Abstract #3225

NI-2901, a CD47xPD-L1 bispecific antibody for dual immune checkpoint blockade with fine-tuned affinity to reduce erythrocyte binding and improve biodistribution

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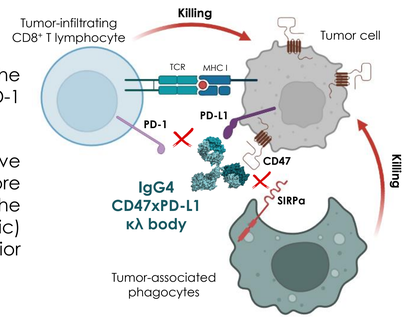
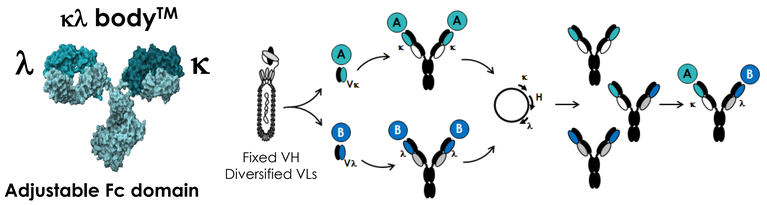
Background

- 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 stand as 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



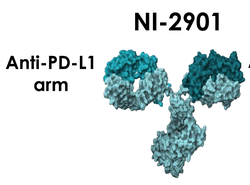
κλ body platform – Native, human bsAbs

- Native, 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 bsAbs in clinical development and multiple κλ body in preclinical development



NI-2901, a CD47xPD-L1 IgG4 κλ body

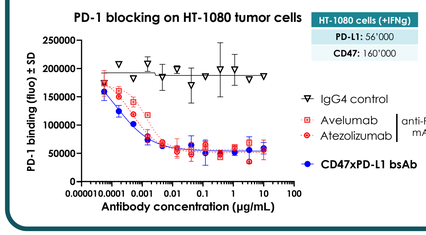
- **Subnanomolar affinity**
- Blocks PD-1/PD-L1 axis
- Cross-reacts with cynomolgus and mouse

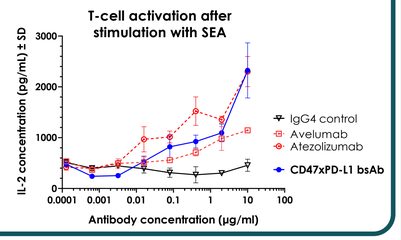


- **2-digit nanomolar affinity**
- Blocks CD47/SIRPa axis
- Cross-reacts with cynomolgus

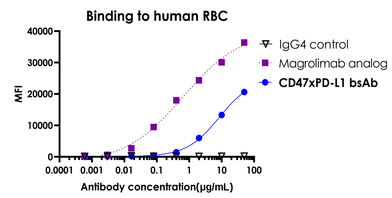
- Moderate affinity of the CD47 arm to limit binding to red blood cells (RBC)
- Effective blockade of PD-1 and SIRPa checkpoints, reinforced by target co-engagement
- Stabilized IgG4 and good CMC properties

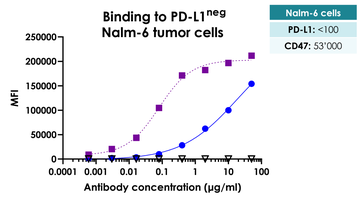
PD-1/PD-L1 blockade and enhancement of T-cell activation



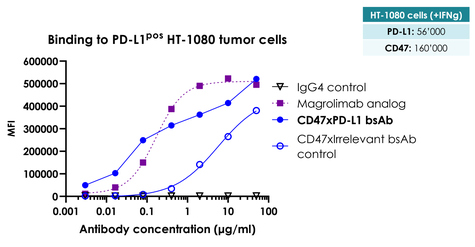


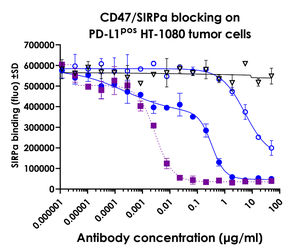
Weaker binding to CD47-expressing cells as compared to magrolimab





