

Press Release

Raludotatug Deruxtecan Continues to Demonstrate Promising Clinical Activity in Patients with Advanced Ovarian Cancer in Early Trial

- Encouraging overall response rate of 46% and disease control rate of 98% with a median duration of response of 11.2 months seen with raludotatug deruxtecan in heavily pretreated patients
- Plans underway to initiate late-stage trial of raludotatug deruxtecan in advanced ovarian cancer

Tokyo and Basking Ridge, NJ – (October 22, 2023) – Updated results from a subgroup analysis of a first-in-human [phase 1 trial](#) showed that raludotatug deruxtecan (R-DXd) continues to demonstrate promising clinical activity in patients with heavily pretreated platinum-resistant advanced ovarian cancer. These data were presented today during a mini-oral session ([745MO](#)) at the 2023 European Society for Medical Oncology (#ESMO23).

Raludotatug deruxtecan is a specifically engineered potential first-in-class CDH6 directed DXd antibody drug conjugate (ADC) being jointly developed by Daiichi Sankyo (TSE: 4568) and Merck & Co., Inc., Rahway, N.J., USA (known as MSD outside of the United States and Canada).

Approximately 70% to 80% of patients diagnosed with ovarian cancer will have a recurrence of disease following standard treatment with platinum-based chemotherapy regimens.¹ An estimated 65% to 85% of patients with ovarian cancer have expression of CDH6, which is associated with poor prognosis.^{2,3}

A confirmed objective response rate (ORR) of 46% (95% CI: 32–61) by investigator assessment was observed in the subgroup of 50 patients with measurable ovarian cancer receiving raludotatug deruxtecan (4.8 to 8.0 mg/kg) in the phase 1 trial. One complete response (CR), 22 partial responses (PRs) and four unconfirmed responses were seen. A disease control rate (DCR) of 98% was observed. Median duration of response (DOR) was 11.2 months (95% CI: 3.0-NE) and median progression-free survival (PFS) was 7.9 months (95% CI: 4.4-12.4) as of the data cutoff of July 14, 2023. Responses were observed in patients with a range of tumor CDH6 expression.

“Following treatment with the current standard of care of platinum-based chemotherapy, disease progression in patients with advanced ovarian cancer is inevitable and underscores the need for new treatment options,” said Erika Hamilton, MD, Director, Breast Cancer and Gynecologic Cancer Research,

Sarah Cannon Research Institute, Nashville, Tennessee. “The response rate seen in these heavily pretreated patients is promising and further study of raludotatug deruxtecan in ovarian cancer is warranted.”

The safety profile of raludotatug deruxtecan was consistent with previous reports from the phase 1 trial. Treatment discontinuations due to treatment-emergent adverse events (TEAEs) occurred in 15% of patients. Grade 3 or higher TEAEs occurred in 51.7% of patients. The most common grade ≥ 3 or higher TEAEs occurring in patients were anemia (18.3%), decreased neutrophil count (11.7%), decreased platelet count (5.0%), fatigue (3.3%), nausea (1.7%), vomiting (1.7%), diarrhea (1.7%) and decreased appetite (1.7%). Two grade 2 interstitial lung disease (ILD) events were confirmed as treatment-related by an independent adjudication committee across the 4.8 to 6.4 mg/kg doses. Two grade 5 treatment-related ILD events were reported at the 8.0 mg/kg dose, which has been discontinued as of October 2022.

“In addition to the response rate seen with raludotatug deruxtecan, the median duration of response of 11.2 months and disease control achieved by more than 98% of patients with platinum-resistant advanced ovarian cancer is encouraging,” said Mark Rutstein, MD, Global Head, Oncology Clinical Development, Daiichi Sankyo. “We look forward to further evaluation of our CDH6 directed antibody drug conjugate in this population of patients that currently face poor outcomes with limited treatment options.”

A majority of patients (91.7%) had platinum-resistant disease with four median prior lines of systemic therapy (range, 1-13) including bevacizumab (68.3%) and a PARP inhibitor (65%). The median follow-up for DOR was 5.8 months (range, 1.4-16.8) and the median follow-up for PFS was 5.6 months (range, 0.03-25.1). The median treatment duration was 18 weeks (range 3-115) and 33 patients remain on treatment with raludotatug deruxtecan.

Summary of Ovarian Cancer Subset Efficacy Analysis of Phase 1 Trial

Efficacy Measure	Patients with ovarian cancer receiving doses of raludotatug deruxtecan (between 4.8 and 8.0 mg/kg), evaluable for RECIST v.1.1 n=50
Confirmed ORR, % (95% CI)	46% (32–61)
CR, n	1
PR, n	22
DCR	98%
DOR, median (95% CI), months	11.2 months (3.0-NE)
PFS, median (95% CI), months	7.9 months (4.4-12.4)

CR, complete response; DCR, disease control rate; DOR, duration of response; ORR, objective response rate; PR, partial response; PFS, progression-free survival.

