ALX148 is a High Affinity SIRPα Fusion Protein that Blocks CD47, Enhances the Activity of Anti-Cancer Antibodies and Checkpoint Inhibitors, and Has a Favorable Safety Profile in Preclinical Models

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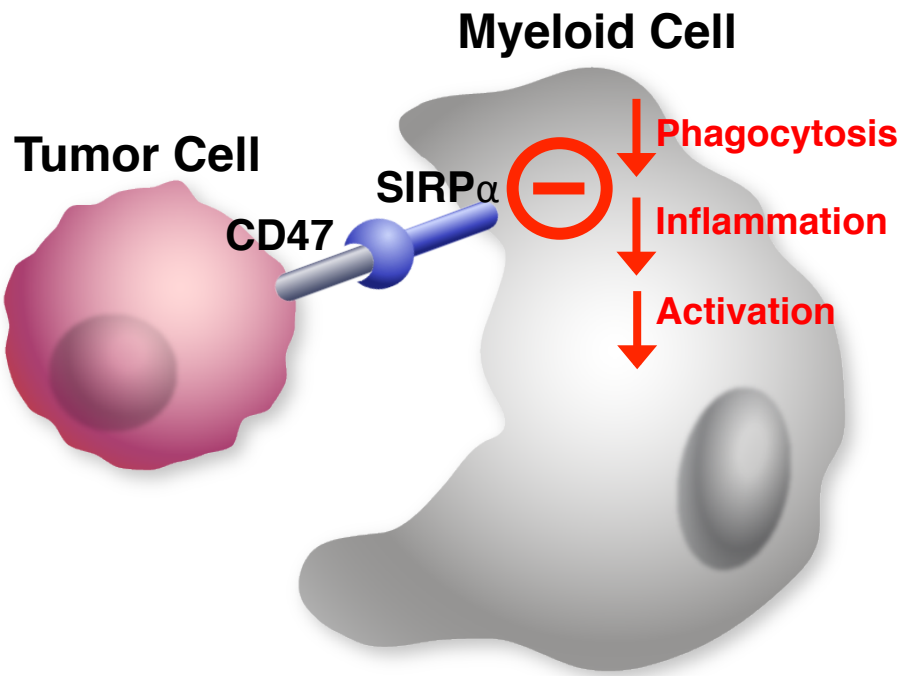
ALEXO THERAPEUTICS

The CD47-SIRPα Interaction Regulates Myeloid Cell Function



- CD47
  - Broadly expressed cell surface protein
  - Overexpressed on tumor cells
- SIRPα
  - Receptor for CD47 on myeloid cells
  - Inhibitory signaling upon CD47 binding
- CD47-SIRPα is an immune checkpoint
- CD47 is a promising therapeutic target

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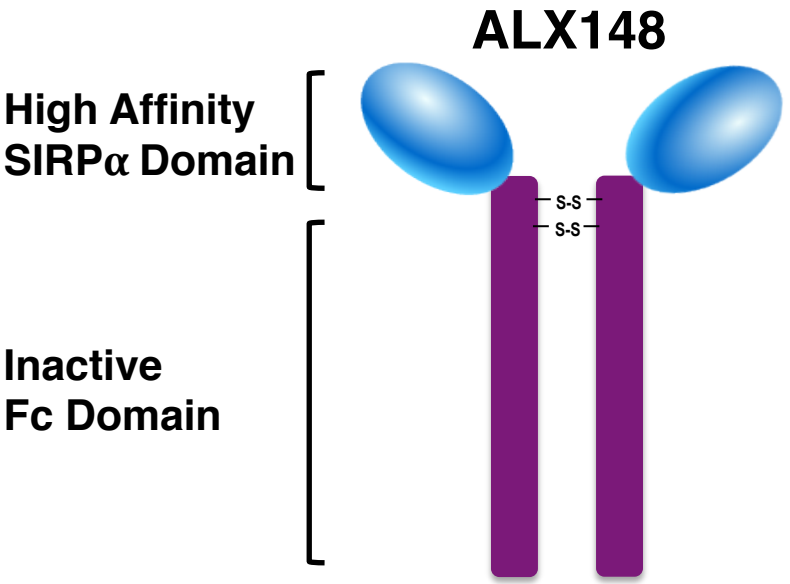
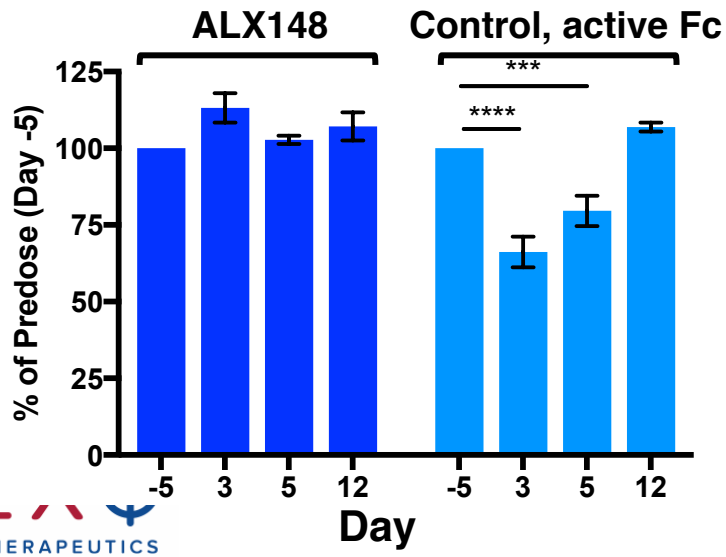
Unique Design of ALX148 is Responsible for Improved Safety

