

## Press Release

# New Research Data Across DXd ADC Portfolio at WCLC Showcases Daiichi Sankyo's Continued Commitment in Lung Cancer

- Interim DESTINY-Lung01 research data from the HER2 overexpressing metastatic non-small cell lung cancer (NSCLC) cohort of ENHERTU® will be featured as late-breaker presentation
- Updated TROPION-PanTumor01 results of datopotamab deruxtecan in patients with advanced NSCLC to be highlighted
- Biomarker analysis from phase 1 trial of patritumab deruxtecan in patients with previously treated metastatic or locally advanced EGFR mutated NSCLC to be presented

**Munich and Basking Ridge, NJ – (January 13, 2021)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that it will present new research data across its DXd ADC portfolio including ENHERTU® (trastuzumab deruxtecan), datopotamab deruxtecan (Dato-DXd; DS-1062) and patritumab deruxtecan (HER3-DXd) at the 2020 World Conference on Lung Cancer (#WCLC20) virtual conference to be held January 28-31, 2021.

Interim results from the pivotal phase 2 [DESTINY-Lung01](#) trial of ENHERTU, a HER2 directed ADC, from the HER2 overexpressing metastatic NSCLC cohort will be featured as a late-breaking oral presentation. Encore results from the HER2 mutant metastatic NSCLC cohort of DESTINY-Lung01, which were previously [presented](#) at the 2020 American Society of Clinical Oncology (ASCO) virtual meeting, will also be presented.

Updated research data from the NSCLC cohort of the [TROPION-PanTumor01](#) study of datopotamab deruxtecan, a TROP2 directed ADC, will be presented, highlighting data that includes additional patients in both the dose escalation and dose expansion parts of the study. A new biomarker analysis from an ongoing [phase 1 study](#) of patritumab deruxtecan, a HER3 directed ADC, will provide initial observations of HER3 expression and its association with prior treatment in patients with previously treated metastatic or locally advanced epidermal growth factor receptor-mutated (EGFR mutated) NSCLC. Encore clinical results from the phase 1 study, which were previously [presented](#) at the 2020 European Society of Clinical Oncology (ESMO) virtual meeting, will also be presented.

“We look forward to presenting new research data from our DXd ADC portfolio, which offer an updated view into the clinical activity of these potential medicines for patients with various types of advanced or metastatic non-small cell lung cancer,” said Antoine Yver, MD, MSc, EVP and Global Head, Oncology Research and Development, Daiichi Sankyo. “These clinical and translational findings further expand our understanding of

the activity and inform clinical development of our DXd ADCs and showcase our commitment to develop durable treatment options for patients with cancer.”

Trial-in-progress updates from the [phase 1b study](#) of ENHERTU in combination with pembrolizumab, [HERTHENA-Lung01](#), a phase 2 study of patritumab deruxtecan in patients with previously treated metastatic or locally advanced EGFR mutated NSCLC, and a [phase 1 study](#) of patritumab deruxtecan in combination with osimertinib in patients with locally advanced or metastatic EGFR mutant NSCLC will also be presented.

Following is an overview of research data from Daiichi Sankyo’s DXd ADC portfolio to be presented at WCLC:

