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Daiichi-Sankyo

Press Release

DATROWAY® Approved in the U.S. for Patients with Previously Treated Metastatic HR Positive, HER2 Negative Breast Cancer

- First approval in the U.S. for Daiichi Sankyo and AstraZeneca's DATROWAY based on TROPION-Breast01 results showing 37% reduction in the risk of disease progression or death versus chemotherapy
- Second DXd antibody drug conjugate approved in U.S. based on Daiichi Sankyo's DXd technology

Tokyo and Basking Ridge, NJ – (January 17, 2025) – DATROWAY® (datopotamab deruxtecan-dlnk) has been approved in the U.S. for the treatment of adult patients with unresectable or metastatic hormone receptor (HR) positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

DATROWAY is a specifically engineered TROP2 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo (TSE: 4568) and being jointly developed by Daiichi Sankyo and AstraZeneca (LSE/STO/Nasdaq: AZN). DATROWAY is the second DXd ADC approved in the U.S. based on Daiichi Sankyo's DXd ADC Technology.

The approval by the U.S. Food and Drug Administration (FDA) was based on results from the TROPION-Breast01 phase 3 trial. In the trial, DATROWAY significantly reduced the risk of disease progression or death by 37% compared to investigator's choice of chemotherapy (hazard ratio [HR]=0.63; 95% confidence interval [CI]: 0.52-0.76; p<0.0001) in patients with HR positive, HER2 negative metastatic breast cancer as assessed by blinded independent central review (BICR). Median progression-free survival (PFS) was 6.9 months in patients treated with DATROWAY versus 4.9 months with chemotherapy. A confirmed objective response rate (ORR) of 36% was observed in the DATROWAY arm compared to an ORR of 23% observed in the chemotherapy arm. Two (0.5%) complete responses (CR) and 131 (36%) partial responses (PR) were observed in the DATROWAY arm compared to zero CR and 84 PR (23%) in the chemotherapy arm. The median duration of response (DoR) was 6.7 months (95% CI: 5.6-9.8) in the DATROWAY arm compared to 5.7 (95% CI: 4.9-6.8) in the chemotherapy arm.

"Despite considerable progress in the HR positive, HER2 negative metastatic breast cancer treatment landscape, new therapies are still needed to tackle the frequent and complex challenge of disease progression after endocrine and initial chemotherapy," said Aditya Bardia, MD, MPH, Program Director of Breast Oncology and Director of Translational Research Integration at the UCLA Health Jonsson Comprehensive Cancer Center and Global Principal Investigator for TROPION-Breast01. "The approval of datopotamab

deruxtecan, a novel TROP2 directed antibody drug conjugate, marks a major therapeutic milestone and provides patients with metastatic breast cancer a new treatment alternative to conventional chemotherapy."

"Only one in three patients with metastatic HR positive, HER2 negative breast cancer live more than five years following diagnosis, highlighting the urgent need for additional effective therapies," said Caitlin Lewis, Senior Vice President of Strategy & Mission, Living Beyond Breast Cancer. "The approval of DATROWAY is a significant advance, offering patients with metastatic HR positive breast cancer a new and much needed treatment option."

In TROPION-Breast01, the safety of DATROWAY (6 mg/kg) was evaluated in 360 patients. The most common (>20%) adverse reactions, including laboratory abnormalities, were stomatitis, nausea, fatigue, decreased leukocytes, decreased calcium, alopecia, decreased lymphocytes, decreased hemoglobin, constipation, decreased neutrophils, dry eye, increased alanine transaminase, vomiting, increased aspartate aminotransferase, increased alkaline phosphatase, and keratitis. Serious adverse reactions among patients who received DATROWAY included urinary tract infection (1.9%), COVID-19 infection (1.7%), interstitial lung disease (ILD)/pneumonitis (1.1%), acute kidney injury (0.6%), pulmonary embolism (0.6%), vomiting (0.6%), diarrhea (0.6%), hemiparesis (0.6%), and anemia (0.6%). One patient fatality (0.3%) was attributed to an adverse reaction (ILD/pneumonitis).

"The approval of DATROWAY provides patients with HR positive, HER2 negative breast cancer previously treated with endocrine-based therapy and traditional chemotherapy with the opportunity to be treated with a new TROP2 directed antibody drug conjugate earlier in the metastatic setting," said Ken Keller, Global Head of Oncology Business, and President and CEO, Daiichi Sankyo, Inc. "DATROWAY is the latest addition to our portfolio of innovative cancer treatments and marks the fourth medicine from our oncology pipeline to receive approval in the U.S."