About the Phase 1 Trial

The phase 1 trial is the first-in-human, open-label study evaluating the safety and efficacy of raludotatug deruxtecan in patients with advanced ovarian cancer resistant or refractory to standard of care and previously treated with platinum-based and taxane chemotherapy. Patients were not selected based on tumor CDH6 expression status.

The first part of the trial (dose escalation) assessed the safety and tolerability of increasing doses of raludotatug deruxtecan to determine the maximum tolerated dose and/or recommended dose for expansion (RDE) in patients with advanced ovarian tumors. The second part of the trial (dose expansion) initially evaluated the safety and efficacy of raludotatug deruxtecan at the RDE of 8.0 mg/kg, which was discontinued as of October 2022. Further assessment is currently ongoing at the 4.8, 5.6 and 6.4 mg/kg doses.

The trial will evaluate safety endpoints including dose-limiting toxicities and adverse events as well as efficacy endpoints including ORR by investigator assessment, DOR, DCR, time to response and PFS. Pharmacokinetic and exploratory biomarker endpoints also will be assessed.

Patient enrollment in the dose expansion part of the trial remains underway in Asia and North America. For more information, please visit [ClinicalTrials.gov](https://clinicaltrials.gov).

About Ovarian Cancer

Approximately 314,000 women were diagnosed with ovarian cancer worldwide in 2020 and more than 207,000 died from the disease.^{4,5} Approximately 70% to 80% of patients diagnosed with ovarian cancer will have a recurrence of disease following standard treatment with platinum-based chemotherapy regimens.¹ For patients that develop resistance to platinum-based chemotherapy, treatment options are limited.⁶

The introduction of targeted treatments has increased treatment options and improved survival outcomes for some patients with ovarian cancer, but new therapeutic approaches are needed for tumors that progress on available medicines.⁷

About CDH6

CDH6 (human cadherin-6) is a cadherin family protein overexpressed in several cancers, particularly ovarian tumors.² An estimated 65% to 85% of patients with ovarian cancer have expression of CDH6,

which is associated with poor prognosis.^{2,3} No CDH6 directed cancer therapies are currently approved for treatment of any cancer.

About the Daiichi Sankyo and Merck & Co., Inc., Rahway, N.J., USA Collaboration

Daiichi Sankyo and Merck & Co., Inc., Rahway, N.J., USA (known as MSD outside of the United States and Canada) entered into a global collaboration in [October 2023](#) to jointly develop and commercialize patritumab deruxtecan (HER3-DXd), ifinatamab deruxtecan (I-DXd) and raludotatug deruxtecan (R-DXd), except in Japan where Daiichi Sankyo will maintain exclusive rights. Daiichi Sankyo will be solely responsible for manufacturing and supply.

About Raludotatug Deruxtecan

Raludotatug deruxtecan (R-DXd) is an investigational potential first-in-class CDH6 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC technology, raludotatug deruxtecan is comprised of a humanized anti-CDH6 IgG1 monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

The ongoing phase 1 trial in advanced ovarian cancer is part of a strategic collaboration with Sarah Cannon Research Institute (SCRI) with study operational oversight and delivery provided through SCRI's early phase oncology clinical research organization, SCRI Development Innovations in Nashville, TN.

About the DXd ADC Portfolio of Daiichi Sankyo

The DXd ADC portfolio of Daiichi Sankyo currently consists of six ADCs in clinical development across multiple types of cancer. ENHERTU, a HER2 directed ADC, and datopotamab deruxtecan (Dato-DXd), a TROP2 directed ADC, 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, N.J., USA. DS-3939, a TA-MUC1 directed ADC, is being developed by Daiichi Sankyo.

Designed using Daiichi Sankyo's proprietary DXd ADC technology to target and deliver a cytotoxic payload inside cancer cells that express a specific cell surface antigen, 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.

Datopotamab deruxtecan, ifinatamab deruxtecan, patritumab deruxtecan, raludotatug deruxtecan and DS-3939 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 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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¹ Pignata S, et al. *Ann Oncol*. 2017 Nov 1;28(suppl_8):viii51-viii56.

² Bartolome RA, et al. *Mol Oncol*. 2021 Jul; 15(7): 1849-18865.

³ Shintani, D, et al. *Gynecol Oncol*. 2022;166(Suppl 1): S116.

⁴ Global Cancer Observatory. [Population Fact Sheet](#). Updated November 2020. Accessed September 2023.

⁵ SEER Cancer Stat Facts: Ovarian Cancer. Data from [SEER](#) 18 2011-2017.

⁶ Mor, G, et al. *Cancer biology & therapy*. 2011;11(8), 708–713.

⁷ Kurnit K et al. *Obstetrics and Gynecology* (2021); 137(1): 108-121.