.
- **Hypophysitis**—Administer corticosteroids and hormone replacement as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher hypophysitis. Hypopituitarism leading to adrenal insufficiency and diabetes insipidus occurred in <0.1% of 1889 patients with various cancers who received IMFINZI.

Immune-Mediated Nephritis

IMFINZI can cause immune-mediated nephritis, defined as evidence of renal dysfunction requiring use of corticosteroids. Fatal cases have occurred. Monitor patients for abnormal renal function tests prior to and periodically during treatment with IMFINZI. Administer corticosteroids as clinically indicated. Withhold IMFINZI for creatinine greater than 1.5 to 3 times the ULN; permanently discontinue IMFINZI and administer corticosteroids in patients with creatinine greater than 3 times the ULN.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, nephritis (reported as any of the following: increased creatinine or urea, acute kidney injury, renal failure, decreased glomerular filtration rate, tubulointerstitial nephritis, decreased creatinine clearance, glomerulonephritis, and nephritis) occurred in 6.3% of the patients including Grade 3 (1.1%), Grade 4 (0.2%), and Grade 5 (0.1%) nephritis. IMFINZI was discontinued in 0.3% of the 1889 patients.

Immune-Mediated Dermatologic Reactions

IMFINZI can cause immune-mediated rash. Bullous dermatitis and Stevens Johnson Syndrome (SJS)/toxic epidermal necrolysis (TEN) have occurred with other products in this class. Administer corticosteroids for Grade 2 rash or dermatitis lasting for more than 1 week or for Grade 3 or 4 rash or dermatitis. Withhold IMFINZI for Grade 2 rash or dermatitis lasting longer than 1 week or Grade 3 rash or dermatitis; permanently discontinue IMFINZI in patients with Grade 4 rash or dermatitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, 26% of patients developed rash or dermatitis and 0.4% of the patients developed vitiligo. Rash or dermatitis led to discontinuation of IMFINZI in 0.1% of the 1889 patients.

Other Immune-Mediated Adverse Reactions

IMFINZI can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system. While immune-mediated reactions usually manifest during treatment with IMFINZI, immune-mediated adverse reactions can also manifest after discontinuation of IMFINZI. For suspected immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. Withhold

IMFINZI for Grade 3 immune-mediated adverse reactions, unless clinical judgment indicates discontinuation; permanently discontinue IMFINZI for Grade 4 adverse reactions.

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in 1889 patients who received IMFINZI: aseptic meningitis, hemolytic anemia, immune thrombocytopenic purpura, myocarditis, myositis, and ocular inflammatory toxicity, including uveitis and keratitis. Additional clinically significant immune-mediated adverse reactions have been seen with other products in this class (see Warnings and Precautions Section 5.7 of IMFINZI full Prescribing Information).

Infection

IMFINZI can cause serious infections, including fatal cases. Monitor patients for signs and symptoms of infection and treat as clinically indicated. Withhold IMFINZI for Grade 3 or 4 infection, until clinically stable.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infections occurred in 43% of patients, including Grade 3 (8%), Grade 4 (1.9%), and Grade 5 (1.0%). In patients with Stage III NSCLC in the PACIFIC study, the most common Grade 3 or higher infection was pneumonia, which occurred in 5% of patients.

Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions. Monitor patients for signs and symptoms of an infusion-related reaction. Interrupt or slow the rate of infusion for Grades 1–2 infusion-related reactions; permanently discontinue for Grades 3–4 infusion-related reactions.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infusion-related reactions occurred in 2.2% of patients, including Grade 3 (0.3%).

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.

Lactation

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 women not to breastfeed during treatment and for at least 3 months after the last dose.

Most Common Adverse Reactions

- In patients with Stage III NSCLC in the PACIFIC study (IMFINZI n=475), the most common adverse reactions (≥20% of patients) were cough (40%),

fatigue (34%), pneumonitis or radiation pneumonitis (34%), upper respiratory tract infections (26%), dyspnea (25%), and rash (23%). The most common Grade 3 or 4 adverse reaction (≥3%) was pneumonia (7%).
- In patients with Stage III NSCLC in the PACIFIC study (IMFINZI n=475), discontinuation due to adverse reactions occurred in 15% of patients in the IMFINZI arm. Serious adverse reactions occurred in 29% of patients receiving IMFINZI. The most frequent serious adverse reactions (≥2% of patients) were pneumonitis or radiation pneumonitis (7%) and pneumonia (6%). Fatal pneumonitis or radiation pneumonitis and fatal pneumonia occurred in <2% of patients and were similar across arms.