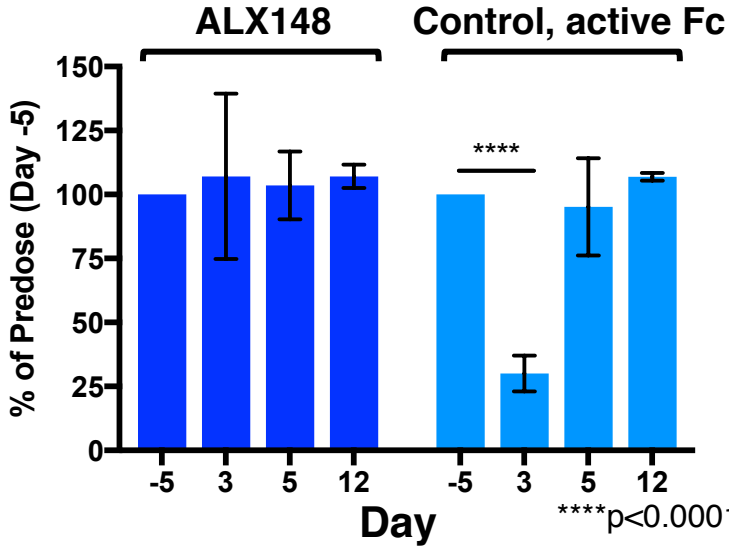


- Engineered SIRPα domain binds CD47 with picomolar affinity
- Blocks CD47-SIRPα interaction
- Binds CD47 from humans, non-human primates, and mice
- Fc domain does not bind Fcγ receptor, binding to neonatal Fc receptor is maintained

