Abstract #481

An affinity-optimized CD47xPD-L1 bispecific antibody for dual immune checkpoint blockade

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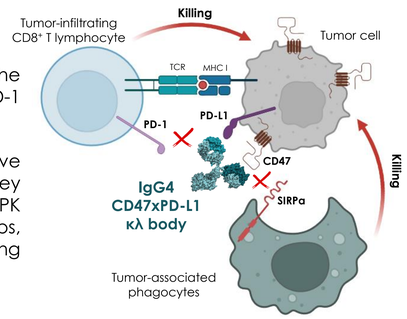
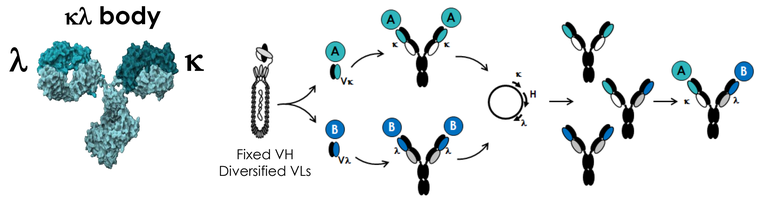
Background

- CD47/SIRPa checkpoint blockade has emerged as an effective approach to mobilize myeloid cells to eliminate cancer cells
- Preclinical data have demonstrated the synergistic benefit of combined SIRPa and PD-1 blockade with monoclonal antibodies
- CD47xPD-L1 bsAbs are an attractive alternative to mAb combinations, even more so as they provide a solution to improve the safety and PK issues faced by (monospecific) CD47 mAbs, but might also provide superior tumor-targeting capabilities



κλ body platform – Native, human bsAbs

- Non-engineered, human bispecific antibodies
- Standard antibody discovery using common heavy chain libraries, kappa and lambda variable light chains drive the specificity to the targets
- Platform purification process, several GMP batches produced
- Two programs in clinical trials and multiple bsAbs in preclinical development



Fischer *et al.*, Nat. Com., 2015

NI-2901, a CD47xPD-L1 IgG4 κλ body

- **High affinity**
- Blocks PD-1/PD-L1 axis
- Cross-reacts with cynomolgus and mouse

NI-2901

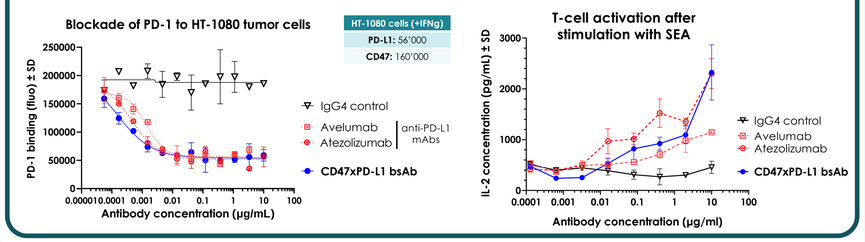
Anti-PD-L1 arm | **Anti-CD47 arm**

IgG4 Fc
Low Fc-mediated effector functions
(ADCP)

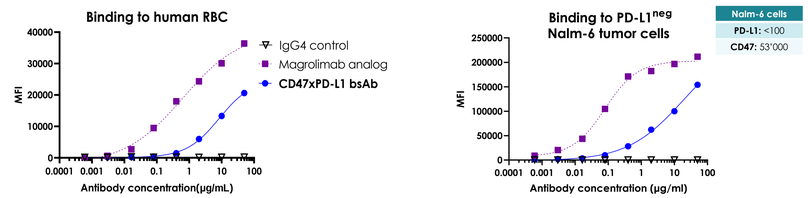
- **Moderate affinity**
- Blocks CD47/SIRPa axis
- Cross-reacts with cynomolgus

- The arms can act independently and also benefit from co-engagement
- Moderate monovalent binding to CD47 on PD-L1-neg cells to mitigate safety concerns
- Stabilized IgG4 for favorable manufacturability

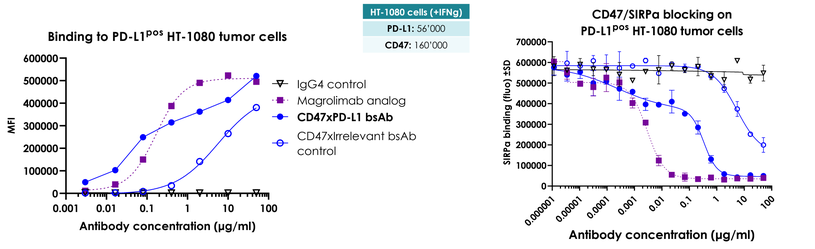
PD-1/PD-L1 blockade and enhancement of T-cell activation



