Press Release

Daiichi-Sankyo

TROPION-Urothelial04 Phase 3 Trial of Datroway® Initiated as Adjuvant Therapy in Patients with High-Risk Muscle Invasive Urothelial Cancer

Tokyo – **(August 26, 2026)** – The first patient has been dosed in the TROPION-Urothelial04 phase 3 trial evaluating Datroway® (datopotamab deruxtecan) plus rilvegostomig or Datroway monotherapy versus current standard of care (durvalumab monotherapy or nivolumab monotherapy or enfortumab vedotin plus pembrolizumab) as an adjuvant treatment (after surgery) in patients with muscle invasive urothelial cancer (MIUC) at high risk of recurrence following radical surgical resection with or without prior neoadjuvant therapy.

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/NYSE: AZN). Rilvegostomig is AstraZeneca's anti-PD-1/TIGIT dual checkpoint inhibitor bispecific antibody.

MIUC is a highly progressive disease, representing approximately 30% of all urothelial cancer cases.[1,2] While adjuvant immunotherapy remains standard of care in the muscle invasive setting, many patients still face a high risk for disease recurrence after surgery, underscoring the need for new treatments that can further improve long-term outcomes.[3] There are currently no TROP2 directed medicines approved for the treatment of urothelial cancer.

"Following the encouraging results in the urothelial cancer cohorts of the TROPION-PanTumor03 and TROPION-PanTumor01 trials, we are now evaluating the combination of Datroway and rilvegostomig in earlier lines of treatment for this disease," said Abderrahmane Laadem, MD, Head, Therapeutic Area Oncology Development, Daiichi Sankyo. "TROPION-Urothelial04 marks our second pivotal trial in urothelial cancer as we continue to identify different types of cancer where Datroway may contribute to improving outcomes for patients."

"Patients with muscle invasive urothelial cancer continue to face a significant risk of disease recurrence despite recent new advances," said Leora Horn, MD, FRCPC, Senior Vice President, Late Development Oncology, AstraZeneca. "TROPION-Urothelial04 will allow us to further evaluate the potential of Datroway in combination with rilvegostomig to help advance treatment approaches and move closer to a cure for these patients with significant unmet need."

Daiichi Sankyo and AstraZeneca also are 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 in the TROPION-Urothelial03 phase 2/3 trial.

About TROPION-Urothelial04

TROPION-Urothelial04 is a global, multicenter, three-arm open-label phase 3 trial where patients will be randomized in a 2:1:2 ratio to evaluate the efficacy and safety of Datroway in combination with rilvegostomig or Datroway monotherapy versus current standard of care (durvalumab monotherapy or nivolumab monotherapy or enfortumab vedotin plus pembrolizumab) in patients with high-risk MIUC, including those with residual disease at surgical resection following neoadjuvant therapy and those with high-risk disease after surgery without neoadjuvant therapy.

The primary endpoint of TROPION-Urothelial04 is disease free survival (DFS) as assessed by investigator for the combination of Datroway and rilvegostomig versus standard of care. Key secondary endpoints include DFS as

assessed by blinded independent central review, disease specific survival, non-urothelial tract recurrence-free survival, distant metastasis-free survival, patient reported outcomes, overall survival and safety.

TROPION-Urothelial04 will enroll approximately 915 patients across multiple sites in Asia, Europe, North America, Oceania and South America. For more information about the trial, visit ClinicalTrials.gov.

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

About Urothelial Cancer

The most common type of bladder cancer is urothelial cancer, accounting for approximately 90% of cases.[4] Urothelial cancer can originate in the upper urinary tract (renal pelvis, ureter) or the lower urinary tract (bladder, urethra).[5] Muscle invasive urothelial cancer is a highly progressive disease, which occurs when the cancer has spread to the muscle walls of the bladder and represents approximately 30% of all urothelial cancer cases.[1,2,6] More than 635,000 bladder cancer cases were diagnosed globally in 2024, and while the five-year survival rate for localized urothelial and bladder cancer is more than 70%, survival decreases to approximately 9% in the metastatic setting.[6,7,8]

While adjuvant immunotherapy remains standard of care in the muscle invasive setting, many patients still face a high risk for disease recurrence after surgery, underscoring the need for new treatments that can further improve long-term outcomes.[3]

TROP2 is a protein broadly expressed in several solid tumors including urothelial cancer.[9] TROP2 expression is positively correlated with disease severity in patients with urothelial cancer.[10]

About Datroway

Datroway (datopotamab deruxtecan; datopotamab deruxtecan-dlnk in the U.S. only) is a TROP2 directed ADC. Designed using the proprietary DXd ADC Technology of Daiichi Sankyo, Datroway is one of seven 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/regions worldwide for the treatment of adult patients with unresectable or metastatic triple negative breast cancer (TNBC) who are not candidates for PD-1/PD-L1 inhibitor therapy based on the results from the TROPION-Breast02 trial.