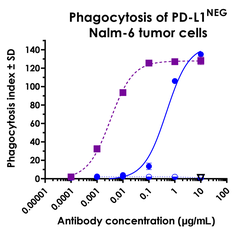
CD47/SIRPa blockade is enhanced by PD-L1 co-engagement

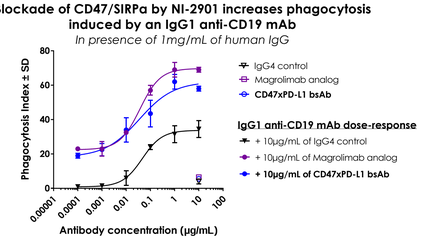




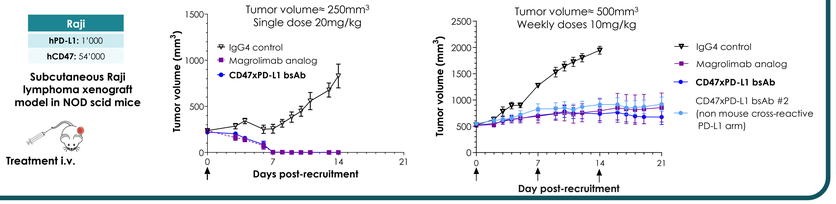
NI-2901 induces robust PD-L1-independent CD47 activity

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



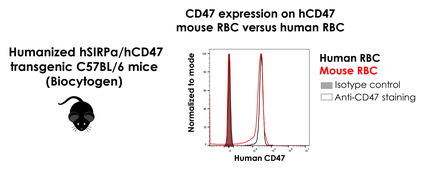


- **Antitumor activity in a PD-L1low lymphoma xenograft model**

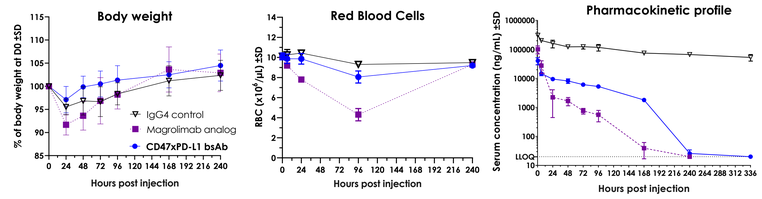


Improved tolerability and PK in hCD47 transgenic mice compared to magrolimab

- **hSIRPa/hCD47 mouse RBC express similar level of hCD47 than human RBC**

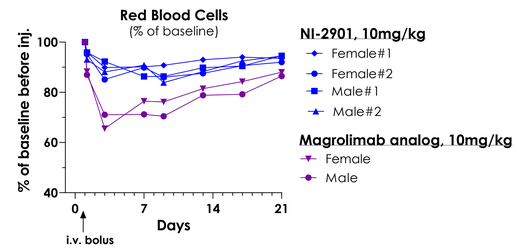


- **NI-2901 is well-tolerated after a single i.v. dose of 10mg/kg, without causing anemia, and shows better pharmacokinetics than magrolimab analog**



Well-tolerated in non-human primates

- **Exploratory single-dose tolerability study in cynomolgus monkey**
  - All the animals were injected with a dose of 10mg/kg (slow i.v. bolus)
  - No clinical signs were reported after injections and during the whole study
  - A significant drop of RBCs (34% maximum decrease) was observed after magrolimab administration



Conclusions

- **NI-2901:**
  - Is a human IgG4 CD47xPD-L1 bispecific antibody, generated using the κλ body™ phage display platform
  - Enhances phagocytosis of tumor cells, increases T-cell activation and demonstrates antitumor activity in xenograft model
  - Has good safety profile in non-human primates and does not cause anemia
- **For partnering opportunities, please reach out to bd@lightchainbio.com**

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