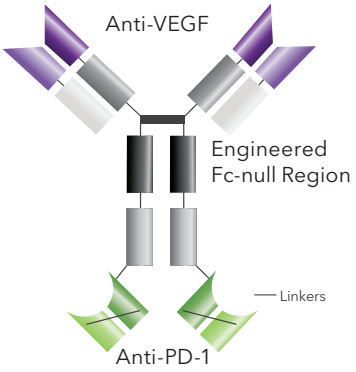
HARMONi-3 Phase 3 Clinical Trial

First Line Metastatic Squamous and Non-Squamous NSCLC / NCT05899608[1]

HARMONi-3

Ivonescimab: Most Advanced PD-1/VEGF Bispecific Antibody in Clinical Development in the U.S. and EU.*
Brings two validated mechanisms in oncology[2-4] into ONE novel tetravalent molecule.



Ivonescimab blocks both PD-1 & VEGF

Globally 2,300+ patients have been treated with ivonescimab across Summit and Akeso clinical trials.[5] Summit is actively recruiting approximately 1,080 patients worldwide for the HARMONi-3 study.

HARMONi-3 STUDY DESIGN

Key Inclusion:
- First line Stage IV squamous and non-squamous NSCLC

Key Exclusion:
- Known actionable mutations for which first line approved agents are available
- Symptomatic CNS metastases
- Major blood vessel or organ invasion
- History of bleeding tendencies or coagulopathy or clinically significant bleeding symptoms or risk (including GI bleeding, hemoptysis)
- Active autoimmune disease

Randomization 1:1, n = ~1080

Non-Squamous	OR	Squamous	Maintenance
Ivonescimab + Carboplatin + Pemetrexed Q3W x 4 cycles		**Ivonescimab** + Carboplatin + Paclitaxel (or nab-paclitaxel) + Q3W x 4 cycles	Non-Squamous: Ivonescimab + Pemetrexed; Squamous: Ivonescimab
Pembrolizumab + Carboplatin + Pemetrexed, Q3W x 4 cycles		**Pembrolizumab** + Carboplatin + Paclitaxel (or nab-paclitaxel) Q3W x 4 cycles	Non-Squamous: Pembrolizumab + Pemetrexed; Squamous: Pembrolizumab

Treatment Until:
- Disease progression
- Unacceptable toxicity
- Withdrawal of consent/death
- Initiation of a new anti-tumor therapy
- Complete 24 months of treatment

Safety and Survival Follow-up

Stratification Factors
- Squamous vs. non-squamous histology
- TPS Score: PD-L1 ≥1% vs <1%
- Sex (female vs male)
- Age (<65 vs ≥65 years)
- East Asia vs Rest of World
- Liver or brain metastases at study entry (present vs. absent)
- Prior PD-1/L1 inhibitor containing therapy (yes vs no)

Study Endpoints

Primary
- OS, PFS by Investigator based on IRRC's assessment

Secondary
- ORR, DCR, DOR by investigator assessments, safety, PK, immunogenicity

KEY ELIGIBILITY CRITERIA

- Metastatic (Stage IV) NSCLC
- Histologically or cytologically confirmed squamous or non-squamous NSCLC
- Patients must have Tumor Proportion Score (TPS) with PD-L1 expression prior to randomization
- No prior systemic treatment for metastatic NSCLC. No histologic or cytopathologic evidence of the presence of small cell lung carcinoma, or non-squamous NSCLC histology
- No known actionable genomic alterations in EGFR, ALK, ROS1 or BRAF V600E) or genes for which first-line approved therapies are available
- No Radiographic evidence of major blood vessel encasement with narrowing of the vessel or intratumor lung cavitation or necrosis that the investigator determines will pose a significantly increased risk of bleeding
- No symptomatic CNS metastases or CNS metastasis ≥1.5 cm
- No history of bleeding tendencies or coagulopathy and/or clinically significant bleeding symptoms or risk within 4 weeks (including GI bleeding, hemoptysis)

Ivonescimab is an investigational therapy not presently approved by any regulatory authority other than China's National Medical Products Administration (NMPA).
*There are no known PD-1-based bispecific antibodies approved by the U.S. Food and Drug Administration ("FDA") or the European Medicines Agency ("EMA").

Abbreviations: ALK=anaplastic lymphoma kinase; CNS=central nervous system; DCR=disease control rate; ECOG=eastern cooperative oncology group; EGFR=epidermal growth factor receptor; GI=gastrointestinal; INV=investigator; IRRC=independent radiologic review committee; MO=months; NSCLC=non-small cell lung cancer; ORR=overall response rate; OS=overall survival; PD-1=programmed cell death protein 1; PFS=progression-free survival; PK=pharmacokinetics; Q3W=every 3 weeks; TME=tumor microenvironment; VEGF=vascular endothelial growth factor.