Weaker binding to CD47-expressing cells as compared to magrolimab

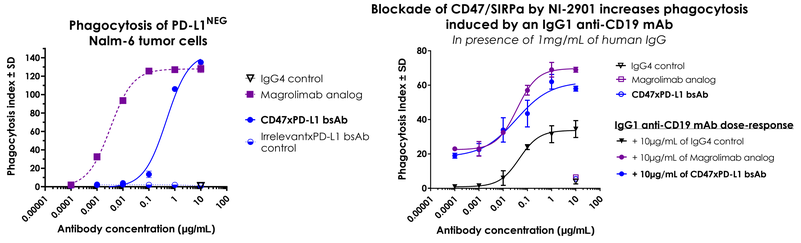


CD47/SIRPa blockade is enhanced by PD-L1 co-engagement

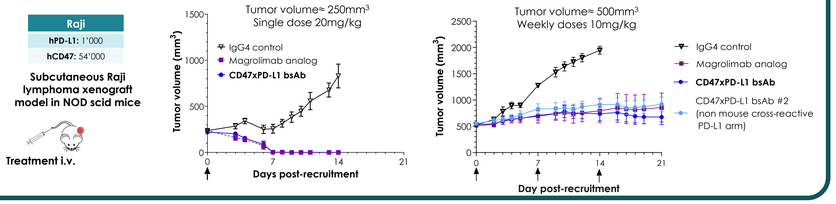


NI-2901 induces robust PD-L1-independent activity

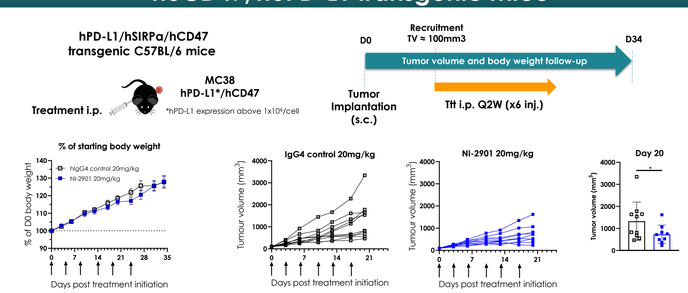
- **Activity in antibody-dependent cellular phagocytosis (ADCP) assays**



- **Antitumor activity in a PD-L1low lymphoma xenograft model**

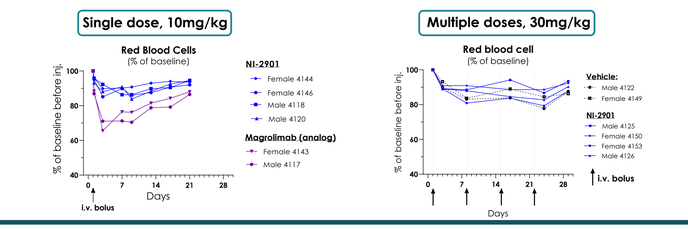


NI-2901 is well-tolerated, demonstrating anti-tumor activity in huCD47/huPD-L1 transgenic mice

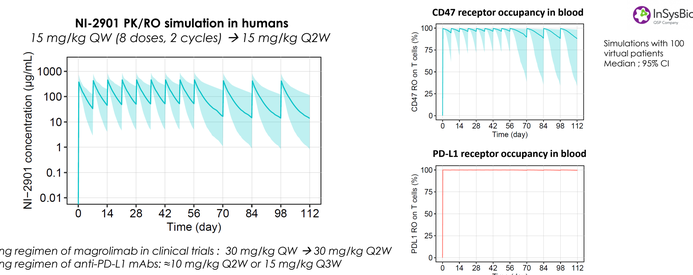


NI-2901 is well-tolerated in non-human primates

- **Exploratory single-dose (10mg/kg) and multiple dose (30mg/kg) tolerability study**
  - No adverse events
  - No change in body weight, food consumption, clinical chemistry and clinical pathology
  - Red blood cells, platelets and leukocytes remained within the normal range



PK modeling and simulations predict favorable patient dosing regimen



Dosing regimen of magrolimab in clinical trials : 30 mg/kg QW → 30 mg/kg Q2W
Dosing regimen of anti-PD-L1 mAbs: ≈10 mg/kg Q2W or 15 mg/kg Q3W

Conclusions

NI-2901:

- Fully human IgG4 CD47xPD-L1 bispecific antibody
- Enhances phagocytosis of tumor cells, increases T-cell activation
- Demonstrates antitumor activity in a syngeneic mouse tumor model
- Well tolerated in NHP, multiple doses at 30mg/kg (highest dose tested)

Next Steps:

- Seeking collaboration or out-licensing opportunities for development

SITC Annual Meeting 2022, November 8-12, Boston, USA