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Daiichi-Sankyo

Press Release

HERTHENA-Lung02 Phase 3 Trial of Patritumab Deruxtecan Initiated in Patients with EGFR-Mutated Metastatic Non-Small Cell Lung Cancer

Tokyo and Basking Ridge, NJ – (August 8, 2022) – Daiichi Sankyo (TSE: 4568) announced today that the first patient has been dosed in the global HERTHENA-Lung02 phase 3 trial evaluating the efficacy and safety of patritumab deruxtecan (HER3-DXd) versus platinum-based chemotherapy in patients with EGFR-mutated locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) with disease progression following treatment with one or more EGFR tyrosine kinase inhibitors (TKIs) including a third-generation EGFR TKI.

Patritumab deruxtecan is a specifically designed potential first-in-class HER3 directed antibody drug conjugate (ADC) discovered and being developed by Daiichi Sankyo.

Lung cancer is the second most common cancer and the leading cause of cancer-related deaths worldwide.[1] Approximately 80% to 85% of lung cancer is classified as NSCLC with EGFR mutations occurring in up to 30% of tumors.[2,3] While the efficacy and safety of targeted therapy with EGFR TKIs is well-established for the treatment of advanced EGFR-mutated NSCLC, the development of a broad range of resistance mechanisms is likely to lead to disease progression.[4,5,6] After failure of one or more EGFR TKIs, platinum-based chemotherapy and subsequent salvage therapies have limited efficacy.[7]

"We are encouraged by the early results seen with patritumab deruxtecan and have initiated HERTHENA-Lung02 to further evaluate whether this HER3 directed antibody drug conjugate will be more effective than standard chemotherapy in treating patients with previously treated EGFR-mutated metastatic non-small cell lung cancer," said Gilles Gallant, BPharm, PhD, FOPQ, Senior Vice President, Global Head, Oncology Clinical Development, Oncology R&D, Daiichi Sankyo. "Initiating this phase 3 trial emphasizes our ongoing commitment to accelerate development of patritumab deruxtecan to potentially improve the standard of care for patients with this specific subtype of lung cancer."

About HERTHENA-Lung02

HERTHENA-Lung02 is a global, multicenter, open-label, phase 3 trial evaluating the efficacy and safety of patritumab deruxtecan (5.6 mg/kg) versus platinum-based chemotherapy (pemetrexed in combination with

cisplatin or carboplatin) in patients with locally advanced or metastatic non-squamous NSCLC with an EGFR-activating mutation (exon 19 deletion or exon 21 L858R mutation) previously treated with an EGFR TKI with disease progression on or after treatment with a third-generation TKI. Patients will be randomized 1:1 to receive patritumab deruxtecan or platinum-based chemotherapy.

The primary endpoint of HERTHENA-Lung02 is progression-free survival (PFS) as assessed by blinded independent central review (BICR). Secondary endpoints include overall survival, investigator-assessed PFS as well as BICR and investigator-assessed objective response rate, clinical benefit rate, disease control rate, duration of response, time to response and safety. HERTHENA-Lung02 will enroll approximately 560 patients at multiple sites across Asia, Europe, North America and Oceania. For more information about the trial, visit ClinicalTrials.gov.

About Non-Small Cell Lung Cancer

Lung cancer is the second most common cancer and the leading cause of cancer-related deaths worldwide.[1] Approximately 80% to 85% of lung cancer is classified as NSCLC with EGFR mutations occurring in up to 30% of tumors.[2,3] NSCLC is diagnosed at an advanced stage in more than 50% of patients and often has a poor prognosis with worsening outcomes after each line of subsequent therapy.[8,9,10]

The introduction of targeted therapies and checkpoint inhibitors in the past decade has improved the treatment landscape for patients with advanced or metastatic NSCLC, and for patients with advanced EGFR-mutated NSCLC targeted therapy with EGFR TKIs offer higher response rates and PFS compared to chemotherapy.[11] However, most patients eventually develop resistance to these therapies and subsequent therapies after EGFR TKI with platinum-based chemotherapy have limited efficacy with PFS of approximately 6.4 months.[7,12]

HER3 is a member of the EGFR family of receptor tyrosine kinases, which are associated with aberrant cell proliferation and survival.[13] It is estimated that about 83% of all NSCLC tumors express the HER3 protein. Overexpression is associated with metastatic progression and decreased relapse-free survival.[14]

New treatment approaches are needed to overcome resistance and improve survival in EGFR-mutated NSCLC. Currently, there is no HER3 directed medicine approved for the treatment of any cancer.

About Patritumab Deruxtecan

Patritumab deruxtecan (HER3-DXd) is one of three lead DXd ADCs in the oncology pipeline of Daiichi Sankyo. 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.

Patritumab deruxtecan is currently being evaluated as both a monotherapy and in combination with other anticancer therapies. In addition to the HERTHENA-Lung02 trial, patritumab deruxtecan is being evaluated in HERTHENA-Lung01, a pivotal phase 2 trial in patients with EGFR-mutated locally advanced or metastatic NSCLC previously treated with a EGFR TKI and platinum-based chemotherapy; a phase 1 trial in combination with osimertinib in EGFR-mutated locally advanced or metastatic NSCLC; and a phase 1 trial in previously treated patients with unresectable or metastatic NSCLC. A phase 1/2 trial in HER3 expressing metastatic breast cancer also has been recently completed.

In December 2021, patritumab deruxtecan was granted Breakthrough Therapy Designation (BTD) by the U.S. Food and Drug Administration (FDA) for the treatment of patients with metastatic or locally advanced EGFR-mutated NSCLC with disease progression on or after treatment with a third-generation TKI and platinum-based therapies.

Patritumab deruxtecan is an investigational medicine that has not been approved for any indication in any country. Safety and efficacy have not been established.

About Daiichi Sankyo

Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose "to contribute to the enrichment of quality of life around the world." In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an "Innovative Global Healthcare Company Contributing to the Sustainable Development of Society." For more information, please visit www.daiichisankyo.com.

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