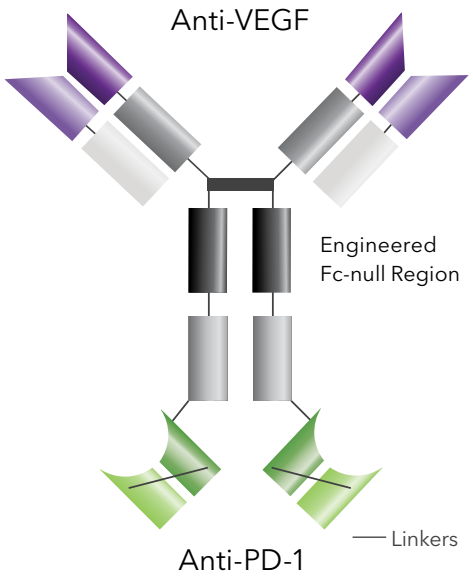
Ivonescimab

Mechanism of Action (MOA)

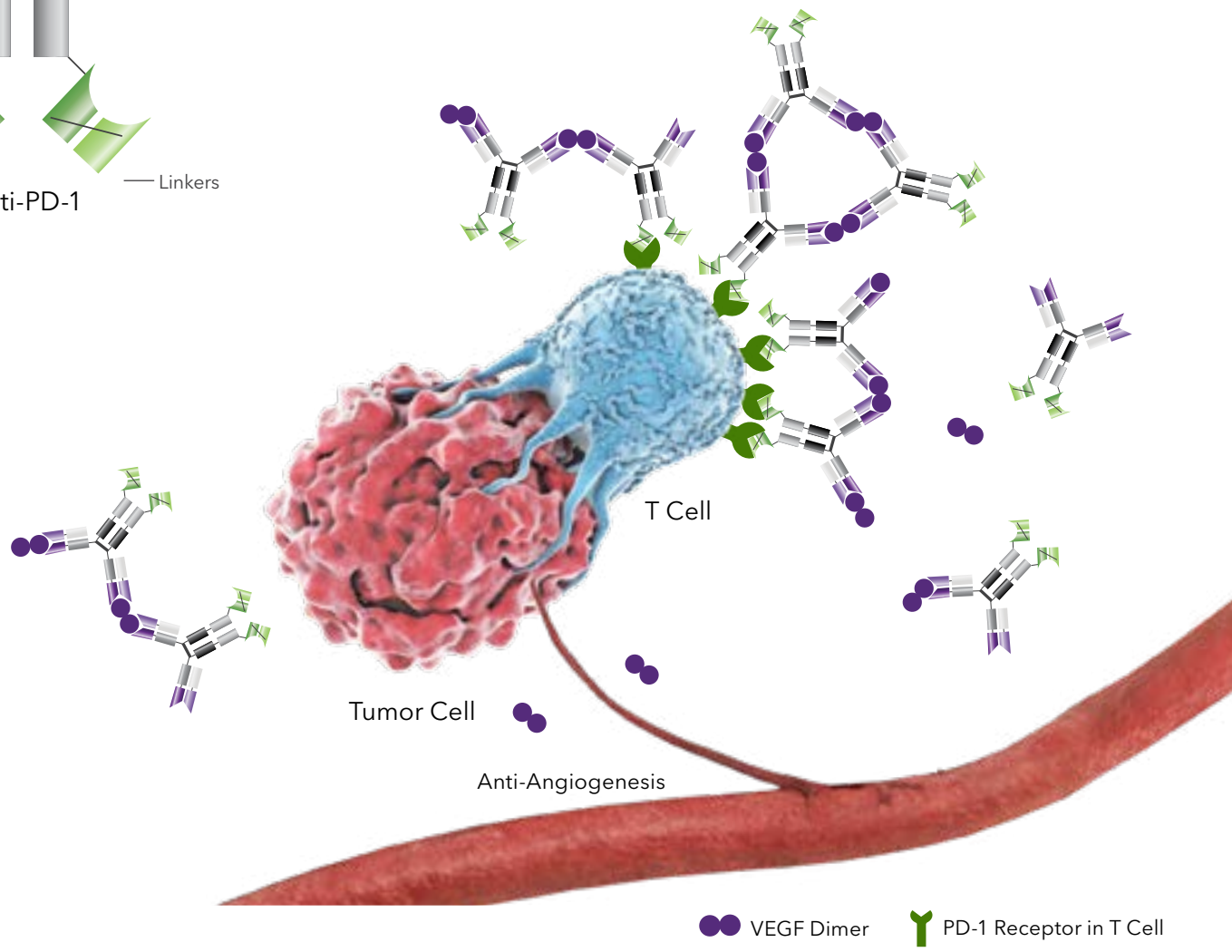
Intended for HCPs / Investors / Media

Designed to Optimize the Balance of Anti-tumor Activity and Safety[1,2]



Potential to drive SYNERGISTIC anti-tumor activity[1,3,4]

- Simultaneous Blocking of PD-1 & VEGF[1,3,4]
- Cooperative Binding[5,6]



1. Zhao Y. et al., eClinicalMedicine. 2023; 3(62): 102106.
2. Zhou C. et al., J Clin Oncol. 2022;40:16_suppl, 9040
3. Manegold C. et al. J Thorac Oncol 2017; 12(2):194-207
4. Data on File. [14, 15] Summit Therapeutics Inc.
5. Zhong T, et al. AACR-NCI-EORTC International Conference 2023 Poster #B123, Abstract #35333, Boston, MA, USA
