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ALPINEImmuneSciences

NEON-1: A first-in-human phase I open-label study of ALPN-202, a conditional CD28 costimulator and dual checkpoint inhibitor, in advanced malignancies

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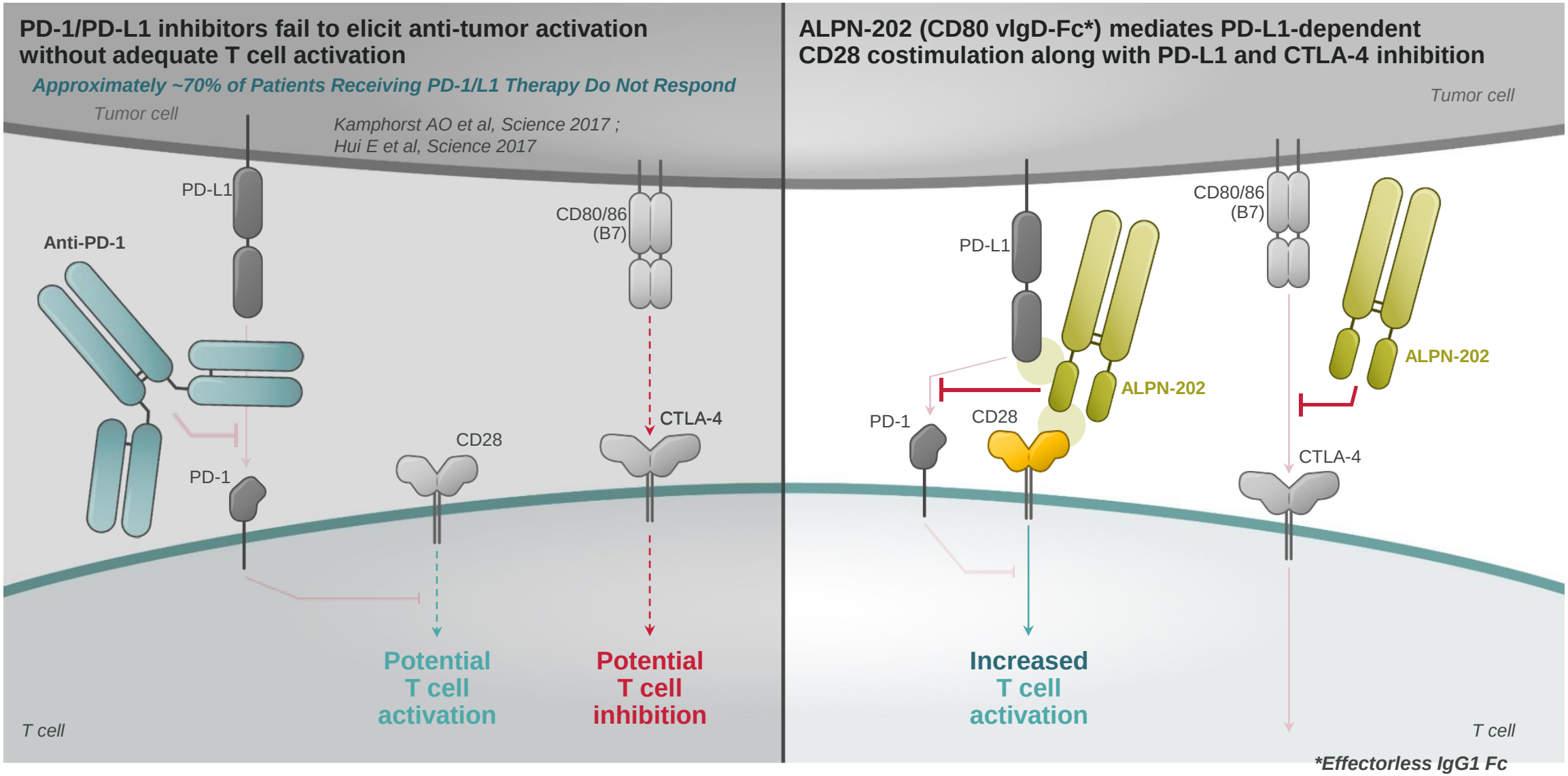
Author Disclosure

- ❑ All authors are employees of Alpine Immune Sciences, Inc.

