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Datroway demonstrated statistically significant and clinically meaningful improvement in overall survival as 1st-line therapy for patients with metastatic triple-negative breast cancer for whom immunotherapy was not an option in TROPION-Breast02

AstraZeneca and Daiichi Sankyo's Datroway is the first and only therapy to significantly improve overall survival vs. chemotherapy in this patient population

Datroway also demonstrated a highly statistically significant and clinically meaningful improvement in the dual primary endpoint of progression-free survival

Positive high-level results from the TROPION-Breast02 Phase III trial showed *Datroway* (datopotamab deruxtecan) demonstrated a statistically significant and clinically meaningful improvement for the dual primary endpoints of overall survival (OS) and progression-free survival (PFS) compared to investigator's choice of chemotherapy as 1st-line treatment for patients with locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC) for whom immunotherapy was not an option.

Approximately 70% of patients with metastatic TNBC are not candidates for immunotherapy, including all patients whose tumours do not express PD-L1 as well as patients with PD-L1 expressing tumours who cannot receive immunotherapy due to other factors.[1] Chemotherapy remains the 1st-line standard of care for these patients.[2]

Susan Galbraith, Executive Vice President, Oncology Haematology R&D, AstraZeneca, said: "TROPION-Breast02 is the only trial ever to show an overall survival benefit in the first-line treatment of patients with metastatic triple-negative breast cancer for whom immunotherapy is not an option. We expect today's results will mark an inflection point in the treatment of these patients who have the poorest prognosis of any type of breast cancer and urgently need better options."

Ken Takeshita, Global Head, R&D, Daiichi Sankyo, said: "*Datroway* is the first antibody drug conjugate and the only therapy to significantly improve overall survival compared to chemotherapy in patients with metastatic triple-negative breast cancer for whom immunotherapy is not an option. These landmark results from TROPION-Breast02 strengthen our confidence in our ongoing clinical development programme for *Datroway* in triple-negative breast cancer and other tumour types. We look forward to discussing these data with global regulatory authorities and to bringing *Datroway* to patients with triple-negative breast cancer as soon as possible."

The safety profile of *Datroway* was consistent with previous clinical trials of *Datroway* in breast cancer. These data will be presented at an upcoming medical meeting and shared with regulatory authorities.

Datroway is a specifically engineered TROP2-directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo and being jointly developed and commercialised by AstraZeneca and Daiichi Sankyo.

AstraZeneca and Daiichi Sankyo are evaluating *Datroway* across stages and treatment settings of TNBC in three additional Phase III trials. TROPION-Breast03 is evaluating *Datroway* with or without *Imfinzi* (durvalumab) in patients with Stage I-III TNBC with residual invasive disease after neoadjuvant systemic therapy. TROPION-Breast04 is evaluating neoadjuvant *Datroway* plus *Imfinzi* in patients with Stage II-III triple-negative or hormone receptor (HR)-low, HER2-low or -negative breast cancer. TROPION-Breast05 is evaluating 1st-line *Datroway* with or without *Imfinzi* in patients with metastatic TNBC whose tumours express PD-L1.

Notes

Triple-negative breast cancer
TNBC accounts for approximately 15% of all breast cancer cases, with an estimated 345,000 diagnoses globally each year.[3,4] TNBC is diagnosed more frequently in younger and premenopausal women, and is more prevalent in Black and Hispanic women.[5-7] Metastatic TNBC is the most aggressive type of breast cancer and has the worst prognosis, with median overall survival of just 12 to 18 months and only about 14% of patients living five years following diagnosis.[5,8,9]

While some breast cancers may test positive for oestrogen receptors, progesterone receptors or overexpression of HER2, TNBC tests negative for all three.[5] Due to its aggressive nature and absence of common breast cancer receptors, TNBC is characteristically difficult to treat.[5] For patients with metastatic disease with PD-L1 expressing tumours, the addition of immunotherapy to chemotherapy has improved outcomes in the 1st-line setting.[10,11] However, for the approximately 70% of patients with metastatic TNBC who are not candidates for immunotherapy, chemotherapy remains the 1st-line standard of care.[1,2]

TROP2 is a protein broadly expressed in several solid tumours including TNBC.[12] TROP2 is associated with increased tumour progression and poor survival in patients with breast cancer.[13,14]

