NEWS RELEASE

# HERTHENA-Breast04 Phase 3 Trial of Patritumab Deruxtecan Initiated in Patients with Metastatic Hormone Receptor Positive, HER2 Negative Breast Cancer Previously Treated with Endocrine Therapy

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BASKING RIDGE, N.J. & RAHWAY, N.J.--(BUSINESS WIRE)-- The first patient has been dosed in the **HERTHENA-Breast04** phase 3 trial evaluating the efficacy and safety of investigational patritumab deruxtecan (HER3-DXd) versus investigator's choice of treatment in patients with unresectable locally advanced or metastatic hormone receptor (HR) positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer with disease progression following endocrine and CDK4/6 inhibitor therapy in either the adjuvant or first-line metastatic settings.

Patritumab deruxtecan is a specifically engineered HER3 directed DXd antibody drug conjugate (ADC) discovered by Daiichi Sankyo (TSE: 4568) and being developed jointly by Daiichi Sankyo and Merck (known as MSD outside of the United States and Canada).

While survival rates are high for those diagnosed with early-stage breast cancer, only about 30% of patients initially diagnosed with advanced disease or having metastatic progression are expected to live five years following diagnosis.1 Patients with HR positive, HER2 negative metastatic breast cancer experience poor outcomes if they progress following initial treatment, highlighting the need for additional options.2

"Despite significant development in the treatment landscape, HR positive, HER2 negative metastatic breast cancer is a highly complex and challenging disease with an overall poor prognosis," said Mark Rutstein, MD, Head, Therapeutic Area Oncology Development, Daiichi Sankyo. "The promising clinical activity observed in our early phase studies including ICARUS-Breast01 suggest that patritumab deruxtecan has the potential to become a

meaningful new treatment option for this specific type of breast cancer."

"The initiation of HERTHENA-Breast04 demonstrates our ongoing commitment to researching innovative approaches that may help treat some of the most challenging cancers," said Marjorie Green, MD, Senior Vice President and Head of Oncology, Global Clinical Development, Merck Research Laboratories. "These patients need new options, and we continue to pursue cutting-edge science to develop therapies that may lead to improved treatment outcomes."

The initiation of HERTHENA-Breast04 is based on results from **ICARUS-Breast01** and a **phase 1/2 breast cancer trial** previously **published** in Journal of Clinical Oncology in June 2022, where patritumab deruxtecan showed promise in patients with metastatic breast cancer.

## About HERTHENA-Breast04

**HERTHENA-Breast04** is an open-label, randomized, phase 3 trial evaluating the safety and efficacy of patritumab deruxtecan (5.6 mg/kg) monotherapy versus physician's choice of treatment in adult patients with unresectable locally advanced or metastatic HR positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer previously treated with endocrine and CDK4/6 inhibitor therapy. Patients in the trial should not be eligible to receive additional endocrine therapy and should not have received chemotherapy or an ADC for advanced or metastatic disease. Further, patients must have experienced disease progression on first-line endocrine and CDK4/6 inhibitor therapy in the advanced or metastatic setting or relapse on or within 24 months of adjuvant endocrine and CDK4/6 inhibitor therapy.

Patients will be randomized 1:1 to receive patritumab deruxtecan or physician's choice of treatment, consisting of either chemotherapy (paclitaxel, nab-paclitaxel, capecitabine, liposomal doxorubicin) or HER2 directed ADC (trastuzumab deruxtecan). Randomization will be stratified by HER2 expression and treatment intent (chemotherapy versus trastuzumab deruxtecan), HER3 expression (low versus high per IHC) and presence of visceral disease.

The dual primary endpoints of HERTHENA-Breast04 are progression-free survival by blinded independent central review and overall survival. Secondary endpoints include objective response rate, duration of response and safety.

HERTHENA-Breast04 will enroll approximately 1,000 patients across Asia, Europe, North America, and South America. For more information, please visit **ClinicalTrials.gov**.

## About Hormone Receptor Positive, HER2 Negative Breast Cancer

More than 2 million cases of breast cancer were diagnosed in 2022, with approximately 670,000 deaths globally.3 While survival rates are high for those diagnosed with early-stage breast cancer, only about 30% of patients initially diagnosed with advanced disease or having metastatic progression are expected to live five years following diagnosis.1

Approximately 70% of diagnosed cases are considered what has been historically called HR positive, HER2 negative breast cancer (as measured as HER2 score of IHC 0, IHC 1+ or IHC 2+/ISH-).4,5 Patients with HR positive, HER2 negative metastatic breast cancer experience poor outcomes if they progress following initial treatment, highlighting the need for additional options.2

## About HER3

HER3 is a member of the HER family of receptor tyrosine kinases.6 HER3 is broadly expressed in about 90% of breast tumors.7,8,9 HER3 is associated with poor treatment outcomes, including shorter relapse-free survival and significantly reduced survival.10,11 There is currently no HER3 directed therapy approved for the treatment of any cancer.

## About Patritumab Deruxtecan

Patritumab deruxtecan (HER3-DXd) is an investigational HER3 directed ADC. Designed using Daiichi Sankyo's proprietary DXd ADC Technology, patritumab deruxtecan is composed of a fully human anti-HER3 IgG1 monoclonal antibody attached to a number of topoisomerase I inhibitor payloads (an exatecan derivative, DXd) via tetrapeptide-based cleavable linkers.

## About the Patritumab Deruxtecan Clinical Development Program

A comprehensive global clinical development program is underway evaluating the efficacy and safety of patritumab deruxtecan across multiple cancers. Trials in combination with other anticancer medicines also are underway.

## About the Daiichi Sankyo and Merck Collaboration

Daiichi Sankyo and Merck (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. 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 & Co., Inc.,

Rahway, N.J., USA will maintain exclusive rights. Merck & Co., Inc., Rahway, N.J., USA 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 & Co., Inc., Rahway, N.J., 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.

## 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 **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**).

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