6. Zhong T, et al. JITC 2022;10(2):521.

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

Ivonescimab

Mechanism of Action (based on *in vitro* studies)

Ivonescimab

First-in-class* PD-1/VEGF bispecific antibody in clinical development
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]

Simultaneous interaction of PD-1 & VEGF blockades and cooperative binding have the potential to drive synergistic anti-tumor activity[1,4,6]

Inhibiting VEGF can help improve the effect of immunotherapy by modulating the tumor microenvironment[4]
Enhancing the PD-1 blockade helps activate T cells[2]

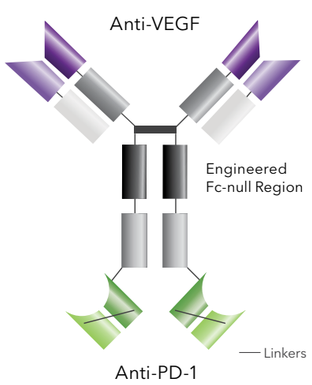
Cooperative Binding

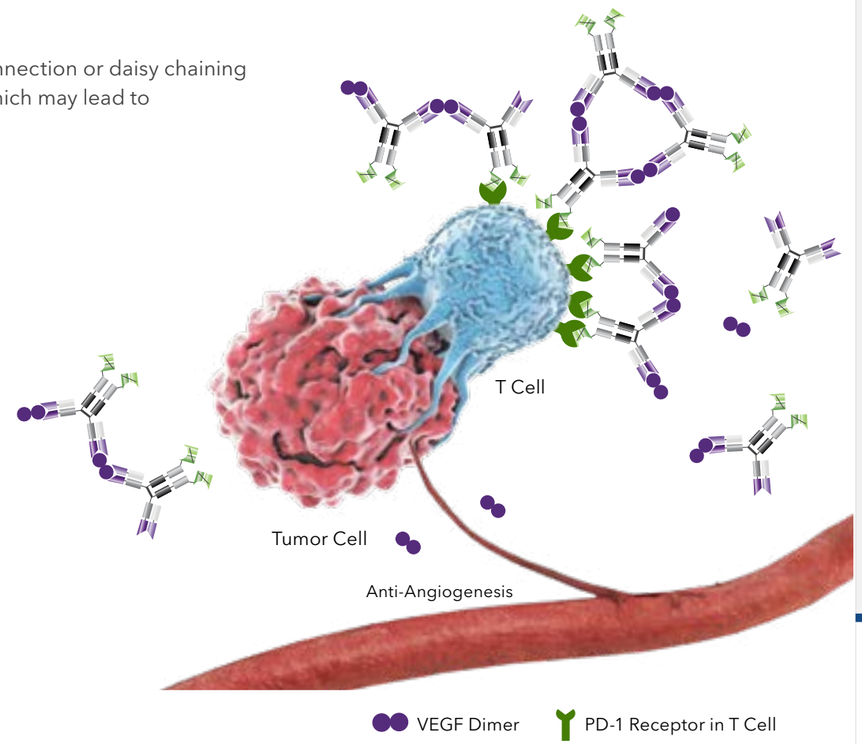
Increased Binding Strength (Affinity)

