Health Technology Briefing
March 2026

Taletrectinib for treating advanced ROS1-positive non-small-cell lung cancer

Company/Developer	Eisai Co Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 33604	NICE ID: Not Available	UKPS ID: 675331

Licensing and Market Availability Plans

Currently in phase II clinical development.

Summary

Taletrectinib is currently in clinical development for the treatment of advanced ROS1-positive non-small cell lung cancer (NSCLC). NSCLC is the most common type of lung cancer. Advanced cancer includes metastatic cancer and means that the cancer has spread and cannot usually be cured, but treatment may help to control the cancer, reduce symptoms, and improve quality of life for some time. Someone with ROS1-positive NSCLC has alterations to the ROS1 gene, which is known to control cell growth. ROS1-positive lung cancer tends to be aggressive and can spread to the brain and the bones, which can lead to increased mortality. Signs are often less obvious than with other forms of lung cancer, but may include a chronic cough, bloody sputum and shortness of breath. Current treatment options tend to cause acquired resistant mutations, which make the treatment of ROS1-positive lung cancers more challenging.

Taletrectinib is a targeted medicine that blocks the activity of abnormal ROS1 proteins that drive cancer growth in certain tumours, particularly NSCLC. It is administered via the mouth (orally). If licensed, taletrectinib will offer an additional treatment option for patients with advanced ROS1-positive NSCLC.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Proposed Indication

Treatment of adult patients with advanced ROS1-positive NSCLC.[1]

Technology

Description

Taletrectinib (DS-6051b, AB-106, Ibtrozi™)[1,2] is an orally available inhibitor of the receptor tyrosine kinases C-ros oncogene 1 (ROS1) and the neurotrophic tyrosine receptor kinase (NTRK) types 1/2/3, with potential antineoplastic activity. It binds to and inhibits ROS1 and the NTRK family members. This inhibition disrupts ROS1- and NTRK-mediated signalling and eventually inhibits the growth of tumour cells that overexpress ROS1 and/or NTRKs. ROS1, overexpressed in certain cancer cells, plays a key role in cancer cell growth and survival. NTRK mutations or rearrangements play a key role in cancer progression.[3]

Taletrectinib is currently in clinical development for the treatment of advanced ROS1-positive NSCLC. In the phase II trials NCT04919811 and NCT04395677, participants are given 400mg or 600mg taletrectinib orally once daily in a 21-day cycle.[1,4]

Key Innovation

There are unmet needs for efficacious, well-tolerated treatments for patients with ROS1-positive NSCLC that achieve strong overall and intracranial responses, prolong disease control, overcome acquired on-target resistance mutations, and have limited neurologic side effects.[5] Taletrectinib addresses several specific unmet clinical needs that earlier ROS1-targeted therapies do not fully solve. The first-generation drugs crizotinib and entrectinib were associated with resistance and limited clinical response, especially in patients with the ROS1 G2032R mutation. Taletrectinib was therefore designed to overcome resistance mutations, including G2032R, making it effective where older TKIs fail. It is not only effective against tumours with primary ROS1 fusions, but also against those with ROS1 resistance mutations.[6]

Another advantage of taletrectinib over the older generation TKIs is its ability to cross the blood-brain barrier and achieve strong intracranial activity, thereby controlling brain metastases more efficiently, while maintaining a favourable safety profile, with fewer clinically important neurological adverse events, which is a significant limitation of the older generation TKIs.[6,7] If licensed, taletrectinib will offer an additional treatment option for patients with advanced ROS1-positive NSCLC.

Regulatory & Development Status

Taletrectinib does not currently have Marketing Authorisation in the EU/UK for any indication.

Taletrectinib is not in phase II/III clinical development for any other indication.

Taletrectinib has the following regulatory designations/awards:

- an orphan drug from the US Food and Drug Administration (FDA) in 2024 for the treatment of ROS1-positive, NTRK-positive, ALK-positive, LTK-positive, ACK1-positive or DDR1-positive NSCLC.[8]
- a Breakthrough Therapy by the US FDA in 2022 for advanced or metastatic ROS1-positive NSCLC in adult patients who were ROS1 inhibitor naïve or who previously received crizotinib.[9]

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Patient Group

Disease Area and Clinical Need

NSCLC, a heterogeneous class of tumours, is the most common class of lung cancers, constituting around 80% to 85% of all diagnosed cases.[7] Advanced cancer can include locally advanced (stage III) NSCLC, which means the cancer has spread into tissues around the lungs and may have spread into nearby lymph nodes, and metastatic NSCLC (stage IV), which indicates the cancer has spread to distant organs, such as the brain, liver, bones, or the other lung.[10] ROS1 gene fusions are oncogenic molecular alterations that result in constitutive activation of the ROS1 kinase domain and drive persistent downstream signalling and dysregulated cell differentiation, proliferation and survival. These ROS1 fusions are rare genetic events reported in multiple solid tumours, including NSCLC.[5] Several environmental and behavioural factors have been correlated with the development of lung cancer: tobacco smoking, second-hand smoke, family history, carcinogenic chemicals and heavy metals, such as radon gas, asbestos, arsenic, chromium, beryllium, and nickel, also highly increase the risk of lung cancer.[11] Symptoms of lung cancer include persistent cough, wheezing and shortness of breath, fatigue and lack of energy, hoarseness, coughing up blood, chest pain, unexplained weight loss or reduced appetite.[12]

