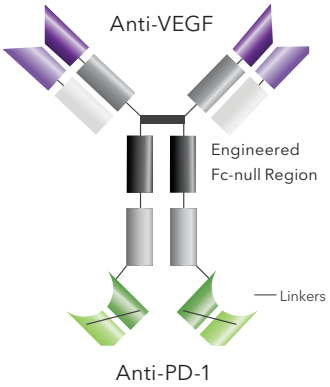
# HARMONi-3 Phase 3 Clinical Trial

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 1,800+ patients have been treated with ivonescimab across Summit and Akeso clinical trials.[2] Summit is actively recruiting approximately 1080 patients worldwide for the HARMONi-3 study.

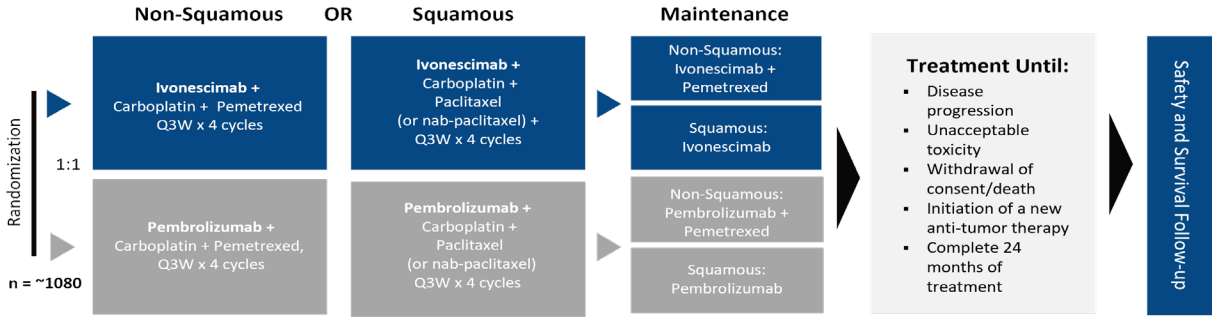
## HARMONi-3 STUDY DESIGN

### 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




### Stratification Factors

- Squamous vs. non-squamous histology
- TPS Score: PD-L1 ≥1% or < 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-(L)1 inhibitor containing therapy (yes vs no)

### Endpoints

**Primary**

- OS, PFS by Investigator Assessments

**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; mo=months; NSCLC=non-small cell lung cancer; PD-1=programmed cell death protein 1; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; PK=pharmacokinetics; Q3W=every 3 weeks; VEGF=vascular endothelial growth factor.

## Ivonescimab: Designed to Potentially Improve the Balance of Anti-tumor Activity & Safety[3-4]

**Brings two validated mechanisms in oncology[5-7] into ONE novel tetravalent molecule**

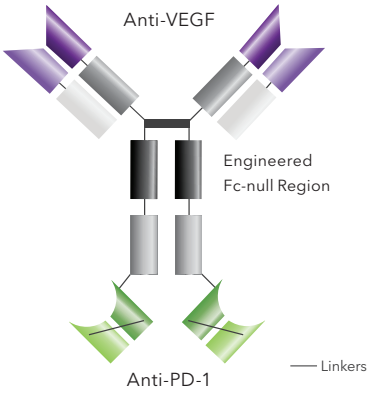
## Cooperative Binding

**Potential to drive synergistic anti-tumor activity[3-4,8]**

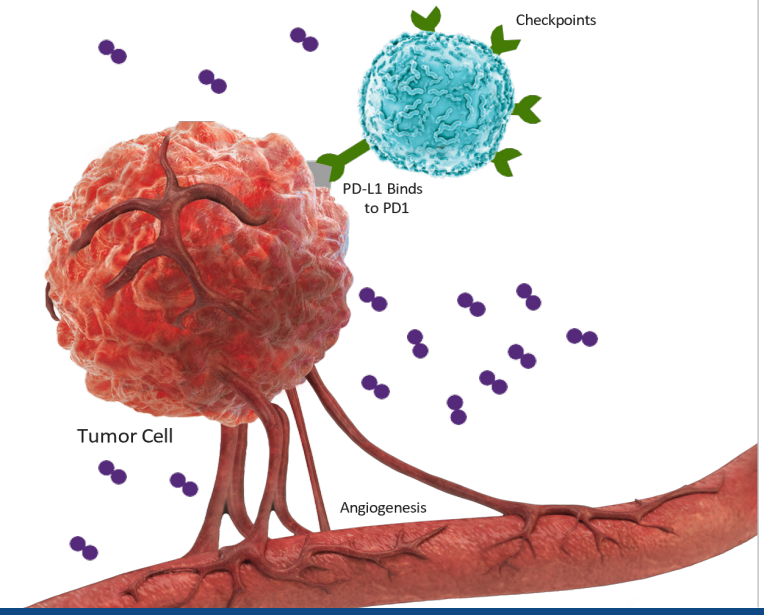
**Simultaneous Blocking of PD-1 & VEGF[8]**

