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Daiichi-Sankyo

Press Release

DATROWAY® Continues to Show Promising Tumor Responses as Part of Combination Regimens in Patients with Early and Advanced Non-Small Cell Lung Cancer

- TROPION-Lung02 and TROPION-Lung04 phase 1b results support combination of Daiichi Sankyo and AstraZeneca's DATROWAY with immunotherapy as first-line treatment for advanced or metastatic NSCLC
- TROPION-Lung02 results include first exploratory QCS analysis of DATROWAY in first-line setting
- NeoCOAST-2 phase 2 results continue to show potential for DATROWAY plus durvalumab and single-agent platinum chemotherapy in neoadjuvant setting

Tokyo and Basking Ridge, NJ – (June 1, 2025) – Results from three trials continue to demonstrate the potential of DATROWAY® (datopotamab deruxtecan) in combination with various immunotherapies to improve outcomes in patients with non-small cell lung cancer (NSCLC) across multiple stages of the disease. These results from TROPION-Lung02, TROPION-Lung04 and NeoCOAST-2 were presented at the 2025 American Society of Clinical Oncology (#ASCO25) Annual Meeting.

DATROWAY is a specifically engineered TROP2 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo (TSE: 4568) and being jointly developed and commercialized by Daiichi Sankyo and AstraZeneca (LSE/STO/Nasdaq: AZN).

"Patients with non-small cell lung cancer have limited treatment options and often experience disease progression due to the aggressive nature of the disease," said Benjamin Levy, MD, Clinical Director, Medical Oncology, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Medicine. "The safety and efficacy data from these trials and the exploratory QCS analysis from TROPION-Lung02 support the potential of DATROWAY to become an important medicine to use in combination with various immunotherapies to improve outcomes for patients across multiple stages of lung cancer."

"These data presented at ASCO continue to reinforce the potential for DATROWAY to become an important part of immunotherapy-based combination regimens for the treatment of certain patients with non-small cell lung cancer," said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. "We look forward to further evaluation of these combinations through our robust clinical development program in order to determine how DATROWAY may help address unmet needs of patients with lung cancer."

"The DATROWAY combination data at ASCO, including results with our own durvalumab and rilvegostomig as well as pembrolizumab, support the combinability of this medicine and its potential to change treatment expectations across stages of lung cancer," said Cristian Massacesi, MD, Chief Medical Officer and Oncology Chief Development Officer, AstraZeneca. "Further, the results from the TROPION-Lung02 exploratory biomarker analysis offer additional evidence that the more precise measurement of TROP2, as enabled by our computational pathology platform, can help identify patients with non-small cell lung cancer more likely to respond to DATROWAY."

DATROWAY plus pembrolizumab with or without platinum-based chemotherapy show consistent tumor responses as first-line treatment of advanced NSCLC

Final results from the TROPION-Lung02 phase 1b trial of DATROWAY plus Merck's (known as MSD outside of the United States and Canada) anti-PD-1 therapy KEYTRUDA® (pembrolizumab) with or without platinum chemotherapy in patients with advanced NSCLC without actionable genomic alterations were featured during an oral presentation (#8501) on Sunday, June 1.

In 42 patients receiving first-line doublet DATROWAY plus pembrolizumab, an objective response rate (ORR) of 54.8% (95% confidence interval [CI]: 38.7-70.2) was observed. In 54 patients receiving first-line triplet DATROWAY plus pembrolizumab and platinum chemotherapy, an ORR of 55.6% (95% CI: 41.4-69.1) was observed. This analysis included patients enrolled during the dose escalation phase of the trial, where 4.8% and 40.7% of patients treated with the doublet and triplet regimens, respectively, received DATROWAY at a dose of 4 mg/kg versus 6 mg/kg. Median treatment duration was 9.7 months for patients receiving the doublet regimen and 5.8 months for those receiving the triplet regimen.

