

**Category**

Best Pharmaceutical Product

**General Information****Company Name \***

Amgen Inc.

**Product/Solution Name \***

IMDELLTRA® (tarlatamab-dlle)

**Compound/Tech Name\***

tarlatamab-dlle

**Trade Name \***

IMDELLTRA®

**Corporate Name \***

Amgen Inc.

**Date of Approval \***

2024-05-16

**Indications \***

IMDELLTRA® (tarlatamab) is approved for adult patients with extensive-stage small cell lung cancer (ES-SCLC) whose disease has progressed on or after platinum-based chemotherapy. It is also being studied in limited stage small cell lung cancer, earlier treatment lines of ES-SCLC and in other DLL3 expressing tumors.

words remaining :

454

**Therapeutic Areas \***

Oncology

words remaining :

499

\*Kindly clearly label your files with company name and asset name.

Attached Files:

- [Amgen Corporate Logo.svg](#)

**Background information and need for drug / device****(please be as specific as possible in your description; limit 500 words)**

Lung cancer represents the most common cause of cancer death, and small cell lung cancer (SCLC) is one of the most aggressive subtypes of lung cancer accounting for approximately 15% of all cases, with an estimated 33,000 new cases of SCLC diagnosed in the United States in 2024. Due to its rapid growth rate and early metastatic spread to other organs, SCLC has an extremely unfavorable prognosis.

Among patients with extensive stage small cell lung cancer (ES-SCLC) who have failed first-line treatment, the median overall survival (mOS) is 4-9 months with standard of care (SoC) second-line chemotherapy. Outcomes for these patients, especially those who relapse within 3 months from end of initial chemotherapy treatment, remain very poor, with uncertain benefits of further chemotherapy and limited treatment options. Therefore, there is a high unmet need for these patients, including identification of new treatment options.

Limited progress has been recently achieved by incorporating anti-PD-L1 inhibitors into first-line treatment; however survival benefits have been modest. As such, ES-SCLC prognosis remains bleak (mOS 12-13 months), and relapse may occur within 6 months.

Screening strategies have not proven to be effective, as most patients are diagnosed at an advanced stage of disease. Standard of care (SoC) treatment has centered around chemotherapy, and despite clinical trials aiming to improve SCLC prognosis, there have been limited therapeutic advances and most ES-SCLC cases remain incurable, with less than 10% of the patients alive at 5 years, highlighting a high unmet need for therapies that can provide durable benefits for patients with SCLC.

Delta-like ligand 3 (DLL3), an inhibitory ligand of the Notch signaling pathway, is aberrantly expressed on the surface of SCLC cells 94% of patients but rarely found on the surface of normal cells, making it an attractive therapeutic target in SCLC. The Notch signaling pathway is involved in multiple developmental processes including the development of pulmonary neuroendocrine cells and is a key regulator of neuroendocrine differentiation in SCLC. IMDELLTRA® is a BiTE® (Bispecific T-cell Engager) immunotherapy that redirects cytotoxic T cells to kill DLL3-expressing tumor cells.

words remaining :

160

\*Kindly clearly label your files with company name and asset name.

Attached Files:

- [Amgen Inc IMDELLTRA Background References.pdf](#)

**History of the development of the solution/product \*****(please be as specific as possible in your description; 500 words)**

Amgen pioneered BiTE technology and achieved the first approval with BLINCYTO®, a CD19-targeted BiTE molecule in B-cell precursor acute lymphoblastic leukemia. The ability of BLINCYTO® to recognize and eliminate CD19-positive B cells in both blood and tissue in B-cell malignancies suggested the potential to develop BiTE therapy in solid tumors.

While advancing T cell-targeted therapy in solid tumors was considered very challenging, due to heterogeneity of target antigen expression and the immunosuppressive tumor microenvironment that hinders T cell activity, Amgen held the conviction that these challenges could be addressed with the right targets and therapeutic modality. Amgen's research team profiled tumors and normal tissue by RNA sequencing and identified DLL3 as a target overexpressed in SCLC. Expression analysis showed that the DLL3 protein is expressed on the surface of most SCLC tumor cells, while it has intracellular localization in select normal cells, making it a compelling therapeutic target for the BiTE modality.

IMDELLTRA® was

designed to bind to DLL3 on tumor cells and CD3 on T cells, enabling targeted T cell activation and tumor cell destruction. Preclinical studies demonstrated that IMDELLTRA® exhibited potent, selective T cell-dependent killing of DLL3-expressing tumor cells including complete clearance of primary and metastatic SCLC lesions in mouse tumor models.

