

## Press Release

# ENHERTU® Demonstrated Robust and Durable Tumor Response of 54.9% in Patients with *HER2* Mutant Metastatic Non-Small Cell Lung Cancer

- First *HER2* directed therapy to show a strong tumor response in this population
- Data from *HER2* mutant cohort of pivotal DESTINY-Lung01 phase 2 trial presented at ESMO and published in *The New England Journal of Medicine*

**Tokyo, Munich and Basking Ridge, NJ – (September 18, 2021)** – Detailed primary results from the positive pivotal [DESTINY-Lung01](#) phase 2 trial of ENHERTU® (trastuzumab deruxtecan), the Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) and AstraZeneca *HER2* directed antibody drug conjugate (ADC), showed a robust and durable tumor response in previously-treated patients with *HER2* mutant unresectable and/or metastatic non-squamous non-small cell lung cancer (NSCLC). Results presented during a late-breaking Proffered Paper session at the European Society for Medical Oncology (#ESMO21) 2021 Virtual Congress (#LBA45) and simultaneously published in [The New England Journal of Medicine](#) confirm ENHERTU as the first *HER2* directed therapy to show a strong anti-tumor response in this patient population.

Lung cancer is the leading cause of cancer-related death among both men and women, and accounts for about one-fifth of all cancer deaths globally,<sup>1</sup> with approximately 80 to 85% of cases classified as NSCLC.<sup>2,3</sup> There are currently no medicines approved specifically for the treatment of *HER2* mutant NSCLC, which affects approximately 2 to 4% of patients with non-squamous NSCLC.<sup>4,5</sup>

Primary results from the *HER2* mutant cohort (cohort 2) of DESTINY-Lung01 in previously-treated *HER2* mutant NSCLC demonstrated a confirmed objective response rate (ORR) of 54.9% (n=50; 95% CI: 44.2-65.4) in patients treated with ENHERTU (6.4 mg/kg) as assessed by independent central review (ICR). Out of a total of 91 patients, one (1.1%) complete response (CR) and 49 (53.8%) partial responses (PR) were observed. A confirmed disease control rate (DCR) of 92.3% (95% CI: 84.8-96.9) was seen with a reduction in tumor size observed in most patients.

After a median follow-up of 13.1 months, the median duration of response (DoR) for ENHERTU was 9.3 months (95% CI: 5.7-14.7). The median progression-free survival (PFS) was 8.2 months (95% CI: 6.0-11.9) and the median overall survival (OS) was 17.8 months (95% CI: 13.8-22.1).

Responses were observed in exploratory analyses of different *HER2* mutation subtypes, as well as in patients with no detectable *HER2* expression or *HER2* gene amplification. Efficacy was observed in subgroups including prior treatment with platinum-based therapy, or platinum-based and anti-PD-(L)1 therapy, as well as asymptomatic brain metastases at baseline.

The overall safety profile of ENHERTU was consistent with previous NSCLC trials of ENHERTU, with no new safety signals identified. The most common grade 3 or higher drug-related treatment-emergent adverse events were neutropenia (18.7%), anemia (9.9%), nausea (8.8%), fatigue (6.6%), leukopenia (4.4%), diarrhea (3.3%) and vomiting (3.3%). Twenty-three patients (25.3%) discontinued treatment due to drug-related treatment-emergent adverse events. Rates of treatment-related interstitial lung disease (ILD) or pneumonitis were consistent with previous trials in lung cancer. There were 24 cases of ILD or pneumonitis, as determined by an independent adjudication committee, with the majority (75%) low grade (grade 1 or 2), four grade 3 and two grade 5 (ILD or pneumonitis-related death).

“Despite more than 20 years of research into *HER2* mutations in non-small cell lung cancer, there are currently no approved *HER2* targeted therapies for non-small cell lung cancer. Patients with *HER2* mutant non-small cell lung cancer are associated with younger age, female sex, never-smoking history, and a poor prognosis with increased incidence of brain metastases, representing an unmet medical need,” said Bob Li, MD, PhD, MPH, Medical Oncologist and Principal Investigator at Memorial Sloan Kettering Cancer Center in New York. “The impressive results from DESTINY-Lung01 showed most patients experienced a reduction in tumor size with ENHERTU treatment, suggesting this medicine has the potential to become the new standard of care for these patients.”

“ENHERTU is the first *HER2* targeted therapy to demonstrate a robust and durable tumor response in patients with *HER2* mutant non-small cell lung cancer,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “This is potentially great news for patients and we are continuing to conduct research, with the goal of bringing ENHERTU to patients with this specific form of lung cancer.”

