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Daiichi-Sankyo

Press Release

DATROWAY® Approved in the U.S. as First TROP2 Directed Therapy for Patients with Previously Treated Advanced EGFR-Mutated Non-Small Cell Lung Cancer

- Based on TROPION-Lung05 phase 2 trial results and supported by data from the TROPION-Lung01 phase 3 trial
- Second U.S. approval for Daiichi Sankyo and AstraZeneca's DATROWAY in less than six months

Tokyo and Basking Ridge, NJ – (June 23, 2025) – DATROWAY® (datopotamab deruxtecan-dlnk) has been approved in the U.S. for the treatment of adult patients with locally advanced or metastatic EGFR-mutated non-small cell lung cancer (NSCLC) who have received prior EGFR-directed therapy and platinum-based chemotherapy. This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DoR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

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).

The approval follows Priority Review and Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA) based on subgroup results from the TROPION-Lung05 phase 2 and TROPION-Lung01 phase 3 trials.

In TROPION-Lung05 and TROPION-Lung01, DATROWAY demonstrated a confirmed ORR of 45% (95% confidence interval [CI]: 35-54) in patients (n=114) with previously treated locally advanced or metastatic EGFR-mutated NSCLC as assessed by blinded independent central review (BICR). Complete responses were seen in 4.4% of patients and partial responses were seen in 40% of patients. The median DoR was 6.5 months (95% CI: 4.2-8.4).

"Addressing disease progression in patients with advanced EGFR-mutated lung cancer after prior targeted therapy and chemotherapy is very challenging with limited later-line treatment options available," said Jacob Sands, MD, Medical Oncology, Dana-Farber Cancer Institute and investigator for TROPION-Lung05 and TROPION-Lung01. "The U.S. approval of datopotamab deruxtecan introduces a novel and needed treatment option to patients with advanced disease."

“For people with advanced EGFR-mutated non-small cell lung cancer whose disease progresses on initial treatments, additional options are limited,” said Andrea E. Ferris, President and CEO, LUNGevity. “Today’s approval of DATROWAY offers a new treatment option for patients whose disease has progressed following treatment with an EGFR-directed therapy and chemotherapy.”

The safety of DATROWAY (6 mg/kg) was evaluated in a pooled analysis of 125 patients with locally advanced or metastatic EGFR-mutated NSCLC who received DATROWAY in the TROPION-Lung05, TROPION-Lung01 and TROPION-PanTumor01 trials. The most common (≥20%) adverse reactions, including laboratory abnormalities, were stomatitis, nausea, alopecia, fatigue, decreased hemoglobin, decreased lymphocytes, constipation, increased calcium, increased aspartate aminotransferase, decreased white blood cell count, increased lactate dehydrogenase, musculoskeletal pain, decreased appetite, increased alanine aminotransferase and rash. Serious adverse reactions occurred in 26% of patients who received DATROWAY. Serious adverse reactions in more than 1% who received DATROWAY included COVID-19, stomatitis and pneumonia.

“With today’s accelerated approval, DATROWAY is now the first TROP2 directed medicine available for certain patients in the U.S. living with lung cancer,” said Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc. “We remain committed to our extensive clinical development program to further identify where DATROWAY may be used in other types of lung and breast cancer.”

“This first approval of DATROWAY in lung cancer provides a much-needed option to patients with advanced EGFR-mutated lung cancer whose disease has become resistant to past treatments, regardless of the driving mutation,” said Dave Fredrickson, Executive Vice President, Oncology Hematology Business Unit, AstraZeneca. “We have long supported patients with EGFR-mutated lung cancer and are proud to bring another innovative treatment option to this community.”

Daiichi Sankyo and AstraZeneca are evaluating DATROWAY alone and/or with osimertinib, AstraZeneca’s EGFR tyrosine kinase inhibitor, in other advanced or metastatic EGFR-mutated NSCLC settings in the TROPION-Lung14 and TROPION-Lung15 phase 3 trials.

Daiichi Sankyo and AstraZeneca are committed to ensuring that patients in the U.S. who are prescribed DATROWAY can access the medication and receive necessary financial support. Provider and patient support, reimbursement and distribution for DATROWAY in the U.S. will be accessible by visiting DATROWAY4U.com or calling 1-855-DATRO4U (1-855-328-7648).