The safety profiles of the doublet and triplet regimens of DATROWAY in TROPION-Lung02 were consistent with previous analyses. Grade 3 or higher treatment-related adverse events (TRAEs) occurred in 40.5% and 55.6% of patients receiving the doublet and triplet regimens, respectively. The most common grade 3 or higher TRAEs occurring in 5% or more of patients treated with the doublet regimen were increased amylase (14%) and stomatitis (5%). The most common grade 3 or higher TRAEs occurring in 5% or more of patients treated with the triplet regimen were decreased neutrophil count (15%), neutropenia (13%), anemia (13%), increased amylase (9%), fatigue (6%) and nausea (6%). Two (4.8%) grade 3 interstitial lung disease (ILD) events in patients treated with the doublet regimen and one (1.9%) grade 3 ILD event in patients treated with the triplet regimen were adjudicated as drug-related by an independent committee.

In TROPION-Lung02, patients across six cohorts received DATROWAY plus pembrolizumab (doublet) or DATROWAY plus pembrolizumab and chemotherapy (triplet). As of data cut-off of April 29, 2024, 96 patients received either the doublet (n=42) or triplet (n=54) combination as first-line therapy.

Summary of TROPION-Lung02 First-Line Efficacy Results

Efficacy Measure	Doublet			Triplet		
	Overall (n=42)	PD-L1<50% (n=30)	PD-L1≥50% (n=5)	Overall (n=54)	PD-L1<50% (n=40)	PD-L1≥50% (n=10)
Confirmed ORR.[i,ii] % (95% CI)	54.8% (38.7–70.2)	53.3% (34.3–71.7)	100% (47.8–100)	55.6% (41.4–69.1)	55% (38.5-70.7)	60% (26.2–87.8)
CR, %	2.4%	3.3%	0%	3.7%	2.5%	10%
PR, %	52.4%	50%	100%	51.9%	52.5%	50%
SD, %	33%	NA	NA	33%	NA	NA
PD, %	7%	NA	NA	4%	NA	NA
DCR, % (n)[iii] (95% CI)	88.1% (37) (74.4–96.0)	96.7% (29) (82.8–99.9)	100% (5) (47.8–100)	88.9% (48) (77.4–95.8)	87.5% (35) (73.2–95.8)	90% (9) (55.5–99.7)
Median DoR, (months) (95% CI)	20.1 months (9.7–NE)	12 months (8.0–NE)	NE (5.5–NE)	13.7 months (5.7–NE)	14.6 months (5.3–NE)	NE (4.1–NE)
Median PFS, (months) (95% CI)	11.2 months (8.2–21.3)	11.1 months (7.2–13.3)	NE (8.3–NE)	6.8 months (5.5–11.1)	6.4 months (5.5–13.2)	6.8 months (0.8–NE)

CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NA, not available; NE, not estimable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease

[i]ORR is CR+ PR

[ii]As assessed by investigator

[iii]Proportion of patients with confirmed CR + confirmed PR + SD.

Tissue samples collected from patients in TROPION-Lung02 were analyzed retrospectively using quantitative continuous scoring (QCS), AstraZeneca's proprietary computational platform. Tumors were considered biomarker positive if ≥75% of tumor cells exhibited a normalized membrane ratio (NMR) below a predetermined value (≤0.56), indicating a greater proportion of TROP2 in the cytoplasm than on the membrane. Results from this exploratory analysis showed that TROP2-NMR biomarker positivity was associated with a trend toward prolonged progression free survival (PFS) in patients treated with the doublet (hazard ratio [HR]: 0.50; 95% CI: 0.19-1.29) and triplet (HR: 0.67; 95% CI: 0.33-1.36) regimens, and a trend toward prolonged overall survival in patients treated with the doublet (HR: 0.35; 95% CI: 0.07-1.72) and triplet (HR: 0.71; 95% CI: 0.31-1.59) regimens compared to the TROP2-NMR biomarker negative population.