Presence of VEGF increases PD-1 binding strength by >18X[7]
Presence of PD-1 increases VEGF binding strength by >4X[7]

Increased Binding of T Cells

VEGF dimer leads to potential interconnection or daisy chaining of multiple ivonescimab molecules, which may lead to increased binding of T cells[7,8]





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Ivonescimab is currently being investigated in Phase 3 clinical studies. Phase 1 and 2 data generated and analyzed by Akeso.
*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").

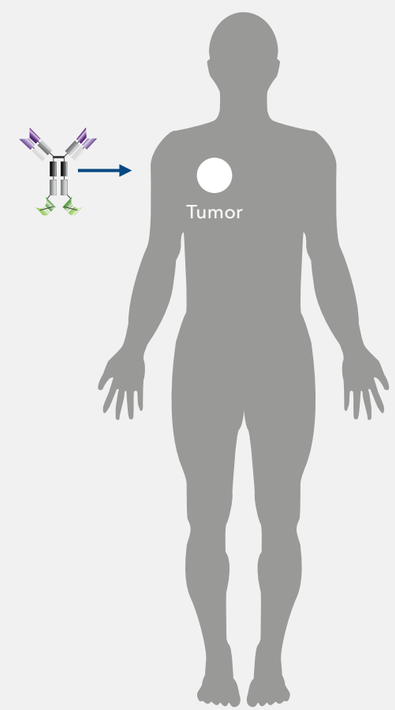
Ivonescimab

Potential Safety Benefits

Ivonescimab has the potential to accumulate in the TME where there are higher levels of PD-1 and VEGF vs. healthy tissue[4,5,7,8]

Half-life ($T_{1/2}$) of 6-7 days[9]

Provides blockade of both PD-1 and VEGF targets with its affiliated clearance, which could potentially lead to a favorable safety profile[4,5]



1. Manegold C, et al. J Thorac Oncol 2017;12(2):194-207
2. Pardoll, D. Nat Rev Cancer 2012;12(4):252-64
3. Tamura R, et al. Med Oncol 2020;37(1):2
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5. Zhou C, et al. J Clin Oncol. 2022;40:16_suppl, 9040.
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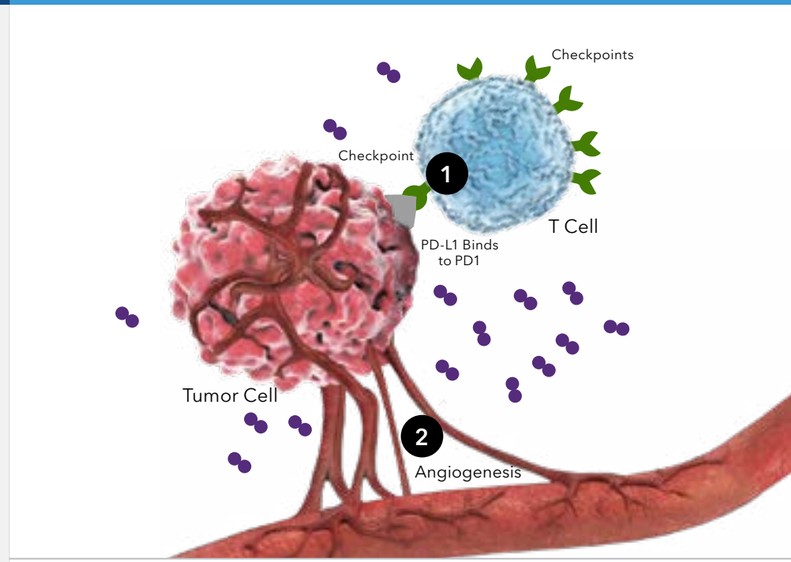
Tumor Microenvironment (TME)