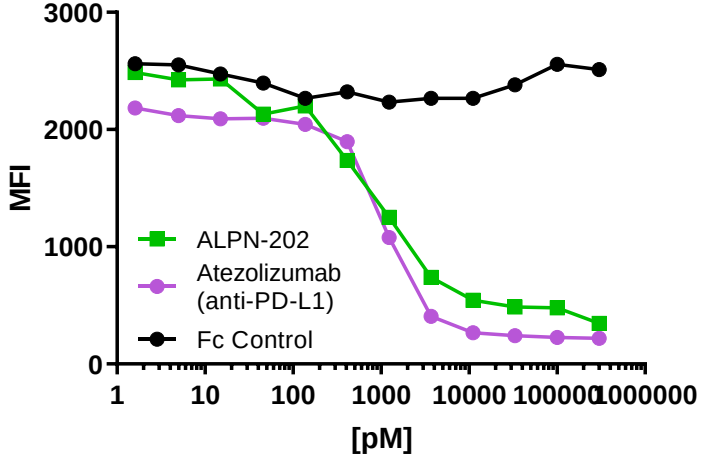
ALPN-202: A Conditional CD28 Costimulator and Dual Checkpoint Inhibitor



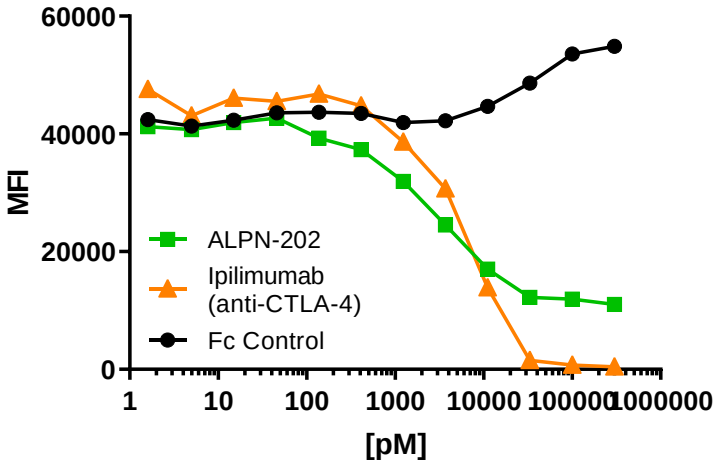
Means GD et al. Abstract 2016 USCAP 2020

Three Primary Mechanisms of Action of ALPN-202:
Conditional CD28 costimulation and dual PD-L1/CTLA-4 inhibition