“Lung cancer is a devastating diagnosis and for patients with *HER2* mutant lung cancer, a targeted treatment for their specific disease has not been an option,” said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology Research and Development, AstraZeneca. “These data reinforce the potential of ENHERTU to become the first *HER2* directed therapy for these patients and reaffirm how this treatment is truly delivering on its transformative potential.”

Patients in DESTINY-Lung01 were previously-treated with a median of two lines of therapy (range, 0-7), including platinum-based chemotherapy (94.5%), immunotherapy (65.9%), platinum-based chemotherapy and immunotherapy (62.6%), docetaxel (19.8%) and HER2 tyrosine kinase inhibitors (14.3%). Of the 91 patients, 36.3% of patients had asymptomatic brain metastases not requiring ongoing glucocorticoid or anticonvulsant therapy at baseline. As of data cut-off on May 3, 2021, 15 patients (16.5%) remain on treatment with ENHERTU.

### Summary of *HER2* mutant cohort of DESTINY-Lung01 Results

Efficacy Measure (ENHERTU 6.4 mg/kg)	<i>HER2</i> Mutant Total Evaluable (n=91) <sup>i</sup>
Confirmed ORR (%) (95% CI) <sup>ii,iii</sup>	54.9% (n=50) (44.2 – 65.4)
CR (%)	1.1% (n=1)
PR (%)	53.8% (n=49)
SD (%)	37.4% (n=34)
DCR (95% CI) <sup>iv</sup>	92.3% (n=84) (84.8-96.9)
Median DoR (months) (95% CI)	9.3 months (5.7-14.7)
Median PFS (months) (95% CI)	8.2 months (6.0-11.9)
Median OS (months) (95% CI)	17.8 months (13.8-22.1)

CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease

<sup>i</sup> ENHERTU 6.4 mg/kg; median follow-up was 13.1 months (range, 0.7-29.1)

<sup>ii</sup> As assessed by independent central review

<sup>iii</sup> ORR is (CR + PR)

<sup>iv</sup> DCR is (CR + PR + SD)

### About DESTINY-Lung01

DESTINY-Lung01 is a global pivotal phase 2, open-label, multi-cohort trial evaluating the safety and efficacy of ENHERTU (6.4 mg/kg and 5.4 mg/kg) in previously-treated patients with *HER2* mutant or *HER2* overexpressing (defined as IHC3+ or IHC2+) unresectable and/or metastatic non-squamous NSCLC. The primary endpoint is confirmed ORR by ICR. Key secondary endpoints include DoR, DCR, PFS, OS and safety.

An interim analysis ENHERTU (6.4 mg/kg) in the *HER2* overexpressing cohort of DESTINY-Lung01 was presented at the 2020 World Conference on Lung Cancer (WCLC) hosted by the International Association for the Study of Lung Cancer (IASLC).

DESTINY-Lung01 enrolled approximately 180 patients at multiple sites, including Asia, Europe and North America. For more information about the trial, visit [ClinicalTrials.gov](https://clinicaltrials.gov).

### **About *HER2* Mutant NSCLC**

Lung cancer is the leading cause of cancer death among both men and women and accounts for about one-fifth of all cancer deaths globally, with 80% to 85% classified as NSCLC.<sup>1,2,3</sup> For patients with metastatic disease, prognosis is particularly poor, as only approximately 6% will live beyond five years after diagnosis.<sup>2</sup>

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of many types of tumors, including lung, breast, gastric and colorectal cancers. HER2 gene alterations (called HER2 mutations) have been identified in NSCLC, as distinct molecular targets and have been reported in approximately 2% to 4% of patients with non-squamous NSCLC.<sup>4,5</sup> These HER2 gene mutations are predominantly seen in younger women, with no smoking history and have been independently associated with cancer cell growth and poor prognosis,<sup>4</sup> with an increased incidence of brain metastases.<sup>4,6,7,8,9,10</sup> Although the role of anti-HER2 treatment is well established in breast and gastric cancers, HER2 is an emerging biomarker in NSCLC with no approved HER2 directed therapies.<sup>4,11</sup>

### **About ENHERTU**

ENHERTU® (trastuzumab deruxtecan; fam-trastuzumab deruxtecan-nxki in the U.S. only) is a HER2 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC technology, ENHERTU is the lead ADC in the oncology portfolio of Daiichi Sankyo and the most advanced program in AstraZeneca's ADC scientific platform. ENHERTU consists of a HER2 monoclonal antibody attached to a topoisomerase I inhibitor payload, an exatecan derivative, via a stable tetrapeptide-based cleavable linker.

ENHERTU (5.4 mg/kg) is approved in Canada, EU, Israel, Japan, UK and U.S. 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.

ENHERTU (6.4 mg/kg) is also approved in Israel, Japan and U.S. for the treatment of adult patients with locally advanced or metastatic HER2 positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen based on the results from the [DESTINY-Gastric01](#) trial.