Red Blood Cells



Platelets



CD-1 mice
30 mg/kg x1
****p<0.0001, ***p<0.001

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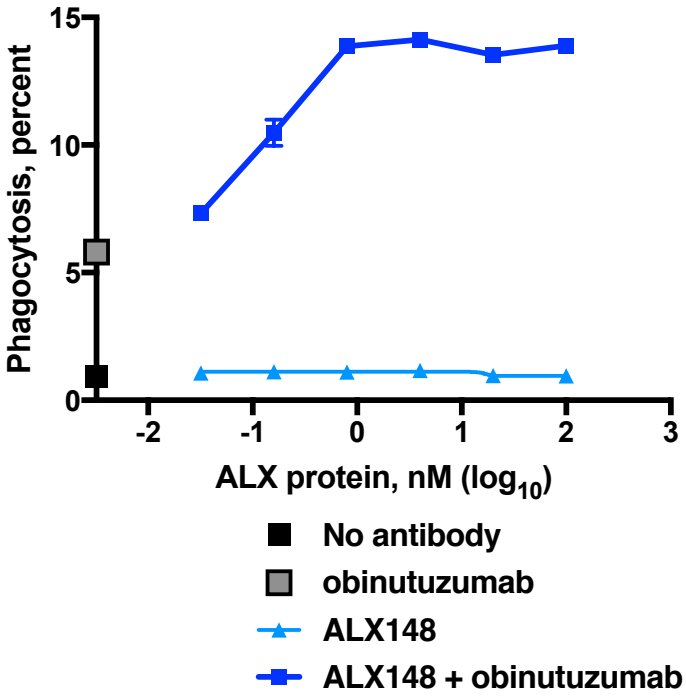
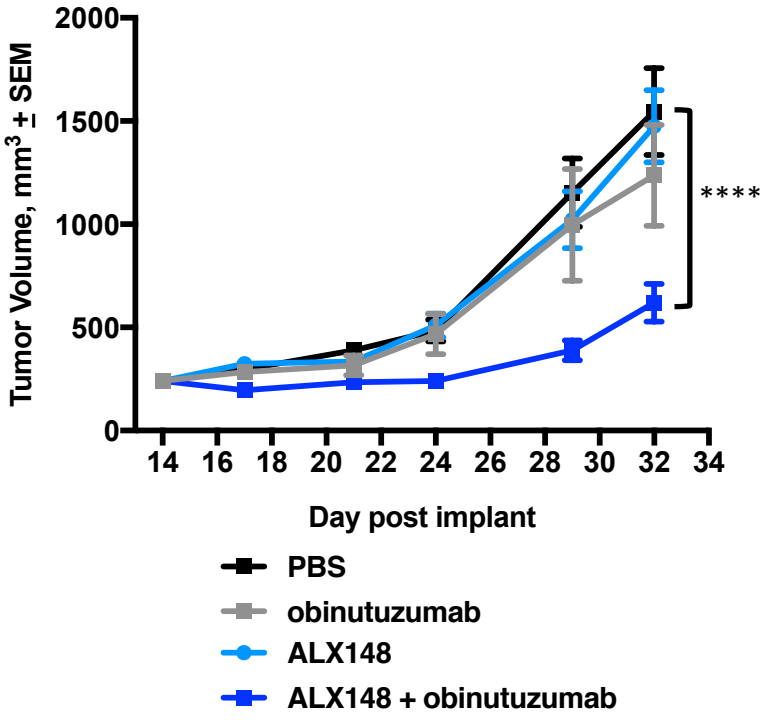
ALX148 Enhances Activity of Targeted Antitumor Antibodies

Phagocytosis of Daudi Tumor Cells *in vitro*



Inhibition of Z138 Xenograft Tumorigenesis



Similar results with rituximab, trastuzumab

NOD SCID Mice
0.05 mg/kg obinutuzumab 2x/week
10 mg/kg ALX148 2x/week
****, p<0.0001

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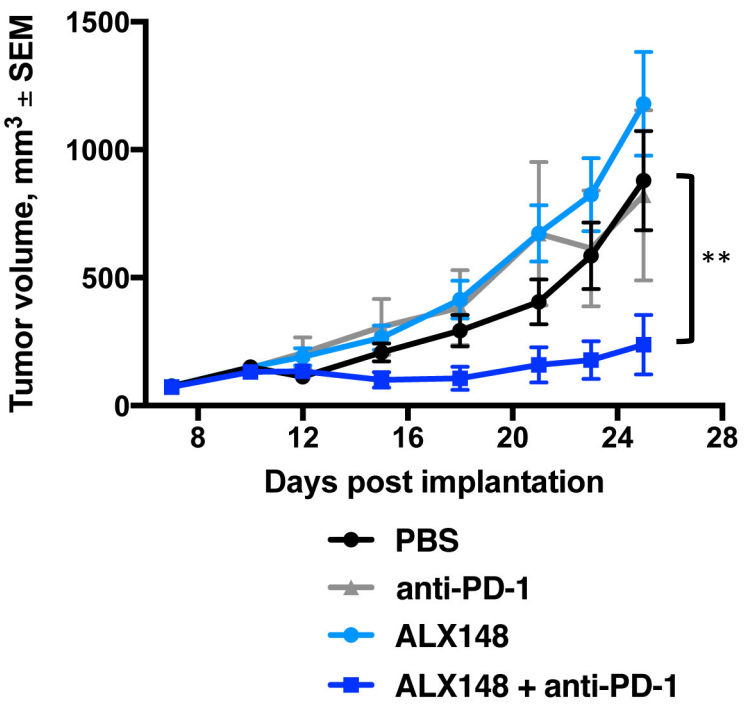
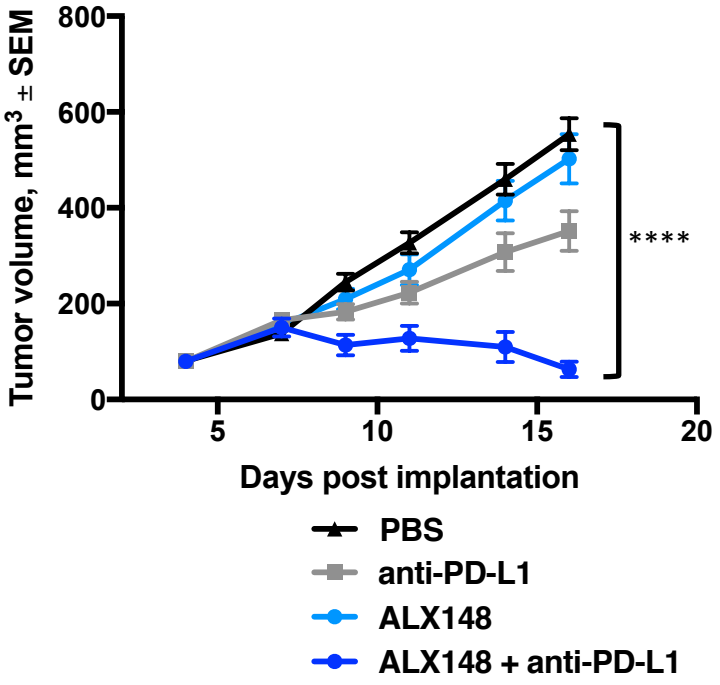
ALX148 Enhances Efficacy of Checkpoint Inhibitors in Multiple Syngeneic Models

