An Open Label Study of ALPN-101, a First-in-Class Dual CD28/ICOS Antagonist, in Subjects with Steroid-Resistant or Steroid-Refractory Acute Graft Versus Host Disease (BALANCE)

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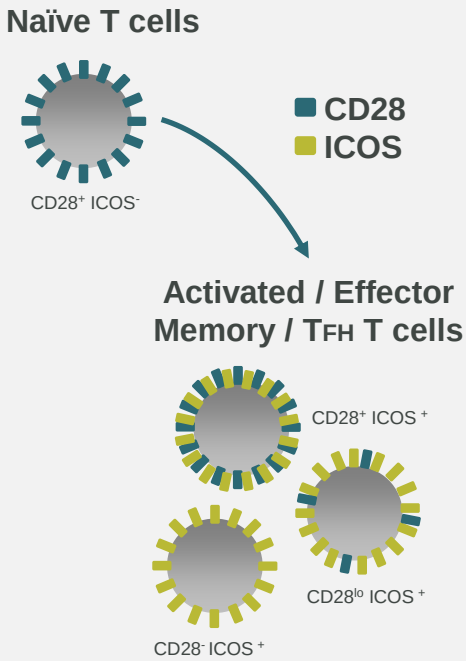
American Society of Hematology 61st Annual Meeting and Exposition

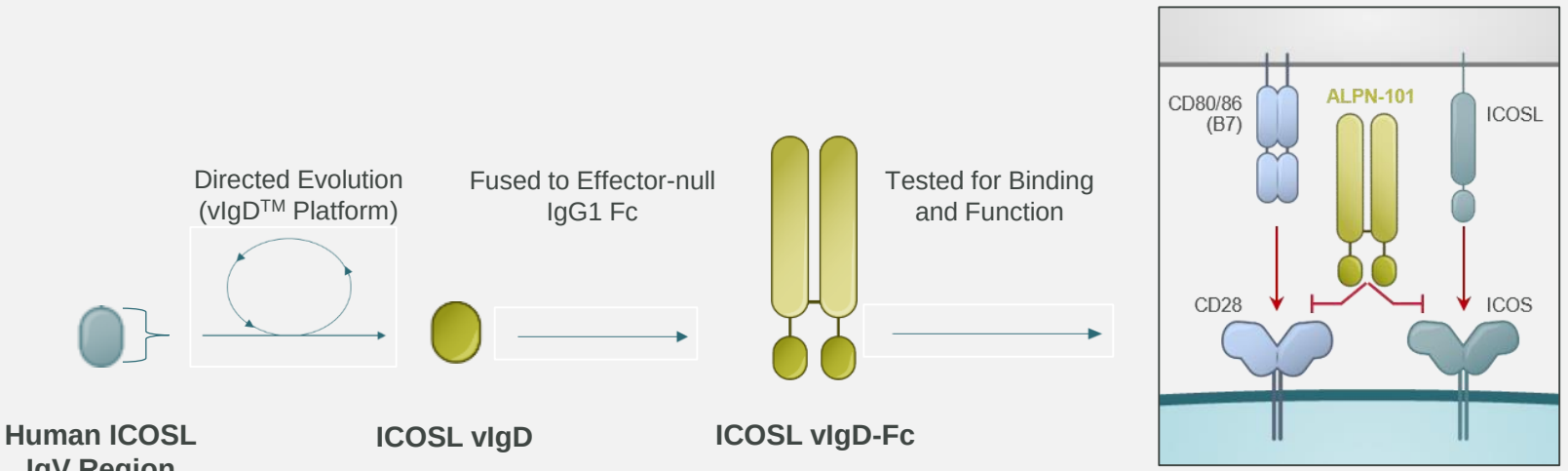
Rationale for Targeting CD28/80/86 and ICOS/ICOSL in GVHD