WCLC Abstract	Presentation Details
<b>ENHERTU (HER2 ADC)</b>	
Trastuzumab deruxtecan in HER2 overexpressing metastatic non-small cell lung cancer: interim results of DESTINY-Lung01	Oral Presentation (OA04.05) Nakagawa, et al. New Data from Rare EGFR Alterations; Friday, January 29, 2021 at 11:45 a.m. SGT/Thursday, January 28, 2021 at 10:45 p.m. EST
Trastuzumab deruxtecan in HER2 mutated metastatic non-small cell lung cancer; interim results of DESTINY-Lung01 (ENCORE)	Mini-Oral Presentation (MA11.03) Smit, et al. Expanding Targetable Genetic Alterations in NSCLC; Sunday, January 31, 2021 at 2:15 p.m. SGT/1:15 a.m. EST
Trastuzumab deruxtecan plus pembrolizumab in advanced/metastatic breast or non-small cell lung cancer: a phase 1b study (TiP ENCORE)	Poster Presentation (P01.02) Borghaei, et al. Antibody Drug Conjugates, Novel Therapeutics and Cytotoxics; Thursday, January 28, 2021; available virtually
<b>Datopotamab Deruxtecan (TROP2 ADC)</b>	
Updated results from the phase 1 study of DS-1062, a TROP2 antibody drug conjugate (ADC), in patients with non-small cell lung cancer (NSCLC)	Oral Presentation (OA03.03) Spira, et al. Promising Antibody Drug Conjugate and Cytotoxic Therapy in NSCLC; Friday, January 29, 2021 at 10:30 a.m. SGT/Thursday, January 28, 2021 at 9:30 p.m. EST
<b>Patritumab Deruxtecan (HER3 ADC)</b>	
Efficacy and safety of patritumab deruxtecan (HER3-DXd; U3-1402) in patients (Pts) with EGFR-mutant (EGFRm) NSCLC (ENCORE)	Oral Presentation (OA03.04) Yu, et al. Promising Antibody Drug Conjugate and Cytotoxic Therapy in NSCLC Friday, January 29, 2021 at 10:30 a.m. SGT/Thursday, January 28, 2021 at 9:30 p.m. EST
Dynamics of molecular markers in EGFR mutated NSCLC patients treated with patritumab deruxtecan (HER3-DXd; U3-1402)	Poster Presentation (P01.04) Jänne, et al. Antibody Drug Conjugates, Novel Therapeutics and Cytotoxics; Thursday, January 28, 2021; available virtually
HERTHENA-Lung01: A randomized phase 2 study of patritumab deruxtecan (HER3-DXd; U3-1402) in previously treated metastatic EGFR mutated NSCLC (TiP)	Poster Presentation (P01.01) Jänne, et al. Antibody Drug Conjugates, Novel Therapeutics and Cytotoxics; Thursday, January 28, 2021; available virtually
Phase 1 study of patritumab deruxtecan (HER3-DXd; U3-1402) in combination with osimertinib in patients with locally advanced or metastatic EGFR mutant NSCLC (TiP)	Poster Presentation (P01.03) Jänne, et al. Antibody Drug Conjugates, Novel Therapeutics and Cytotoxics; Thursday, January 28, 2021; available virtually

### **About the DXd ADC Portfolio of Daiichi Sankyo**

The DXd ADC portfolio of Daiichi Sankyo currently consists of seven antibody drug conjugates (ADCs) of which five are currently in clinical development across multiple types of cancer. These include ENHERTU (T-DXd; DS-8201), a HER2 directed ADC, and datopotamab deruxtecan (Dato-DXd; DS-1062), a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca; patritumab deruxtecan (HER3-DXd), a HER3 directed ADC; and DS-7300, a B7-H3 directed ADC; and DS-6157, a GPR20 directed ADC, which are being developed through a strategic research collaboration with Sarah Cannon Cancer Institute.

Each ADC is engineered using Daiichi Sankyo's proprietary and portable DXd ADC technology to target and deliver chemotherapy inside cancer cells that express a specific cell surface antigen. Each ADC consists of a monoclonal antibody attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a stable tetrapeptide-based cleavable linker.

### **About ENHERTU**

ENHERTU<sup>®</sup> (trastuzumab deruxtecan; fam-trastuzumab deruxtecan-nxki in the U.S. only) (5.4 mg/kg) is approved in the U.S. under accelerated approval and Japan for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting based on the results from the [DESTINY-Breast01](#) trial and has been recommended for conditional marketing authorization in the European Union as monotherapy for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received two or more prior anti-HER2 based regimens. ENHERTU is approved in the U.S. with Boxed WARNINGS for Interstitial Lung Disease and Embryo-Fetal Toxicity.

ENHERTU (6.4 mg/kg) is also approved in Japan for the treatment of patients with HER2 positive unresectable advanced or recurrent gastric cancer that has progressed after chemotherapy based on the results from the [DESTINY-Gastric01](#) trial. ENHERTU has not been approved in the EU, or countries outside of the U.S. and Japan for any indication.

