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Daiichi-Sankyo

Press Release

ENHERTU® Granted Priority Review in the U.S. for Patients with HER2 Low Metastatic Breast Cancer

- Based on DESTINY-Breast04 results which showed Daiichi Sankyo and AstraZeneca's ENHERTU is the first HER2 directed therapy to demonstrate a survival benefit in this population
- Application being evaluated under FDA Real-Time Oncology Review and Project Orbis

Tokyo and Basking Ridge, NJ – (July 25, 2022) – Daiichi Sankyo (TSE: 4568) and AstraZeneca (LSE/STO/Nasdaq: AZN) have received notification of acceptance by the U.S. Food and Drug Administration (FDA) of the supplemental Biologics License Application (sBLA) of ENHERTU® (fam-trastuzumab deruxtecan-nxki) for the treatment of adult patients with unresectable or metastatic HER2 low (immunohistochemistry (IHC) 1+ or IHC 2+/*in-situ* hybridization (ISH)-negative) breast cancer who have received a prior therapy in the metastatic setting. The application has been granted Priority Review.

ENHERTU is a specifically engineered HER2 directed antibody drug conjugate (ADC) being jointly developed and commercialized by Daiichi Sankyo and AstraZeneca.

The FDA grants Priority Review to applications for medicines that, if approved, would offer significant improvements over available options by demonstrating safety or efficacy improvements, preventing serious conditions or enhancing patient compliance. The Prescription Drug User Fee Act date (PDUFA), the FDA action date for their regulatory decision, is during the fourth quarter of the 2022 calendar year. The Priority Review follows receipt of Breakthrough Therapy Designation, granted by the FDA in April 2022 for ENHERTU in metastatic HER2 low breast cancer.

The sBLA is being reviewed under the Real-Time Oncology Review (RTOR) program and Project Orbis, two initiatives of the FDA which are designed to bring safe and effective cancer treatments to patients as early as possible. RTOR allows the FDA to review components of an application before submission of the complete application. Project Orbis provides a framework for concurrent submission and review of oncology medicines among participating international partners.

"The results seen in the DESTINY-Breast04 trial represent a significant advance and reinforce the potential for ENHERTU to become a new standard of care for patients with previously treated HER2 low metastatic breast cancer," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "The prioritization of this

application by the FDA and inclusion in both the Real-Time Oncology Review and Project Orbis initiatives support the importance of these data, and we look forward to working with the FDA to potentially bring ENHERTU to patients with HER2 low metastatic breast cancer as quickly as possible."

"The data from DESTINY-Breast04 represent the first time a HER2 targeted therapy has shown a survival benefit in patients with HER2 low metastatic breast cancer," said Susan Galbraith, MBBChir, PhD, Executive Vice President, Oncology R&D, AstraZeneca. "For more than two decades, only patients with HER2 positive breast cancer have been able to benefit from HER2 targeted therapies. If approved, ENHERTU will redefine how we classify and treat metastatic breast cancer, enabling patients whose tumors have lower levels of HER2 expression the opportunity to benefit from a HER2 directed therapy."

The sBLA is based on data from the DESTINY-Breast04 phase 3 trial recently presented at the presidential plenary session of the American Society of Clinical Oncology (#ASCO22) Annual Meeting and simultaneously published in *The New England Journal of Medicine*. In DESTINY-Breast04, ENHERTU demonstrated superior and clinically meaningful efficacy in progression-free survival (PFS) and overall survival (OS) in previously treated patients with HER2 low unresectable and/or metastatic breast cancer with hormone receptor (HR) positive or HR negative disease versus standard of care physician's choice of chemotherapy. The safety profile of ENHERTU was consistent with previous clinical trials with no new safety concerns identified. Interstitial lung disease (ILD) or pneumonitis rates were consistent with those observed in other late-line HER2 positive breast cancer trials of ENHERTU, as determined by an independent adjudication committee.

