

## Press Release

### **Daiichi Sankyo Presents Updated Phase 1 Data for U3-1402 in Patients with HER3-Expressing Metastatic Breast Cancer at 2018 San Antonio Breast Cancer Symposium (SABCS)**

- Updated efficacy and safety results presented from ongoing phase 1/2 study with U3-1402, an investigational and potential first-in-class HER3-targeting antibody drug conjugate (ADC), in patients with heavily pretreated HER3-positive metastatic breast cancer
- Preliminary efficacy data demonstrated a 42.9 percent confirmed overall response rate and a 90.5 percent disease control rate at a median follow-up time of 10.5 months
- No therapies are specifically approved for HER3-expressing breast cancer, and findings with U3-1402 continue to support the portability of Daiichi Sankyo's proprietary DXd and linker ADC technology

**Tokyo, Munich, and Basking Ridge, NJ – (December 5, 2018)** – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that updated efficacy and safety results from the ongoing phase 1/2 study of U3-1402, an investigational and potential first-in-class HER3-targeting antibody drug conjugate (ADC), in 42 heavily pretreated patients with HER3-positive metastatic breast cancer were presented during a Spotlight Session at the 2018 San Antonio Breast Cancer Symposium (SABCS).

Updated efficacy data for 42 evaluable patients who received U3-1402 in dose levels between 1.6 mg/kg to 8.0 mg/kg in the dose escalation and dose finding parts of the study showed a confirmed overall response rate of 42.9 percent (18/42 patients) and a disease control rate of 90.5 percent (38/42 patients) at a median follow-up time of 10.5 months. A median duration of response was not reached (range: 2.8, 13.8+). The median progression-free survival was 8.3 months (range: 1.2, 16.8+). Efficacy was observed in all molecular subtypes. A total of 21 patients remain on treatment at the time of data cut-off on November 6, 2018.

“These results offer preliminary evidence of U3-1402 activity in HER3-positive metastatic breast cancer and further study is warranted,” said Norikazu Masuda, MD, PhD, National Hospital Organization, Osaka National Hospital, Osaka, Japan, and an investigator for the trial. “The initial efficacy and safety data suggest that a HER3-targeting agent such as U3-1402 could provide a new treatment approach for patients with HER3-expressing metastatic breast cancer, who are in need of additional options to manage their disease.”

Updated safety results were also reported. With a median exposure to treatment of 7.6 months, U3-1402 showed a manageable safety profile. The most common adverse events ( $\geq 30$  percent, any grade) included nausea (85.7 percent), thrombocytopenia (71.4 percent), decreased appetite (66.7 percent), neutropenia (64.3 percent), leukopenia (59.5 percent), vomiting (54.8 percent), AST increased (47.6 percent), ALT

increased (45.2 percent), anemia (38.1 percent), stomatitis (35.7 percent) and diarrhea (31.0 percent). The most common adverse events Grade  $\geq 3$  (>10 percent of patients) were thrombocytopenia (35.7 percent), neutropenia (28.6 percent), leukopenia (21.4 percent), anemia (16.7 percent) and ALT increased (11.9 percent). Fourteen (14) patients (33.3 percent) experienced serious adverse events regardless of causality, and seven (7) patients (16.7 percent) experienced serious adverse events that were treatment-related. One (1) patient experienced an adverse event leading to treatment discontinuation (2.4 percent), and there were no adverse events leading to death.

“We are encouraged by these preliminary findings with U3-1402, particularly because there are no therapies specifically approved for HER3-expressing breast cancer,” said Kouichi Akahane, PhD, MBA, Executive Officer, Head of Oncology Function, R&D Division, Daiichi Sankyo. “Additionally, these findings continue to build evidence that supports the portability of Daiichi Sankyo’s proprietary DXd and linker ADC technology to other targets such as HER3.”

