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Daiichi-Sankyo

Press Release

IDeate-Esophageal01 Phase 3 Trial of Ifinatamab Deruxtecan Initiated in Certain Patients with Pretreated Advanced or Metastatic Esophageal Squamous Cell Carcinoma

Basking Ridge, NJ and Rahway, NJ – (May 19, 2025) – The first patient has been dosed in the IDeate-Esophageal01 phase 3 trial evaluating the efficacy and safety of investigational ifinatamab deruxtecan (I-DXd) versus investigator's choice of chemotherapy in patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) with disease progression following treatment with a platinum-containing systemic therapy and an immune checkpoint inhibitor.

Ifinatamab deruxtecan is a specifically engineered, potential first-in-class B7-H3 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo (TSE: 4568) and being jointly developed with Merck (NYSE: MRK), known as MSD outside of the United States and Canada.

ESCC accounts for nearly 90% of esophageal cancers globally with a five-year overall survival rate around 15% to 20% and has a worse prognosis for those diagnosed at an advanced stage of the disease.[1,2] While the evolved landscape in the first-line metastatic setting of ESCC has helped to improve outcomes for patients, treatment options are limited for patients progressing after first-line therapy, reinforcing the need for new approaches.

"Patients with metastatic esophageal squamous cell carcinoma continue to experience poor outcomes despite currently available treatments," said Mark Rutstein, MD, Head, Therapeutic Area Oncology Development, Daiichi Sankyo. "The encouraging clinical activity seen in our early-phase signal finding trial supports further evaluation of ifinatamab deruxtecan as a potential treatment strategy for these patients."

"Advanced esophageal squamous cell carcinoma is a difficult-to-treat disease, and unfortunately overall survival remains low," said Marjorie Green, MD, Senior Vice President and Head of Oncology, Global Clinical Development, Merck Research Laboratories. "The initiation of the pivotal phase 3 IDeate-Esophageal01 clinical trial demonstrates our shared commitment with Daiichi Sankyo to further expand our clinical development program evaluating this potentially first-in-class ADC across multiple solid tumors where there are unmet needs for new treatment options."

The initiation of IDeate-Esophageal01 is based on results from the IDeate-PanTumor01 phase 1/2 trial presented at both the 2022 and 2023 European Society of Medical Oncology (ESMO) where ifinatamab deruxtecan showed promising responses in heavily pretreated patients with ESCC.

About the IDeate-Esophageal01 Trial

IDeate-Esophageal01 is a global, multicenter, open-label, randomized phase 3 trial evaluating the safety and efficacy of ifinatamab deruxtecan (12 mg/kg) versus treatment of physician's choice of chemotherapy (paclitaxel, docetaxel or irinotecan hydrochloride) in patients with advanced or metastatic ESCC with disease progression following treatment with platinum-based chemotherapy therapy and an immune checkpoint inhibitor. Eligible patients must have received no more than one prior line of systemic therapy in the advanced or metastatic setting.

The primary endpoint of the trial is overall survival. Secondary endpoints include progression-free survival and objective response rate as assessed by blinded independent central review, and safety.

IDeate-Esophageal01 will enroll approximately 510 patients across Asia, Europe and North America. For more information, please visit ClinicalTrials.gov.

About Esophageal Squamous Cell Carcinoma

More than half a million esophageal cancer cases were diagnosed in 2022, with nearly half a million deaths globally.[3] ESCC accounts for nearly 90% of esophageal cancers globally with a five-year overall survival rate around 15% to 20% and has a worse prognosis for those diagnosed at an advanced stage of the disease.[1,2] ESCC is most prevalent in Eastern Asia where mortality rates are also the highest.[1,2]

While the evolved landscape in the first-line metastatic setting of ESCC has helped to improve outcomes for patients, treatment options are limited for patients progressing after first-line therapy, reinforcing the need for new approaches.