Combination With αPD-1 in CT26 Model



BALB/c mice
αPD-1 5 mg/kg 3q5d
ALX148 10 mg/kg 2q10d
**p<0.01

Combination With αPD-L1 in MC38 Model



C57BL/6 mice
αPD-L1 2 mg/kg 2q7d
ALX148 30 mg/kg 2q10d
****p<0.0001

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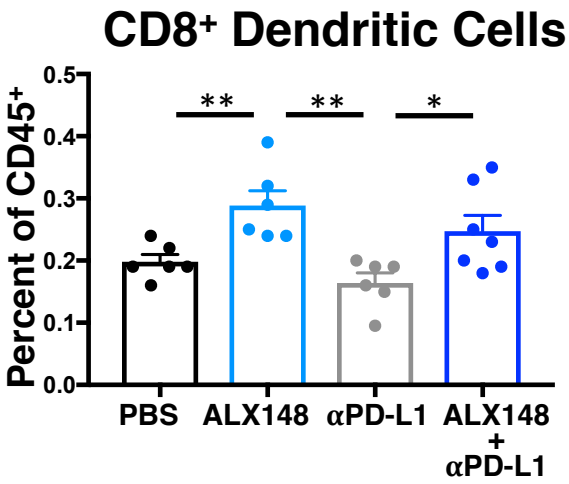
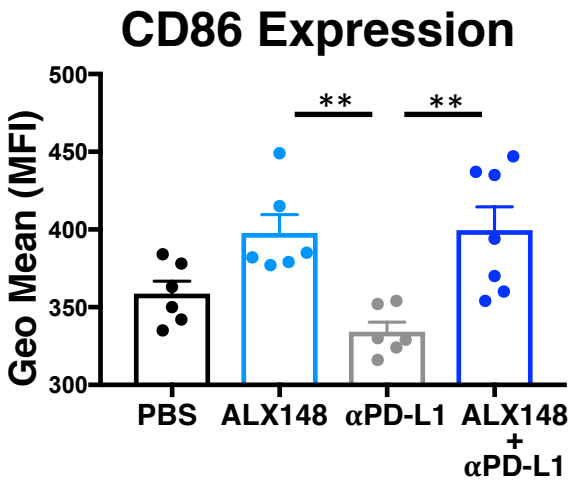
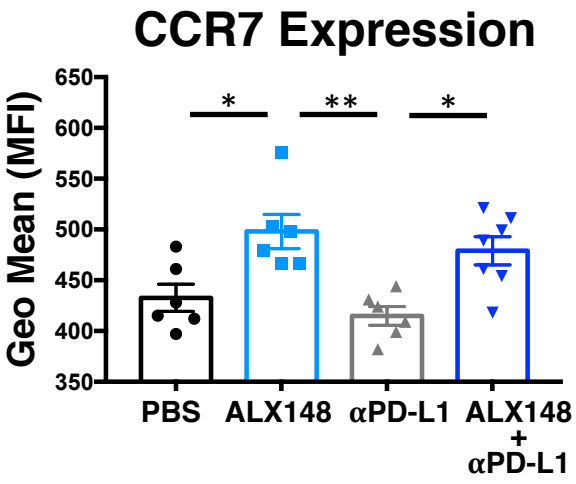
ALX148 Activates Splenic Dendritic Cells in Tumor-Bearing Mice