Datroway (6 mg/kg) is approved in more than 45 countries/regions 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 Brazil, Russia, Singapore 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 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 a 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 urothelial cancer. The program includes eight phase 3 trials in lung cancer, five phase 3 trials in breast cancer, one phase 3 trial and one phase 2/3 trial in urothelial 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.

Datroway U.S. Indication and Important Safety Information

Indications

DATROWAY® (datopotamab deruxtecan-dlnk) 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 triple-negative breast cancer (TNBC) who are not candidates for PD-1/PD-L1 inhibitor therapy.

- 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.

Important Safety Information

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 first 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 841 patients with breast cancer from TROPION-Breast01, TROPION-Breast02, TROPION-PanTumor01 and TROPION-PanTumor02, ILD/pneumonitis occurred in 3.0% of patients treated with DATROWAY, including 0.4% of patients with Grade 3. There were two fatal cases (0.2%). The median time to first onset for ILD was 5.3 months (range: 1.1 months to 19.3 months) and with a median duration of 1.2 months (range: 0.3 months to 5.2 months). Eight patients (1.0%) had DATROWAY withheld and 10 patients (1.2%) permanently discontinued DATROWAY due to ILD/pneumonitis. Systemic corticosteroids were required in 64% (16/25) 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 38% of patients treated with DATROWAY. Forty-two patients (3.1%) experienced Grade 3 ocular adverse reactions, which included keratitis and dry eye, and four patients (0.3%) experienced a Grade 4 ocular adverse reaction of keratitis, corneal epithelium defect, corneal lesion, and conjunctival hemorrhage. The most common (≥5%) ocular adverse reactions were dry eye (18%), keratitis (16%), increased lacrimation (6%), and conjunctivitis (5%). The median time to first onset for ocular adverse reactions was 2.3 months (range: 0.03 months to 30 months) and with a median duration of 2.3 months (range: 0.03 months to 19.5 months). Of the patients who experienced ocular adverse reactions, 39% had complete resolution, and 8% 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 4.3% of patients, dosage reductions in 2.8% of patients, and permanent discontinuation of DATROWAY in 0.9% of patients.

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

Advise patients to use preservative-free lubricant eye drops at least four times daily and as needed 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, at end of treatment, and as clinically indicated. While on treatment, conduct visual acuity testing and slit lamp examination every 3 cycles.

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 19.8 months) and with a median duration of 1.1 months (range: 0.03 months to 33.2 months). Stomatitis led to dosage interruption in 5% of patients, dosage reductions in 11% of patients, and permanent discontinuation of DATROWAY in 0.4% of patients.

In patients who received DATROWAY in TROPION-Breast01 and TROPION-Breast02, 39% and 51% respectively 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 1365 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, 319 patients with TNBC in TROPION-Breast02, 50 patients with NSCLC and 83 patients with breast cancer in TROPION-PanTumor01, and 40 patients with NSCLC and 79 patients with breast cancer in TROPION-PanTumor02. Among the 1365 patients who received DATROWAY, 48% were exposed for greater than 6 months and 22% were exposed for greater than one year. In this pooled safety population, the most common (≥20%) adverse reactions were stomatitis (63%), nausea (51%), fatigue (42%), alopecia (38%), constipation (30%), vomiting (23%), decreased appetite (22%), and rash (20%). In this pooled safety population, the most common (≥2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes (8%), decreased hemoglobin (3.7%), decreased sodium (3.0%), and decreased blood potassium (2.3%).

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. 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 Triple-Negative Breast Cancer (TNBC)

TROPION-Breast02

The safety of DATROWAY was evaluated in 319 patients with triple-negative breast cancer who received at least one dose of DATROWAY 6 mg/kg in TROPION-Breast02. DATROWAY was administered by intravenous infusion once every three weeks. The median duration of treatment was 8.5 months (range: 0.7 months to 38.0 months) for patients who received DATROWAY.

Serious adverse reactions occurred in 17% of patients who received DATROWAY. Serious adverse reactions in >1% of patients who received DATROWAY were pneumonia (2.2%), vomiting (1.9%), COVID-19 (1.6%), and anemia (1.3%). Fatal adverse reactions occurred in one patient (0.3%) who received DATROWAY and was due to ILD/pneumonitis.

