News Release

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Imfinzi-based treatment before and after surgery reduced the risk of disease recurrence, progression events or death by 32% in resectable non-small cell lung cancer in the AEGEAN Phase III trial

Results presented at AACR 2023 found that four times as many patients treated with Imfinzi plus chemotherapy before surgery achieved pathologic complete response versus those treated with neoadjuvant chemotherapy alone

Positive results from the AEGEAN Phase III trial showed that treatment with AstraZeneca's *Imfinzi* (durvalumab) in combination with neoadjuvant chemotherapy before surgery and as adjuvant monotherapy after surgery led to a statistically significant and clinically meaningful improvement in event-free survival (EFS) versus neoadjuvant chemotherapy alone followed by surgery for patients with resectable early-stage (IIA-IIIB) non-small cell lung cancer (NSCLC).

The combination of *Imfinzi* and neoadjuvant chemotherapy also demonstrated a statistically significant and meaningful improvement in pathologic complete response (pCR), a dual primary endpoint, compared to neoadjuvant chemotherapy alone, at a previously reported interim analysis. The final analysis was consistent with these previously announced positive results.

Results will be presented today in a plenary session at the American Association for Cancer Research (AACR) Annual Meeting in Orlando, Florida (abstract #CT005).

In a planned interim analysis of EFS, patients treated with the *Imfinzi*-based regimen before and after surgery showed a 32% reduction in the risk of recurrence, progression events or death versus chemotherapy alone (32% data maturity, EFS hazard ratio [HR] of 0.68, 95% confidence interval [CI] 0.53-0.88; p=0.003902). In a final analysis of pCR, treatment with *Imfinzi* plus neoadjuvant chemotherapy before surgery resulted in a pCR rate of 17.2% versus 4.3% for patients treated with neoadjuvant chemotherapy alone (difference in pCR 13.0%; 95% CI 8.7-17.6). The trial will continue as planned to assess key secondary endpoints including disease-free survival (DFS) and overall survival (OS).

John V. Heymach, MD, PhD, Professor and Chair Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center in Houston, Texas, said: "Too many patients with resectable non-small cell lung cancer experience disease recurrence and poor clinical outcomes today. Adding durvalumab both before and after surgery has the potential to become a backbone combination approach that may alter the course of a patient's cancer, significantly increasing the potential for cure."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "The AEGEAN trial shows this novel *Imfinzi*-based regimen meaningfully improved outcomes in resectable lung cancer, further validating the importance of moving lung cancer diagnosis and treatment to earlier stages of disease where patients have the highest potential for cure. We look forward

to discussing these data with global regulatory authorities with the goal of providing this important new treatment option to patients."

Summary of results: AEGEAN

	***Imfinzi*-based regimen (n=366)**	**Chemotherapy alone (n=374)**
pCR		
Number of patients who achieved pCR (%)	63 (17.2)	16 (4.3)
Difference in pCR rate % (95% CI)	13.0 (8.7–17.6)[a]	
p-value	p=0.000036 Assessed at IA[b]	
EFS		
Number of patients with event (%)	98 (26.8)	138 (36.9)
Median EFS (95% CI) (in months)	NR (31.9-NR) [c]	25.9 (18.9-NR)
Hazard ratio (95% CI)	0.68 (0.53-0.88)[d]	
p-value	0.003902[e]	
Data maturity	32%	

[a]CIs by stratified Miettinen and Nurminen's method.
[b]Statistical significance achieved at the interim analysis (402 pts, data cutoff, 14 Jan 2022), no testing performed at FA. The statistically significant p-value was 0.000036 based on Cochran-Mantel-Haenszel test.
[c]Kaplan-Meier method.
[d]Stratified Cox proportional hazards model.
[e]Stratified log rank test.
NR, not reached

Imfinzi was generally well tolerated and no new safety signals were observed in the neoadjuvant and adjuvant settings. Further, adding *Imfinzi* to neoadjuvant chemotherapy was consistent with the known profile for this combination and did not compromise patients' ability to complete surgery versus chemotherapy alone. Of patients treated with the *Imfinzi*-based regimen, 77.6% completed surgery compared to 76.7% of patients treated with chemotherapy alone. Grade 3/4 any-cause adverse events occurred in 42.3% of patients treated with the *Imfinzi*-based regimen versus 43.4% for chemotherapy alone.

Notes

Lung cancer

Each year, an estimated 2.2 million people are diagnosed with lung cancer globally.[1] Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-fifth of all cancer deaths.[1] Lung cancer is broadly split into NSCLC and small cell lung cancer (SCLC), with 80-85% of patients diagnosed with NSCLC.[2,3]

The majority of NSCLC patients are diagnosed with advanced disease while approximately 25-30% are diagnosed early enough to have surgery with curative intent.[4,5] Early-stage lung

cancer diagnoses are often only made when the cancer is found on imaging for an unrelated condition.[6,7]

The majority of patients with resectable disease eventually develop recurrence despite complete tumour resection and adjuvant chemotherapy.[4] Only around 56-65% of patients with Stage II disease will survive for five years.[8] This decreases to 41% for patients with Stage IIIA and 24% for patients with Stage IIIB disease, reflecting a high unmet medical need.[8]

AEGEAN

AEGEAN is a randomised, double-blind, multi-centre, placebo-controlled global Phase III trial evaluating *Imfinzi* as perioperative treatment for patients with resectable Stage IIA-IIIB (Eighth Edition AJCC Cancer Staging Manual) NSCLC, irrespective of PD-L1 expression. Perioperative therapy includes treatment before and after surgery, also known as neoadjuvant/adjuvant therapy. In the trial, 802 patients were randomised to receive a 1500mg fixed dose of *Imfinzi* plus chemotherapy or placebo plus chemotherapy every three weeks for four cycles prior to surgery, followed by *Imfinzi* or placebo every four weeks (for up to 12 cycles) after surgery. Patients with known EGFR or ALK genomic tumour aberrations were excluded from the primary efficacy analyses.

