

## Press Release

# Daiichi Sankyo Showcases Latest Research Towards Creating New Standards of Care for Patients with Cancer with Data at ASCO and EHA

- DESTINY-PanTumor02 late-breaking interim data and DESTINY-CRC02 primary results further support potential of ENHERTU across multiple HER2 expressing cancers
- TROPION-Lung02 updated results continue to demonstrate promising clinical activity of datopotamab deruxtecan-based combinations in patients with non-small cell lung cancer
- Investor meeting to discuss ASCO presentations and oncology development updates

**Basking Ridge, NJ – (May 25, 2023)** – Daiichi Sankyo (TSE: 4568) will present new clinical research across its oncology portfolio at the 2023 American Society of Clinical Oncology Scientific Program (#ASCO23) and the European Hematology Association Congress (#EHA23).

Presentations at ASCO showcasing the company’s leadership in developing multiple innovative medicines for patients with cancer will include the [DESTINY-PanTumor02](#) late-breaking ([LBA #3000](#)) and [DESTINY-CRC02](#) oral presentations ([#3501](#)) evaluating ENHERTU® (trastuzumab deruxtecan) across multiple HER2 expressing cancers. Data from DESTINY-PanTumor02 will be featured in an ASCO press briefing.

Additional data from Daiichi Sankyo’s DXd antibody drug conjugate (ADC) portfolio at ASCO include oral presentations featuring [TROPION-Lung02](#) updated results of datopotamab deruxtecan (Dato-DXd)-based combinations in patients with advanced or metastatic non-small cell lung cancer (NSCLC) and the first results from [BRE-354](#), a collaborative trial with Sarah Cannon Research Institute, evaluating patritumab deruxtecan (HER3-DXd) in patients with metastatic breast cancer.

Two analyses from the [QuANTUM-First](#) trial evaluating the addition of quizartinib to standard induction and consolidation chemotherapy followed by continuation monotherapy for the treatment of patients with newly diagnosed *FLT3*-ITD positive acute myeloid leukemia (AML) will be highlighted at EHA.

“Our data at ASCO and EHA represent another step forward in realizing our vision to create new standards of care for patients with cancer. Data from our ENHERTU clinical development program will be presented at ASCO showcasing how this medicine potentially may change the way HER2 targetable solid tumors are treated beyond breast, gastric and lung cancer,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “New datopotamab deruxtecan-based combination data from our TROPION-Lung02 trial will be reported at ASCO

along with analyses from our QuANTUM-First trial of quizartinib in newly diagnosed acute myeloid leukemia at EHA.”

### **ENHERTU Redefining HER2 Targetable Cancers**

Data from an interim analysis of the DESTINY-PanTumor02 phase 2 trial evaluating ENHERTU in patients with pre-treated metastatic HER2 expressing solid tumors, including biliary tract, bladder, cervical, endometrial, ovarian, pancreatic and other rare cancers will be presented as a late-breaking presentation and included in an ASCO press briefing on Sunday, June 4.

In [topline results](#) from DESTINY-PanTumor02, ENHERTU demonstrated clinically meaningful and durable responses across many of these HER2 expressing cancers, potentially redefining how these tumors may be treated. The safety profile observed in the DESTINY-PanTumor02 trial was consistent with that seen in other trials of ENHERTU with no new safety signals identified.

Other ENHERTU data being presented include two oral presentations featuring the primary results from the DESTINY-CRC02 phase 2 trial evaluating ENHERTU in patients with previously treated HER2 overexpressing metastatic colorectal cancer and age-specific pooled analysis of ENHERTU from three global breast cancer trials ([DESTINY-Breast01](#), [DESTINY-Breast02](#) and [DESTINY-Breast03](#)).

### **Datopotamab Deruxtecan-Based Combinations Continuing to Show Promise in NSCLC**

Updated results from the TROPION-Lung02 phase 1b trial evaluating datopotamab deruxtecan in combination with pembrolizumab with or without platinum-based chemotherapy in patients with previously untreated or pretreated advanced or metastatic NSCLC without actionable genomic alterations will be featured in an ASCO oral presentation.