"With this first approval of DATROWAY in the U.S., we continue to deliver on our ambition for antibody drug conjugates to improve upon and replace conventional chemotherapy for the treatment of multiple cancers," said Dave Fredrickson, Executive Vice President, Oncology Hematology Business Unit, AstraZeneca. "We are proud to bring DATROWAY to people living with metastatic HR positive, HER2 negative breast cancer, and this approval marks the eighth new medicine of the 20 we have set out to deliver across AstraZeneca by 2030."

DATROWAY will be available by prescription in the U.S. in approximately two weeks. 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-DAT-RO4U (1-855-328-7648).

Additional regulatory submissions for DATROWAY in breast cancer are under review in the EU, China and other regions.

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

About TROPION-Breast01

TROPION-Breast01 is a global, randomized, multicenter, open-label phase 3 trial evaluating the efficacy and safety of intravenous DATROWAY (6 mg/kg) once per 21-day cycle versus investigator's choice of single-agent chemotherapy (eribulin, capecitabine, vinorelbine or gemcitabine) in adult patients with unresectable or metastatic HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have progressed on and are not suitable for endocrine therapy per investigator assessment and have received at least one prior line of chemotherapy for unresectable or metastatic disease.

Following disease progression or discontinuation of DATROWAY or chemotherapy, patients had the option to receive a subsequent treatment at the discretion of their physician. Crossover between trial arms was not permitted.

The dual primary endpoints of TROPION-Breast01 are PFS as assessed by BICR and OS. Key secondary endpoints include ORR, duration of response, investigator-assessed PFS, disease control rate, time to first subsequent therapy and safety. The PFS data and additional results for key secondary endpoints of TROPION-Breast01 were published in the *Journal of Clinical Oncology*.

TROPION-Breast01 enrolled 732 patients in Africa, Asia, Europe, North America and South America. For more information visit ClinicalTrials.gov.

About Hormone Receptor Positive, HER2 Negative Breast Cancer

In the U.S., more than 300,000 cases of breast cancer are diagnosed annually.[1] While survival rates are high for those diagnosed with early breast cancer, only about 30% of patients diagnosed with or who progress to metastatic disease are expected to live five years following diagnosis.[2]

Approximately 70% of diagnosed cases are considered what has been historically called HR positive, HER2 negative breast cancer (measured as HER2 score of IHC 0, IHC 1+ or IHC 2+/ISH-).[2] Endocrine therapies are widely given consecutively in the early lines of treatment for HR positive metastatic breast cancer.[3]

However, after initial treatment, further efficacy from endocrine therapy is often limited.[3] The current standard of care following endocrine therapy is chemotherapy, which is associated with poor response rates and outcomes.[3,4,5,6]

About DATROWAY

DATROWAY (datopotamab deruxtecan-dlnk) 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 the U.S. and Japan for the treatment of adult patients with unresectable or metastatic HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease based on the results from the TROPION-Breast01 trial.

About the DATROWAY Clinical Development Program

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

About the Daiichi Sankyo and AstraZeneca Collaboration

Daiichi Sankyo and AstraZeneca entered into a global collaboration to jointly develop and commercialize ENHERTU® in March 2019 and DATROWAY in July 2020, except in Japan where Daiichi Sankyo maintains exclusive rights for each ADC. Daiichi Sankyo is responsible for the manufacturing and supply of ENHERTU and DATROWAY.

About the ADC Portfolio of Daiichi Sankyo

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

The ADC platform furthest in clinical development is Daiichi Sankyo's DXd ADC Technology where each ADC consists of a monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an

exatecan derivative, DXd) via tetrapeptide-based cleavable linkers. The DXd ADC portfolio currently consists of ENHERTU, a HER2 directed ADC, and DATROWAY, a TROP2 directed ADC, which are being jointly developed and commercialized globally with AstraZeneca. Patritumab deruxtecan (HER3-DXd), a HER3 directed ADC, ifinatamab deruxtecan (I-DXd), a B7-H3 directed ADC, and raludotatug deruxtecan (R-DXd), a CDH6 directed ADC, are being jointly developed and commercialized globally with Merck & Co., Inc, Rahway, NJ, USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

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

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

DATROWAY U.S. Important Safety Information

Indication
DATROWAY® is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic, hormone receptor (HR)-positive, HER2negative (IHC 0, IHC 1+, or IHC 2+/ISH−) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

Contraindications
None.

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

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

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

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

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

In TROPION-Breast01, ocular adverse reactions occurred in 51% of patients treated with DATROWAY. Seven patients (1.9%) experienced Grade 3 ocular adverse reactions, including dry eye, keratitis, and blurred vision. The most common (≥5%) ocular adverse reactions were dry eye (27%), keratitis (24%), blepharitis and increased lacrimation (8% each), and meibomian gland dysfunction (7%). Patients with clinically significant corneal disease were excluded from TROPION-Breast01.