Lung cancer remains the leading cause of cancer-related mortality worldwide.[13] There were 20,236 diagnosed cases of stage III-IV NSCLC in 2023 in England.[14] Since ROS1 fusions occur in 1%-2% of patients with NSCLC[15], there were approximately 202-405 diagnosed stage III-IV ROS1-positive NSCLC patients. In England (2024-25), there were 128,356 finished consultant episodes (FCEs) and 108,616 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34), which resulted in 83,351 day cases and 220,624 FCE bed days.[16]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends crizotinib and entrectinib for advanced or metastatic ROS1-positive NSCLC.[17,18]

Clinical Trial Information

Trial	**TRUST-II;** NCT04919811; A Single-Arm, Open-Label, Multicentre Phase 2 Study to Evaluate the Efficacy and Safety of Taletrectinib in Patients With Advanced or Metastatic ROS1 Positive NSCLC and Other Solid Tumours **Phase II:** Active, not recruiting **Locations**: four EU countries, USA, Canada and other countries **Primary Completion Date:** June 2025
Trial Design	Open label, single group assignment
Population	N=217 (actual) adults with histologically or cytologically confirmed diagnosis of locally advanced or metastatic NSCLC or other solid tumours, with evidence of ROS1 fusion by a validated assay
Intervention(s)	Taletrectinib, 400mg or 600mg once daily in a 21-day cycle
Comparator(s)	No comparator

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Outcome(s)	Primary outcome: objective response rate according to Response Evaluation Criteria in Solid Tumours (RECIST) 1.1, by an independent radiology review committee (time frame - up to four years) See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	**Trust-I:** NCT04395677; A Multicentre, Open Label, Single Arm Phase 2 Study of AB-106 in the Treatment of Locally Advanced and Metastatic NSCLC **Phase II:** Active, not recruiting **Location:** China **Primary Completion Date:** June 2024
Trial Design	Open label, single group assignment
Population	N=173 (estimated) adults with ROS-1 positive, histologically or cytologically confirmed locally advanced or metastatic NSCLC, in either TKI treatment naïve subjects or subjects with disease progression following the treatment of crizotinib
Intervention(s)	Stage 1 (dose finding) taletrectinib, 400mg or 600mg once daily Stage 2 (efficacy) taletrectinib, 600mg once daily in 21-day cycles
Comparator(s)	No comparator
Outcome(s)	Primary outcome: best overall response based on independent radiology review by Independent Review Committee according to RECIST 1.1 (time frame - up to six months) See trial record for full list of other outcomes
Results (efficacy)	In TKI-naïve patients, the confirmed objective response rate (cORR) and intracranial cORR were 91% and 88%, respectively; and 52% and 73% in crizotinib-pretreated patients, respectively. In TKI-naive patients, median duration of response (DOR) and median progression-free survival (PFS) were not reached (NR) with 22.1-month and 23.5-month follow-up, respectively. In crizotinib-pretreated patients, the median DOR was 10.6 months (95% CI, 6.3 months to NR; 8.4-month follow-up), and the median PFS was 7.6 months (95% CI, 5.5 to 12.0 months; 9.7-month follow-up). Eight of 12 patients (67%) with G2032R mutations responded.[19]
Results (safety)	The most common TEAEs were increased liver function enzymes: ALT (n = 117, 67.6%), AST (n = 132, 76.3%), diarrhoea (n = 121, 69.9%) and vomiting (n = 92, 53.2%), and anaemia (n = 85, 49.1%); most of these events were grade 1 and 2. Neurologic TEAEs reported in ≥5% of patients were dizziness (23.1%), dysgeusia (10.4%), headache (8.7%), and hypesthesia (7.5%), and most were grade 1 (88.0%).

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

	Two crizotinib-pretreated patients experienced interstitial lung disease (one grade 3 and one grade 4). TEAEs leading to dose reduction were reported in 33 (19.1%) patients, with the most common being abnormal hepatic function (4.0%), increased AST (2.9%), and diarrhoea (2.9%). Three patients experienced a treatment-related AE per investigator, leading to death: two TKI-naïve patients (one hepatic failure, one pneumonia) and one crizotinib-pretreated patient (hepatic function abnormal).[19]

Estimated Cost

The cost of taletrectinib is not yet known

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Crizotinib for treating ROS1-positive advanced NSCLC (TA1021). December 2024.
- NICE technology appraisal. Entrectinib for treating ROS1-positive advanced NSCLC (TA643). August 2020.
- NICE guideline. Lung cancer: diagnosis and management (NG122). Updated March 2024.
- NICE quality standard. Lung cancer in adults (QS17). Updated December 2019.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a

Other Guidance

- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2023[20]
- National Comprehensive Cancer Network. NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 2. 2021[21]

References

1 ClinicalTrials.gov. *Taletrectinib Phase 2 Global Study in ROS1 Positive NSCLC (TRUST-II). Trial ID: NCT04919811*. September 2021. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/study/NCT04919811 [Accessed 27 January 2026].