Please visit www.DATROWAY.com for full Prescribing Information, including the Medication Guide.

Financial Considerations

Following approval in the U.S., an amount of $45 million is due from AstraZeneca to Daiichi Sankyo as a milestone payment for the locally advanced or metastatic EGFR-mutated NSCLC indication. Sales of DATROWAY in the U.S. are recognized by Daiichi Sankyo. For further details on the financial arrangements, please consult the collaboration agreement from July 2020.

About TROPION-Lung05

TROPION-Lung05 is a global, multicenter, single-arm, open-label phase 2 trial evaluating the efficacy and safety of DATROWAY in patients with locally advanced or metastatic NSCLC with actionable genomic alterations who have progressed on at least one line of targeted therapy and on or after one regimen of platinum-based chemotherapy. Patients receiving up to four prior lines of treatment with tumors with one or more genomic alterations including EGFR, ALK, ROS1, NTRK, BRAF, RET or MET were eligible for the trial.

The primary trial endpoint of TROPION-Lung05 is ORR as assessed by BICR. Secondary efficacy endpoints include DoR, disease control rate (DCR), clinical benefit rate, PFS, time to response (TTR), OS and safety. Primary results from TROPION-Lung05 were published in the *Journal of Clinical Oncology*.

TROPION-Lung05 enrolled 137 patients globally in Asia, Europe and North America. For more information, visit ClinicalTrials.gov.

About TROPION-Lung01

TROPION-Lung01 is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of DATROWAY versus docetaxel in adult patients with locally advanced or metastatic NSCLC with and without actionable genomic alterations who require systemic therapy following prior treatment. Patients with actionable genomic alterations were previously treated with an approved targeted therapy and platinum-based chemotherapy. Patients without known actionable genomic alterations were previously treated, concurrently or sequentially, with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor.

The dual primary endpoints of TROPION-Lung01 are PFS as assessed by BICR and OS. Key secondary endpoints include investigator-assessed PFS, ORR, DoR, TTR, and DCR as assessed by both BICR and investigator, and safety. Primary PFS results and interim OS results from TROPION-Lung01 were presented at the 2023 ESMO (#ESMO23) Congress. Final OS results were presented at IASLC 2024 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer (#WCLC24) and simultaneously published in the *Journal of Clinical Oncology*.

TROPION-Lung01 enrolled 590 patients in Asia, Europe, North America, Oceania and South America. For more information visit ClinicalTrials.gov.

About TROPION-PanTumor01

TROPION-PanTumor01 is a first-in-human, open-label, two-part, multicenter phase 1 trial evaluating the safety and preliminary efficacy of DATROWAY in patients with advanced solid tumors that have relapsed or are refractory to standard treatment or for which no standard treatment is available. The dose escalation portion of the trial enrolled patients with NSCLC to assess the safety and tolerability of DATROWAY to determine the recommended dose for expansion (6 mg/kg). The dose expansion part of TROPION-PanTumor01 enrolled several different cohorts including patients with NSCLC, triple negative breast cancer (TNBC), HR positive, HER2 negative breast cancer, small cell lung cancer, urothelial, gastric, pancreatic, castration resistant prostate and esophageal cancer.

Safety endpoints include dose-limiting toxicities and serious adverse events. Efficacy endpoints include ORR, DoR, TTR, PFS and OS. Pharmacokinetic, biomarker and immunogenicity endpoints also are being evaluated.

TROPION-PanTumor01 enrolled 890 patients in Asia and North America. For more information, visit ClinicalTrials.gov.

About Advanced Non-Small Cell Lung Cancer

Nearly 2.5 million lung cancer cases were diagnosed globally in 2022.[1] Lung cancer is broadly split into small or NSCLC, with NSCLC accounting for about 87% of cases.[2] Approximately 10% to 15% of patients with NSCLC in the U.S. and Europe, and 30% to 40% of patients in Asia have an EGFR mutation.[3,4] The majority of EGFR mutations occur in tumors of nonsquamous histology.[5] TROP2 is a protein broadly expressed in the majority of NSCLC tumors.[6]

For patients with tumors that have an EGFR mutation, the established first-line treatment in the metastatic setting includes EGFR-directed therapy with or without platinum-based chemotherapy.[7] While these therapies have improved outcomes in earlier lines of treatment, most patients eventually experience disease progression and receive subsequent therapies.[8,9,10,11]

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 (6 mg/kg) is approved in more than 30 countries worldwide 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.

