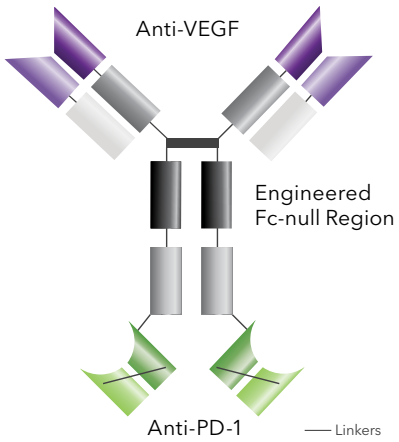
HARMONi Phase 3 Clinical Trial

EGFR+ Advanced NSCLC Who Have Progressed After 3rd Generation EGFR-TKI (osimertinib)

HARMONi™

Ivonescimab: Most Advanced PD-1/VEGF Bispecific Antibody in Clinical Development in the U.S. and EU.*

Brings two validated mechanisms in oncology[1,2,3] into ONE novel tetravalent molecule.



Ivonescimab simultaneously engages both PD-1 & VEGF.

To-date 825+ patients have been treated with ivonescimab in clinical trials in China and Australia. Summit is actively recruiting 100+ patients in the U.S., Canada and Europe; the overall study will include over 400 patients worldwide.

HARMONi PHASE 3 STUDY DESIGN NCT05184712

Locally advanced or metastatic non-squamous NSCLC:

- → Positive sensitive EGFR mutation
- → Progressed on 1st/2nd generation EGFR-TKI with negative T790, or on 3rd generation EGFR-TKI
- → ECOG = 0 or 1
- → Regardless of PD-L1 expression

Stratification factor:

- → Exposure to 3rd generation EGFR-TKI before (Yes or No)
- → Brain metastases at baseline (Yes or No)

1:1

Group A
Ivonescimab 20 mg/kg Q3W + Pemetrexed 500 mg/m² Q3W + Carboplatin AUC 5 Q3W 4 cycles (3 weeks/cycle)

Group A
Ivonescimab 20 mg/kg Q3W + Pemetrexed 500 mg/m² Q3W + Maintenance Period

Group B
Placebo Q3W + Pemetrexed 500 mg/m² Q3W + Carboplatin AUC 5 Q3W 4 cycles (3 weeks/cycle)

Group B
Placebo Q3W + Pemetrexed 500 mg/m² Q3W Maintenance Period

Treatment Until

- → Intolerable toxicity
- → No clinical benefit (Investigator assessment)
- → Initiation of a new anti-tumor therapy
- → Complete 24 months of treatment

Primary Endpoints: OS, PFS assessed by IRRC
Secondary Endpoints: ORR by IRRC, DoR, safety and tolerability

Safety and Survival Follow up

KEY ELIGIBILITY CRITERIA

- Expected survival ≥3 months
- Locally advanced (Stage IIIB/IIIC) or metastatic NSCLC that has progressed on 3rd generation EGFR-TKI (e.g., osimertinib)
- At least 1 measurable noncerebral lesion
- Adequate organ and hematologic function
- Has not received other systemic antitumor therapy for the advanced stage (IIIB to IV) of NSCLC
- Tumor does not surround important blood vessels, have obvious necrosis and/or cavitation or invade the surrounding vital organs and blood vessels
- No symptomatic metastases of the central nervous system
- No history of esophageal gastric varices, severe ulcers or wounds that do not heal
- No history of severe bleeding tendencies or coagulopathy, or hemoptysis within last 4 weeks

Ivonescimab is an investigational therapy that is not approved by any regulatory authority.

*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").

1. Manegold et al., (2016); *JTO* 12:2.194-207.; **2.** Pardoll, Drew M. (2012) *Nature Reviews Cancer* vol. 12,4 :252-64.;
3. Tamura et al., (2020) *Med Oncol* 37:2, 10.1007.

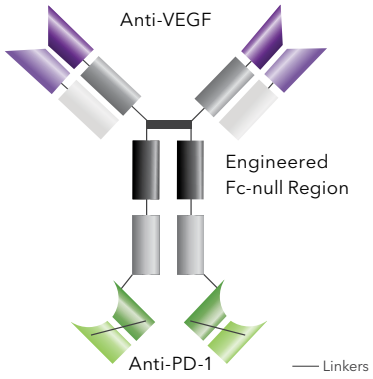
Ivonescimab: Most Advanced PD-1/VEGF Bispecific Antibody in Clinical Development in the U.S. and EU*