In the Phase I first-in-human DeLLphi-300 trial, IMDELLTRA® showed early evidence of antitumor activity against previously treated SCLC patients in the second-line and beyond setting, with a favorable safety profile. In the pivotal phase 2 DeLLphi-301 trial, IMDELLTRA® showed durable anticancer activity [objective response rate (ORR): 40%; median duration of response (mDOR): 9.7 months] and promising survival outcomes (mOS: 15.2 months) in patients with previously treated SCLC in the third-line and beyond, with 46% of patients alive at 18 months. These findings far exceeded historical control benchmarks of 15% ORR. The survival benefit observed with IMDELLTRA® far exceeded the mOS of 4-9 months observed with current second-line treatment options. This unprecedented benefit drove the accelerated approval of IMDELLTRA® in May 2024 for ES-SCLC patients whose disease has progressed on or after platinum-based chemotherapy.

These encouraging data prompted phase 3 clinical trials to evaluate the potential benefit of IMDELLTRA® in all lines of therapy for SCLC (e.g. limited-stage, first-line extensive-stage, and second-line settings).

IMDELLTRA® fills a critical treatment gap for SCLC patients who have exhausted standard treatment options with transformative survival potential in limited-stage and first-line extensive-stage disease.

The approval of IMDELLTRA® represents a major milestone in the fight against SCLC, offering an innovative first-in-class targeted therapy where traditional treatments have failed. The IMDELLTRA® mechanism of action bypasses key pathways of immune resistance in SCLC. Instead of relying on antigen presentation by tumor cells and recognition by T-cells, IMDELLTRA® directly binds T cells and tumor cells, forming a cytolytic synapse that mediates activation of cytotoxic T cells and tumor cell killing. By leveraging the patient's immune system through Amgen's BiTE® technology, IMDELLTRA® introduces a new therapeutic paradigm for solid tumors, paving the way for future research into DLL3-expressing tumors.

words remaining :

8

\*Kindly clearly label your files with company name and asset name.

Attached Files:

- [Amgen Inc IMDELLTRA History of Development References.pdf](#)

### **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition \***

IMDELLTRA® (tarlatamab) is a first-in-class therapy that revolutionizes the treatment of SCLC by utilizing BiTE® technology to redirect the body's own immune system to attack tumors. Unlike conventional chemotherapy, which kills both healthy and cancerous cells indiscriminately, BiTE® molecules like IMDELLTRA® offer a precision approach, improving efficacy while reducing systemic toxicity. Immunotherapy had revolutionized the treatment of multiple solid tumors resulting in durable anticancer responses, however, immune checkpoint inhibitors have shown limited success in this disease. IMDELLTRA provides a DLL3-targeted immunotherapeutic approach with a distinct mechanism of action than immune checkpoint blockade and offers a new strategy for treatment of SCLC patients.

This innovation is significant for several reasons:

- This is the first and only approved DLL3-directed therapy.
- IMDELLTRA® is the first approved therapy targeting DLL3, a tumor-associated antigen present on SCLC cells of 94% patients but absent from the surface of healthy cells.
- IMDELLTRA®'s high specificity and pharmacokinetic profile make it an effective

therapy with manageable toxicities. \n\nThis is the first BiTE® therapy approved for a major solid tumor[iii] \n\nWhile BiTE® technology has been used in blood cancers (e.g., BLINCYTO® in precursor B-cell acute lymphoblastic leukemia), IMDELLTRA® is the first BiTE® immunotherapy effective against a major solid tumor, setting a precedent for future cancer therapies. \n\nIt is the first BiTE® therapy based on the fully human/cynomolgus monkey-cross reactive BiTE® platform and the first BiTE® therapy based on Amgen's platform single chain Fc-BiTE® scaffold. It is a breakthrough in SCLC treatment. \n\nHistorically, SCLC has lacked effective targeted therapies. Despite lacking long-term effectiveness, chemotherapy has remained the mainstay treatment for decades. \n\nIMDELLTRA® provides new hope for patients who previously had no options beyond platinum-based chemotherapy. \n\nIt has future research and broader implications. \n\nThe success of IMDELLTRA® in SCLC suggests DLL3 could be a viable target in other hard-to-treat cancers, such as neuroendocrine prostate tumors.

words remaining :

197

\*Kindly clearly label your files with company name and asset name.