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

Indication

IMFINZI is indicated for the treatment of patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Please see complete Prescribing Information, including Medication Guide.

NOTES TO EDITORS

About Stage III NSCLC
Stage III (locally advanced) non-small cell lung cancer (NSCLC) is commonly divided into three sub-categories (IIIA, IIIB and IIIC), defined by how much the cancer has spread locally and the possibility of surgery. Stage III disease is different from Stage IV disease, when the cancer has spread (metastasized) to distant organs, as Stage III is currently treated with curative intent.

Approximately one in four patients with NSCLC in the United States present with Stage III disease, which is estimated to affect over 43,000 patients. The majority of Stage III NSCLC patients are determined to have unresectable tumors. Until recently, the standard of care beyond CRT was active surveillance to monitor for progression as there had been no FDA approved treatments following CRT.

About PACIFIC
The PACIFIC trial is a Phase III, randomized, double-blinded, placebo-controlled, multi-center trial of IMFINZI® (durvalumab) as treatment in ”all-comer” patients (i.e. regardless of PD-L1 status) with unresectable Stage III NSCLC whose disease has not progressed following platinum-based chemotherapy concurrent with radiation therapy (CRT).

The trial is being conducted in 235 centers across 26 countries involving 713 patients. The primary endpoints of the trial are progression-free survival (PFS) and overall survival (OS), and secondary endpoints include landmark PFS and OS, overall response rate (ORR) and duration of response (DoR).

About IMFINZI® (durvalumab)
IMFINZI® (durvalumab) is a human monoclonal antibody that binds to PD-L1 and blocks the

interaction of PD-L1 with PD-1 and CD80, countering the tumor's immune-evading tactics and releasing the inhibition of immune responses.

IMFINZI is approved for unresectable Stage III NSCLC in the US, EU, Canada, Switzerland, India, Japan, and Brazil based on the Phase III PACIFIC trial.

As part of a broad development program, IMFINZI is also being tested as a monotherapy and in combination with chemotherapy, radiation therapy, small molecules and tremelimumab, an investigational anti-CTLA4 monoclonal antibody, as a first- or second-line treatment for patients with NSCLC, small cell lung cancer, locally advanced or metastatic urothelial carcinoma, head and neck cancer and other solid tumors.

About AstraZeneca Support Programs
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 affordability and reimbursement programs, such as Access 360™.

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. Find out more about Lighthouse at LighthouseProgram.com or call 1-855-LHOUSE1 (1-855-546-8731).

About AstraZeneca in Lung Cancer
Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-quarter of all cancer deaths in the US.

AstraZeneca has a comprehensive portfolio of approved and investigational medicines in late-stage clinical development for the treatment of different forms of lung cancer across all stages of disease and lines of therapy. We aim to address the unmet needs of patients with EGFR-mutated tumors as a genetic driver of disease, which occur in approximately 7-23% of patients in Western populations, and 30-50% of patients in Asia, with our other approved medicines and ongoing FLAURA, ADAURA and LAURA Phase III trials. Our extensive late-stage Immuno-Oncology program focuses on 75-80% of patients with lung cancer without a known genetic mutation. The portfolio includes IMFINZI, an anti-PD-L1 antibody, which is in development as monotherapy (ADJUVANT BR.31, PACIFIC2, MYSTIC and PEARL Phase III trials) and in combination with tremelimumab and/or chemotherapy (MYSTIC, NEPTUNE, POSEIDON and CASPIAN Phase III trials).

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 clear 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 advancing Oncology as a growth driver for AstraZeneca, 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 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, Renal & 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 therapy areas – Oncology, Cardiovascular, Renal & Metabolism and Respiratory. 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.