DATROWAY plus rilvegostomig show encouraging activity in first-line treatment of advanced NSCLC

First results from cohort 5 of the TROPION-Lung04 phase 1b trial, presented during a poster session (#8521) on Saturday, May 31, showed DATROWAY plus AstraZeneca's PD-1/TIGIT bispecific antibody rilvegostomig as a first-line treatment demonstrated an ORR of 57.5% (95% CI: 40.9-73.0), including one

complete response (CR) and 22 partial responses (PRs) in 40 patients with advanced or metastatic NSCLC. A disease control rate (DCR) of 95% (95% CI: 83.1-99.4) was seen. Objective responses were observed across both squamous (45.5%; 95% CI: 16.7-76.6) and nonsquamous (62.1%; 95% CI: 42.3-79.3) histologies and all PD-L1 expression levels. Median duration of response (DoR) was 5.8 months (4.5-not evaluable [NE]).

The safety profile of DATROWAY and rilvegostomig was consistent with the known safety profile of each agent with no new safety signals identified. Grade 3 or higher treatment-emergent adverse events (TEAEs) occurred in 60% of patients. The most common grade 3 or greater TEAEs were pneumonia (10%), pneumonitis (7.5%), anemia (2.5%), decreased appetite (2.5%), increased amylase (2.5%), musculoskeletal pain (2.5%), rash (2.5%) and stomatitis (2.5%). Three (7.5%) grade 2 ILD events and two (5%) grade 3 ILD events were adjudicated as drug-related by an independent committee.

Cohort 5 of TROPION-Lung04 enrolled patients with untreated advanced NSCLC without actionable genomic alterations. As of data cut-off of October 24, 2024, 40 patients received DATROWAY plus rilvegostomig with a median treatment duration of 5.1 months. DATROWAY treatment was ongoing in 19 patients and rilvegostomig treatment was ongoing in 20 patients.

Daiichi Sankyo and AstraZeneca are evaluating DATROWAY plus rilvegostomig as first-line treatment for patients with advanced or metastatic nonsquamous NSCLC with PD-L1 ≥50% and without actionable genomic alterations in the TROPION-Lung10 phase 3 trial.

DATROWAY plus durvalumab and chemotherapy demonstrate encouraging pathological response rates in patients with early-stage resectable NSCLC

Final results from Arm 4 of the NeoCOAST-2 phase 2 platform trial evaluating neoadjuvant DATROWAY plus AstraZeneca's anti-PD-L1 therapy IMFINZI® (durvalumab) and single-agent platinum chemotherapy were presented during a poster session (#8046) on Saturday, May 31 and showed the combination demonstrated a pathologic complete response (pCR) rate of 35.2% (95% CI: 22.7-49.4) and a major pathologic response (mPR) rate of 63% (95% CI: 48.7-75.7). This was numerically higher than response rates shown by other combination regimens evaluated in Arm 1 and Arm 2 of NeoCOAST-2; however, the trial was not powered to make direct statistical comparisons between arms. These results, along with results from these other two arms of NeoCOAST-2, were simultaneously published in *Nature Medicine.*

The safety profile of DATROWAY, durvalumab and single-agent platinum chemotherapy was consistent with the known safety profile of each agent with no new safety signals identified. Feasibility of surgery was

maintained with this arm of NeoCOAST-2 relative to the standard of care. Grade 3 or higher TEAEs occurred in 24.1% of patients in the neoadjuvant period.

About TROPION-Lung02

TROPION-Lung02 is an ongoing global, open-label, six-cohort phase 1b trial evaluating the safety and efficacy of DATROWAY at two dose levels (4 mg/kg and 6 mg/kg) in combination with Merck's anti-PD-1 therapy KEYTRUDA® (pembrolizumab; 200 mg) with or without four cycles of platinum chemotherapy (carboplatin or cisplatin) in patients with previously untreated or pretreated locally advanced or metastatic NSCLC without actionable genomic alterations (e.g., EGFR, ALK, ROS1, NTRK, BRAF, RET, MET or other known AGAs). Participants with tumors that harbor KRAS mutations are eligible for this study.

The primary endpoints of TROPION-Lung02 are dose-limiting toxicities and treatment-emergent adverse events. Secondary endpoints include ORR, DoR, PFS as assessed by investigator, overall survival, pharmacokinetics and anti-drug antibodies for DATROWAY and pembrolizumab.