### **About the ENHERTU Clinical Development Program**

A comprehensive development program is underway globally with nine pivotal trials evaluating the efficacy and safety of ENHERTU monotherapy across multiple HER2 targetable cancers including breast, gastric and lung cancers. Trials in combination with other anticancer treatments, such as immunotherapy, are also underway.

In October 2020, ENHERTU was granted Priority Review from the U.S. Food and Drug Administration (FDA) for the treatment of patients with HER2 positive metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma. In May 2020, ENHERTU received a Breakthrough Therapy Designation (BTD) and Orphan Drug Designation (ODD) for gastric cancer, including GEJ adenocarcinoma.

In May 2020, ENHERTU also received a BTD for the treatment of patients with metastatic NSCLC whose tumors have a HER2 mutation and with disease progression on or after platinum-based therapy.

ENHERTU, datopotamab deruxtecan and patritumab deruxtecan are investigational agents globally for various indications. Datopotamab deruxtecan and patritumab deruxtecan are investigational agents that have not been approved for any indication in any country. The profile of clinical safety and efficacy for datopotamab deruxtecan and patritumab deruxtecan has not been established.

### **About the Datopotamab Deruxtecan Clinical Development Program**

Datopotamab deruxtecan is currently being evaluated in a broad and comprehensive development program, including [TROPION-Lung01](#), a phase 3 study in patients with advanced or metastatic NSCLC without actionable genomic alterations, [TROPION-Lung05](#), a phase 2 study in patients with advanced or metastatic NSCLC with actionable genomic alterations previously treated with a kinase inhibitor and platinum chemotherapy, [TROPION-Lung02](#), a phase 1b study in combination with pembrolizumab in patients with advanced or metastatic NSCLC without actionable genomic alterations and previously treated with platinum-based chemotherapy with or without prior immunotherapy, [TROPION-Lung04](#), a phase 1b study in combination with durvalumab in patients with advanced or metastatic NSCLC without actionable genomic alterations and previously treated with platinum-based chemotherapy with or without prior immunotherapy, and [TROPION-PanTumor01](#), a phase 1 study in patients with advanced solid tumors that have progressed on standard treatments or for whom no standard treatment is available, which has completed enrollment of patients into a unresectable advanced NSCLC cohort and is currently enrolling patients into a triple negative breast cancer (TNBC) cohort.

### **About the Patritumab Deruxtecan Clinical Development Program**

Patritumab deruxtecan is currently being evaluated in a [phase 2 study](#) in patients with advanced or metastatic colorectal cancer who are resistant, refractory, or intolerant to at least two prior lines of systemic therapy, a [phase 1/2 study](#) in patients with HER3 expressing metastatic breast cancer, a [phase 1 study](#) in previously treated patients with metastatic or unresectable NSCLC, and a [phase 1 study](#) in combination with osimertinib in patients with locally advanced or metastatic EGFR mutant NSCLC.

### **U.S. FDA-Approved Indication for ENHERTU**

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

**WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY**

- **Interstitial lung disease (ILD) and pneumonitis, including fatal cases, have been reported with ENHERTU. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue ENHERTU in all patients with Grade 2 or higher ILD/pneumonitis. Advise patients of the risk and to immediately report symptoms.**
- **Exposure to ENHERTU during pregnancy can cause embryo-fetal harm. Advise patients of these risks and the need for effective contraception.**

**Contraindications**

None.

**WARNINGS AND PRECAUTIONS**

**Interstitial Lung Disease / Pneumonitis**

Severe, life-threatening, or fatal interstitial lung disease (ILD), including pneumonitis, can occur in patients treated with ENHERTU. In clinical studies, of the 234 patients with unresectable or metastatic HER2-positive breast cancer treated with ENHERTU, ILD occurred in 9% of patients. Fatal outcomes due to ILD and/or pneumonitis occurred in 2.6% of patients treated with ENHERTU. Median time to first onset was 4.1 months (range: 1.2 to 8.3).