DATROWAY (6 mg/kg) is approved in Russia and the U.S. for the treatment of adult patients with locally advanced or metastatic EGFR-mutated NSCLC who have received prior EGFR-directed therapy and platinum-based chemotherapy based on the results from the TROPION-Lung05 and TROPION-Lung01 trials. Continued approval for this indication in the U.S. may be contingent upon verification and description of clinical benefit in the confirmatory 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, TNBC 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

Indications
DATROWAY® is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of:

- adult patients with locally advanced or metastatic epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer (NSCLC) who have received prior EGFR-directed therapy and platinum-based chemotherapy.

  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 the confirmatory trial.

- adult patients with unresectable or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (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.

Locally Advanced or Metastatic NSCLC
In the pooled safety population of 484 patients with NSCLC from TROPION-Lung01, TROPION-Lung05, and TROPION-PanTumor01, ILD/pneumonitis occurred in 7% of patients treated with DATROWAY, including 0.6% of patients with Grade 3 and 0.4% with Grade 4. There were 8 (1.7%) fatal cases. The median time to onset for ILD was 1.4 months (range: 0.2 months to 9 months). Eleven patients (2.3%) had DATROWAY withheld and 20 patients (4.1%) permanently discontinued DATROWAY due to ILD/pneumonitis. Systemic corticosteroids were required in 79% (26/33) of patients with ILD/pneumonitis. ILD/pneumonitis resolved in 45% of patients.

Unresectable or Metastatic Breast Cancer
In the pooled safety population of 443 patients with breast cancer from TROPION-Breast01 and TROPION-PanTumor01, ILD/pneumonitis occurred in 3.6% of patients treated with DATROWAY, including 0.7% of patients with Grade 3. There was one fatal case (0.2%). The median time to onset for ILD was 2.8 months (range: 1.1 months to 10.8 months). Four patients (0.9%) had DATROWAY withheld and 7 patients (1.6%) permanently discontinued DATROWAY due to ILD/pneumonitis. Systemic corticosteroids were required in 60% (9/15) of patients with ILD/pneumonitis. ILD/pneumonitis resolved in 40% of patients.

Patients were excluded from clinical studies 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 (e.g., dyspnea, cough, fever) during treatment with DATROWAY. For asymptomatic (Grade 1) ILD/pneumonitis, consider corticosteroid treatment (e.g., ≥0.5 mg/kg/day prednisolone or equivalent). For symptomatic ILD/pneumonitis (Grade 2 or greater), promptly initiate systemic corticosteroid treatment (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.

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 the pooled safety population, ocular adverse reactions occurred in 36% of patients treated with DATROWAY. Twenty patients (2.2%) experienced Grade 3 ocular adverse reactions, which included keratitis, dry eye, and blurred vision, and one patient experienced a Grade 4 ocular adverse reaction of conjunctival hemorrhage. The most common (≥5%) ocular adverse reactions were dry eye (17%), keratitis (14%), and increased lacrimation (7%). The median time to onset for ocular adverse reactions was 2.3 months (range: 0.03 months to 23.2 months). Of the patients who experienced ocular adverse reactions, 39% had complete resolution, and 10% 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 dosage interruption in 3.6% of patients, dosage reductions in 2.5% of patients, and permanent discontinuation of DATROWAY in 1% of patients.

Patients with clinically significant corneal disease were excluded from clinical studies.

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, withhold, reduce the dose, or permanently discontinue DATROWAY based on severity.

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

In the pooled safety population, stomatitis occurred in 63% of patients treated with DATROWAY, including 8% of patients with Grade 3 events and one patient with a Grade 4 reaction. The median time to first onset of stomatitis was 0.5 months (range: 0.03 months to 18.6 months). Stomatitis led to dosage interruption in 6% of patients, dosage reductions in 11% of patients, and permanent discontinuation of DATROWAY in 0.5% of patients.