TROPION-Lung02 is one of three clinical trials along with the phase 3 TROPION-Lung07 and TROPION-Lung08 trials in a collaboration and supply agreement between Daiichi Sankyo, AstraZeneca and Merck (known as MSD outside of the United States and Canada) to evaluate the combination of DATROWAY and pembrolizumab.

TROPION-Lung02 enrolled 145 patients in Asia, Europe and North America. For more information visit ClinicalTrials.gov.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

About TROPION-Lung04

TROPION-Lung04 is an ongoing global, open-label, 15-cohort phase 1b trial evaluating the safety and efficacy of DATROWAY (4 mg/kg or 6 mg/kg) in combination with immunotherapy (durvalumab, rilvegostomig or volrustomig) with or without up to four cycles of carboplatin in patients with advanced or metastatic NSCLC without actionable genomic alterations. Participants with tumors that harbor KRAS mutations are eligible for this study. Patients enrolled in the cohorts evaluating durvalumab were previously untreated or had received one or fewer lines of systemic chemotherapy without concomitant immunotherapy.

The primary endpoints of TROPION-Lung04 are safety and tolerability. Secondary endpoints include ORR, DCR, duration of response and progression-free survival as assessed by investigator.

Rilvegostomig is AstraZeneca's PD-1/TIGIT bispecific antibody. The TIGIT component of rilvegostomig is derived from the clinical-stage anti-TIGIT antibody, COM902, developed by Compugen Ltd. (Nasdaq/TASE: CGEN).

TROPION-Lung04 will enroll more than 370 patients in Asia, Europe and North America. For more information visit ClinicalTrials.gov.

About NeoCOAST-2

NeoCOAST-2 is a global, randomized, multicenter, open-label, multi-arm phase 2 platform trial conducted by AstraZeneca evaluating the efficacy and safety of durvalumab in multiple novel combinations, before and after surgery, in patients with resectable, early-stage (stage IIA-IIIB) NSCLC.

The dual primary endpoints of NeoCOAST-2 are antitumor activity of neoadjuvant treatment assessed by pCR and the safety and tolerability of neoadjuvant and adjuvant treatment. Secondary endpoints include event-free survival, disease-free survival and ORR as determined by investigator using RECIST version 1.1, OS, feasibility of surgery, and mPR determined by central blinded independent pathologist review.

NeoCOAST-2 will enroll approximately 630 patients in Asia, Europe and North America. For more information visit ClinicalTrials.gov.

About Non-Small Cell Lung Cancer

Nearly 2.5 million lung cancer cases were diagnosed globally in 2022.[1] NSCLC is the most common type of lung cancer, accounting for about 87% of cases.[2] While most NSCLC cases are diagnosed in the advanced setting, between 25 to 30% of diagnoses occur in the early stage of the disease.[3,4]

Despite improvements in treatment for early-stage NSCLC, patients may experience disease recurrence even after complete tumor resection with or without treatment with adjuvant therapy.[5,6,7] For patients with advanced NSCLC without actionable genomic alterations, immunotherapy with or without platinum-based chemotherapy is the standard first-line treatment. While these medicines have improved outcomes in the first-line metastatic setting, most patients experience disease progression.[8,9,10]

TROP2 is a protein broadly expressed in the majority of NSCLC tumors.[11] There is currently no TROP2 directed ADC approved in the U.S. for the treatment of lung cancer.[12,13]

About DATROWAY

DATROWAY (datopotamab deruxtecan; datopotamab deruxtecan-dlnk in the U.S. only) is a TROP2 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, DATROWAY is one of six DXd ADCs in the oncology pipeline of Daiichi Sankyo, and one of the most advanced programs in AstraZeneca's ADC scientific platform. DATROWAY is comprised of a humanized anti-TROP2 IgG1 monoclonal antibody, developed in collaboration with Sapporo Medical University, attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

DATROWAY is approved in more than 30 countries for the treatment of adult patients with unresectable or metastatic HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease based on the results from the TROPION-Breast01 trial.