Trials-in-progress presentations also will be featured including the [TROPION-Lung04](#) phase 1b trial evaluating datopotamab deruxtecan in various immunotherapy combinations with or without carboplatin in patients with advanced or metastatic NSCLC, and the [TROPION-PanTumor03](#) phase 2 trial evaluating datopotamab deruxtecan monotherapy as well as combination therapy with other anticancer treatments (immunotherapy, PARP inhibitor, VEGF inhibitor or chemotherapy) in patients with advanced/metastatic endometrial, gastric, ovarian, colorectal and castration-resistant prostate cancer.

Daiichi Sankyo will hold a hybrid investor meeting/conference call for investors on Monday, June 5, 2023 from 7:30 to 9:00 pm CDT / Tuesday, June 6, 2023 from 9:30 to 11:00 am JST. Executives from Daiichi Sankyo will provide an overview of the ASCO research data and address questions.

Highlights of data from Daiichi Sankyo's DXd ADC portfolio at 2023 ASCO include:

Presentation Title		Author	Abstract #	Presentation
<b>ENHERTU (trastuzumab deruxtecan; T-DXd)</b>				
Pan-Tumor	Efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients with HER2 expressing solid tumors: DESTINY-PanTumor02 (DP-02) interim results	F. Meric-Bernstam	LBA 3000	Oral Presentation Monday, June 5 8:00 - 11:00 am CDT
GI	Trastuzumab deruxtecan (T-DXd) in patients with HER2 overexpressing/amplified (HER2+) metastatic colorectal cancer: primary results from the multicenter, randomized, phase 2 DESTINY-CRC02 study	K. Raghav	3501	Oral Presentation Sunday, June 4 8:00 - 11:00 am CDT
Breast	An age-specific pooled analysis of trastuzumab deruxtecan (T-DXd) in patients with HER2 positive metastatic breast cancer from DESTINY-Breast01, 02, and 03	I. Krop	1006	Oral Presentation Monday, June 5 11:30 am - 2:30 pm CDT
	Trastuzumab deruxtecan (T-DXd) versus treatment of physician's choice in patients with HER2 low, hormone receptor-positive unresectable and/or metastatic breast cancer: exploratory biomarker analysis of DESTINY-Breast04	S. Modi	1020	Poster Presentation Sunday, June 4 11:30 am - 1:00 pm CDT
	Interim real-world treatment patterns in patients with HER2+ unresectable or metastatic breast cancer: interim results from HER2 REAL Asia cohort	S. Lee	1047	Poster Presentation Sunday, June 4 8:00 - 11:00 am CDT
Lung	Analytical and clinical validation of OncoPrint Dx Target (ODxT) test and local testing for identifying patients with HER2 (ERBB2) mutant non-small cell lung cancer for treatment with trastuzumab deruxtecan (T-DXd) in DESTINY-Lung01/02 (DL-01/02)	B. Li	9033	Poster Presentation Sunday, June 4 8:00 - 11:00 am CDT
<b>Datopotamab Deruxtecan (Dato-DXd)</b>				
Lung	TROPION-Lung02: datopotamab deruxtecan (Dato-DXd) plus pembrolizumab with or without platinum chemotherapy in advanced non-small cell lung cancer	Y. Goto	9004	Oral Presentation Tuesday, June 6 9:45 am - 12:45 pm CDT
	TROPION-Lung04: phase 1b, multicenter study of datopotamab deruxtecan (Dato-DXd) in combination with immunotherapy ± carboplatin in advanced/metastatic non-small cell lung cancer	H. Borghaei	TPS3158	Poster Presentation Saturday, June 3 8:00 - 11:00 am CDT
Pan-Tumor	TROPION-PanTumor03: phase 2, multicenter study of datopotamab deruxtecan (Dato-DXd) as monotherapy and in combination with anticancer agents in patients with advanced/metastatic solid tumors	Y. Janjigian	TPS3153	Poster Presentation Saturday, June 3 8:00 - 11:00 am CDT
<b>Patritumab Deruxtecan (HER3-DXd)</b>				
Breast	A phase 2 study of HER3-DXd in patients with metastatic breast cancer	E. Hamilton	1004	Oral Presentation Monday, June 5 11:30 am - 2:30 pm CDT

### Quizartinib Analyses in Newly Diagnosed *FLT3*-ITD Positive AML

Two analyses of data from the QuANTUM-First phase 3 trial of quizartinib in combination with standard induction and consolidation chemotherapy and as continuation monotherapy in patients with newly diagnosed *FLT3*-ITD positive AML will be presented at EHA. An oral presentation will feature data reporting the impact of hematopoietic stem cell transplantation (HSCT) following first complete remission followed by up to three years of quizartinib monotherapy. An analysis of *FLT3*-ITD-specific measurable residual disease (MRD) and how it

impacted patient outcomes in QuANTUM-First will be reported in a poster presentation. The primary manuscript of the QuANTUM-First trial was recently published online in *The Lancet* along with approval received in Japan [today](#) for use in this AML patient population.