Advise patients to immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms. Monitor patients for signs and symptoms of ILD. Promptly investigate evidence of ILD. Evaluate patients with suspected ILD by radiographic imaging. Consider consultation with a pulmonologist. For asymptomatic ILD/pneumonitis (Grade 1), interrupt ENHERTU until resolved to Grade 0, then if resolved in  $\leq 28$  days from date of onset, maintain dose. If resolved in  $> 28$  days from date of onset, reduce dose one level. Consider corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g.,  $\geq 0.5$  mg/kg prednisolone or equivalent). For symptomatic ILD/pneumonitis (Grade 2 or greater), permanently discontinue ENHERTU. Promptly initiate corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g.,  $\geq 1$  mg/kg prednisolone or equivalent). Upon improvement, follow by gradual taper (e.g., 4 weeks).

**Neutropenia**

Severe neutropenia, including febrile neutropenia, can occur in patients treated with ENHERTU. Of the 234 patients with unresectable or metastatic HER2-positive breast cancer who received ENHERTU, a decrease in neutrophil count was reported in 30% of patients and 16% had Grade 3 or 4 events. Median time to first onset was 1.4 months (range: 0.3 to 18.2). Febrile neutropenia was reported in 1.7% of patients.

Monitor complete blood counts prior to initiation of ENHERTU and prior to each dose, and as clinically indicated. Based on the severity of neutropenia, ENHERTU may require dose interruption or reduction. For Grade 3 neutropenia (Absolute Neutrophil Count [ANC]  $< 1.0$  to  $0.5 \times 10^9/L$ ) interrupt ENHERTU until resolved to Grade 2 or less, then maintain dose. For Grade 4 neutropenia (ANC  $< 0.5 \times 10^9/L$ ) interrupt ENHERTU until resolved to Grade 2 or less. Reduce dose by one level. For febrile neutropenia (ANC  $< 1.0 \times$

10<sup>9</sup>/L and temperature >38.3°C or a sustained temperature of ≥38°C for more than 1 hour), interrupt ENHERTU until resolved. Reduce dose by one level.

### **Left Ventricular Dysfunction**

Patients treated with ENHERTU may be at increased risk of developing left ventricular dysfunction. Left ventricular ejection fraction (LVEF) decrease has been observed with anti-HER2 therapies, including ENHERTU. In the 234 patients with unresectable or metastatic HER2-positive breast cancer who received ENHERTU, two cases (0.9%) of asymptomatic LVEF decrease were reported. Treatment with ENHERTU has not been studied in patients with a history of clinically significant cardiac disease or LVEF <50% prior to initiation of treatment.

Assess LVEF prior to initiation of ENHERTU and at regular intervals during treatment as clinically indicated. Manage LVEF decrease through treatment interruption. Permanently discontinue ENHERTU if LVEF of <40% or absolute decrease from baseline of >20% is confirmed. When LVEF is >45% and absolute decrease from baseline is 10-20%, continue treatment with ENHERTU. When LVEF is 40-45% and absolute decrease from baseline is <10%, continue treatment with ENHERTU and repeat LVEF assessment within 3 weeks. When LVEF is 40-45% and absolute decrease from baseline is 10-20%, interrupt ENHERTU and repeat LVEF assessment within 3 weeks. If LVEF has not recovered to within 10% from baseline, permanently discontinue ENHERTU. If LVEF recovers to within 10% from baseline, resume treatment with ENHERTU at the same dose. When LVEF is <40% or absolute decrease from baseline is >20%, interrupt ENHERTU and repeat LVEF assessment within 3 weeks. If LVEF of <40% or absolute decrease from baseline of >20% is confirmed, permanently discontinue ENHERTU. Permanently discontinue ENHERTU in patients with symptomatic congestive heart failure.

### **Embryo-Fetal Toxicity**

ENHERTU can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risks to a fetus. Verify the pregnancy status of females of reproductive potential prior to the initiation of ENHERTU. Advise females of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose of ENHERTU. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for at least 4 months after the last dose of ENHERTU.