### **About the Phase 1 Study**

In this three-part open-label global phase 1/2 study, U3-1402 is given as an intravenous infusion every three weeks. The first part of the study (dose escalation) assessed the safety, tolerability and maximum tolerated dose of U3-1402 in HER3-positive (defined as IHC [immunohistochemistry] 2+/3+) metastatic breast cancer patients who are refractory or intolerant to standard treatment or for whom no standard treatment is available. A maximum tolerated dose has not been reached. Based on preliminary results, dose levels of 4.8 mg/kg and 6.4 mg/kg are being further evaluated. The second part of the study (dose finding) is assessing the safety and efficacy of U3-1402 and determining the recommended phase 2 dose in HER3-positive metastatic breast cancer patients who have received six or fewer prior chemotherapy regimens. The third part of the study (phase 2) is assessing the safety and efficacy of the recommended dose of U3-1402 in HER3-positive metastatic breast cancer patients who have received six or fewer prior chemotherapy regimens. The study is currently enrolling patients in Japan and the U.S. For more information about this study, please visit [ClinicalTrials.gov](https://clinicaltrials.gov).

### **About HER3-Positive Metastatic Breast Cancer**

HER3 is a member of the human epidermal growth factor receptor family of tyrosine kinase receptors, which are associated with aberrant cell growth.<sup>1</sup> HER3 is overexpressed in several types of solid tumors including breast cancer.<sup>2</sup> HER3 overexpression has been independently associated with a poorer prognosis and reduced survival for patients with invasive breast cancer.<sup>1</sup> A wide range of incidence of HER3 overexpression has been reported in breast cancer, depending on the screening method and published series.<sup>1</sup> There are currently no targeted therapies approved specifically for HER3-expressing breast cancer or any HER3-expressing cancer.

## **About U3-1402**

Part of the investigational ADC Franchise of the Daiichi Sankyo Cancer Enterprise, U3-1402 is an investigational and potential first-in-class HER3-targeting ADC. ADCs are targeted cancer medicines that deliver cytotoxic chemotherapy ("payload") to cancer cells via a linker attached to a monoclonal antibody that binds to a specific target expressed on cancer cells. Designed using Daiichi Sankyo's proprietary ADC technology, U3-1402 is comprised of a human anti-HER3 antibody attached to a novel topoisomerase I inhibitor payload by a tetrapeptide-based linker. It is designed to target and deliver chemotherapy inside cancer cells and reduce systemic exposure to the cytotoxic payload (or chemotherapy) compared to the way chemotherapy is commonly delivered.

U3-1402 is currently being evaluated in two clinical studies, including the phase 1/2 study for HER3-expressing metastatic or unresectable breast cancer in Japan and the U.S., and a phase 1 study for metastatic or unresectable EGFR-mutated non-small cell lung cancer (NSCLC) in the U.S.

U3-1402 is an investigational agent that has not been approved for any indication in any country. Safety and efficacy have not been established.

## **About Daiichi Sankyo Cancer Enterprise**

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by three pillars including our investigational Antibody Drug Conjugate Franchise, Acute Myeloid Leukemia Franchise and Breakthrough Science, we aim to deliver seven distinct new molecular entities over eight years during 2018 to 2025. Our powerful research engines include two laboratories for biologic/immuno-oncology and small molecules in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. Compounds in pivotal stage development include: [fam-] trastuzumab deruxtecan, an antibody drug conjugate (ADC) for HER2 expressing breast, gastric and other cancers; quizartinib, an oral selective FLT3 inhibitor, for newly diagnosed and relapsed/refractory *FLT3*-ITD acute myeloid leukemia (AML); and pexidartinib, an oral CSF1R inhibitor, for tenosynovial giant cell tumor (TGCT). For more information, please visit:

[www.DSCancerEnterprise.com](http://www.DSCancerEnterprise.com).

## **About Daiichi Sankyo**

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for hypertension and

thrombotic disorders, under the Group’s 2025 Vision to become a “Global Pharma Innovator with Competitive Advantage in Oncology,” Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit: [www.daiichisankyo.com](http://www.daiichisankyo.com).

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