**Increased Avidity in the Tumor Microenvironment (TME)[8]**
VEGF increases affinity to **PD-1 by >18X** PD-1 increases affinity to **VEGF by >4X** *(in vitro)*

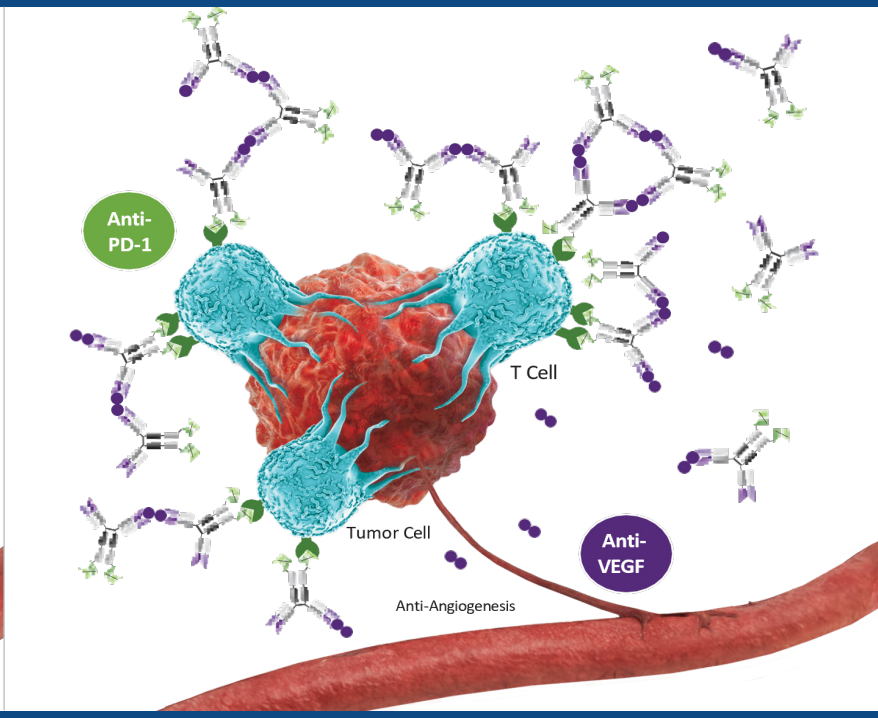
**Enhanced Activity of T Cells[8]**
VEGF dimer leads to potential interconnection of ivonescimab molecules, which may increase activity of T cells *(in vitro)*




### Tumor Microenvironment




### Tumor Microenvironment with Ivonescimab Cooperative Binding




Images for illustrative purposes only

VEGF Dimer  PD-1 Receptor in T Cell

**Ivonescimab is an investigational therapy that is not presently approved by any regulatory authority other than China's National Medical Products Administration (NMPA).**

**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 2024, May 14).; 2. Summit Therapeutics. Press Release. Aug 6, 2024. Available at: https://www.smmttx.com/pressrelease/; 3. Zhao Y, et al. eClinicalMedicine.2023; 3(62): 102106.; 4. Wang L, et al. J Thorac Oncol. 2024 Mar;19(3):465-475.; 5. Manegold C, et al .J Thorac Oncol 2017;12(2):194-207.; 6. Pardoll, D. Nat Rev Cancer 2012;12(4):252-64.; 7. Tamura R, et al. Med Oncol 2020;37(1):2.; 8. Zhong T, et al. AACR-NCI-EORTC, 2023. Poster #B123, Abstract #35333, Boston, MA, USA.



**Ivonescimab is an investigational therapy not presently approved by any regulatory authority other than China's National Medical Products Administration (NMPA).**



**SMMTTX.com**
**medinfo@smmttx.copm**