About the DATROWAY Clinical Development Program

A comprehensive global clinical development program is underway with more than 20 trials evaluating the efficacy and safety of DATROWAY across multiple cancers, including NSCLC, triple negative breast cancer and HR positive, HER2 negative breast cancer. The program includes eight phase 3 trials in lung cancer and five phase 3 trials in breast cancer evaluating DATROWAY as a monotherapy and in combination with other anticancer treatments in various settings.

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 DATROWAY in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights for each ADC. Daiichi Sankyo is responsible for the manufacturing and supply of ENHERTU and DATROWAY.

About the ADC Portfolio of Daiichi Sankyo

The Daiichi Sankyo ADC portfolio consists of seven ADCs in clinical development crafted from two distinct ADC technology platforms discovered in-house by Daiichi Sankyo.

The ADC platform furthest in clinical development is Daiichi Sankyo's DXd ADC Technology where 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. The DXd ADC portfolio currently consists of ENHERTU, a HER2 directed ADC, and DATROWAY, a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca. Patritumab deruxtecan (HER3-DXd), a HER3 directed ADC, ifinatamab deruxtecan (I-DXd), a B7-H3 directed ADC, and raludotatug deruxtecan

(R-DXd), a CDH6 directed ADC, are being jointly developed and commercialized globally with Merck & Co., Inc, Rahway, NJ, USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

The second Daiichi Sankyo ADC platform consists of a monoclonal antibody attached to a modified pyrrolobenzodiazepine (PBD) payload. DS-9606, a CLDN6 directed PBD ADC, is the first of several planned ADCs in clinical development utilizing this platform.

Ifinatamab deruxtecan, patritumab deruxtecan, raludotatug deruxtecan, DS-3939 and DS-9606 are investigational medicines that have not been approved for any indication in any country. Safety and efficacy have not been established.

DATROWAY U.S. Important Safety Information

Indication
DATROWAY® is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic, hormone receptor (HR)-positive, HER2-negative (IHC 0, IHC 1+, or IHC 2+/ISH−) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

Contraindications
None.

Warnings and Precautions
Interstitial Lung Disease/Pneumonitis
DATROWAY can cause severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis.

In TROPION-Breast01, ILD/pneumonitis occurred in 4.2% of patients treated with DATROWAY, including 0.5% of patients with Grade 3-4 ILD/pneumonitis, and 0.3% with fatal ILD/pneumonitis. Six patients (1.7%) permanently discontinued DATROWAY due to ILD/pneumonitis. The median time to onset of ILD/pneumonitis was 3.5 months (range: 1.2 months to 10.8 months). Patients were excluded from TROPION-Breast01 for a history of ILD/pneumonitis requiring treatment with steroids or for ongoing ILD/pneumonitis.

Monitor patients for new or worsening respiratory symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever) during treatment with DATROWAY. For asymptomatic (Grade 1) ILD/pneumonitis, consider corticosteroid treatment (eg, ≥0.5 mg/kg/day prednisolone or equivalent). For symptomatic ILD/pneumonitis (Grade 2 or greater), promptly initiate systemic corticosteroid treatment (eg, ≥1 mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks.

Withhold DATROWAY in patients with suspected ILD/pneumonitis and permanently discontinue DATROWAY if Grade ≥2 ILD/pneumonitis is confirmed.

Ocular Adverse Reactions
DATROWAY can cause ocular adverse reactions including dry eye, keratitis, blepharitis, meibomian gland dysfunction, increased lacrimation, conjunctivitis, and blurred vision.

In TROPION-Breast01, ocular adverse reactions occurred in 51% of patients treated with DATROWAY. Seven patients (1.9%) experienced Grade 3 ocular adverse reactions, including dry eye, keratitis, and blurred

vision. The most common (≥5%) ocular adverse reactions were dry eye (27%), keratitis (24%), blepharitis and increased lacrimation (8% each), and meibomian gland dysfunction (7%). Patients with clinically significant corneal disease were excluded from TROPION-Breast01.

