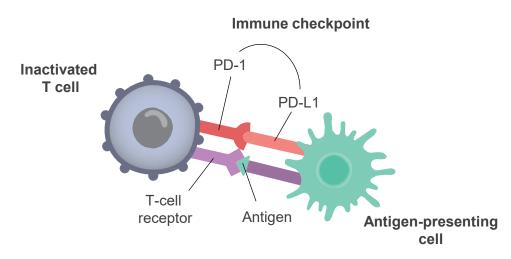
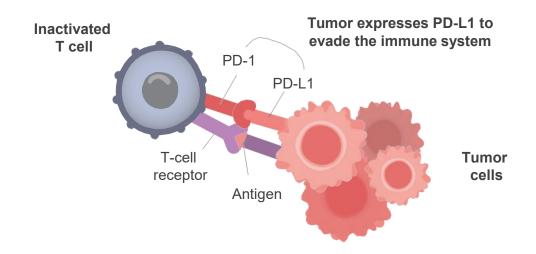


The PD-1/PD-L1 Pathway Is an Important Regulator of the Immune System



- PD-1 is a co-inhibitory receptor expressed on the surface of activated T cells and other immune cells.
 Its ligands, PD-L1 and PD-L2, are mainly expressed on antigen-presenting cells and tumor cells
- The binding of PD-1 to its ligands regulates T-cell effector functions during various physiological responses—such as acute and chronic infection and the maintenance of immune tolerance



Cancer cells use the PD-1/PD-L1 pathway to escape T-cell–mediated destruction.

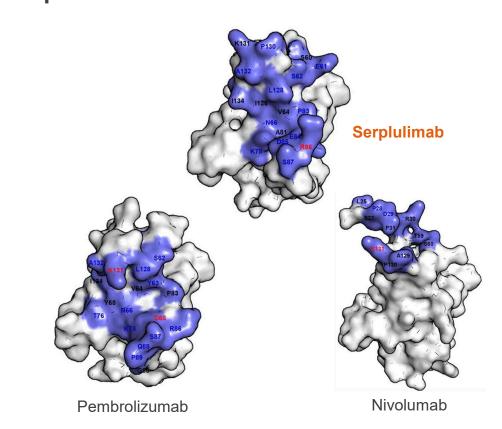
- PD-L1 is highly expressed in a variety of cancers, including lung cancer
- Increased expression of PD-L1 in tumor tissues and on antigen-presenting cells in the tumor microenvironment results in T-cell immunosuppression, exhaustion of tumorspecific T cells, and cancer escape



Serplulimab: An Anti-Programmed Cell Death 1 (PD-1) mAb With a Favorable Binding Profile

- Novel fully humanized anti–PD-1 IgG4 mAb
- Activates T-cell proliferation and cytokine secretion in T-cells in in vivo studies
- Similar or better PD-L1 and PD-L2 blockade than a nivolumab analogue based on flow cytometry
- Similar antitumor activity compared with pembrolizumab based on in vivo mouse models
- Unique mode of recognition of the PD-1 receptor when comparing complex structure models with currently available anti–PD-1 mAbs

Comparison of Binding Epitope Regions (Blue) of Serplulimab With Pembrolizumab and Nivolumab



MOA is hypothesized and is not meant to imply clinical efficacy.

Serplulimab is not approved for use in the United States (US). Clinical investigation of serplulimab in the US is underway.

IgG4=human immunoglobulin G4; mAb=monocolonal antibody; PD-1=programmed death-1; PD-L1=programmed death ligand-1; PD-L2=programmed death ligand-2.