Cooperative Binding Offers Potential to Drive Synergistic Activity[6-8]

Brings two validated mechanisms in oncology[2-4] into ONE novel tetravalent molecule

Increased Avidity in TME[8*]

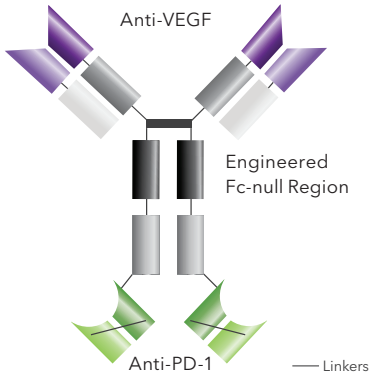
Enhanced Activity of T Cells[8*]

VEGF dimer leads to potential interconnection of ivonescimab molecules, which may increase activity of T Cells

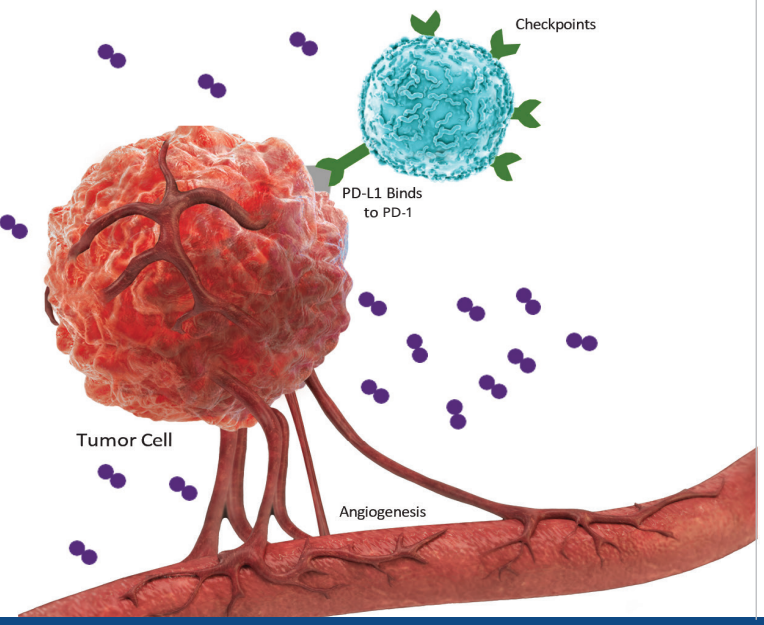
T½ ~10 days[9] and Fc-null region[8]

VEGF dimer leads to potential interconnection of ivonescimab molecules, which may increase activity of T Cells

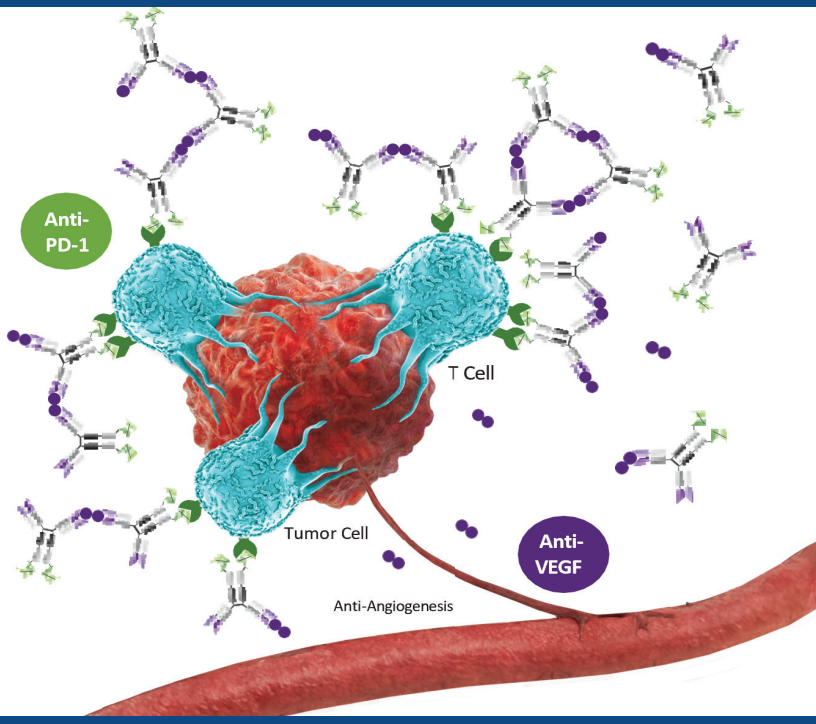
**in vitro*



Tumor Microenvironment



Tumor Microenvironment with Ivonescimab Cooperative Binding



Images for illustrative purposes only

VEGF Dimer PD-1 Receptor in T Cell

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For more information contact medinfo@smmttx.com

1. Clinical Study of Ivonescimab for First-line Treatment of Metastatic Squamous NSCLC Patients. ClinicalTrials.gov identifier: NCT05899608. https://clinicaltrials.gov/study/NCT05899608. (Accessed 2025, May 12).; 2. Manegold C, et al. J Thorac Oncol 2017;12(2):194-207.; 3. Pardoll, D. Nat Rev Cancer 2012;12(4):252-64.; 4. Tamura R, et al. Med Oncol 2020;37(1):2.; 5. Data on File 38. Summit Therapeutics Inc.; 6. Zhao Y. et al., eClinicalMedicine. 2023; 3(62): 102106.; 7. Wang L, et al. J Thorac Oncol. 2024 Mar;19(3):465-475; 8. Zhong T, et al. iScience. 2024;28(3):111722.; 9. Data on File 39. Summit Therapeutics Inc.

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