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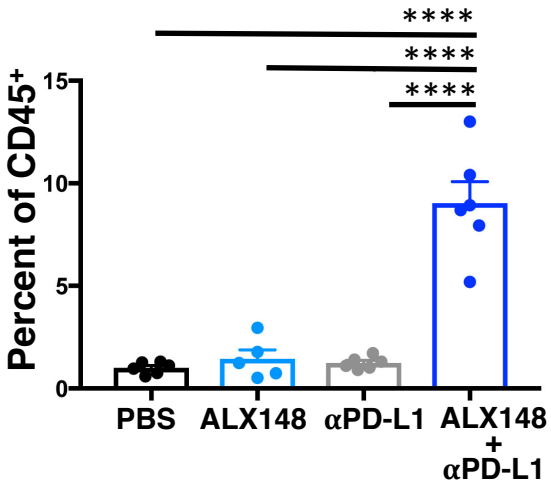
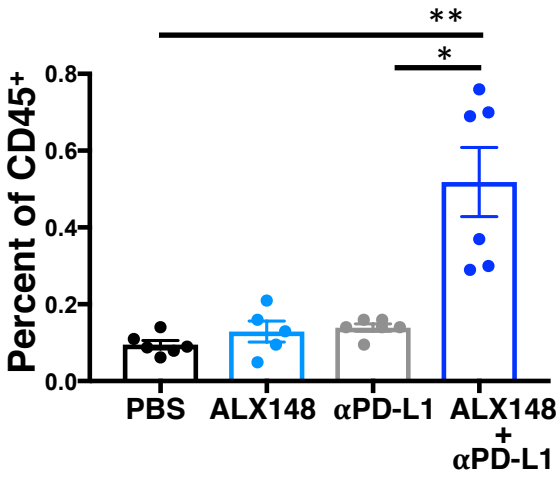
C57BL/6 mice
αPD-L1 2 mg/kg 2q7d
ALX148 30 mg/kg 2q10d
**p<0.01, *p<0.05

ALX148 and Anti-PD-L1 Cooperatively Increase CD8+ T Cell Function in the Tumor

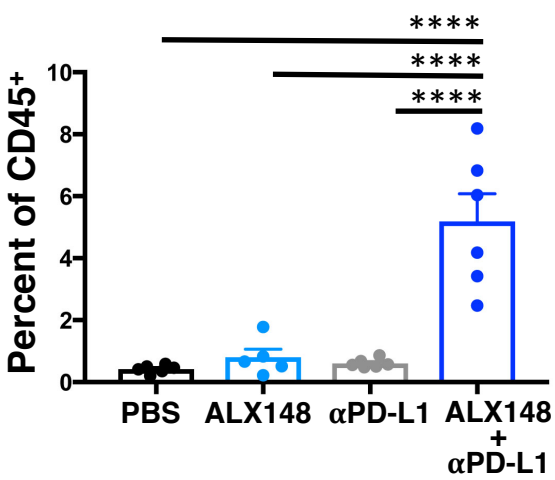
Infiltrating CD8+ T Cells



IFNγ+ CD8+ T Cells



Granzyme B+ CD8+ T Cells



C57BL/6 mice
αPD-L1 2 mg/kg 2q7d
ALX148 30 mg/kg 2q10d
****p<0.0001, **p<0.01, *p<0.05