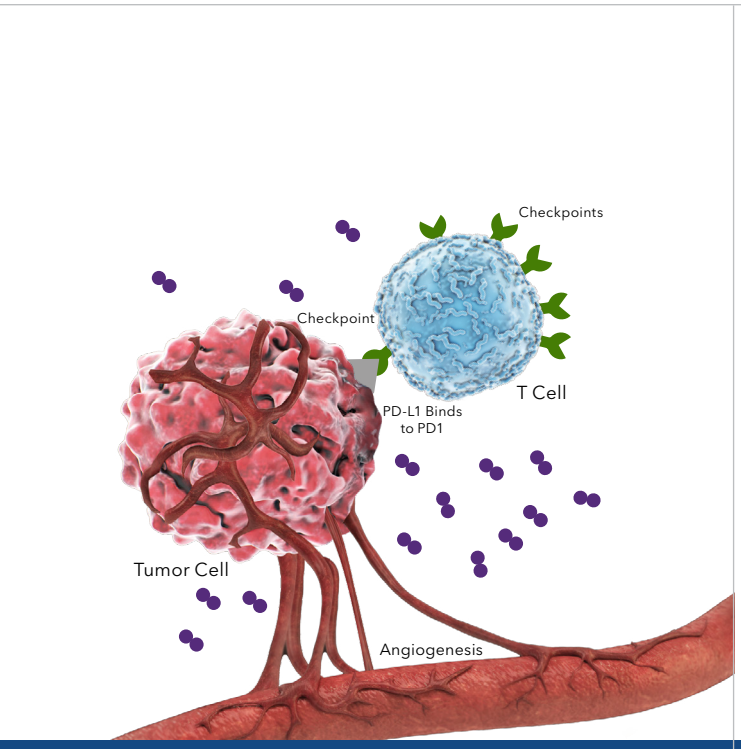
Brings two validated mechanisms in oncology[1,2,3] into ONE novel tetravalent molecule

Designed to Optimize the Balance of Anti-tumor Activity and Safety[4,5]

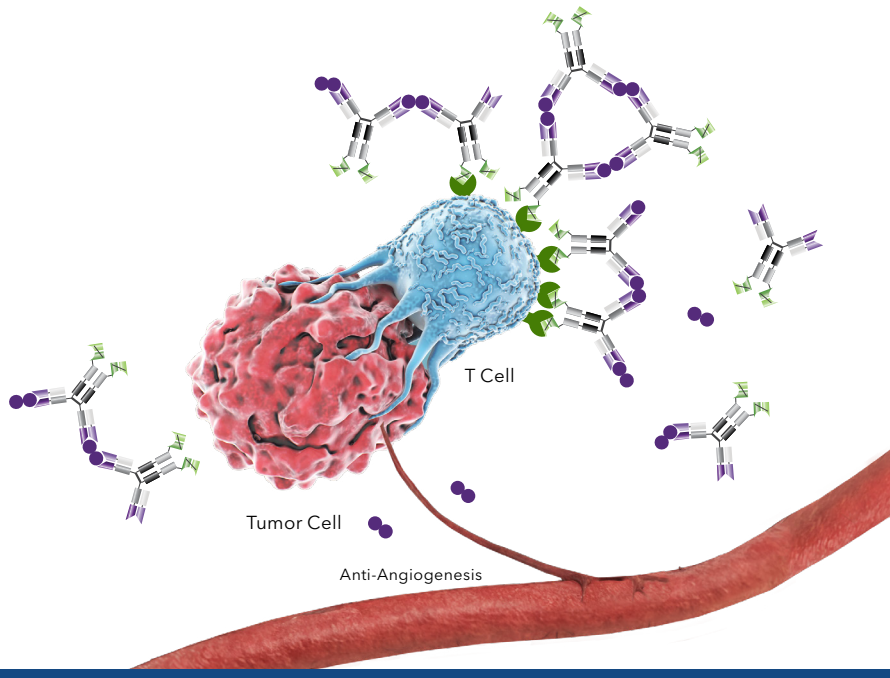
Cooperative Binding

- Presence of VEGF increases binding of PD-1 by >10-fold in-vitro[6]
- VEGF dimer leads to potential interconnection of multiple ivonescimab molecules, which may lead to increased binding of T-cells in-vitro[6]





Without Ivonescimab PD-1/VEGF Bispecific Antibodies



With Ivonescimab PD-1/VEGF Bispecific Antibody Cooperative Binding

VEGF Dimer PD-1 Receptor in T Cell

Summit Medical Monitor: Dr. Lori Styles / +1.510.325.4823 / Lori.Styles@summitplc.com or email medinfo@smmttx.com

*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").

1. Manegold et al., (2016); *JTO* 12:2.194-207.; **2.** Pardoll, Drew M. (2012) *Nature Reviews Cancer* vol. 12,4 :252-64.; **3.** Tamura et al., (2020) *Med Oncol* 37:2, 10.1007.; **4.** Zhao Y. et al., (August 2023) *eClinicalMedicine vol* 62: 102106.; **5.** Zhou C. et al., *Journal of Clinical Oncology* 40, no. 16_suppl (June 01, 2022) 9040.; **6.** Zhong T et al., (2022) *Journal for ImmunoTherapy of Cancer 10(2) 521.*

Intended for Clinical Site Staff Use Only

Ivonescimab is an investigational therapy that is not approved by any regulatory authority.

SMMTTX.com
medinfo@smmttx.com

Summit therapeutics