The median time to onset for ocular adverse reactions was 2.1 months (range: 0.03 months to 23.2 months). Of the patients who experienced ocular adverse reactions, 45% had complete resolution; 9% had partial improvement (defined as a decrease in severity by one or more grades from the worst grade at last follow up). Ocular adverse reactions led to permanent discontinuation of DATROWAY in 0.8% of patients.

Advise patients to use preservative-free lubricant eye drops several times daily for prophylaxis. Advise patients to avoid use of contact lenses unless directed by an eye care professional.

Refer patients to an eye care professional for an ophthalmic exam including visual acuity testing, slit lamp examination (with fluorescein staining), intraocular pressure, and fundoscopy at treatment initiation, annually while on treatment, at end of treatment, and as clinically indicated.

Promptly refer patients to an eye care professional for any new or worsening ocular adverse reactions. Monitor patients for ocular adverse reactions during treatment with DATROWAY, and if diagnosis is confirmed, dose delay, dose reduce, or permanently discontinue DATROWAY based on severity.

Stomatitis
DATROWAY can cause stomatitis, including mouth ulcers and oral mucositis.

In the TROPION-Breast01 study, stomatitis occurred in 59% of patients treated with DATROWAY, including 7% of patients with Grade 3-4 events. Median time to first onset was 0.7 months (range: 0.03 months to 8.8 months). Stomatitis led to interruption of DATROWAY in 1.9%, dosage reductions in 13%, and permanent discontinuation in 0.3% of patients.

In patients who received DATROWAY, 38% used a mouthwash containing corticosteroid for management or prophylaxis of stomatitis/oral mucositis at any time during the treatment.

Advise patients to use a steroid-containing mouthwash for prophylaxis and treatment of stomatitis. Instruct the patient to hold ice chips or ice water in the mouth throughout the infusion of DATROWAY.

Monitor patients for signs and symptoms of stomatitis. If stomatitis occurs, increase the frequency of mouthwash and administer other topical treatments as clinically indicated. Based on the severity of the adverse reaction, withhold, dose reduce, or permanently discontinue DATROWAY.

Embryo-Fetal Toxicity
Based on its mechanism of action, DATROWAY can cause embryo-fetal harm when administered to a pregnant woman because the topoisomerase inhibitor component of DATROWAY, DXd, is genotoxic and affects actively dividing cells.

Advise patients of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with DATROWAY and for 7 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with DATROWAY and for 4 months after the last dose.

Adverse Reactions
The safety of DATROWAY was evaluated in 360 patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH−) breast cancer who received at least one dose of DATROWAY 6 mg/kg in TROPION-Breast01. DATROWAY was administered by intravenous infusion

once every three weeks. The median duration of treatment was 6.7 months (range: 0.7 months to 16.1 months) for patients who received DATROWAY.

Serious adverse reactions occurred in 15% of patients who received DATROWAY. Serious adverse reactions in >0.5% of patients who received DATROWAY were urinary tract infection (1.9%), COVID-19 infection (1.7%), ILD/pneumonitis (1.1%), acute kidney injury, pulmonary embolism, vomiting, diarrhea, hemiparesis, and anemia (0.6% each). Fatal adverse reactions occurred in 0.3% of patients who received DATROWAY and were due to ILD/pneumonitis.

Permanent discontinuation of DATROWAY due to an adverse reaction occurred in 3.1% of patients. Adverse reactions which resulted in permanent discontinuation of DATROWAY in >0.5% of patients included ILD/pneumonitis (1.7%) and fatigue (0.6%). Dosage interruptions of DATROWAY due to an adverse reaction occurred in 22% of patients. Adverse reactions which required dosage interruption in >1% of patients included COVID-19 (3.3%), infusion-related reaction (1.4%), ILD/pneumonitis (1.9%), stomatitis (1.9%), fatigue (1.7%), keratitis (1.4%), acute kidney injury (1.1%), and pneumonia (1.1%). Dose reductions of DATROWAY due to an adverse reaction occurred in 23% of patients. Adverse reactions which required dose reduction in >1% of patients included stomatitis (13%), fatigue (3.1%), nausea (2.5%), and weight decrease (1.9%).