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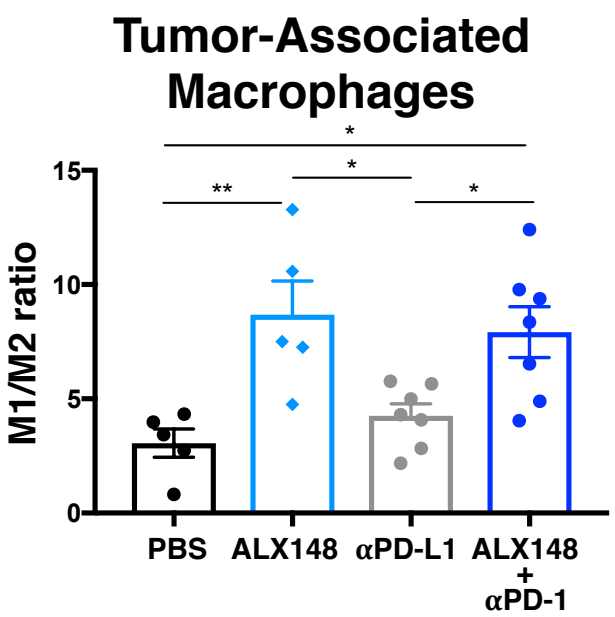
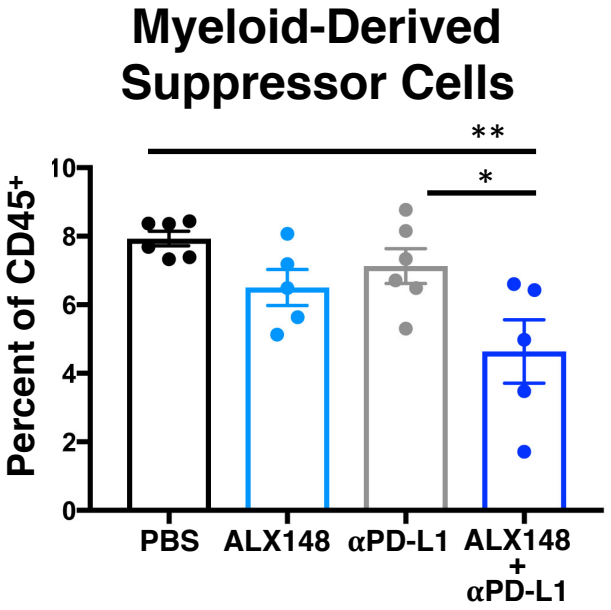
ALX148 Reduces Immunosuppressive Populations in the Tumor Microenvironment



BALB/c mice
CT26 tumor
αPD-1 5 mg/kg x1
ALX148 30 mg/kg x1
*p<0.05, **p<0.01



C57BL/6 mice
MC38 tumor
αPD-L1 2 mg/kg 2q7d
ALX148 30 mg/kg 2q10d
*p<0.05, **p<0.01

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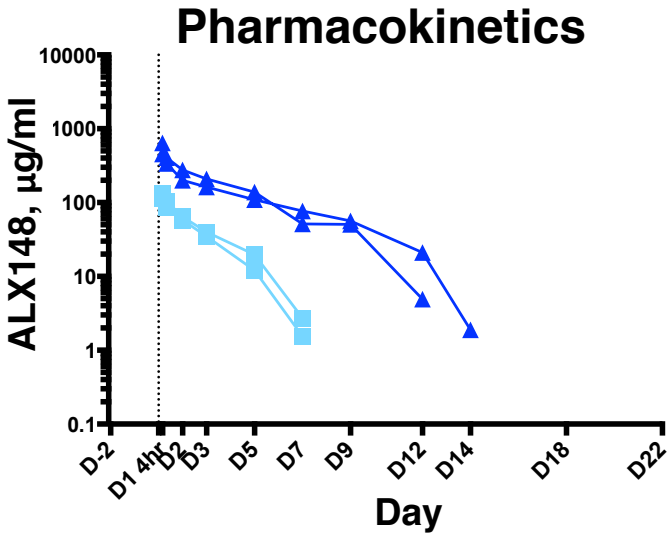
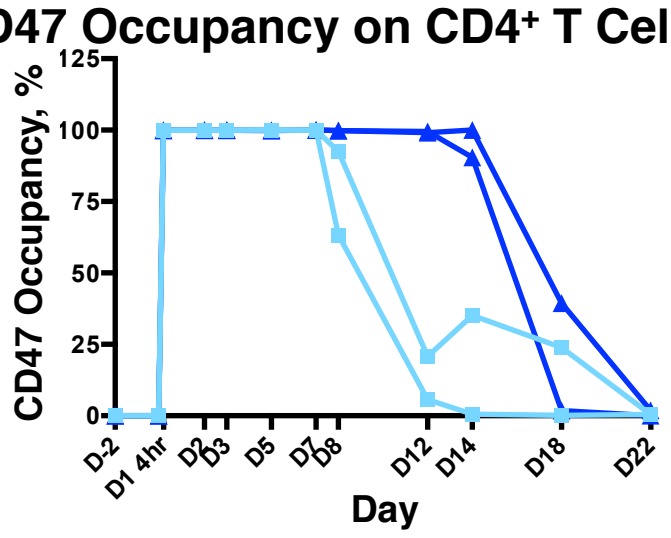
ALX148 Has a Favorable Safety Profile in Nonhuman Primates