In patients who received DATROWAY in TROPION-Breast01, 39% 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, reduce the dose, 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 pooled safety population described in WARNINGS AND PRECAUTIONS reflects exposure to DATROWAY in 927 patients as a single agent at 6 mg/kg administered as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity. This included 137 patients with NSCLC in TROPION-Lung05, 297 patients with NSCLC in TROPION-Lung01, 360 patients with HR-positive, HER2-negative breast cancer in TROPION-Breast01, and 50 patients with NSCLC and 83 patients with breast cancer in TROPION-PanTumor01 (NCT03401385). Among 927 patients who received DATROWAY, 45% were exposed for 6 months or longer and 19% were exposed for greater than one year. In this pooled safety population, the most common (≥20%) adverse reactions were stomatitis (63%), nausea (52%), fatigue (45%), alopecia (38%), constipation (28%), decreased appetite (23%), rash (23%), vomiting (22%), and musculoskeletal pain (20%). In this pooled safety population, the most common (≥2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes (9%) and decreased hemoglobin (3.5%).

Locally Advanced or Metastatic EGFR-Mutated Non-Small Cell Lung Cancer

TROPION-Lung05, TROPION-Lung01, TROPION-PanTumor01

The safety of DATROWAY was evaluated in 125 patients with EGFR-mutated NSCLC who received DATROWAY 6 mg/kg administered as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity in TROPION-Lung05 and TROPION-Lung01 as well as TROPION-PanTumor01 (NCT03401385). Among these patients, the median duration of treatment was 6.1 months (range 0.7 months to 41.7 months).

The median age was 63 years (range: 36 to 81), 56% of patients were <65 years, 62% of patients were female; 66% were Asian, 26% were White, 0.8% were Black, 6% were other races; and 2.4% were of Hispanic ethnicity.

Serious adverse reactions occurred in 26% of patients who received DATROWAY. Serious adverse reactions in >1% of patients who received DATROWAY were COVID-19 (4%), stomatitis (2.4%), and pneumonia (1.6%). Fatal adverse reactions occurred in 1.6% of patients who received DATROWAY, due to death not otherwise specified.

Permanent discontinuation of DATROWAY due to an adverse reaction occurred in 8% of patients. Adverse reactions which resulted in permanent discontinuation of DATROWAY in >1% of patients included ILD/pneumonitis (2.4%) and abnormal hepatic function (1.6%).

Dosage interruptions of DATROWAY due to an adverse reaction occurred in 43% of patients. Adverse reactions which required dosage interruption in >1% of patients included COVID-19 (13%), stomatitis (7%), fatigue (6%), pneumonia (4%), anemia (2.4%), amylase increased (2.4%), keratitis (2.4%), ILD/pneumonitis (1.6%), decreased appetite (1.6%), dyspnea (1.6%), rash (1.6%), and infusion-related reaction (1.6%).

Dose reductions of DATROWAY due to an adverse reaction occurred in 26% of patients. Adverse reactions which required dose reduction in >1% of patients included stomatitis (14%), keratitis (1.6%), fatigue (1.6%), decreased weight (1.6%) and COVID-19 (1.6%).

The most common (≥20%) adverse reactions, including laboratory abnormalities, were stomatitis (71%), nausea (50%), alopecia (49%), fatigue (42%), decreased hemoglobin (34%), decreased lymphocytes (32%), constipation (31%), increased calcium (31%), increased AST (28%), decreased white blood cell count (27%), increased lactate dehydrogenase (23%), musculoskeletal pain (22%), decreased appetite (20%), increased ALT (20%), and rash (20%).

Clinically relevant adverse reactions occurring in <10% of patients who received DATROWAY included dry skin, blurred vision, abdominal pain, conjunctivitis, dry mouth, ILD/pneumonitis, skin hyperpigmentation, increased lacrimation, and visual impairment.

Unresectable or Metastatic, HR-Positive, HER2-Negative Breast Cancer

TROPION-Breast01

The safety of DATROWAY was evaluated in 360 patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC1+ or IHC2+/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 125 patients with EGFR-mutated NSCLC in TROPION-Lung05, TROPION-Lung01, TROPION-PanTumor01 treated with DATROWAY 6 mg/kg, 44% were ≥65 years of age and 10% were ≥75 years of age. No clinically meaningful differences in efficacy and safety were observed between patients ≥65 years of age versus younger patients. 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 WARNINGS AND PRECAUTIONS, and 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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