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Daiichi-Sankyo

Press Release

DATROWAY® Plus Rilvegostomig Showed Promising Tumor Responses in Patients with Metastatic Urothelial Cancer in TROPION-PanTumor03 Phase 2 Trial

- A confirmed objective response rate of 68.2% and a disease control rate of 95.5% was observed with Daiichi Sankyo and AstraZeneca's DATROWAY in combination with rilvegostomig in previously untreated, cisplatin ineligible patients
- TROPION-Urothelial03 phase 2/3 trial initiated to further evaluate the role of DATROWAY plus platinum-based chemotherapy in previously treated metastatic urothelial cancer

Tokyo and Basking Ridge, NJ – (October 17, 2025) – Initial results from one sub-study of the TROPION-PanTumor03 phase 2 trial showed that DATROWAY® (datopotamab deruxtecan) plus rilvegostomig showed promising tumor responses and disease control as first-line and second-line combination therapy in patients with locally advanced or metastatic urothelial cancer. These results were presented today as a mini oral session (3072MO) at the 2025 European Society for Medical Oncology (#ESMO25) Congress.

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). Rilvegostomig is AstraZeneca's PD-1/TIGIT bispecific antibody.

In a sub-study of patients with locally advanced or metastatic urothelial cancer, DATROWAY plus rilvegostomig was evaluated in both the first-line and second-line treatment settings. As first-line treatment for patients not eligible for cisplatin (n=22), DATROWAY plus rilvegostomig demonstrated a confirmed objective response rate (ORR) of 68.2% (95% confidence interval [CI]: 45.1-86.1) and a disease control rate (DCR) of 95.5% (80% CI: 83.4-99.5). Median progression free survival (PFS) was not reached in the first-line setting and the PFS rate was 73.5% (95% CI: 46.5-88.4) at 12 months. As second-line treatment for patients who previously received platinum-based chemotherapy and no prior treatment with immunotherapy (n=18), DATROWAY plus rilvegostomig demonstrated a confirmed ORR of 38.9% (95% CI: 17.3-64.3) and a DCR of 83.3% (80% CI: 66.6-93.7). Median PFS was 12.5 months (95% CI: 4.2-NR) and the PFS rate was 60.0% (95% CI: 33.7–78.7) at 12 months. Median duration of response (DoR) was not yet reached in either setting.

“Despite recent advances in the treatment of metastatic urothelial cancer, there are limited treatment options in both the first-line and second-line settings and many patients still experience disease progression after first-line therapy,” said Sun Young Rha, MD, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea. “The response rates seen with TROPION-PanTumor03 across the first-line and second-line settings, including the disease control rate of 95.5% observed in the first-line setting, highlight the potential of datopotamab deruxtecan plus rilvegostomig and warrant further evaluation across lines of therapy.”

The safety profile of DATROWAY plus rilvegostomig was consistent with the known safety profiles of each agent. Grade 3 or higher treatment-related adverse events (TRAEs) were observed in four of 22 patients (18.2%) receiving first-line treatment and in seven of 18 patients (38.9%) receiving second-line treatment. The most common grade 3 or higher TRAEs occurring in patients treated with DATROWAY plus rilvegostomig in the first-line (n=22) and second-line (n=18) settings, respectively, were increased amylase (13.6%, 16.7%), neutropenia (4.5%, 5.6%), stomatitis (0%, 5.6%), decreased appetite (0%, 5.6%) and anemia (0%, 5.6%). There was one (4.5%) interstitial lung disease (ILD) event adjudicated as drug-related in first-line and two (11.1%) in second-line setting with no grade 3 or higher ILD events observed.

Daiichi Sankyo has initiated the TROPION-Urothelial03 phase 2/3 trial evaluating DATROWAY plus platinum-based chemotherapy compared to gemcitabine and platinum-based chemotherapy in patients with metastatic urothelial carcinoma following progression during or after treatment with enfortumab vedotin in combination with pembrolizumab.

“The five-year survival rate for patients with metastatic urothelial cancer remains very low, underscoring the urgent need for new therapeutic options in this difficult-to-treat population,” said Abderrahmane Laadem, MD, Head, Late-Stage Oncology Development, Daiichi Sankyo. “These results from TROPION-PanTumor03, coupled with results from TROPION-PanTumor01, support further clinical development of DATROWAY in urothelial cancer and we have initiated the TROPION-Urothelial03 phase 2/3 trial, our first pivotal trial outside of breast and lung cancer.”

“These initial TROPION-PanTumor03 results offer further support for our strategy of combining the potency of DATROWAY with the dual PD-1 and TIGIT blockade of rilvegostomig to enhance patients’ immune responses and ultimately, improve outcomes,” said Leora Horn, MD, MSC, FRCPC, Senior Vice President, Late Development Oncology, AstraZeneca. “We are encouraged by the responses observed in patients with metastatic urothelial cancer and hope to further evaluate this combination in the early-line setting.”