1 T cells & Binding of PD-1 to PD-L1[10,11,12]

- PD-1: Protein, found on T cell
- PD-L1: Protein, found on tumor cell
- Found in tumor microenvironment
- Helps immune system fight germs and protect from disease
- One role is to attack and kill tumor cells

Drugs That Block PD-1 & PD-L1 From Binding[12]

Anti-PD-1 / PD-L1 Drugs
(Immunotherapy or Checkpoint Inhibitors/ICIs)

- Blocking PD-1 & PD-L1 allows T cells to attack tumor cells

2 Angiogenesis & VEGF[13,14]

Tumor cells need a blood supply to grow

Angiogenesis

- Formation of new blood vessels that feed the tumor cell
- VEGF (vascular endothelial growth factor)
  - Is a "dimer" (structure with two identical units)
  - Found in high abundance around tumor cell in TME
  - Promotes angiogenesis

Anti-VEGF Drugs or Angiogenesis Inhibitors

- Helps block angiogenesis by cutting blood supply to tumor
- Causes tumor to wither and die

Glossary of Terms

Intended for HCPs / Investors / Media

Affinity	The measure of the binding strength between one of the binding sites of the antibody and its target.
Angiogenesis	The formation of new blood vessels which feed a tumor and make it grow.
Antibody	A protein produced by the immune system (B cells). Protects the body from disease.
Anti-PD-1	Blocking binding of PD-1 to PD-L1 which can be achieved by an immune checkpoint inhibitor (ICI).
Anti-tumor Activity	Preventing or inhibiting the formation or growth of tumors.
Anti-VEGF / Anti-angiogenic	Stops the growth of new blood vessels, starves the tumor.
Adverse Events	Any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related.
Avidity	Measure of the total binding strength of the antibody.
Bispecific Antibody	Type of protein that can simultaneously (at the same time) bind to two different targets.
Cooperative Binding	In the case of ivonescimab, "cooperative binding" occurs because there are both anti-PD-1 and anti-VEGF binding sites in one molecule. Presence of VEGF increases PD-1 binding strength by >18X *in vitro*. Presence of PD-1 increases VEGF binding strength by >4X *in vitro*. Also, the VEGF dimer leads to potential interconnection or daisy chaining, which may lead to increased binding of T cells *in vitro*.
Daisy chaining	Interconnecting multiple molecules together which can potentially multiply its biological effect.
Dimer	Structure containing two identical or similar units.
FC-null Region	A region of the antibody responsible for additional biological activities.
Half-life or $T_{1/2}$	The time it takes for the amount of a drug's active substance to reduce by half.
Immunotherapy also called immune checkpoint inhibitors or ICIs	Treatments that promote or support the body's immune system response to a disease such as cancer.
In vitro	Performed in a test tube, culture dish or outside something that is living.
IV infusion	Delivery of a drug into the patient's blood stream (veins).
Mechanism of Action (MOA)	The process by which a molecule, such as a drug, functions to produce a pharmacological effect.
Metastatic	The process by which cancer cells spread to other parts of the body.
Molecule	Two or more atoms connected by chemical bonds.
PD-1 (Programmed cell death protein 1)	Protein, found on the T cell that can prevent the immune system from killing cancer cells.
PD-L1 (Programmed cell death ligand 1)	Protein, found on the tumor cell can prevent the immune system from killing cancer cells.
T Cells	Type of cell that helps your immune system fight germs and cancer.
Tumor	An abnormal lump or mass of tissue. Tumors can be benign (not cancerous) or malignant (cancerous).
Tumor microenvironment (TME)	The ecosystem that surrounds a tumor.
Tetravalent Molecule	Having the capacity to bind four targets simultaneously.
Vascular Endothelial Growth Factor (VEGF)	Promotes the growth of new blood vessels. Promotes angiogenesis.
VEGF Dimer	VEGF, which is a structure containing two identical or similar units.

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Summit therapeutics