Hutloff 1999; Coyle 2000; Dong 2001; McAdam 2001; Tafuri 2001

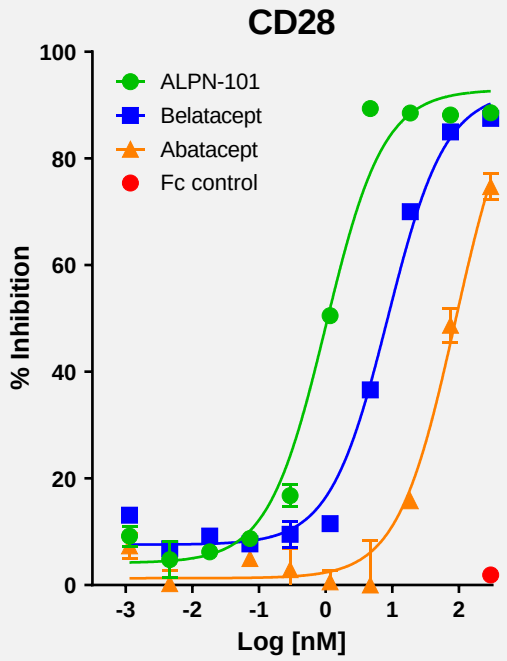
- CD28-CD80/86 blockade (abatacept) shows benefit for acute GVHD in humans
  Nahas 2018; Jaiswal 2016; Elfeki 2014
- ICOS blockade or deficiency reduces acute GVHD in animal models
  Taylor 2005; Adom 2018; Li 2016; Watkins 2018; Hubbard 2005; Burlion 2017
- Dual blockade of CD28 and ICOS with ALPN-101 demonstrates benefit in GVHD and other models
  Dillon 2018; Adom 2018