### **Adverse Reactions**

The safety of ENHERTU was evaluated in a pooled analysis of 234 patients with unresectable or metastatic HER2-positive breast cancer who received at least one dose of ENHERTU 5.4 mg/kg in DESTINY-Breast01 and Study DS8201-A-J101. ENHERTU was administered by intravenous infusion once every three weeks. The median duration of treatment was 7 months (range: 0.7 to 31).

Serious adverse reactions occurred in 20% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were interstitial lung disease, pneumonia, vomiting, nausea, cellulitis, hypokalemia, and intestinal obstruction. Fatalities due to adverse reactions occurred in 4.3% of patients including interstitial lung disease (2.6%), and the following events occurred in one patient each (0.4%): acute hepatic failure/acute kidney injury, general physical health deterioration, pneumonia, and hemorrhagic shock.

ENHERTU was permanently discontinued in 9% of patients, of which ILD accounted for 6%. Dose interruptions due to adverse reactions occurred in 33% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were neutropenia, anemia, thrombocytopenia, leukopenia, upper respiratory tract infection, fatigue, nausea, and ILD. Dose reductions occurred in 18% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were fatigue, nausea, and neutropenia.

The most common adverse reactions (frequency  $\geq 20\%$ ) were nausea (79%), fatigue (59%), vomiting (47%), alopecia (46%), constipation (35%), decreased appetite (32%), anemia (31%), neutropenia (29%), diarrhea (29%), leukopenia (22%), cough (20%), and thrombocytopenia (20%).

### Use in Specific Populations

- **Pregnancy:** ENHERTU can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risks to a fetus. There are clinical considerations if ENHERTU is used in pregnant women, or if a patient becomes pregnant within 7 months following the last dose of ENHERTU.
- **Lactation:** There are no data regarding the presence of ENHERTU in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with ENHERTU and for 7 months after the last dose.
- **Females and Males of Reproductive Potential:** Pregnancy testing: Verify pregnancy status of females of reproductive potential prior to initiation of ENHERTU. Contraception: *Females:* ENHERTU can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with ENHERTU and for at least 7 months following the last dose. *Males:* Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for at least 4 months following the last dose. Infertility: ENHERTU may impair male reproductive function and fertility.
- **Pediatric Use:** Safety and effectiveness of ENHERTU have not been established in pediatric patients.
- **Geriatric Use:** Of the 234 patients with HER2-positive breast cancer treated with ENHERTU 5.4 mg/kg, 26% were  $\geq 65$  years and 5% were  $\geq 75$  years. No overall differences in efficacy were observed between patients  $\geq 65$  years of age compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients aged  $\geq 65$  years (53%) as compared to younger patients (42%).
- **Hepatic Impairment:** In patients with moderate hepatic impairment, due to potentially increased exposure, closely monitor for increased toxicities related to the topoisomerase inhibitor.

To report SUSPECTED ADVERSE REACTIONS, contact Daiichi Sankyo, Inc. at 1-877-437-7763 or FDA at 1-800-FDA-1088 or [fda.gov/medwatch](http://fda.gov/medwatch).

Please see accompanying full [Prescribing Information](#), including [Boxed WARNINGS](#), and [Medication Guide](#).

### About Daiichi Sankyo Cancer Enterprise

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by our DXd antibody drug conjugate (ADC) technology, our powerful research engines include biologics, medicinal chemistry, modality and other research laboratories in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. For more information, please visit:

[www.DSCancerEnterprise.com](http://www.DSCancerEnterprise.com).

### About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical therapies to improve standards of care and address diversified, unmet medical needs of people globally by leveraging our world-class science and technology. With more than 100 years of scientific expertise and a presence in more

than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for cardiovascular diseases, under the Group’s 2025 Vision to become a “Global Pharma Innovator with Competitive Advantage in Oncology,” Daiichi Sankyo is primarily focused on providing novel therapies in oncology, as well as other research areas centered around rare diseases and immune disorders. For more information, please visit: [www.daiichisankyo.com](http://www.daiichisankyo.com).

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