Permanent discontinuation of DATROWAY due to an adverse reaction occurred in 4.7% of patients. Adverse reactions which resulted in permanent discontinuation of DATROWAY in >0.5% of patients included ILD/pneumonitis (0.9%) and keratitis (0.9%).

Dosage interruptions of DATROWAY due to an adverse reaction occurred in 35% of patients. Adverse reactions which required dosage interruption in >1% of patients included stomatitis (5%), increased amylase (4.1%), keratitis (3.4%), neutropenia (3.1%), COVID-19 (2.8%), pneumonia (2.2%), dry eye (1.9%), upper respiratory tract infection (1.6%), anemia (1.3%), leukopenia (1.3%), IRR (1.3%), and ILD/pneumonitis (1.3%).

Dose reductions of DATROWAY due to an adverse reaction occurred in 28% of patients. Adverse reactions which required dose reduction in >1% of patients included stomatitis (11%), keratitis (4.1%), fatigue (3.8%), increased amylase (2.8%), and pneumonia (1.3%).

The most common (≥20%) adverse reactions, including laboratory abnormalities in patients receiving DATROWAY, were stomatitis (63%), increased amylase (54%), nausea (48%), alopecia (43%), decreased hemoglobin (43%), decreased white blood cells (41%), constipation (40%), decreased calcium (39%), decreased lymphocytes (36%), fatigue (36%), decreased neutrophils (35%), increased ALT (28%), increased AST (27%), dry eye (26%), keratitis (26%), decreased albumin (25%), vomiting (23%), musculoskeletal pain (22%), decreased sodium (21%), and increased blood alkaline phosphatase (20%).

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

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, 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 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 841 patients with breast cancer in TROPION-Breast01, TROPION-Breast02, TROPION-PanTumor01, and TROPION-PanTumor02 treated with DATROWAY 6 mg/kg, 23% were ≥65 years of age and 4.5% were ≥75 years of age. Grade ≥3 and serious adverse reactions were more common in patients ≥65 years (45% and 22%, respectively) compared to patients <65 years (38% and 16%, respectively). No other meaningful differences in efficacy and safety were observed between patients ≥65 years of age versus younger patients.
- **Renal Impairment:** Monitor patients with renal impairment for increased adverse reactions, including respiratory reactions. A higher incidence of ILD/pneumonitis has been observed in patients with creatinine clearance (CLcr) 30 to <90 mL/min (estimated by Cockcroft Gault). No dosage adjustment is recommended in patients with CLcr 30 to <90 mL/min. The pharmacokinetics of datopotamab deruxtecan-dlnk or DXd in patients with CLcr <30 mL/min is unknown.
- **Hepatic Impairment:** Monitor patients with moderate hepatic impairment (total bilirubin >1.5 to 3 times ULN and any AST) for increased adverse reactions. Limited data are available in patients with moderate 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). 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 Prescribing Information and Medication Guide for additional Important Safety Information.

About the ADC Portfolio of Daiichi Sankyo

The Daiichi Sankyo ADC portfolio consists of eight ADCs in clinical development crafted from ADC technology discovered in-house by Daiichi Sankyo.

The DXd ADC Technology platform of Daiichi Sankyo consists of seven ADCs in clinical development where each ADC is comprised of a monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers. The DXd ADCs include Enhertu and Datroway, which are being jointly developed and commercialized globally with AstraZeneca, and ifinatamab deruxtecan (I-DXd), raludotatug deruxtecan (R-DXd) and patritumab deruxtecan (HER3-DXd), which are being jointly developed and commercialized globally with Merck & Co., Inc, Rahway, NJ, USA. DS-3939 and DS3790 are being developed by Daiichi Sankyo.

An additional ADC being developed by Daiichi Sankyo is DS3610, which consists of an antibody attached to a novel payload that acts as an agonist of STING.

Ifinatamab deruxtecan, raludotatug deruxtecan, patritumab deruxtecan, DS-3939, DS3610 and DS3790 are investigational medicines that have not been approved for any indication in any country. Safety and efficacy have not been established.

About Daiichi Sankyo

Daiichi Sankyo (TSE: 4568) is a global healthcare company committed to becoming a trusted healthcare innovator, transforming the lives of people through its strength in science and technology. The company discovers and develops new standards of care to address diverse medical needs to fulfill its purpose of contributing to the enrichment of quality of life around the world. With a strategic focus on oncology, Daiichi Sankyo is advancing an industry-leading antibody drug conjugate portfolio along with identifying new breakthrough generating technologies to deliver practice-changing medicines to patients, healthcare professionals and society. For more information, please visit www.daiichisankyo.com.

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