ALPN-101: First-in-Class Dual Inhibitor of CD28 and ICOS

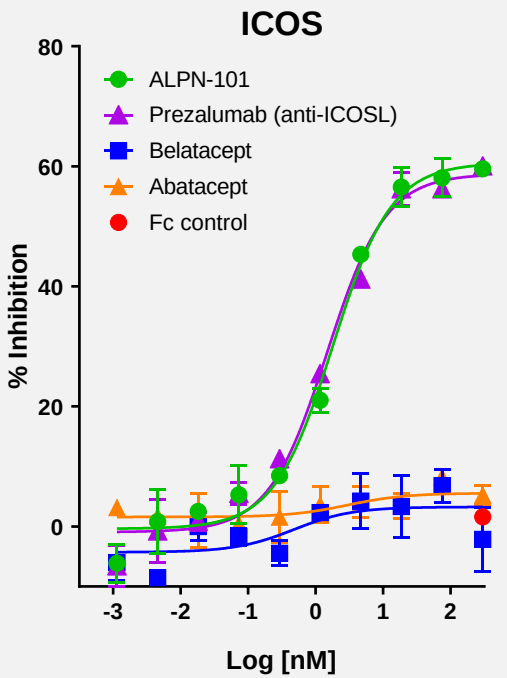


ALPN-101: Highly Potent Dual Inhibition of CD28 and ICOS

Inhibition of CD28-CD80/86 Costimulation



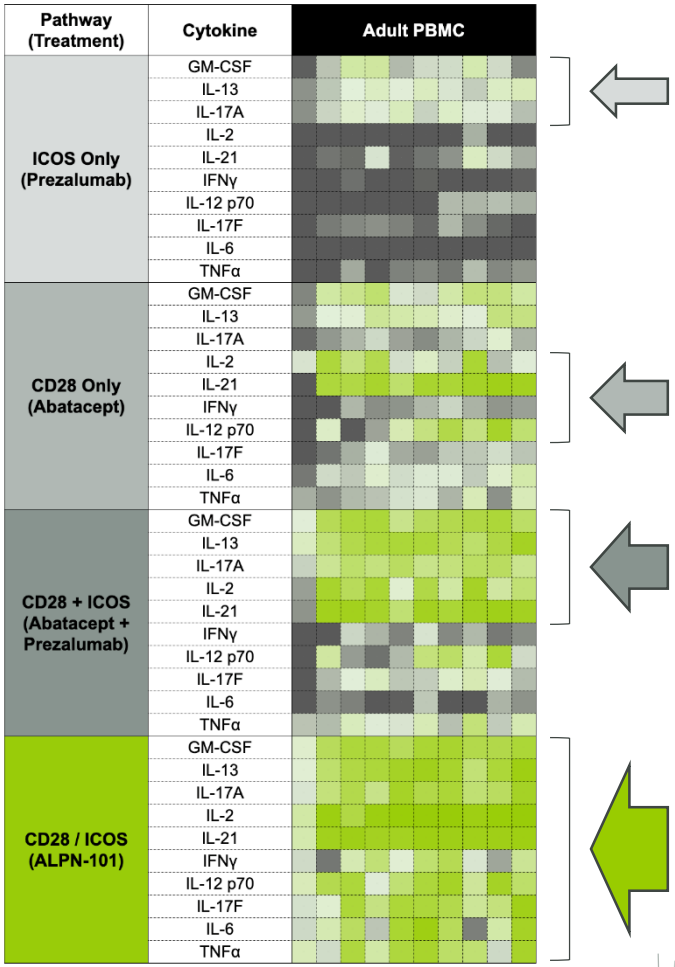
Inhibition of ICOS-ICOSL Costimulation



Dillon 2019

Superior Inhibition of Cytokine Secretion from Stimulated PBMCs by ALPN-101 Relative to Comparators

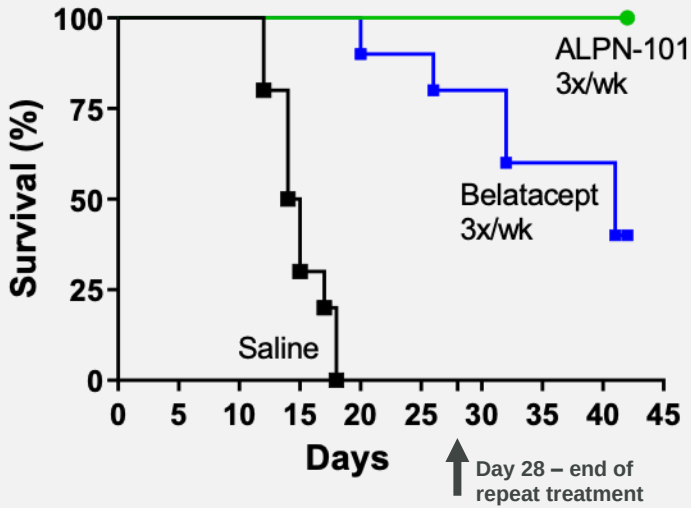
- PBMCs from healthy donors were stimulated with artificial antigen presenting cells
- After 48 hours, cytokines were assessed in supernatants
- Data are represented as percent cytokine inhibition relative to the Fc control