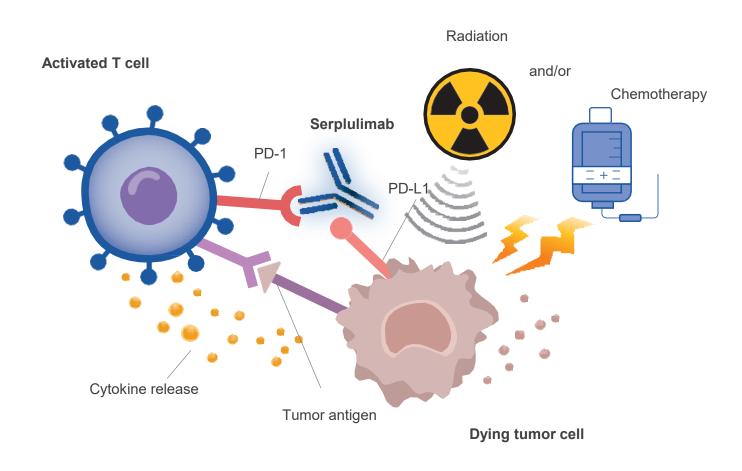


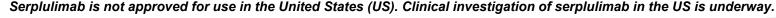
Serplulimab Can Restore T-cell Immunity by Blocking the PD-1/PD-L1 Pathway¹

 Inhibition of the PD-1/PD-L1 pathway can enable tumor-reactive T cells to recognize tumor antigens and enhance the T-cell anti-tumor response¹

Serplulimab works synergistically with chemotherapy and/or radiation to enhance tumor-killing effects^{2,3}

- The cytotoxic effects of chemotherapy and/or radiation on tumor cells increase the release and presentation of tumor antigens to T cells²
- Inhibition of the PD-1/PD-L1 pathway and subsequent restoration of T-cell immunity with serplulimab may produce a stronger and more durable response against these tumor antigens¹

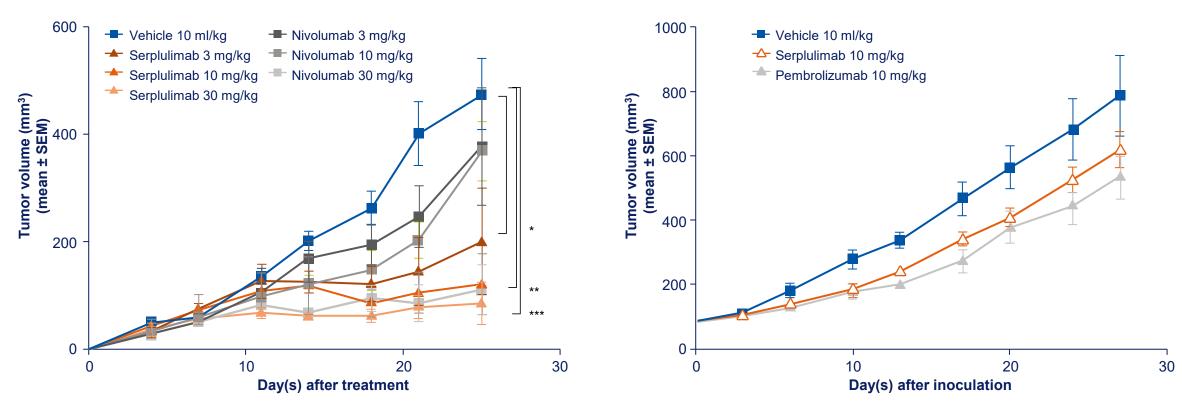






Antitumor Activity With Serplulimab Showed a Pronounced Effect on Tumor Growth In Vivo

When compared with currently available anti–PD-1 antibodies in in vivo mouse models, serplulimab showed similar or better PD-L1 blockade and antitumor activity



^{*}P<0.05. **P<0.001. ***P<0.0001.

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mAb=monocolonal antibody; PD-1=programmed death-1; PD-L1=programmed death ligand-1; SEM=standard error of the mean.



Issafras H, et al. *PLoS One*. 2021;16(12):e0257972.



Global Development Pathway for Serplulimab, an Anti-PD-1 Monoclonal Antibody for the Treatment of ES-SCLC

China NMPA

Approval in previously treated MSI-H tumors¹ (March 2022)

Serplulimab for previously treated advanced unresectable or metastatic MSI-H solid tumors China NMPA

Approval as 1L treatment for advanced sqNSCLC² (Nov 2022)

Serplulimab plus carboplatin/ paclitaxel as 1L treatment for unresectable locally advanced or metastatic sqNSCLC China NMPA

Approval as 1L treatment for ES-SCLC³
(January 2023)

Serplulimab plus carboplatin/ etoposide to treat ES-SCLC⁶

China NMPA

Approval as treatment for advanced ESCC⁴ (Sept 2023)

Serplulimab plus chemotherapy to treat PD-L1+ unresectable locally advanced/recurrent or metastatic ESCC

2022

EC grants serplulimab orphan drug designation for SCLC⁵ (Dec 2022) 2023

EMA validates marketing authorization application for serplulimab plus chemotherapy for 1L treatment of ES-SCLC⁶

(March 2023)

2024

Positive CHMP opinion⁷ (Sep 2024)

The Committee for Medicinal Products for Human Use adopted a positive opinion, recommending the granting of a marketing authorization for the medicinal product Hetronifly, intended for the treatment of ES-SCLC.

