NI-3201, a PD-L1xCD28 bispecific antibody for immune checkpoint-dependent CD28 costimulation


Light Chain Bioscience – Novimmune SA | Plan-Les-Ouates – Geneva | Switzerland

*Corresponding author: sara.majocchi@lightchainbio.com

NI-3201 combines PD-L1 blockade with CD28 co-stimulation

1. Blocks PD-L1 | PD-1 interaction to remove the brake on CD28 signaling
2. Provides T cell activation signal 2 when bridging PD-L1⁺ cells and T cells

The κλ body platform – Truly native bispecific IgGs

- Unmodified native human antibody sequence and structure
- Indistinguishable from natural human IgGs
- Light chain CDRs drive specific binding to selected antigen
- Favorable CMC properties
- Platform purification process
- Multiple GMP runs performed
- 2 clinical stage programs and several other κλ bodies in development, including various partnered programs

PD-L1-dependent delivery of Signal 2

- Blocks PD-L1 | PD-1 interaction
- Clusters CD28 on T cells
- Cyto & mouse cross-reactive

Unbalanced affinity

anti-PD-L1 arm

- Blocks PD-L1 | PD-1 interaction
- Clusters CD28 on T cells
- Cyto & mouse cross-reactive

anti-CD28 arm

- Agonist arm: PD-L1 dependent CD28 activation
- Cyto cross-reactive

Silenced Fc part

NI-3201 shows single-agent anti-tumor activity in vivo

1. NI-3201 controls established MC38-HD-PD-L1 tumors in immunocompetent huCD28 mice
2. NI-3201 is well tolerated in immunocompetent huCD28 mice
3. NI-3201 induces immunological memory against WT MC38

NI-3201 arm of NI-3201 is not superagonist

1. Sensitive in vitro cytokine release assays
2. T cell activation by NI-3201 is signal 1 dependent and effective even at low E:T ratios

NI-3201 does not induce CD28-mediated CRS

1. NI-3201 is well tolerated in a model sensitive to CD28-mediated CRS

NI-3201 is well tolerated in cynomolgus monkeys

1. Ongoing NHP study suggests favorable pharmacokinetics
2. Upon NI-3201 administration to NHP, only a mild and transient IL-6 release was observed

Conclusions and Perspectives

- PD-L1 blockade to release the brake, CD28 agonistic activity to fuel the engine
- Universal combination partner enhancing T cell-mediated immunity to tumors
- Superior single-agent anti-tumor activity to PD-L1 mAbs in vivo
- No flag raised in in vitro and in vivo safety studies
- Several other TAAxCD28 κλ bodies under development:

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