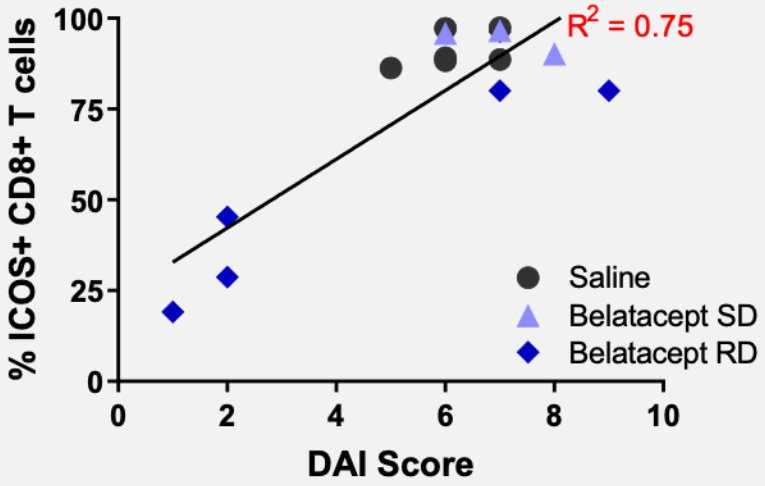
GVHD Models

ALPN-101: Effective in the Human Xenograft PBMC-NSG GVHD Mouse Model

Repeated Doses of 100 μg ALPN-101 or Belatacept Through 28 Days



ICOS Expression on Human T Cells Correlates with Disease Activity



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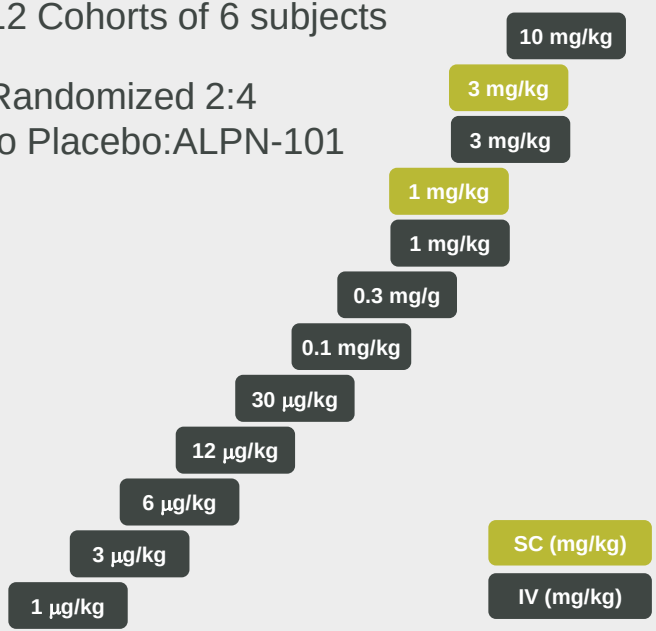
Phase 1 Results: AIS-A01 Part A

ALPN-101: Well Tolerated in First-in-Human Study in Healthy Volunteers

Part A: Single Ascending Dose Study of Safety, PK, and PD

12 Cohorts of 6 subjects

Randomized 2:4
to Placebo:ALPN-101



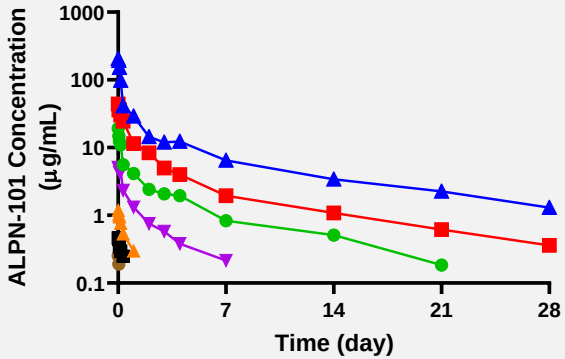
Safety in Doses That Maintain Target Saturation up to 4 Weeks

- No dose limiting toxicities
- No grade 3 or 4 adverse events
  - The most common AEs were self-limited upper respiratory tract infections and headaches
- No infusion reactions
- No cytokine release (CytokineMAP A&B)

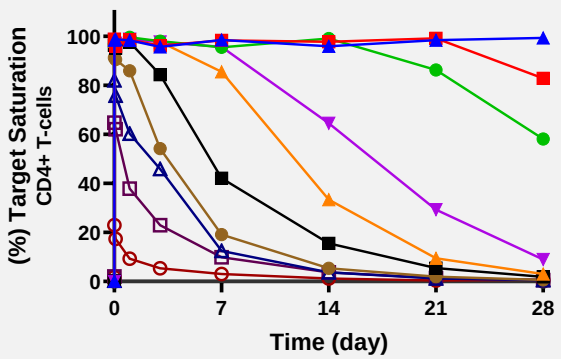
ALPN-101 Achieved Targeted Pharmacodynamic Activity