About B7-H3

B7-H3 is a transmembrane protein that belongs to the B7 family of proteins which bind to the CD28 family of receptors that includes PD-1.[4,5] B7-H3 is overexpressed in a wide range of cancer types, including ESCC, and its overexpression has been shown to correlate with poor prognosis, making B7-H3 a promising therapeutic target.[6-9] There are currently no B7-H3 directed medicines approved for the treatment of any cancer.

About Ifinatamab Deruxtecan

Ifinatamab deruxtecan is an investigational potential first-in-class B7-H3 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, ifinatamab deruxtecan is comprised of a humanized anti-B7-H3 IgG1 monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

In addition to IDeate-Esophageal01, ifinatamab deruxtecan is being evaluated in a global development program that includes IDeate-Lung01, a phase 2 monotherapy trial in patients with previously treated extensive-stage small cell lung cancer (ES-SCLC); IDeate-Lung02, a phase 3 trial in patients with relapsed SCLC versus investigator's choice of chemotherapy; IDeate-Lung03, a phase 1b/2 trial in patients with ES-SCLC in combination with atezolizumab with or without carboplatin as first-line induction or maintenance therapy; IDeate-PanTumor02, a phase 2 monotherapy trial in patients with recurrent or metastatic solid tumors; and, IDeate-PanTumor01, a phase 1/2 first-in-human monotherapy trial in patients with advanced solid malignant tumors in 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.

Ifinatamab deruxtecan has been granted orphan drug designation in the EU, Japan, Taiwan and US for the treatment of SCLC.

About the Daiichi Sankyo and Merck Collaboration

Daiichi Sankyo and Merck 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. In August 2024, the global co-development and co-commercialization agreement was expanded to include gocatamig (MK-6070/DS3280), which the companies will jointly develop and commercialize worldwide, except in Japan where Merck will maintain exclusive rights. Merck will be solely responsible for manufacturing and supply for gocatamig.

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. 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.

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 needs. For more information, please visit www.daiichisankyo.com.

Merck's Focus on Cancer

Every day, we follow the science as we work to discover innovations that can help patients, no matter what stage of cancer they have. As a leading oncology company, we are pursuing research where scientific opportunity and medical need converge, underpinned by our diverse pipeline of more than 25 novel mechanisms. With one of the largest clinical development programs across more than 30 tumor types, we strive to advance breakthrough science that will shape the future of oncology. By addressing barriers to clinical trial participation, screening and treatment, we work with urgency to reduce disparities and help ensure patients have access to high-quality cancer care. Our unwavering commitment is what will bring us closer to our goal of bringing life to more patients with cancer. For more information, visit https://www.merck.com/research/oncology.

About Merck

At Merck, known as MSD outside of the United States and Canada, we are unified around our purpose: We use the power of leading-edge science to save and improve lives around the world. For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals. We foster a diverse and inclusive global workforce and operate responsibly every day to enable a safe, sustainable and healthy future for all people and communities. For more information, visit www.merck.com and connect with us on X (formerly Twitter), Facebook, Instagram, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Rahway, N.J., USA

This news release of Merck & Co., Inc., Rahway, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's Annual Report on Form 10-K for the year ended December 31, 2024 and the company's

other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

Media Contacts:

Global/US Media:
Jennifer Brennan
Daiichi Sankyo, Inc.
jennifer.brennan@daiichisankyo.com
+1 908 900 3183 (mobile)

Japan:
Daiichi Sankyo Co., Ltd.
DS-PR_jp@daiichisankyo.com

Investor Relations Contact:
DaiichiSankyoIR_jp@daiichisankyo.com

Merck
Media:
Julie Cunningham
(617) 519-6264
julie.cunningham@merck.com

Michael McArdle
(908) 447-9453
michael.mcardle@merck.com

Investors:
Peter Dannenbaum
(732) 594-1579
peter.dannenbaum@merck.com

Steven Graziano
(732) 594-1583
steven.graziano@merck.com

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