- Four week repeat dose toxicity study
- No ALX148 mechanism-related toxicity or adverse events up to 100 mg/kg
- Separate PK/PD study: PK profile similar to CD47 antibody; Sustained CD47 target occupancy





10 mg/kg 30 mg/kg

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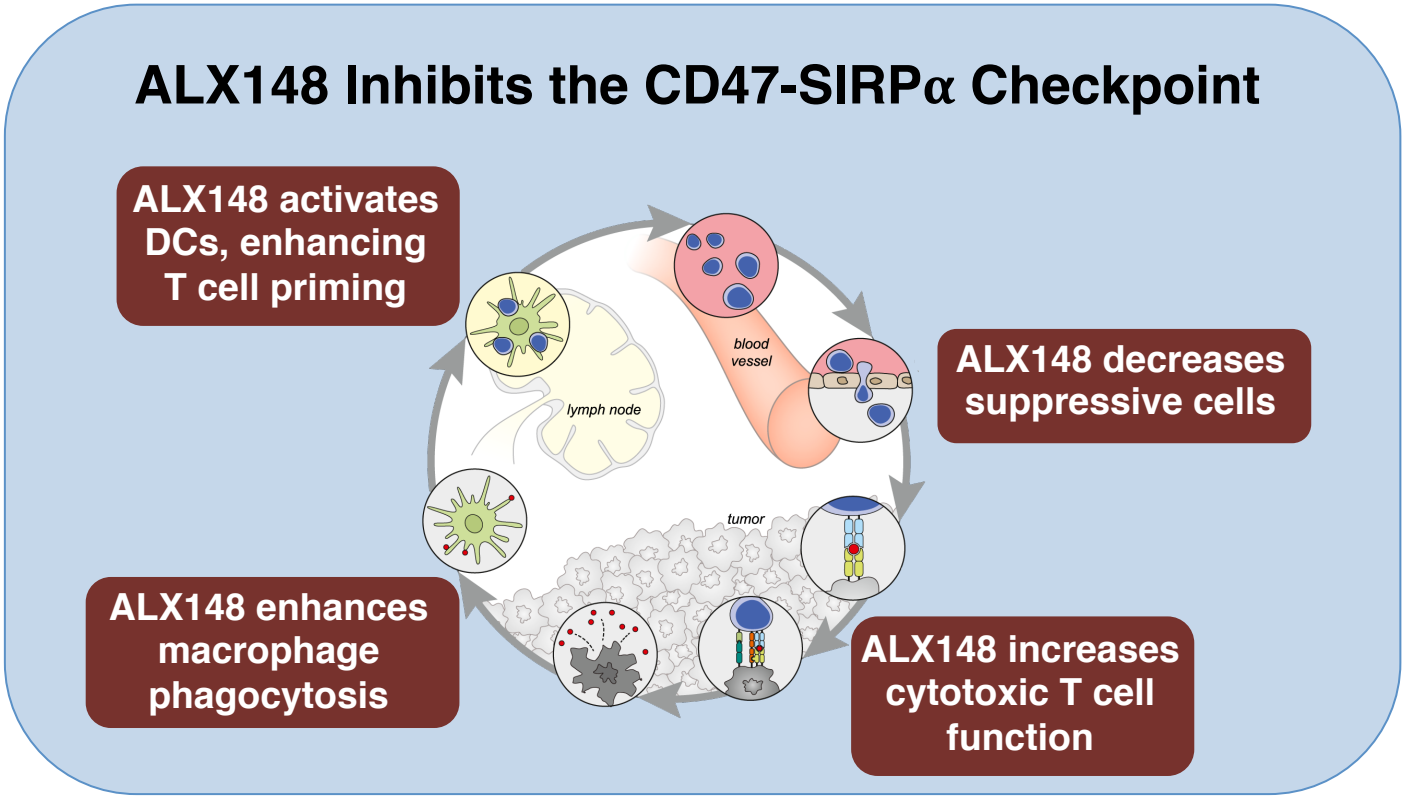
Summary