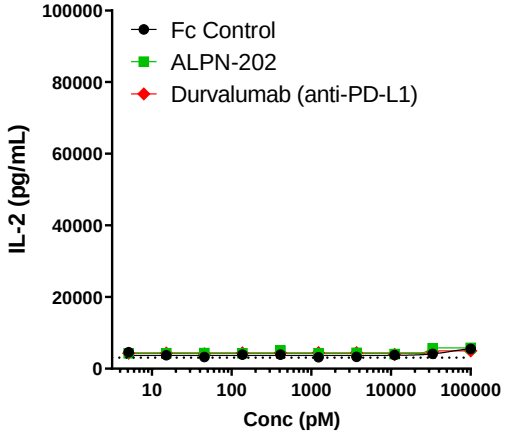
1. PD-L1 – PD-1 Antagonism



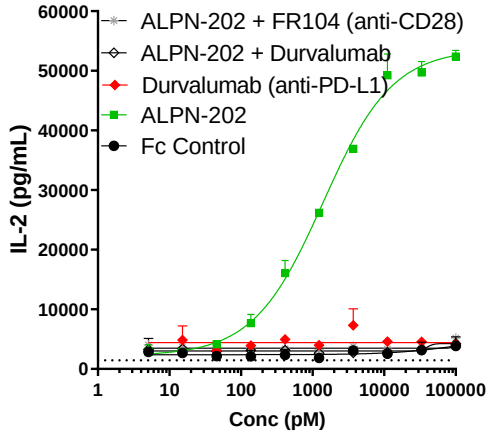
2. CTLA-4 – B7 Antagonism



3. PD-L1-Dependent CD28 Costimulation



No PD-L1

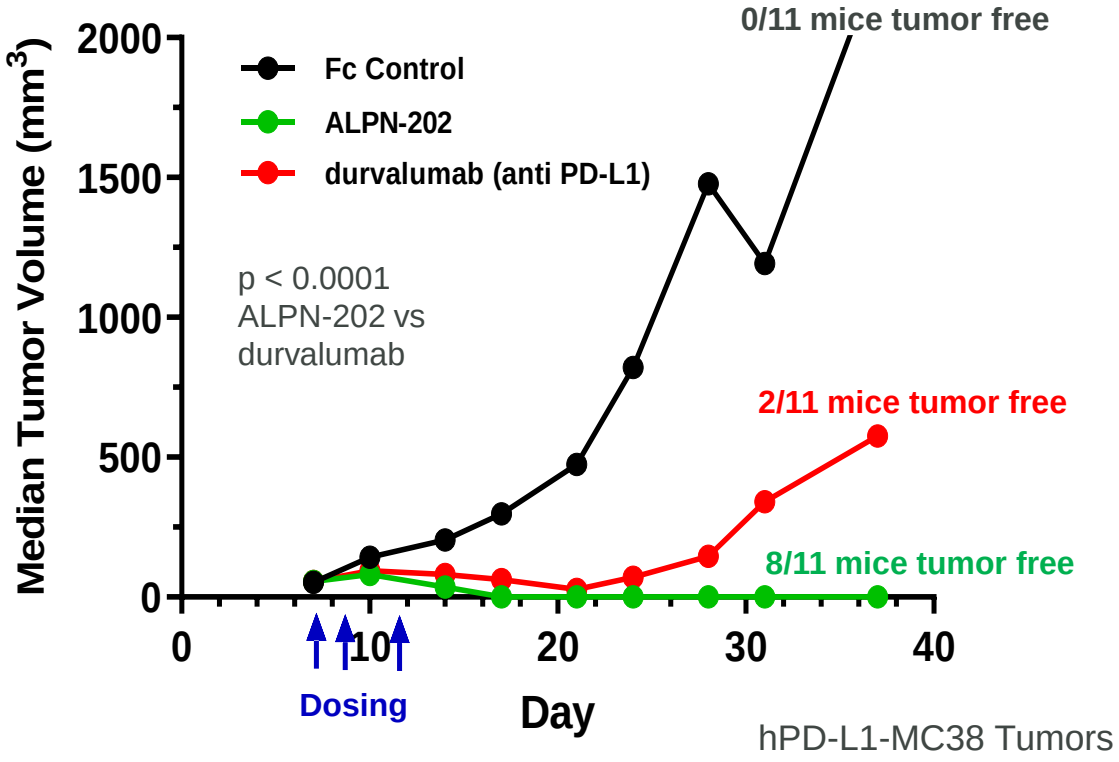


+ PD-L1

Primary T cells + K562 ± hPD-L1

ALPN-202 Exhibits Potent yet Well-Tolerated Anti-Tumor Activity *in vivo*

Monotherapy Efficacy Superior to PD-L1 Inhibition Alone



hPD-L1-MC38 Tumors

Safety in Nonclinical Studies

- Well tolerated in rats and cynomolgus monkeys (MTD not reached)
- No evidence of cytokine release or systemic agonism at all dose levels up to 150 mg/kg (rat) or 200 mg/kg (monkey)
- No clinically-significant colitis or other immune-related AEs as previously reported with dual checkpoint blockade in cynomolgus monkeys*