Approved in the EU for First-Line Treatment of Extensive-Stage Small Cell Lung Cancer

2025

(ES-SCLC)⁸ (Feb 2025)

Serplulimab is not approved for use in the United States (US). Clinical investigation of serplulimab in the US is underway.

1L=first-line; EC=European Commission; EMA=European Medical Agency; ESCC=esophageal squamous cell carcinoma; ES-SCLC=extensive-stage small cell lung cancer; MSI-H=microsatellite instability-high; NMPA=National Medical Products Administration; PD-1=programmed death-1; PD-L1=programmed death ligand-1; SCLC=small cell lung cancer; sqNSCLC=squamous non-small cell lung cancer.

1. Press release. Shanghai Henlius Biotech, Inc. March 25, 2022. https://www.henlius.com/en/NewsDetails-3512-26.html 2. Press release. Shanghai Henlius Biotech, Inc. November 1, 2022. https://www.henlius.com/en/NewsDetails-3837-26.html 3. Press release. Shanghai Henlius Biotech, Inc. January 17, 2023. https://www.henlius.com/en/NewsDetails-3949-26.html 4. Press release. Shanghai Henlius Biotech, Inc. September 22, 2023. https://www.henlius.com/en/NewsDetails-4283-26.html 5. Press release. Shanghai Fosun Pharmaceutical Co., Ltd. December 15, 2022. https://www.fosunpharma.com/en/content/details38_12122.html 6. Press release. Shanghai Helius Biotech, Inc. March 23, 2023. https://www.henlius.com/en/NewsDetails-4074-26.html 7. Press release. Shanghai Henlius Biotech, Inc. September 21, 2024. https://www.henlius.com/en/NewsDetails-4712-26.html, 8. Press release. Shanghai Henlius Biotech, Inc. February 5, 2025.



Development Pathway for Serplulimab in the US



April 7

Orphan drug designation¹

The FDA grants serplulimab orphan drug designation for SCLC

September 28

ASTRUM-005 published²

ASTRUM-005, a global Phase 3 trial of serplulimab for 1L treatment of ES-SCLC, is the first clinical study of immunotherapy for SCLC published in *JAMA* November 29

ASTRIDE commences³

First patient treated in ASTRIDE, a Phase 3 study of the treatment for ES-SCLC in the US

January 5

ASTRUM-020 commences^{4,5}

First patient treated in ASTRUM-020, a Phase 3 study of the treatment for LS-SCLC in the US Current

2023

ASTRIDE trial is ongoing and recruiting in the US⁶

2022

Serplulimab is not approved for use in the United States (US). Clinical investigation of serplulimab in the US is underway.

1L=first-line; ES-SCLC=extensive-stage small cell lung cancer; FDA=US Food and Drug Administration; LS-SCLC=limited-stage small cell lung cancer; NDA=new drug application; SCLC=small cell lung cancer.

1. Press release. Shanghai Henlius Biotech, Inc. April 7, 2022. https://www.henlius.com/en/NewsDetails-3525-26.html 2. Press release. Shanghai Henlius Biotech, Inc. September 28, 2022. https://www.henlius.com/en/NewsDetails-3768-26.html 3. Press release. Shanghai Henlius Biotech, Inc. November 29, 2022. https://www.henlius.com/en/NewsDetails-3880-26.html 4. Press release. Shanghai Henlius Biotech, Inc. January 5, 2023. https://www.henlius.com/en/NewsDetails-3935-26.html 5. ClinicalTrials.gov. NCT05353257. https://classic.clinicaltrials.gov/ct2/show/NCT05353257 6. ClinicalTrials.gov. NCT05468489. https://classic.clinicaltrials.gov/ct2/show/NCT05468489