2 OncoDaily. *Taletrectinib (Ibtrozi) 2025 Updates: Uses in Cancer, Side effects, Dosage, Expectations and more*. 2025. Available from: https://oncodaily.com/drugs/taletrectinib-ibtrozi [Accessed 27 January 2026].

3 National Library of Medicines. *Taletrectinib*. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Taletrectinib [Accessed 27 January 2026].

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

4 ClinicalTrials.gov. *A Study of AB-106 in Subjects With Advanced NSCLC Harboring ROS1 Fusion Gene*. *Trial ID: NCT04395677*. Available from: https://clinicaltrials.gov/study/NCT04395677 [Accessed 02 February 2026].

5 Pérol M, Li W, Pennell NA, Liu G, Ohe Y, De Braud F, et al. Taletrectinib in ROS1+ Non-Small Cell Lung Cancer: TRUST. *J Clin Oncol*. 2025;43(16):1920-9. Available from: https://doi.org/10.1200/jco-25-00275.

6 Nagasaka M, Ohe Y, Zhou C, Choi C-m, Yang N, Liu G, et al. TRUST-II: a global phase II study of taletrectinib in ROS1-positive non-small-cell lung cancer and other solid tumors. *Future Oncology*. 2023;19(2):123-35. Available from: https://doi.org/10.2217/fon-2022-1059.

7 Zahra F-T, Naveed F, Fatima M. Taletrectinib in ROS1-positive NSCLC: bridging clinical trials and real-world practice. *Annals of Medicine and Surgery*. 2025;87(11):6954-6. Available from: https://doi.org/10.1097/ms9.0000000000003945.

8 US Food & Drug Administration. *Taletrectinib- Orphan Drug Designations*. 2024. Available from: https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=946023 [Accessed 28 January 2026].

9 OncLive. *FDA Grants Breakthrough Therapy Designation to Taletrectinib for ROS1+ NSCLC*. 2022. Available from: https://www.onclive.com/view/fda-grants-breakthrough-therapy-designation-to-taletrectinib-for-ros1-nsclc [Accessed 28 January 2026].

10 Cancer Research UK. *What is metastatic lung cancer?* Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/metastatic/what-is [Accessed 28 January 2026].

11 Alduais Y, Zhang H, Fan F, Chen J, Chen B. Non-small cell lung cancer (NSCLC): A review of risk factors, diagnosis, and treatment. *Medicine*. 2023;102(8):e32899. Available from: https://doi.org/10.1097/md.0000000000032899.

12 Cancer Research UK. *Symptoms of lung cancer*. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/symptoms [Accessed 02 February 2026].

13 Jeon H, Wang S, Song J, Gill H, Cheng H. Update 2025: Management of Non-Small-Cell Lung Cancer. *Lung*. 2025;203(1):53. Available from: https://doi.org/10.1007/s00408-025-00801-x.

14 NHS England Digital. *Cancer Registration Statistics, England, 2023*. 2025. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/cancer-registration-statistics/england-2023 [Accessed 28 January 2026].

15 Boulanger MC, Schneider JL, Lin JJ. Advances and future directions in ROS1 fusion-positive lung cancer. *The Oncologist*. 2024;29(11):943-56. Available from: https://doi.org/10.1093/oncolo/oyae205.

16 NHS England Digital. *Hospital Admitted Patient Care Activity, 2024-25*. 2025. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2024-25 [Accessed 28 January 2026].

17 National Institute for Health and Care Excellence. *Crizotinib for treating ROS1-positive advanced non-small-cell lung cancer*. 2024. Available from: https://www.nice.org.uk/guidance/ta1021 [Accessed 28 January 2026].

18 National Institute for Health and Care Excellence. *Entrectinib for treating ROS1-positive advanced non-small-cell lung cancer- Technology appraisal guidance*. 2020. Available from: https://www.nice.org.uk/guidance/ta643 [Accessed 28 January 2026].

19 Li W, Xiong A, Yang N, Fan H, Yu Q, Zhao Y, et al. Efficacy and Safety of Taletrectinib in Chinese Patients With ROS1+ Non-Small Cell Lung Cancer: The Phase II TRUST-I Study. *J Clin Oncol*. 2024;42(22):2660-70. Available from: https://doi.org/10.1200/jco.24.00731.

20 Hendriks LE, Kerr KM, Menis J, Mok TS, Nestle U, Passaro A, et al. Oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis,

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

treatment and follow-up[☆]. *Annals of Oncology*. 2023;34(4):339-57. Available from: https://doi.org/10.1016/j.annonc.2022.12.009.

21 David S, Ettinger S, Wood E, Aisner L, Akerley W, Bauman R, et al. *NCCN Guidelines Insights: Non–Small Cell Lung Cancer, Version 2.2021*. 2021. Available from: https://jnccn.org/view/journals/jnccn/19/3/article-p254.xml [Accessed 27 January 2026].

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.