About DESTINY-Breast04

DESTINY-Breast04 is a global, randomized, open-label, pivotal phase 3 trial evaluating the efficacy and safety of ENHERTU (5.4 mg/kg) versus physician's choice of chemotherapy (capecitabine, eribulin, gemcitabine, paclitaxel or nab-paclitaxel) in patients with HR positive or HR negative, HER2 low unresectable and/or metastatic breast cancer previously treated with one or two prior lines of chemotherapy. Patients were randomized 2:1 to receive either ENHERTU or chemotherapy.

The primary endpoint of DESTINY-Breast04 is PFS in patients with HR positive disease based on blinded independent central review (BICR). Key secondary endpoints include PFS based on BICR in all randomized patients (HR positive and HR negative disease), OS in patients with HR positive disease and OS in all randomized patients (HR positive and HR negative disease). Other secondary endpoints include PFS based on investigator assessment, objective response rate based on BICR and on investigator assessment, duration of response based on BICR and safety. DESTINY-Breast04 enrolled 557 patients at multiple sites in Asia, Europe and North America. For more information about the trial, visit ClinicalTrials.gov.

About Breast Cancer and HER2 Expression

Breast cancer is the most common cancer and is one of the leading causes of cancer-related deaths worldwide.[1] More than two million cases of breast cancer were diagnosed in 2020 with nearly 685,000 deaths globally.[1] In the U.S., more than 290,000 new cases are expected to be diagnosed in 2022, with more than 43,000 deaths.[2] Approximately one in five cases of breast cancer are considered HER2 positive.[3]

HER2 is a tyrosine kinase receptor growth-promoting protein expressed on the surface of many types of tumors including breast, gastric, lung and colorectal cancers, and is one of many biomarkers expressed in breast cancer tumors.[4]

HER2 expression is currently defined as either positive or negative, and is determined by an IHC test which estimates the amount of HER2 protein on a cancer cell, and/or an ISH test, which counts the copies of the *HER2* gene in cancer cells.[4,5] HER2 positive cancers are defined as IHC 3+, IHC 2+/ISH+.[4] HER2 negative cancers are currently defined as IHC 0, IHC 1+ or IHC 2+/ISH-.[4] Approximately half of all patients with breast cancer have tumors with low HER2 expression, with a HER2 IHC score of 1+, or a HER2 IHC score of 2+ in combination with a negative ISH test, an expression level not currently eligible for HER2 targeted therapy.[3,6,7,8] Low HER2 expression occurs in both HR positive and HR negative disease.[9]

HER2 testing is routinely used to determine appropriate treatment options for patients with metastatic breast cancer. Targeting the lower range of expression in the HER2 spectrum may offer another approach to delay disease progression and extend survival in patients with metastatic breast cancer.[10] Currently, patients with low HER2 expression with HR positive tumors have limited treatment options following progression on endocrine (hormone) therapy.[11] Few targeted options are available for those who are HR negative.[12]

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 more than 30 countries 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, based on results from the DESTINY-Breast03

trial. ENHERTU also is approved in several countries 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 based on the results from the DESTINY-Breast01 trial.

ENHERTU (6.4 mg/kg) is approved in several countries for the treatment of adult patients with locally advanced or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) 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 the 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, also are underway.

Regulatory applications for ENHERTU are currently under review in China, Japan and several other countries for the treatment of adult patients with HER2 positive unresectable or metastatic breast cancer who have received a prior anti-HER2-based regimen based on the results from the DESTINY-Breast03 trial.

ENHERTU is under review in Europe and Japan for the treatment of adult patients with unresectable or metastatic HER2 low (IHC 1+ or IHC 2+/ISH-negative) breast cancer who have received a prior systemic therapy in the metastatic setting or developed disease recurrence during or within six months of completing adjuvant chemotherapy, based on the results from the DESTINY-Breast04 trial. Patients with HR positive breast cancer must additionally have received or be ineligible for endocrine therapy.