Highlights of data from Daiichi Sankyo at 2023 EHA include:

Presentation Title		Author	Abstract #	Presentation
<b>Quizartinib</b>				
AML	Impact of allogeneic hematopoietic cell transplantation in first complete remission plus FLT3 inhibition with quizartinib in acute myeloid leukemia with <i>FLT3</i> -ITD: results from QuANTUM-First	R. Schlenk	<a href="#">S137</a>	Oral Presentation Sunday, June 11 12:00 - 12:15 pm CEST
	QuANTUM-First trial: <i>FLT3</i> -ITD-specific measurable residual disease (MRD) clearance is associated with improved overall survival	M. Levis	<a href="#">P483</a>	Poster Presentation Friday, June 9 6:00 - 7:00 pm CEST

### About the DXd ADC Portfolio of Daiichi Sankyo

The DXd ADC portfolio of Daiichi Sankyo currently consists of five ADCs in clinical development across multiple types of cancer. The company’s clinical trial stage DXd ADCs include ENHERTU, a HER2 directed ADC and datopotamab deruxtecan (Dato-DXd), a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca; and patritumab deruxtecan (HER3-DXd), a HER3 directed ADC. Two additional ADCs including ifinatamab deruxtecan (I-DXd; DS-7300), a B7-H3 directed ADC, and raludotatug deruxtecan (R-DXd; DS-6000), a CDH6 directed ADC, are being developed through a strategic early-stage research collaboration with Sarah Cannon Research Institute.

Designed using Daiichi Sankyo’s proprietary DXd ADC technology to target and deliver a cytotoxic payload inside cancer cells that express a specific cell surface antigen, each ADC consists of a monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

Datopotamab deruxtecan, ifinatamab deruxtecan, patritumab deruxtecan and raludotatug deruxtecan are investigational medicines that have not been approved for any indication in any country. Safety and efficacy have not been established.

### ENHERTU U.S. Important Safety Information

#### Indications

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 a prior anti-HER2-based regimen either:
  - In the metastatic setting, or
  - In the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy
- Unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-approved test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy
- Unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy

This indication is approved under accelerated approval based on objective 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.

- Locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen

**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. A higher incidence of Grade 1 and 2 ILD/pneumonitis has been observed in patients with moderate renal impairment. 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/day prednisolone or equivalent). For symptomatic ILD/pneumonitis (Grade 2 or greater), permanently discontinue ENHERTU. Promptly initiate systemic corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g.,  $\geq 1$  mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks.

Metastatic Breast Cancer and HER2-Mutant NSCLC (5.4 mg/kg)

In patients with metastatic breast cancer and HER2-mutant NSCLC treated with ENHERTU 5.4 mg/kg, ILD occurred in 12% of patients. Fatal outcomes due to ILD and/or pneumonitis occurred in 1.0% of patients treated with ENHERTU. Median time to first onset was 5 months (range: 0.9 to 23).

#### Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, ILD occurred in 10% of patients. Median time to first onset was 2.8 months (range: 1.2 to 21).

#### **Neutropenia**

Severe neutropenia, including febrile neutropenia, can occur in patients treated with ENHERTU. Monitor complete blood counts prior to initiation of ENHERTU and prior to each dose, and as clinically indicated. 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, then reduce dose by one level. For febrile neutropenia (ANC  $<1.0 \times 10^9/L$  and temperature  $>38.3^\circ C$  or a sustained temperature of  $\geq 38^\circ C$  for more than 1 hour), interrupt ENHERTU until resolved, then reduce dose by one level.