The most common (≥20%) adverse reactions, including laboratory abnormalities, were stomatitis (59%), nausea (56%), fatigue (44%), decreased leukocytes (41%), decreased calcium (39%), alopecia (38%), decreased lymphocytes (36%), decreased hemoglobin (35%), constipation (34%), decreased neutrophils (30%), dry eye (27%), vomiting (24%), increased ALT (24%), keratitis (24%), increased AST (23%), and increased alkaline phosphatase (23%).

Clinically relevant adverse reactions occurring in <10% of patients who received DATROWAY included infusion-related reactions (including bronchospasm), ILD/pneumonitis, headache, pruritus, dry skin, dry mouth, conjunctivitis, blepharitis, meibomian gland dysfunction, blurred vision, increased lacrimation, photophobia, visual impairment, skin hyperpigmentation, and madarosis.

Use in Specific Populations

- **Pregnancy:** Based on its mechanism of action, DATROWAY can cause embryo-fetal harm when administered to a pregnant woman because the topoisomerase inhibitor component of DATROWAY, DXd, is genotoxic and affects actively dividing cells. There are no available data on the use of DATROWAY in pregnant women to inform a drug-associated risk. Advise patients of the potential risks to a fetus.
- **Lactation:** There are no data regarding the presence of datopotamab deruxtecan-dlnk or its metabolites 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 DATROWAY and for 1 month after the last dose.
- **Females and Males of Reproductive Potential:** Pregnancy Testing: Verify pregnancy status of females of reproductive potential prior to initiation of DATROWAY. Contraception: *Females:* Advise females of reproductive potential to use effective contraception during treatment with DATROWAY and for 7 months after the last dose. *Males:* Because of the potential for genotoxicity, advise male patients with female partners of reproductive potential to use effective contraception during treatment with DATROWAY and for 4 months after the last dose. Infertility: Based on findings in animal toxicity studies, DATROWAY may impair male and female reproductive function and fertility. The effects on reproductive organs in animals were irreversible.
- **Pediatric Use:** Safety and effectiveness of DATROWAY have not been established in pediatric patients.
- **Geriatric Use:** Of the 365 patients in TROPION-Breast01 treated with DATROWAY 6 mg/kg, 25% were ≥65 years of age and 5% were ≥75 years of age. Grade ≥3 and serious adverse reactions were more common in patients ≥65 years (42% and 25%, respectively) compared to patients <65 years

(33% and 15%, respectively). In TROPION-Breast01, no other meaningful differences in safety or efficacy were observed between patients ≥65 years of age versus younger patients.

- **Renal Impairment:** A higher incidence of ILD/pneumonitis has been observed in patients with mild and moderate renal impairment (creatinine clearance [CLcr] 30 to <90 mL/min). Monitor patients with renal impairment for increased adverse reactions, including respiratory reactions. No dosage adjustment is recommended in patients with mild to moderate renal impairment. The effect of severe renal impairment (CLcr <30 mL/min) on the pharmacokinetics of datopotamab deruxtecan-dlnk or DXd is unknown.
- **Hepatic Impairment:** No dosage adjustment is recommended in patients with mild hepatic impairment (total bilirubin ≤ULN and any AST >ULN or total bilirubin >1 to 1.5 times ULN and any AST). Limited data are available in patients with moderate hepatic impairment (total bilirubin >1.5 to 3 times ULN and any AST). Monitor patients with moderate hepatic impairment for increased adverse reactions. The recommended dosage of DATROWAY 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.

Please see accompanying full Prescribing Information, including the Medication Guide.

About Daiichi Sankyo

Daiichi Sankyo is an innovative global healthcare company contributing to the sustainable development of society that discovers, develops and delivers new standards of care to enrich the quality of life around the world. With more than 120 years of experience, Daiichi Sankyo leverages its world-class science and technology to create new modalities and innovative medicines for people with cancer, cardiovascular and other diseases with high unmet medical need. For more information, please visit www.daiichisankyo.com.

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