ENHERTU is approved in the U.S. with Boxed WARNINGS for Interstitial Lung Disease and Embryo-Fetal Toxicity. For more information, please see accompanying full [Prescribing Information](#), including Boxed WARNINGS, and [Medication Guide](#).

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

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

ENHERTU was highlighted in the [Clinical Cancer Advances 2021](#) report as one of two significant advancements in the “ASCO Clinical Advance of the Year: Molecular Profiling Driving Progress in GI Cancers,” based on data from both the [DESTINY-Gastric01](#) and [DESTINY-CRC01](#) trials, as well as one of the targeted therapy advances of the year in non-small cell lung cancer (NSCLC), based on the interim results of the *HER2* mutant cohort of the [DESTINY-Lung01](#) trial.

In May 2020, ENHERTU received [Breakthrough Therapy Designation](#) in the U.S. for the treatment of patients with metastatic non-small cell lung cancer whose tumors have a HER2 mutation and with disease progression on or after platinum-based therapy.

### **About the Daiichi Sankyo and AstraZeneca Collaboration**

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize ENHERTU in [March 2019](#) and datopotamab deruxtecan (Dato-DXd) in [July 2020](#), except in Japan where Daiichi Sankyo maintains exclusive rights for each ADC. Daiichi Sankyo is responsible for manufacturing and supply of ENHERTU and datopotamab deruxtecan.

### **U.S. Important Safety Information for ENHERTU**

#### **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 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.

- 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. 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**

In clinical studies, of the 234 patients with unresectable or metastatic HER2-positive breast cancer treated with ENHERTU 5.4 mg/kg, 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).

**Locally Advanced or Metastatic Gastric Cancer**

In DESTINY-Gastric01, of the 125 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 21.0).

**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. 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. Reduce dose by one level.

**Metastatic Breast Cancer**

In clinical studies, of the 234 patients with unresectable or metastatic HER2-positive breast cancer who received ENHERTU 5.4 mg/kg, a decrease in neutrophil count was reported in 62% of patients. Sixteen

percent had Grade 3 or 4 decrease in neutrophil count. Median time to first onset of decreased neutrophil count was 23 days (range: 6 to 547). Febrile neutropenia was reported in 1.7% of patients.

#### Locally Advanced or Metastatic Gastric Cancer

In DESTINY-Gastric01, of the 125 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. 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. In DESTINY-Gastric01, of the 125 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. 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. 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.

#### **Additional Dose Modifications**

##### **Thrombocytopenia**

For Grade 3 thrombocytopenia (platelets <50 to 25 x 10<sup>9</sup>/L) interrupt ENHERTU until resolved to Grade 1 or less, then maintain dose. For Grade 4 thrombocytopenia (platelets <25 x 10<sup>9</sup>/L) interrupt ENHERTU until resolved to Grade 1 or less. Reduce dose by one level.

#### **Adverse Reactions**

##### Metastatic Breast Cancer

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 ( $\geq 20\%$ ) adverse reactions, including laboratory abnormalities, were nausea (79%), white blood cell count decreased (70%), hemoglobin decreased (70%), neutrophil count decreased (62%), fatigue (59%), vomiting (47%), alopecia (46%), aspartate aminotransferase increased (41%), alanine aminotransferase increased (38%), platelet count decreased (37%), constipation (35%), decreased appetite (32%), anemia (31%), diarrhea (29%), hypokalemia (26%), and cough (20%).

#### Locally Advanced or Metastatic Gastric Cancer

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 once 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) in the ENHERTU group and 2.8 months (range: 0.5 to 13.1) in the irinotecan/paclitaxel group.

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 hemoglobin decreased (75%), white blood cell count decreased (74%), neutrophil count decreased (72%), lymphocyte count decreased (70%), platelet count decreased (68%), nausea (63%), decreased appetite (60%), anemia (58%), aspartate aminotransferase increased (58%), fatigue (55%), blood alkaline phosphatase increased (54%), alanine aminotransferase increased (47%), diarrhea (32%), hypokalemia (30%), vomiting (26%), constipation (24%), blood bilirubin increased (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 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%). 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.
- **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 in Oncology**

The oncology portfolio of Daiichi Sankyo is powered by our team of world-class scientists that push beyond traditional thinking to create transformative medicines for people with cancer. Anchored by our DXd antibody drug conjugate (ADC) technology, our 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 the U.S. We also work alongside leading academic and business collaborators to further advance the understanding of cancer as Daiichi Sankyo builds towards our ambitious goal of becoming a global leader in oncology by 2025.

### **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 16,000 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).

*Disclosure: Dr. Li has provided uncompensated advisory services to Daiichi Sankyo and AstraZeneca.*

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