#### Metastatic Breast Cancer and HER2-Mutant NSCLC (5.4 mg/kg)

In patients with metastatic breast cancer and HER2-mutant NSCLC treated with ENHERTU 5.4 mg/kg, a decrease in neutrophil count was reported in 65% of patients. Sixteen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 22 days (range: 2 to 664). Febrile neutropenia was reported in 1.1% of patients.

#### Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, a decrease in neutrophil count was reported in 72% of patients. Fifty-one percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 16 days (range: 4 to 187). Febrile neutropenia was reported in 4.8% of patients.

#### **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. Assess LVEF prior to initiation of ENHERTU and at regular intervals during treatment as clinically indicated. Manage LVEF decrease through treatment interruption. 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. 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.

#### Metastatic Breast Cancer and HER2-Mutant NSCLC (5.4 mg/kg)

In patients with metastatic breast cancer and HER2-mutant NSCLC treated with ENHERTU 5.4 mg/kg, LVEF decrease was reported in 3.6% of patients, of which 0.4% were Grade 3.

#### Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

In patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg, no clinical adverse events of heart failure were reported; however, on echocardiography, 8% were found to have asymptomatic Grade 2 decrease in LVEF.

#### **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 7 months after the last dose of ENHERTU. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for 4 months after the last dose of ENHERTU.

### **Additional Dose Modifications**

#### **Thrombocytopenia**

For Grade 3 thrombocytopenia (platelets  $<50$  to  $25 \times 10^9/L$ ) interrupt ENHERTU until resolved to Grade 1 or less, then maintain dose. For Grade 4 thrombocytopenia (platelets  $<25 \times 10^9/L$ ) interrupt ENHERTU until resolved to Grade 1 or less, then reduce dose by one level.

### **Adverse Reactions**

#### Metastatic Breast Cancer and HER2-Mutant NSCLC (5.4 mg/kg)

The pooled safety population reflects exposure to ENHERTU 5.4 mg/kg intravenously every 3 weeks in 984 patients in Study DS8201-A-J101 (NCT02564900), DESTINY-Breast01, DESTINY-Breast03, DESTINY-Breast04, and DESTINY-Lung02. Among these patients 65% were exposed for  $>6$  months and 39% were exposed for  $>1$  year. In this pooled safety population, the most common ( $\geq 20\%$ ) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (71%), decreased hemoglobin (66%), decreased neutrophil count (65%), decreased lymphocyte count (55%), fatigue (54%), decreased platelet count (47%), increased aspartate aminotransferase (48%), vomiting (44%), increased alanine aminotransferase (42%), alopecia (39%), increased blood alkaline phosphatase (39%), constipation (34%), musculoskeletal pain (32%), decreased appetite (32%), hypokalemia (28%), diarrhea (28%), and respiratory infection (24%).

#### HER2-Positive Metastatic Breast Cancer

##### *DESTINY-Breast03*

The safety of ENHERTU was evaluated in 257 patients with unresectable or metastatic HER2-positive breast cancer who received at least one dose of ENHERTU 5.4 mg/kg intravenously every three weeks in DESTINY-Breast03. The median duration of treatment was 14 months (range: 0.7 to 30).

Serious adverse reactions occurred in 19% of patients receiving ENHERTU. Serious adverse reactions in  $>1\%$  of patients who received ENHERTU were vomiting, interstitial lung disease, pneumonia, pyrexia, and urinary tract infection. Fatalities due to adverse reactions occurred in 0.8% of patients including COVID-19 and sudden death (one patient each).

ENHERTU was permanently discontinued in 14% of patients, of which ILD/pneumonitis accounted for 8%. Dose interruptions due to adverse reactions occurred in 44% of patients treated with ENHERTU. The most frequent adverse reactions ( $>2\%$ ) associated with dose interruption were neutropenia, leukopenia, anemia, thrombocytopenia, pneumonia, nausea, fatigue, and ILD/pneumonitis. Dose reductions occurred in 21% of patients treated with ENHERTU. The most frequent adverse reactions ( $>2\%$ ) associated with dose reduction were nausea, neutropenia, and fatigue.