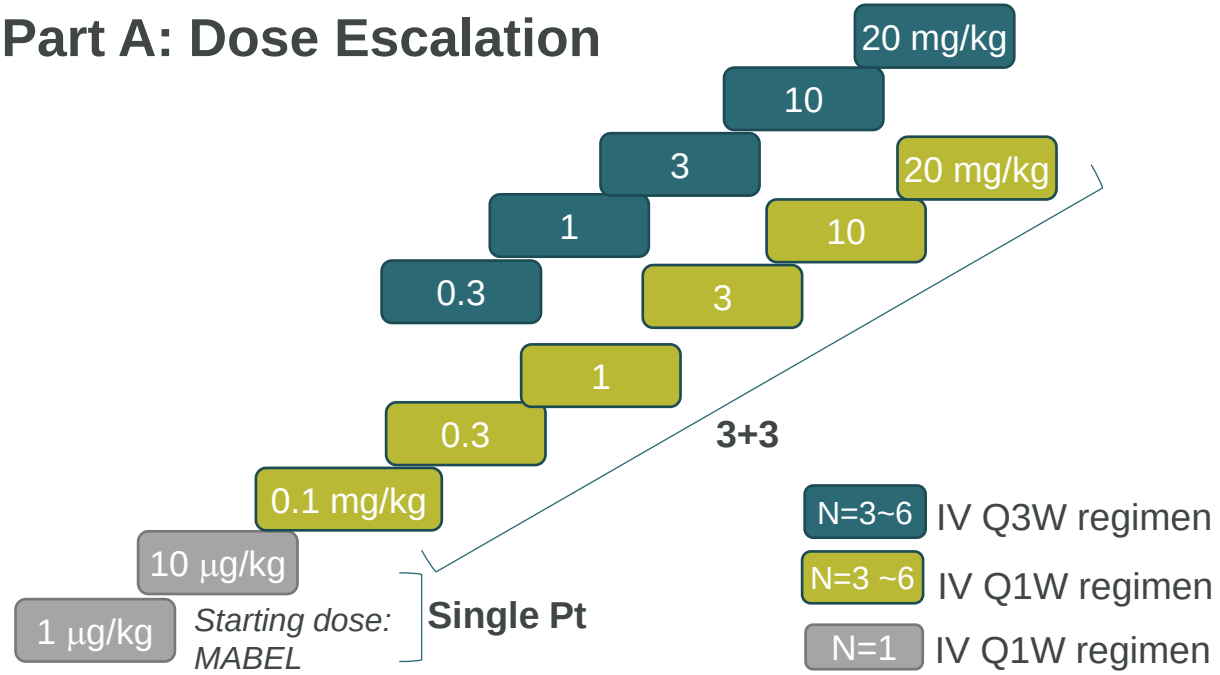
** Selby et al. PLoS One 11:e061779, 2016*

Study NEON-1: ALPN-202 in Advanced Malignancies (Phase 1)

Study Population

- Adults
- Advanced solid malignancies and lymphoma
- Refractory or resistant to standard therapy including CPIs
- Measurable disease
- ECOG: grade 0-2
- Adequate hematological, renal and hepatic function

Part A: Dose Escalation



Part B: Expansion Cohorts (N=15/cohort)

- Specific PD-1-refractory indications and/or populations
- Biomarker-selected when appropriate

Study Endpoints

- **Safety: DLTs, adverse events, immunogenicity, cytokines**
- **Efficacy: ORR, DOR, DCR, PFS, OS**
- **PK and PD: target saturation, immunophenotyping, ex vivo costimulatory capacity analysis**

PK/PD model: Yang J et al, Abstract 705, ASCPT 2019

Summary

- Current checkpoint inhibitor therapies may be limited by a lack of sufficient T cell costimulatory ligands (e.g., the CD28 ligands CD80 and/or CD86) in the tumor microenvironment

- ALPN-202 is a first-in-class:
  - Conditional (i.e., PD-L1-dependent) CD28 costimulator, and,
  - Dual checkpoint (PD-L1 and CTLA-4) inhibitor

- Preclinical studies demonstrate superior anti-tumor efficacy vs. checkpoint inhibition alone with excellent tolerability in GLP toxicology studies

- **NEON-1 (NCT04186637) is:**
  - **An open-label, dose escalation & expansion study of ALPN-202 in advanced malignancies**
  - **Currently open for enrollment**

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