TROPION-Breast02

TROPION-Breast02 is a global, multicentre, randomised, open-label Phase III trial evaluating the efficacy and safety of *Datroway* versus investigator's choice of chemotherapy (paclitaxel, nab-paclitaxel, capecitabine, carboplatin or eribulin) in patients with previously untreated locally recurrent inoperable or metastatic TNBC for whom immunotherapy was not an option. This included patients whose tumours did not express PD-L1 as well as patients with PD-L1 expressing tumours who could not receive immunotherapy due to prior exposure in early-stage disease, comorbidities or immunotherapy not being accessible in their geography. Enrolment included patients with de novo or recurrent disease, regardless of disease-free interval, and those with poor prognostic factors such as brain metastases.

The dual primary endpoints of TROPION-Breast02 are PFS as assessed by blinded independent central review and

OS. Key secondary endpoints include PFS as assessed by investigator, objective response rate, duration of response, disease control rate, pharmacokinetics and safety.

TROPION-Breast02 enrolled 644 patients at sites in Africa, Asia, Europe, North America and South America. For more information, visit ClinicalTrials.gov.

Datroway
Datroway (datopotamab deruxtecan; datopotamab deruxtecan-dlnk in the US only) is a TROP2-directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, *Datroway* 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. *Datroway* 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.

Datroway is approved in more than 35 countries/regions worldwide for the treatment of adult patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease based on results from the TROPION-Breast01 trial.

Datroway is available in the US under accelerated approval for the treatment of adult patients with locally advanced or metastatic *EGFR*-mutated non-small cell lung cancer (NSCLC) who have received prior *EGFR*-directed therapy and platinum-based chemotherapy based on results from the TROPION-Lung05 and TROPION-Lung01 trials. Continued approval for this indication in the US may be contingent upon verification and description of clinical benefit in a confirmatory trial. *Datroway* is approved in Russia for the same population.

***Datroway* clinical development programme**
A comprehensive global clinical development programme is underway with more than 20 trials evaluating the efficacy and safety of *Datroway* across multiple cancers, including NSCLC, TNBC and urothelial cancer. The programme includes eight Phase III trials in lung cancer and five Phase III trials in breast cancer evaluating *Datroway* as a monotherapy and in combination with other anticancer treatments in various settings.

Daiichi Sankyo collaboration
AstraZeneca and Daiichi Sankyo entered into a global collaboration to jointly develop and commercialise *Enhertu* in March 2019 and *Datroway* 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 *Datroway*.

AstraZeneca in breast cancer
Driven by a growing understanding of breast cancer biology, AstraZeneca is challenging, and redefining, the current clinical paradigm for how breast cancer is classified and treated to deliver even more effective treatments to patients in need - with the bold ambition to one day eliminate breast cancer as a cause of death.

AstraZeneca has a comprehensive portfolio of approved and promising compounds in development that leverage different mechanisms of action to address the biologically diverse breast cancer tumour environment.

With *Enhertu*, AstraZeneca and Daiichi Sankyo are aiming to improve outcomes in previously treated HER2-positive, HER2-low and HER2-ultralow metastatic breast cancer, and are exploring its potential in earlier lines of treatment and in new breast cancer settings.

In HR-positive breast cancer, AstraZeneca continues to improve outcomes with foundational medicines *Faslodex* (fulvestrant) and *Zoladex* (goserelin) and aims to reshape the HR-positive space with first-in-class AKT inhibitor, *Truqap* (capivasertib), the TROP2-directed ADC, *Datroway*, and next-generation oral SERD and potential new medicine camizestrant.

PARP inhibitor *Lynparza* (olaparib) is a targeted treatment option that has been studied in early and metastatic breast cancer patients with an inherited BRCA mutation. AstraZeneca with MSD (Merck & Co., Inc. in the US and Canada) continue to research *Lynparza* in these settings. AstraZeneca is also exploring the potential of saruparib, a potent and selective inhibitor of PARP1, in combination with camizestrant in BRCA-mutated, HR-positive, HER2-negative advanced breast cancer.

To bring much-needed treatment options to patients with triple-negative breast cancer, an aggressive form of breast cancer, AstraZeneca is collaborating with Daiichi Sankyo to evaluate the potential of *Datroway* alone and in combination with immunotherapy *Imfinzi*.

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's innovative medicines are sold in more than 125 countries and 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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Matthew Bowden
Company Secretary
AstraZeneca PLC

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