In the AEGEAN trial, the primary endpoints were pCR, defined as no viable tumour in the resection specimen (including lymph nodes) following neoadjuvant therapy, and EFS, defined as the time from randomisation to an event like tumour recurrence, progression precluding definitive surgery, or death. Key secondary endpoints were major pathologic response, defined as residual viable tumour of less than or equal to 10% in the resected primary tumour following neoadjuvant therapy, DFS, OS, safety and quality of life. The final pathologic response analyses were performed after all patients had the opportunity for surgery and pathology assessment per the trial protocol. The trial enrolled participants from 264 centres in more than 25 countries including in the US, Canada, Europe, South America and Asia.

Imfinzi

Imfinzi (durvalumab) is a human monoclonal antibody that binds to the PD-L1 protein and blocks the interaction of PD-L1 with the PD-1 and CD80 proteins, countering the tumour's immune-evading tactics and releasing the inhibition of immune responses.

Imfinzi is the only approved immunotherapy and the global standard of care in the curative-intent setting of unresectable, Stage III NSCLC in patients whose disease has not progressed after chemoradiation therapy based on the PACIFIC Phase III trial.

Imfinzi is also approved in the US, EU, Japan, China and many other countries around the world for the treatment of extensive-stage SCLC based on the CASPIAN Phase III trial. In an exploratory analysis in 2021, updated results from the CASPIAN trial showed *Imfinzi* plus chemotherapy tripled patient survival at three years versus chemotherapy alone. Additionally, *Imfinzi* is approved in combination with a short course of *Imjudo* (tremelimumab) and chemotherapy for the treatment of metastatic NSCLC in the US, EU and Japan based on the POSEIDON Phase III trial.

In addition to its indications in lung cancer, *Imfinzi* is also approved in combination with chemotherapy in locally advanced or metastatic biliary tract cancer in the US, EU, Japan and several other countries; in combination with *Imjudo* in unresectable hepatocellular carcinoma in the US, EU and Japan; and in previously treated patients with advanced bladder cancer in a small number of countries.

Since the first approval in May 2017, more than 150,000 patients have been treated with *Imfinzi*.

AstraZeneca has several ongoing registrational trials focused on testing *Imfinzi* in earlier stages of lung cancer, including in resectable NSCLC (ADJUVANT BR.31) and unresectable NSCLC (PACIFIC-2, 4, 5, 8 and 9), and in limited-stage SCLC (ADRIATIC).

As part of a broad development programme, *Imfinzi* is being tested as a single treatment and in combinations with other anti-cancer treatments for patients with SCLC, NSCLC, bladder cancer, several gastrointestinal (GI) cancers, ovarian cancer, endometrial cancer and other solid tumours.

AstraZeneca in lung cancer
AstraZeneca is working to bring patients with lung cancer closer to cure through the detection and treatment of early-stage disease, while also pushing the boundaries of science to improve outcomes in the resistant and advanced settings. By defining new therapeutic targets and investigating innovative approaches, the Company aims to match medicines to the patients who can benefit most.

The Company's comprehensive portfolio includes leading lung cancer medicines and the next wave of innovations, including *Tagrisso* (osimertinib) and *Iressa* (gefitinib); *Imfinzi* and *Imjudo*; *Enhertu* (trastuzumab deruxtecan) and datopotamab deruxtecan in collaboration with Daiichi Sankyo; *Orpathys* (savolitinib) in collaboration with HUTCHMED; as well as a pipeline of potential new medicines and combinations across diverse mechanisms of action.

AstraZeneca is a founding member of the Lung Ambition Alliance, a global coalition working to accelerate innovation and deliver meaningful improvements for people with lung cancer, including and beyond treatment.

AstraZeneca in immuno-oncology (IO)
AstraZeneca is a pioneer in introducing the concept of immunotherapy into dedicated clinical areas of high unmet medical need. The Company has a comprehensive and diverse IO portfolio and pipeline anchored in immunotherapies designed to overcome evasion of the anti-tumour immune response and stimulate the body’s immune system to attack tumours.

AstraZeneca aims to reimagine cancer care and help transform outcomes for patients with *Imfinzi* as a single treatment and in combination with *Imjudo* as well as other novel immunotherapies and modalities. The Company is also exploring next-generation immunotherapies like bispecific antibodies and therapeutics that harness different aspects of immunity to target cancer.

AstraZeneca is boldly pursuing an innovative clinical strategy to bring IO-based therapies that deliver long-term survival to new settings across a wide range of cancer types. With an extensive clinical programme, the Company also champions the use of IO treatment in earlier disease stages, where there is the greatest potential for cure.

AstraZeneca in oncology
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca
AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

Contacts
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