In TROPION-PanTumor03, patients were enrolled across seven sub-studies that evaluated DATROWAY as monotherapy or in combination with other approved or investigational cancer medicines. In a sub-study evaluating patients with locally advanced or metastatic urothelial cancer (sub-study 6, cohort 6B [n=40]), patients received DATROWAY in combination with rilvegostomig in either the first-line setting (cisplatin ineligible patients with no prior systemic therapy, or progression more than 12 months after neoadjuvant or adjuvant therapy) or the second-line setting (previous platinum-based chemotherapy in the locally advanced or metastatic setting, or progression less than 12 months after platinum-based neoadjuvant or adjuvant therapy). Of the second-line patients who were not previously treated with immunotherapy (n=18), six had previous treatment in the adjuvant or neoadjuvant setting with progression within 12 months and 12 had been treated in the metastatic setting. Median duration of follow-up was 10.8 months and 9.7 months in the first-line and second-line setting, respectively.

Summary of Sub-study 6, Cohort 6B of TROPION-PanTumor03 Efficacy Results

Efficacy Measure	**First-Line Subset (n=22)**	**Second-Line Subset (n=18)**
Confirmed ORR,[i,ii] (%) (95% CI)	68.2% (45.1–86.1)	38.9% (17.3–64.3)
CR, n (%)	1 (4.5%)	0
PR, n (%)	14 (63.6%)	7 (38.9%)
SD, n (%)	6 (27.3%)	8 (44.4%)
PD, n (%)	1 (4.6%)[iii]	3 (16%)
DCR at 12 weeks,[iv] (%) (80% CI)	95.5% (83.4–99.5)	83.3% (66.6–93.7)
DoR, median [ii] (months) (95% CI)	NR (9.4 months–NR)	NR (6.9 months–NR)
PFS median[ii] (months) (95% CI)	NR (10.8 months–NR)	12.5 months (4.2 months–NR)

CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NR, not reached; 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]Patient has no post-baseline assessment and died less than 13 weeks after first dose
[iv]Proportion of patients who had achieved a CR or PR in the first 13 weeks or who had SD for at least 11 weeks after start of treatment as assessed by investigator

About TROPION-PanTumor03

TROPION-PanTumor03 is a global, multicenter, multi-cohort, open-label, phase 2 trial evaluating the efficacy and safety of DATROWAY as monotherapy and in combination with various approved or investigational cancer medicines across seven sub-studies in several metastatic solid cancers, including endometrial, gastric, prostate, ovarian, colorectal, urothelial and biliary tract cancer.

Cohort 6B is evaluating DATROWAY (6 mg/kg) plus rilvegostomig as first-line and second-line combination therapies in patients with locally advanced or metastatic urothelial cancer. The primary endpoint is ORR as assessed by investigator as well as safety and tolerability. Secondary endpoints include investigator-assessed DCR, DoR, PFS as assessed by investigator as well as pharmacokinetics.

TROPION-PanTumor03 will enroll approximately 580 patients across all sub-studies in Asia, Europe and North America. For more information visit ClinicalTrials.gov.

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).

About TROPION-Urothelial03

TROPION-Urothelial03 is a global, multicenter, randomized, open-label phase 2/3 trial evaluating the efficacy and safety of DATROWAY plus platinum-based chemotherapy (carboplatin or cisplatin) versus gemcitabine plus platinum-based chemotherapy in patients with locally advanced or metastatic urothelial carcinoma with disease progression during or after enfortumab vedotin plus pembrolizumab combination treatment. The phase 2 part of the trial will determine the recommended dose of DATROWAY (4 mg/kg or 6 mg/kg) in combination with carboplatin or cisplatin. The phase 3 part will evaluate the efficacy and safety of DATROWAY at the recommended dose plus carboplatin or cisplatin versus gemcitabine plus carboplatin or cisplatin.

The primary endpoint of the phase 2 part of TROPION-Urothelial03 is ORR assessed by investigator. Secondary endpoints include DoR, PFS, DCR, time to response (TTR), overall survival (OS) and safety.

The dual primary endpoints of the phase 3 part of TROPION-Urothelial03 are PFS assessed by blinded independent central review (BICR) and OS. Secondary endpoints include PFS by investigator, ORR, DoR, TTR, DCR, each assessed by BICR and by investigator, and safety.

TROPION-Urothelial03 will enroll approximately 630 patients at sites in Asia, Europe, North America, Oceania and South America. For more information visit ClinicalTrials.gov.

About Urothelial (Bladder) Cancer

More than 610,000 bladder cancer cases were diagnosed globally in 2022.[1] The most common type of bladder cancer is urothelial cancer, accounting for approximately 90% of cases.[2] While the five-year survival rate for localized bladder cancer is more than 70%, survival decreases to approximately 9% in the metastatic setting.[3,4]

While targeted therapies have improved outcomes in the first-line metastatic setting, disease progression is common and treatment options in the second-line setting are limited.[5]

TROP2 is a protein broadly expressed in several solid tumors including urothelial cancer.[6] TROP2 expression is positively correlated with disease severity in patients with urothelial cancer.[7]

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 35 countries/regions 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 non-small cell lung cancer (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, triple negative breast cancer and urothelial 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 cancer 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%).

<u>Locally Advanced or Metastatic EGFR-Mutated Non-Small Cell Lung Cancer</u>

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 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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