The most common ( $\geq 20\%$ ) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (74%), decreased neutrophil count (70%), increased aspartate aminotransferase (67%), decreased hemoglobin (64%), decreased lymphocyte count (55%), increased alanine aminotransferase (53%), decreased platelet count (52%), fatigue (49%), vomiting (49%), increased blood alkaline phosphatase (49%), alopecia (37%), hypokalemia (35%), constipation (34%), musculoskeletal pain (31%), diarrhea (29%), decreased appetite (29%), respiratory infection (22%), headache (22%), abdominal pain (21%), increased blood bilirubin (20%), and stomatitis (20%).

#### HER2-Low Metastatic Breast Cancer

##### *DESTINY-Breast04*

The safety of ENHERTU was evaluated in 371 patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who received ENHERTU 5.4 mg/kg intravenously every 3 weeks in DESTINY-

Breast04. The median duration of treatment was 8 months (range: 0.2 to 33) for patients who received ENHERTU.

Serious adverse reactions occurred in 28% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, pneumonia, dyspnea, musculoskeletal pain, sepsis, anemia, febrile neutropenia, hypercalcemia, nausea, pyrexia, and vomiting. Fatalities due to adverse reactions occurred in 4% of patients including ILD/pneumonitis (3 patients); sepsis (2 patients); and ischemic colitis, disseminated intravascular coagulation, dyspnea, febrile neutropenia, general physical health deterioration, pleural effusion, and respiratory failure (1 patient each).

ENHERTU was permanently discontinued in 16% of patients, of which ILD/pneumonitis accounted for 8%. Dose interruptions due to adverse reactions occurred in 39% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were neutropenia, fatigue, anemia, leukopenia, COVID-19, ILD/pneumonitis, increased transaminases, and hyperbilirubinemia. Dose reductions occurred in 23% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were fatigue, nausea, thrombocytopenia, and neutropenia.

The most common ( $\geq 20\%$ ) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (70%), decreased hemoglobin (64%), decreased neutrophil count (64%), decreased lymphocyte count (55%), fatigue (54%), decreased platelet count (44%), alopecia (40%), vomiting (40%), increased aspartate aminotransferase (38%), increased alanine aminotransferase (36%), constipation (34%), increased blood alkaline phosphatase (34%), decreased appetite (32%), musculoskeletal pain (32%), diarrhea (27%), and hypokalemia (25%).

#### Unresectable or Metastatic HER2-Mutant NSCLC (5.4 mg/kg)

DESTINY-Lung02 evaluated two dose levels (5.4 mg/kg [n=101] and 6.4 mg/kg [n=50]); however, only the results for the recommended dose of 5.4 mg/kg intravenously every 3 weeks are described below due to increased toxicity observed with the higher dose in patients with NSCLC, including ILD/pneumonitis.

The safety of ENHERTU was evaluated in 101 patients with unresectable or metastatic HER2-mutant NSCLC who received ENHERTU 5.4 mg/kg intravenously every three weeks in DESTINY-Lung02. Nineteen percent of patients were exposed for >6 months.

Serious adverse reactions occurred in 30% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, thrombocytopenia, dyspnea, nausea, pleural effusion, and increased troponin I. Fatality occurred in 1 patient with suspected ILD/pneumonitis (1%).

ENHERTU was permanently discontinued in 8% of patients. Adverse reactions which resulted in permanent discontinuation of ENHERTU were ILD/pneumonitis, diarrhea, hypokalemia, hypomagnesemia, myocarditis, and vomiting. Dose interruptions of ENHERTU due to adverse reactions occurred in 23% of patients. Adverse reactions which required dose interruption (>2%) included neutropenia and ILD/pneumonitis. Dose reductions due to an adverse reaction occurred in 11% of patients.

The most common ( $\geq 20\%$ ) adverse reactions, including laboratory abnormalities, were nausea (61%), decreased white blood cell count (60%), decreased hemoglobin (58%), decreased neutrophil count (52%), decreased lymphocyte count (43%), decreased platelet count (40%), decreased albumin (39%), increased aspartate aminotransferase (35%), increased alanine aminotransferase (34%), fatigue (32%), constipation (31%), decreased appetite (30%), vomiting (26%), increased alkaline phosphatase (22%), and alopecia (21%).

#### Locally Advanced or Metastatic Gastric Cancer (6.4 mg/kg)

The safety of ENHERTU was evaluated in 187 patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma in DESTINY-Gastric01. Patients intravenously received at least one dose of either ENHERTU (N=125) 6.4 mg/kg every 3 weeks or either irinotecan (N=55) 150 mg/m<sup>2</sup> biweekly or paclitaxel (N=7)



80 mg/m<sup>2</sup> weekly for 3 weeks. The median duration of treatment was 4.6 months (range: 0.7 to 22.3) for patients who received ENHERTU.