Attached Files:

- [Amgen Inc IMDELLTRA Innovation References.pdf](#)

#### **Please provide appropriate references (PubMed, Abstract, Website) \***

Siegel RL, et al. Cancer statistics, 2022. CA Cancer J Clin. 2022 Jan;72(1):7-33. doi: 10.3322/caac.21708. Epub 2022 Jan 12. \n\nSabari JK, et al. Unravelling the biology of SCLC: implications for therapy. Nat Rev Clin Oncol. 2017;14:549-56. \n\nSEER\*Explorer: An interactive website for SEER cancer statistics. Surveillance Research Program, National Cancer Institute; 2024 Apr 17. [updated: 2024 Nov 5; cited 2025 Apr 14]. \n\nSlotman B, et al. Prophylactic cranial irradiation in extensive small-cell lung cancer. N Engl J Med. 2007;357:664-672. \n\nTakahashi T, et al. Prophylactic cranial irradiation versus observation in patients with extensive-disease small-cell lung cancer: a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol. 2017;18(5):663-671. \n\nPaz-Ares L, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. Lancet. 2019;394:1929-1939. \n\nHorn L, et al. First-Line Atezolizumab plus Chemotherapy in Extensive-Stage Small-Cell Lung Cancer. N Engl J Med. 2018;379:2220-2229. \n\nvon Pawel J, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol. 1999;17:658-667. \n\nvon Pawel J, et al. Randomized phase III trial of amrubicin versus topotecan as second-line treatment for patients with small-cell lung cancer. J Clin Oncol. 2014;32:4012-4019. \n\nFarago AF, et al. ATLANTIS: a Phase III study of lurbinectedin/doxorubicin versus topotecan or cyclophosphamide/doxorubicin/vincristine in patients with small-cell lung cancer who have failed one prior platinum-containing line. Future Oncol. 2019;15:231-239. \n\nTrigo J, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. Lancet Oncol. 2020;21:645-654. \n\nOnoda S, et al. Phase II trial of amrubicin for treatment of refractory or relapsed small-cell lung cancer: Thoracic Oncology Research Group Study 0301. J Clin Oncol. 2006;24:5448-5453. \n\nHorita N, et al. Topotecan for Relapsed Small-cell Lung Cancer: Systematic Review and Meta-Analysis of 1347 Patients. Sci Rep. 2015;5:15437. \n\nOwen DH, et al. DLL3: an emerging target in small cell lung cancer. J Hematol Oncol. 2019;12(1):61. \n\nPaz-Ares L, et al. Tarlatamab, a First-in-Class DLL3-Targeted Bispecific T-Cell Engager, in Recurrent Small-Cell Lung Cancer: An Open-Label, Phase I Study. J Clin Oncol. 2023;41(16):2893-2903. \n\nAhn MJ, et al.

Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer. N Engl J Med. 2023;389(22):2063-2075. \n\nGiffin MJ, et al. AMG 757, a Half-Life Extended, DLL3-Targeted Bispecific T-Cell Engager, Shows High Potency and Sensitivity in Preclinical Models of Small-Cell Lung Cancer. Clin Cancer Res. 2021;27(5):1526-1537. \n\nSands J, et al. Tarlatamab Sustained Clinical Benefit and Safety in Previously Treated SCLC: DeLLphi-301 Phase 2 Extended Follow-up. Journal of Thoracic Oncology. OA10.03. 2024;19(10):S30 - S31. \n\nReady N, et al. Third-line nivolumab monotherapy in recurrent SCLC: CheckMate 032. J Thorac Oncol. 2019;14: 237-44. \n\nChung HC, et al. Pembrolizumab after two or more lines of previous therapy in patients with recurrent or metastatic SCLC: results from the KEYNOTE-028 and KEYNOTE-158 studies. J Thorac Oncol. 2020;15: 618-27. \n\nFDA Approval Announcement: U.S. Food and Drug Administration (FDA) website --- IMDELLTRA® (tarlatamab) approval, May 16, 2024. \n\nEinsele H, et al. The BiTE® (bispecific T-cell engager) platform: Development and future potential of a targeted immuno-oncology therapy across tumor types. Cancer. 2020;126(14):3192-3201. \n\nWolf E, et al. BiTEs®: bispecific antibody constructs with unique anti-tumor activity, Drug Discov Today. 2005;10(18):1237-1244. \n\nTendler S, et al. Tarlatamab: New Star on the Horizon for Small-Cell Lung Cancer? J Clin Oncol. 2023;41(16):2877-2880.

\*Kindly clearly label your files with company name and asset name.

Attached Files:

- [Amgen Inc IMDELLTRA All References.pdf](#)