ENHERTU also is currently under review in the U.S. for the treatment of adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have a *HER2 (ERBB2)* mutation and who have received a prior systemic therapy based on the results from the DESTINY-Lung01 trial, and in Europe for the treatment of adult patients with locally advanced or metastatic HER2 positive gastric or GEJ adenocarcinoma who have received a prior anti-HER2-based regimen based on the DESTINY-Gastric01 and DESTINY-Gastric02 trials.

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo Company, Limited (referred to as 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 the manufacturing and supply of ENHERTU and datopotamab deruxtecan.

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 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
- 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 ≤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., ≥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., ≥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 491 patients with unresectable or metastatic HER2-positive breast cancer treated with ENHERTU 5.4 mg/kg, ILD occurred in 13% of patients. Fatal outcomes due to ILD and/or pneumonitis

occurred in 1.4% of patients treated with ENHERTU. Median time to first onset was 5.5 months (range: 1.1 to 20.8).

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 x 10^9/L) interrupt ENHERTU until resolved to Grade 2 or less, then maintain dose. For Grade 4 neutropenia (ANC <0.5 x 10^9/L) interrupt ENHERTU until resolved to Grade 2 or less. Reduce dose by one level. For febrile neutropenia (ANC <1.0 x 10^9/L and temperature >38.3ºC or a sustained temperature of ≥38ºC for more than 1 hour), interrupt ENHERTU until resolved. Reduce dose by one level.
Metastatic Breast Cancer
In clinical studies, of the 491 patients with unresectable or metastatic HER2-positive breast cancer who received ENHERTU 5.4 mg/kg, a decrease in neutrophil count was reported in 68% of patients. Eighteen percent had Grade 3 or 4 decrease in neutrophil count. Median time to first onset of decreased neutrophil count was 22 days (range: 6 to 664). Febrile neutropenia was reported in 1.2% 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. 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
In the 491 patients with unresectable or metastatic HER2-positive breast cancer who received ENHERTU 5.4 mg/kg, 13 cases (2.6%) of asymptomatic LVEF decrease were reported.

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

Adverse Reactions
Metastatic Breast Cancer
The pooled safety population for patients with metastatic breast cancer reflects exposure to ENHERTU at 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) in 491 patients in DESTINY-Breast03, DESTINY-Breast01, and Study DS8201-A-J101. The median duration of treatment was 13 months (range: 0.7 to 37). In this pooled safety population, the most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea (78%), decreased white blood cell count (74%), decreased hemoglobin (68%), decreased neutrophil count (68%), increased aspartate aminotransferase (58%), fatigue (57%), decreased lymphocyte count (56%), vomiting (50%), decreased platelet count (49%), increased alanine aminotransferase (48%), increased blood alkaline phosphatase (45%), alopecia (41%), constipation (35%), hypokalemia (33%), decreased appetite (32%), diarrhea (31%), musculoskeletal pain (28%), increased transaminases (27%), respiratory infection (24%), headache (21%), and abdominal pain (21%).

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 in DESTINY-Breast03. ENHERTU was administered by intravenous infusion once every three weeks. 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 (≥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%).

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 DESTINYGastric01. Patients intravenously received at least one dose of either ENHERTU (N=125) 6.4 mg/kg once every three weeks or either irinotecan (N=55) 150 mg/m^2 biweekly or paclitaxel (N=7) 80 mg/m^2 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 (≥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 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 491 patients with HER2-positive breast cancer treated with ENHERTU 5.4 mg/kg, 22% were ≥65 years and 4% were ≥75 years. No overall differences in efficacy within clinical studies were observed between patients ≥65 years of age compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients aged ≥65 years (60%) as compared to younger patients (49%). 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 ≥65 years and 14% were ≥75 years. No overall differences in efficacy or safety were observed between patients ≥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 or severe renal impairment.

- **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.

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 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.

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