Serious adverse reactions occurred in 44% of patients receiving ENHERTU 6.4 mg/kg. Serious adverse reactions in >2% of patients who received ENHERTU were decreased appetite, ILD, anemia, dehydration, pneumonia, cholestatic jaundice, pyrexia, and tumor hemorrhage. Fatalities due to adverse reactions occurred in 2.4% of patients: disseminated intravascular coagulation, large intestine perforation, and pneumonia occurred in one patient each (0.8%).

ENHERTU was permanently discontinued in 15% of patients, of which ILD accounted for 6%. Dose interruptions due to adverse reactions occurred in 62% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were neutropenia, anemia, decreased appetite, leukopenia, fatigue, thrombocytopenia, ILD, pneumonia, lymphopenia, upper respiratory tract infection, diarrhea, and hypokalemia. Dose reductions occurred in 32% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were neutropenia, decreased appetite, fatigue, nausea, and febrile neutropenia.

The most common ( $\geq 20\%$ ) adverse reactions, including laboratory abnormalities, were decreased hemoglobin (75%), decreased white blood cell count (74%), decreased neutrophil count (72%), decreased lymphocyte count (70%), decreased platelet count (68%), nausea (63%), decreased appetite (60%), increased aspartate aminotransferase (58%), fatigue (55%), increased blood alkaline phosphatase (54%), increased alanine aminotransferase (47%), diarrhea (32%), hypokalemia (30%), vomiting (26%), constipation (24%), increased blood bilirubin (24%), pyrexia (24%), and alopecia (22%).

### 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 after 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 7 months after the last dose. *Males:* Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for 4 months after 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 883 patients with breast cancer treated with ENHERTU 5.4 mg/kg, 22% were  $\geq 65$  years and 3.6% were  $\geq 75$  years. No overall differences in efficacy within clinical studies 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 (60%) as compared to younger patients (48%). Of the 101 patients with unresectable or metastatic HER2-mutant NSCLC treated with ENHERTU 5.4 mg/kg, 40% were  $\geq 65$  years and 8% were  $\geq 75$  years. No overall differences in efficacy or safety were observed between patients  $\geq 65$  years of age compared to younger patients. Of the 125 patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma treated with ENHERTU 6.4 mg/kg in DESTINY-Gastric01, 56% were  $\geq 65$  years and 14% were  $\geq 75$  years. No overall differences in efficacy or safety were observed between patients  $\geq 65$  years of age compared to younger patients.
- **Renal Impairment:** A higher incidence of Grade 1 and 2 ILD/pneumonitis has been observed in patients with moderate renal impairment. Monitor patients with moderate renal impairment more frequently. The recommended dosage of ENHERTU has not been established for patients with severe renal impairment (CLcr <30 mL/min).

- **Hepatic Impairment:** In patients with moderate hepatic impairment, due to potentially increased exposure, closely monitor for increased toxicities related to the topoisomerase inhibitor. The recommended dosage of ENHERTU has not been established for patients with severe hepatic impairment (total bilirubin >3 times ULN and any AST).

**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**

Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose “to contribute to the enrichment of quality of life around the world.” In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 17,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an “Innovative Global Healthcare Company Contributing to the Sustainable Development of Society.” For more information, please visit: [www.daiichisankyo.com](http://www.daiichisankyo.com).

### **Media Contacts:**

#### **Global:**

Jennifer Brennan  
Daiichi Sankyo, Inc.  
[jbrennan2@dsi.com](mailto:jbrennan2@dsi.com)  
+ 1 908 900 3183 (mobile)

#### **Japan:**

Koji Ogiwara  
Daiichi Sankyo Co., Ltd.  
[ogiwara.koji.ay@daiichisankyo.co.jp](mailto:ogiwara.koji.ay@daiichisankyo.co.jp)  
+81 3 6225 1126 (office)

#### **Investor Relations Contact:**

[DaiichiSankyoIR@daiichisankyo.co.jp](mailto:DaiichiSankyoIR@daiichisankyo.co.jp)