- 10 mg/kg
- 3 mg/kg
- 1 mg/kg
- 0.3 mg/kg
- 0.1 mg/kg
- 0.03 mg/kg
- 0.012 mg/kg
- 0.006 mg/kg
- 0.003 mg/kg
- 0.001 mg/kg
- Placebo

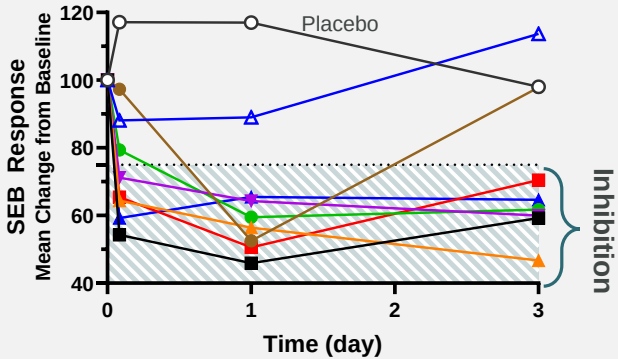
PK



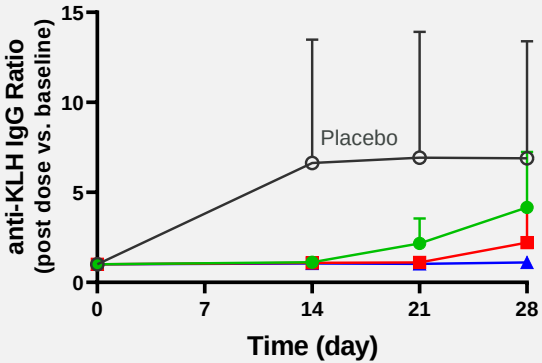
Target Saturation



SEB ex vivo IL-2 Induction



Anti-KLH IgG Response



Phase 2 GVHD Study Design

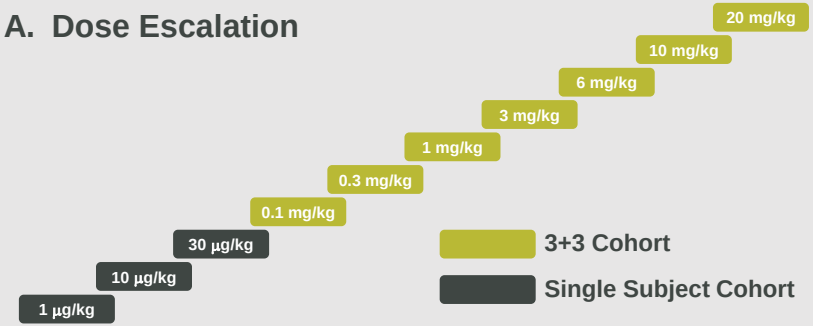
BALANCE (AIS-A02): ALPN-101 in Steroid-Refractory Acute GVHD (Phase 1b/2)

A first-in-disease study to establish minimal effective dose and recommended Phase 2 dose

Study Population

- Adults
- 1st allogeneic stem cell transplant
- Grade 2-4 aGVHD by MAGIC criteria
- Steroid resistant or refractory aGVHD
- ALPN-101 in combination with Investigator's choice of salvage therapy

A. Dose Escalation



B: Expansion at selected dose or doses

- Simon 2-stage expansion rules, start with up to 10 subjects
- Partial or complete response in at least 3 patients will lead to increase cohort by additional 15 patients

Study Endpoints

- Safety over 28 days
- Viral activation; cytokines
- PK; immunogenicity
- Standard response rates
- Use of glucocorticoids
- Long term survival
- Target saturation, immunophenotyping, & other exploratory biomarkers

ALPN-101 Conclusions

- First-in-class dual inhibitor of CD28 and ICOS
- Effective compared to inhibitors of each pathway alone in *ex vivo* and *in vivo* models
- Well tolerated through doses sustaining targeted pharmacodynamic activity
- Phase 1b/2 acute GVHD study in startup

Collaborators

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With Appreciation to Participating Volunteers, Patients, and Health Care Providers