The median time to onset for ocular adverse reactions was 2.1 months (range: 0.03 months to 23.2 months). Of the patients who experienced ocular adverse reactions, 45% had complete resolution; 9% had partial improvement (defined as a decrease in severity by one or more grades from the worst grade at last follow up). Ocular adverse reactions led to permanent discontinuation of DATROWAY in 0.8% of patients. Advise patients to use preservative-free lubricant eye drops several times daily for prophylaxis. Advise patients to avoid use of contact lenses unless directed by an eye care professional.

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

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

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

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

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

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

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

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

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

Adverse Reactions
The safety of DATROWAY was evaluated in 360 patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH−) breast cancer who received at least one dose of DATROWAY 6 mg/kg in TROPION-Breast01. DATROWAY was administered by intravenous infusion once every three weeks. The median duration of treatment was 6.7 months (range: 0.7 months to 16.1 months) for patients who received DATROWAY.

Serious adverse reactions occurred in 15% of patients who received DATROWAY. Serious adverse reactions in >0.5% of patients who received DATROWAY were urinary tract infection (1.9%), COVID19 infection (1.7%), ILD/pneumonitis (1.1%), acute kidney injury, pulmonary embolism, vomiting, diarrhea, hemiparesis, and anemia (0.6% each). Fatal adverse reactions occurred in 0.3% of patients who received DATROWAY and were due to ILD/pneumonitis.

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

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

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

Use in Specific Populations
- **Pregnancy:** Based on its mechanism of action, DATROWAY can cause embryo-fetal harm when administered to a pregnant woman because the topoisomerase inhibitor component of DATROWAY, DXd, is genotoxic and affects actively dividing cells. There are no available data on the use of DATROWAY in pregnant women to inform a drug-associated risk. Advise patients of the potential risks to a fetus.
- **Lactation:** There are no data regarding the presence of datopotamab deruxtecan-dlnk or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with DATROWAY and for 1 month after the last dose.
- **Females and Males of Reproductive Potential:** Pregnancy Testing: Verify pregnancy status of females of reproductive potential prior to initiation of DATROWAY. Contraception: *Females:* Advise females of reproductive potential to use effective contraception during treatment with DATROWAY and for 7 months after the last dose. *Males:* Because of the potential for genotoxicity, advise male patients with female partners of reproductive potential to use effective contraception during treatment with DATROWAY and for 4 months after the last dose. Infertility: Based on findings in animal toxicity studies, DATROWAY may impair male and female reproductive function and fertility. The effects on reproductive organs in animals were irreversible.

- **Pediatric Use:** Safety and effectiveness of DATROWAY have not been established in pediatric patients.
- **Geriatric Use:** Of the 365 patients in TROPION-Breast01 treated with DATROWAY 6 mg/kg, 25% were ≥65 years of age and 5% were ≥75 years of age. Grade ≥3 and serious adverse reactions were more common in patients ≥65 years (42% and 25%, respectively) compared to patients <65 years (33% and 15%, respectively). In TROPION-Breast01, no other meaningful differences in safety or efficacy were observed between patients ≥65 years of age versus younger patients.
- **Renal Impairment:** A higher incidence of ILD/pneumonitis has been observed in patients with mild and moderate renal impairment (creatinine clearance [CLcr] 30 to <90 mL/min). Monitor patients with renal impairment for increased adverse reactions, including respiratory reactions. No dosage adjustment is recommended in patients with mild to moderate renal impairment. The effect of severe renal impairment (CLcr <30 mL/min) on the pharmacokinetics of datopotamab deruxtecan-dlnk or DXd is unknown.
- **Hepatic Impairment:** No dosage adjustment is recommended in patients with mild hepatic impairment (total bilirubin ≤ULN and any AST >ULN or total bilirubin >1 to 1.5 times ULN and any AST). Limited data are available in patients with moderate hepatic impairment (total bilirubin >1.5 to 3 times ULN and any AST). Monitor patients with moderate hepatic impairment for increased adverse reactions. The recommended dosage of DATROWAY has not been established for patients with severe hepatic impairment (total bilirubin >3 times ULN and any AST).

To report SUSPECTED ADVERSE REACTIONS, contact Daiichi Sankyo, Inc. at 1-877-437-7763 or FDA at 1-800-FDA-1088 or fda.gov/medwatch.

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

About Daiichi Sankyo

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

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References

[1] American Cancer Society. Key Statistics for Breast Cancer. Accessed January 2025.
[2] National Cancer Institute. SEER Cancer Stat Facts: Female Breast Cancer Subtypes. Accessed January 2025.
[3] Manohar P, et al. *Cancer Biol Med*. 2022 Feb 15; 19(2):202–212.
[4] Cortes J, et al. *Lancet*. 2011;377:914-923.
[5] Yuan P, et al. *Eur J Cancer*. 2019;112:57-65.
[6] Jerusalem G, et al. *JAMA Oncol*. 2018;4(10):1367–1374.