

Press Release

Patritumab Deruxtecan Granted U.S. FDA Breakthrough Therapy Designation in Patients with Metastatic EGFR-Mutated Non-Small Cell Lung Cancer

- First Breakthrough Therapy Designation for patritumab deruxtecan based on results of phase 1 trial
- Seventh Breakthrough Therapy Designation granted by FDA across Daiichi Sankyo's oncology portfolio

Tokyo, Munich and Basking Ridge, NJ – (December 23, 2021) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) to patritumab deruxtecan (HER3-DXd), a potential first-in-class HER3 directed antibody drug conjugate (ADC), for the treatment of patients with metastatic or locally advanced EGFR-mutated non-small cell lung cancer (NSCLC) with disease progression on or after treatment with a third-generation tyrosine kinase inhibitor (TKI) and platinum-based therapies.

Lung cancer is the second most common cancer and the leading cause of cancer-related mortality worldwide, with 80% to 85% classified as NSCLC.^{1,2,3} While the efficacy of targeted therapy with EGFR TKIs is well-established in the treatment of advanced EGFR-mutated NSCLC, which comprises approximately 30% of patients, the development of a broad range of resistance mechanisms commonly leads to disease progression.^{4,5,6} After failure of an EGFR TKI, platinum-based chemotherapy has limited efficacy with progression-free survival (PFS) of approximately 4.4 to 6.4 months.⁷ Subsequent salvage therapies after EGFR TKI and platinum-based chemotherapy have PFS of 2.8 to 3.2 months.⁸

The U.S. FDA's BTD is designed to accelerate the development and regulatory review of potential new medicines that are intended to treat a serious condition and address a significant unmet medical need. The new medicine needs to have shown encouraging preliminary clinical results that demonstrate substantial improvement on a clinically significant endpoint over available medicines.

The FDA granted the BTD based on data from the dose escalation portion and two expansion cohorts of a three-cohort phase 1 study of patritumab deruxtecan (cohorts 1 and 3a). Extended follow-up data from the dose escalation portion and dose expansion cohort 1 of the study were recently [presented](#) at the 2021 American Society of Clinical Oncology (ASCO) annual meeting and published in [Cancer Discovery](#). This is the first BTD for patritumab deruxtecan and the seventh BTD across Daiichi Sankyo's oncology portfolio.

“The Breakthrough Therapy Designation for patritumab deruxtecan acknowledges the need for new treatment approaches to overcome resistance and improve survival in patients with metastatic TKI-resistant, EGFR-mutated non-small cell lung cancer,” said Ken Takeshita, MD, Global Head, R&D, Daiichi Sankyo. “We are proud that the FDA has once again recognized our innovative science and technology and we look forward to bringing this potential first-in-class HER3 directed antibody drug conjugate to patients with this specific type of lung cancer as quickly as possible.”

About Non-Small Cell Lung Cancer

Lung cancer is the most common cancer and the leading cause of cancer mortality worldwide, with 80% to 85% classified as NSCLC.^{1,2,3} There were an estimated 2.2 million new cases of lung cancer and 1.8 million deaths in 2020.⁹ 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.^{10,11,12}

The introduction of targeted therapies and checkpoint inhibitors in the past decade has improved the treatment landscape for patients with advanced or metastatic NSCLC. For patients with advanced EGFR-mutated NSCLC, targeted therapy with EGFR TKIs offer higher response rates and PFS compared to chemotherapy.¹³ However, most patients eventually develop resistance to these therapies and subsequent therapy after EGFR TKI with platinum-based chemotherapy have limited efficacy with PFS of approximately 4.4 to 6.4 months.^{7,14} Subsequent salvage therapies after EGFR TKI and platinum-based chemotherapy have PFS of 2.8 to 3.2 months.⁸ New treatment approaches are needed to overcome resistance and improve survival in this subtype of NSCLC.

About HER3

HER3 is a member of the EGFR family of receptor tyrosine kinases, which are associated with aberrant cell proliferation and survival.¹⁵ Approximately 25% to 30% of lung cancers have an EGFR-activating mutation, and it is estimated that about 83% of all NSCLC tumors express the HER3 protein, which can be associated with an increased incidence of metastases, reduced survival and resistance to standard of care treatment.^{16,17,18} Currently, no HER3 directed medicines are approved for the treatment of cancer.

About the Phase 1 Non-Small Cell Lung Cancer Study

The global, multicenter, open label, two-part phase 1 study is evaluating patritumab deruxtecan in previously treated patients with metastatic or unresectable NSCLC.

The dose escalation part of the study evaluated patients with EGFR-mutated disease either with progression on osimertinib or T790M-negative after progression on erlotinib, gefitinib or afatinib. The primary objective of this part of the study was to assess the safety and tolerability of patritumab deruxtecan and determine the recommended dose for expansion (RDE).

The dose expansion part of the study is evaluating patritumab deruxtecan at the RDE (5.6 mg/kg every three weeks) in three cohorts. Cohort 1 includes patients with locally advanced or metastatic EGFR-mutated NSCLC who experienced disease progression after taking one or more EGFR TKIs and one or more platinum-based chemotherapy regimens. Cohort 2 includes patients with squamous or non-squamous NSCLC without EGFR-activating mutations following platinum-based chemotherapy and following an anti-PD-1 or anti-PD-L1 antibody regimen. Cohort 3 includes patients with NSCLC with EGFR-activating mutations including any histology other than combined small cell and non-small cell lung cancer; patients in Cohort 3 are randomized 1:1 to receive the 5.6 mg/kg RDE regimen (Cohort 3a) or an escalating up-titration regimen of patritumab deruxtecan (Cohort 3b).

The primary objective of the dose expansion part of the study is to assess efficacy of patritumab deruxtecan as measured by confirmed objective response rate (ORR) assessed by blinded independent central review. Secondary study endpoints include investigator-assessed ORR, safety and pharmacokinetics. The study enrolled patients at multiple sites in Asia, Europe and North America. For more information, visit [ClinicalTrials.gov](https://clinicaltrials.gov).

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 comprised of a fully human anti-HER3 IgG1 monoclonal antibody attached to a topoisomerase I inhibitor payload (an exatecan derivative, DXd) via a stable tetrapeptide-based cleavable linker.

Patritumab deruxtecan is currently being evaluated in a comprehensive development program across multiple cancers as both a monotherapy and in combination with other anticancer treatments. The development program includes [HERTHENA-Lung01](#), a pivotal phase 2 study in patients with locally advanced or metastatic EGFR-mutated NSCLC previously treated with a TKI and platinum-based chemotherapy; a [phase 1/2 study](#) in HER3 expressing metastatic breast cancer; a [phase 1 study](#) in combination with osimertinib in locally advanced/metastatic EGFR-mutated NSCLC; and, a [phase 1 study](#) in previously treated patients with metastatic or unresectable NSCLC.

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 in Oncology

The oncology portfolio of Daiichi Sankyo is powered by our team of world-class scientists that push beyond traditional thinking to create transformative medicines for people with cancer. Anchored by our DXd antibody drug conjugate (ADC) technology, our research engines include biologics, medicinal chemistry, modality and other research laboratories in Japan, and [Plexxikon](#), our small molecule structure-guided R&D center in the U.S. We also work alongside leading academic and business collaborators to further advance the understanding of cancer as Daiichi Sankyo builds towards our ambitious goal of becoming a global leader in oncology by 2025.

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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