After Chen and Mellman, 2013

- **ALX148 enhances the efficacy of antitumor and checkpoint inhibitor antibodies**
- **ALX148 has a favorable preclinical toxicity profile**

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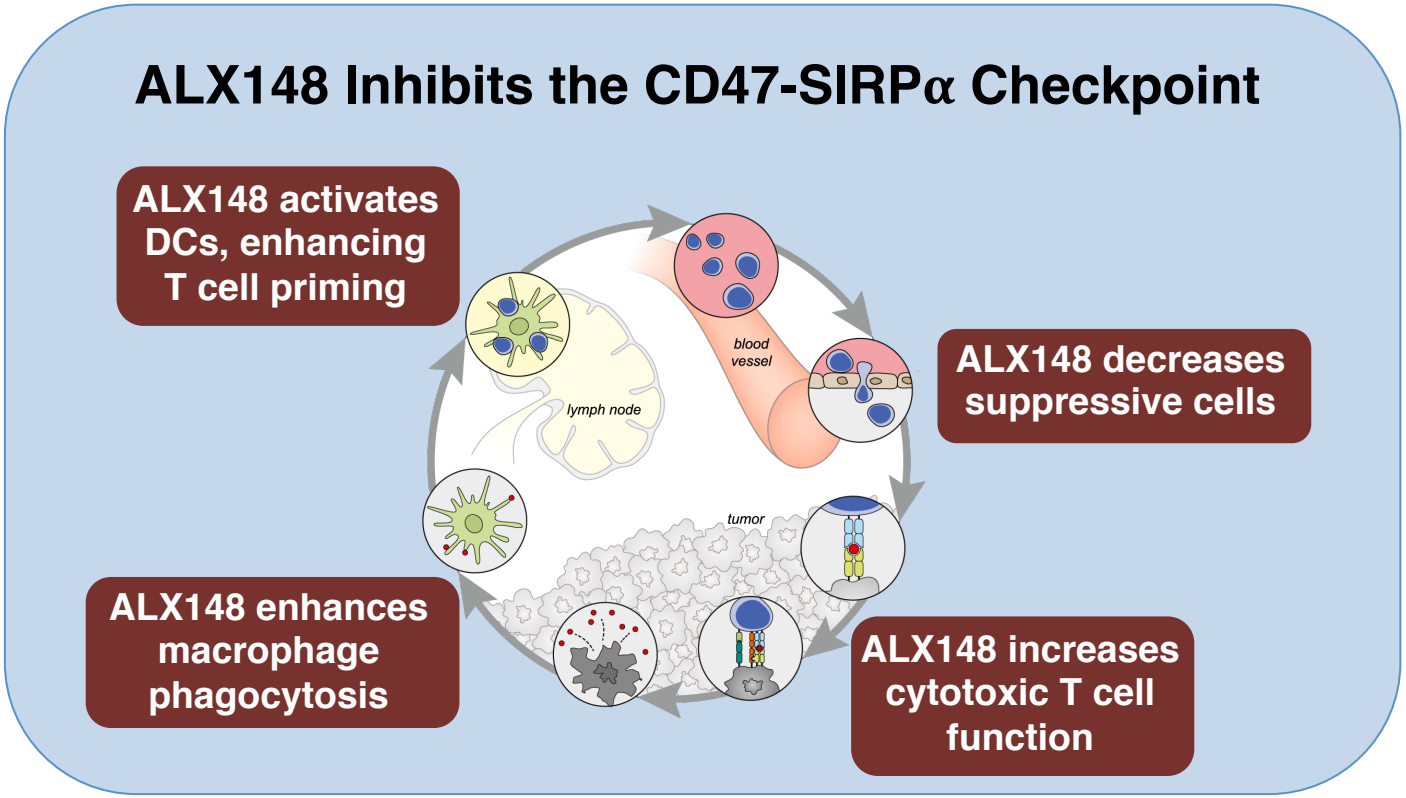
Summary



After Chen and Mellman, 2013

- **ALX148 is currently being investigated in a Phase 1 clinical trial (NCT03013218)**
  - **Clinical safety profile consistent with preclinical studies**
  - **Clinical data presented at 2017 SITC Annual Meeting**

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