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This announcement contains inside information

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Datopotamab deruxtecan showed clinically meaningful overall survival improvement vs. chemotherapy in patients with advanced nonsquamous non-small cell lung cancer in TROPION-Lung01 Phase III trial

In the overall trial population, survival results numerically favoured AstraZeneca and Daiichi Sankyo's datopotamab deruxtecan but did not reach statistical significance

TROPION-Lung01 previously met the dual primary endpoint of progression-free survival in the overall trial population

Results support applications currently under review by regulatory authorities globally including in the US and EU

High-level overall survival (OS) results from the TROPION-Lung01 Phase III trial, which previously met the dual primary endpoint of progression-free survival (PFS), numerically favoured datopotamab deruxtecan (Dato-DXd) compared to docetaxel in the overall trial population of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) treated with at least one prior line of therapy. Survival results did not reach statistical significance in the overall trial population. In the prespecified subgroup of patients with nonsquamous NSCLC, datopotamab deruxtecan showed a clinically meaningful improvement in OS compared to docetaxel, the current standard-of-care chemotherapy.

The final analysis of OS builds on the positive progression-free survival (PFS) results presented at the 2023 European Society for Medical Oncology Congress which showed datopotamab deruxtecan demonstrated a statistically significant improvement in PFS in the overall trial population and a clinically meaningful PFS benefit in patients with nonsquamous NSCLC. In TROPION-Lung01, patient enrolment by tumour histology was balanced across treatment arms and consistent with real-world incidence with approximately 75% of patients having nonsquamous NSCLC.[1,2]

The safety profile of datopotamab deruxtecan in TROPION-Lung01 was consistent with the previous analysis including fewer dose reductions or discontinuations due to adverse events compared to docetaxel, and no new safety concerns identified. No new interstitial lung disease events of any grade were adjudicated as drug-related.

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "Datopotamab deruxtecan is the only investigational therapy to show a clinically meaningful survival improvement in patients with previously treated nonsquamous non-small cell lung cancer versus docetaxel, which has long been unsurpassed in this post-targeted treatment and post-immunotherapy setting. These results reinforce the potential for datopotamab deruxtecan to replace conventional chemotherapy in this late-line setting and underscore our confidence in ongoing trials evaluating this therapy in first-line lung cancer."

Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo, said: "The improvement in overall survival seen with datopotamab deruxtecan coupled with the previously reported clinically meaningful progression-free survival, more than doubling of overall response and prolonged duration of response compared to docetaxel suggest that this TROP2-directed antibody drug conjugate could potentially become an important new treatment for patients with nonsquamous non-small cell lung cancer in this advanced setting. These data will support our ongoing discussions with regulatory authorities globally to potentially bring datopotamab deruxtecan to patients as quickly as possible and mark another step forward in creating new standards of care for patients with cancer."

Datopotamab deruxtecan is a specifically engineered TROP2-directed DXd antibody drug conjugate discovered by Daiichi Sankyo and being jointly developed by AstraZeneca and Daiichi Sankyo.

The data will be presented at a forthcoming medical meeting and will support regulatory applications currently under review globally, including in the US and EU for the treatment of adult patients with locally advanced or metastatic nonsquamous NSCLC who have received prior systemic therapy.

Notes

Advanced non-small cell lung cancer

Nearly 2.5 million lung cancer cases were diagnosed globally in 2022.[3] NSCLC is the most common type of lung cancer, accounting for about 80% of cases.[4] Approximately 75% and 25% of NSCLC tumours are of nonsquamous or squamous histology, respectively.[1] While immunotherapy and targeted therapies have improved outcomes in the 1st-line setting, most patients eventually experience disease progression and receive chemotherapy.[5-7] For decades, chemotherapy has been the last treatment available for patients with advanced NSCLC, despite limited effectiveness and known side effects.[5-7]

TROP2 is a protein broadly expressed in the majority of NSCLC tumours.[8] There is currently no TROP2-directed ADC approved for the treatment of lung cancer.[9,10]

TROPION-Lung01
TROPION-Lung01 is a global, randomised, multicentre, open-label Phase III trial evaluating the efficacy and safety of datopotamab deruxtecan (6.0mg/kg) versus docetaxel (75mg/m^2) in adult patients with locally advanced or metastatic NSCLC with and without actionable genomic alterations who require systemic therapy following prior treatment. Patients with actionable genomic alterations were previously treated with platinum-based chemotherapy and an approved targeted therapy. Patients without known actionable genomic alterations were previously treated, concurrently or sequentially, with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor.

The dual primary endpoints of TROPION-Lung01 are PFS as assessed by blinded independent central review (BICR) and OS. Key secondary endpoints include investigator-assessed PFS, objective response rate, duration of response, time to response, disease control rate as assessed by both BICR and investigator, and safety.

TROPION-Lung01 enrolled approximately 600 patients in Asia, Europe, North America and South America. For more information visit ClinicalTrials.gov.

Datopotamab deruxtecan (Dato-DXd)
Datopotamab deruxtecan (Dato-DXd) is an investigational TROP2-directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, datopotamab deruxtecan is one of six DXd ADCs in the oncology pipeline of Daiichi Sankyo, and one of the most advanced programmes in AstraZeneca's ADC scientific platform. Datopotamab deruxtecan is comprised of a humanised anti-TROP2 IgG1 monoclonal antibody, developed in collaboration with Sapporo Medical University, attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

A comprehensive global clinical development programme is underway with more than 20 trials evaluating the efficacy and safety of datopotamab deruxtecan across multiple cancers, including NSCLC, triple-negative breast cancer and HR-positive, HER2-negative breast cancer.

Daiichi Sankyo collaboration
AstraZeneca and Daiichi Sankyo entered into a global collaboration to jointly develop and commercialise *Enhertu* in March 2019 and datopotamab deruxtecan in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights for each ADC. Daiichi Sankyo is responsible for the manufacturing and supply of *Enhertu* and datopotamab deruxtecan.

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* (durvalumab) and *Imjudo* (tremelimumab); *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 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 social media @AstraZeneca.

Contacts
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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