2021 ASCO® ANNUAL MEETING

FIRST IN HUMAN DOSE ESCALATION OF ALPN-202, A CONDITIONAL CD28 COSTIMULATOR AND DUAL CHECKPOINT INHIBITOR, IN ADVANCED MALIGNANCIES (NEON-1)

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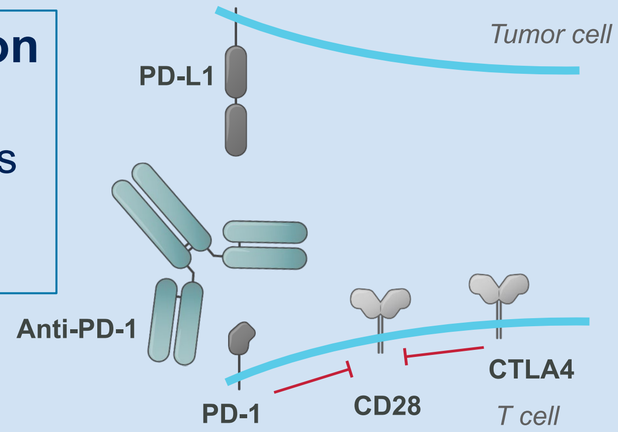
ALPN-202: A First-In-Class, PD-L1-Dependent CD28 Costimulator and Dual PD-L1/CTLA-4 Checkpoint Inhibitor

Background

- Inadequate CD28 costimulation may underlie T cell hyporesponsiveness during checkpoint inhibition, accounting for therapeutic resistance
- ALPN-202 includes a variant CD80 domain, engineered by directed evolution to localize CD28 costimulation safely within the tumor microenvironment, while also inhibiting PD-L1 and CTLA-4
- Preclinical studies demonstrated favorable efficacy and safety compared to checkpoint inhibition

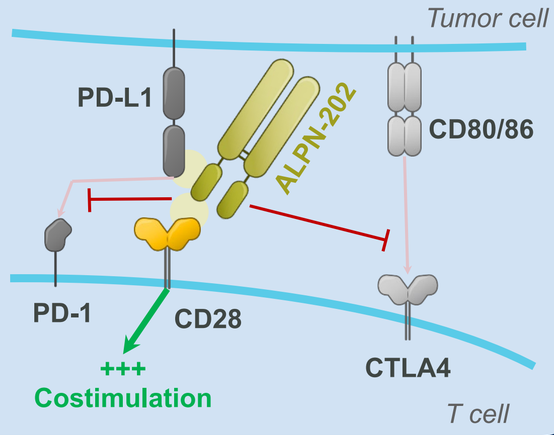
Checkpoint-Only Inhibition

Releases inhibition of, but does not actively agonize, CD28 in the immunosuppressive TME



ALPN-202

- Mediates PD-L1-dependent CD28 costimulation
- Blocks PD-L1 and CTLA-4



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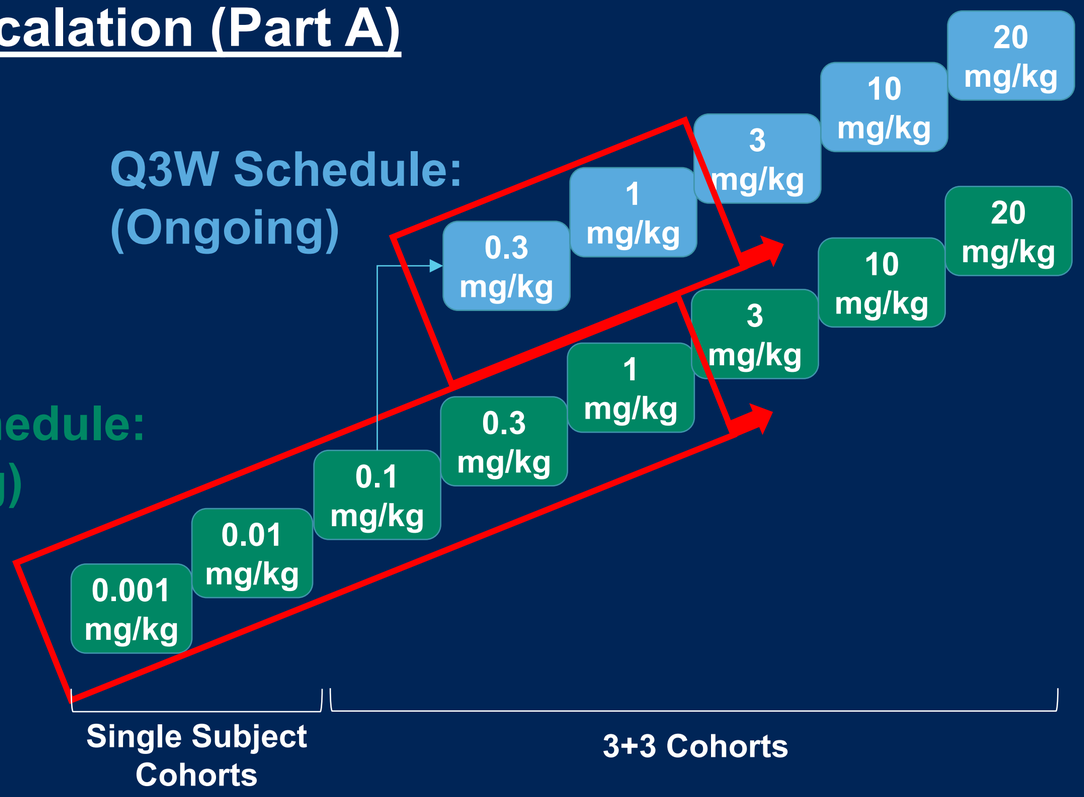
NEON-1: A First-In-Human Dose Escalation and Expansion Study of ALPN-202 in Advanced Malignancies

Dose Escalation (Part A)



Expansion Cohorts (Part B): TBD

NCT04186637

Data: 22APR2021

Characteristic	Total (N=32)
Age (mean yr ± SD)	63 ± 12
Female	13 (41%)
Caucasian	25 (78%)
Dose regimen: Weekly	20 (63%)
Prior lines of therapy (mean ± SD)	3.9 ± 2.3
Received ≥ 1 prior I/O therapy	9 (28%)
Tumor Type:	
- Pancreatic	8 (25%)
- Colorectal	7 (22%)
- Mesothelioma	3 (9%)
- Cholangiocarcinoma	2 (6%)
- Head & Neck	2 (6%)
- Uterine	2 (6%)
- Other (1 each of esophageal, melanoma, ovarian/fallopian, porocarcinoma, prostate, renal, thymoma, uveal melanoma)	8 (25%)

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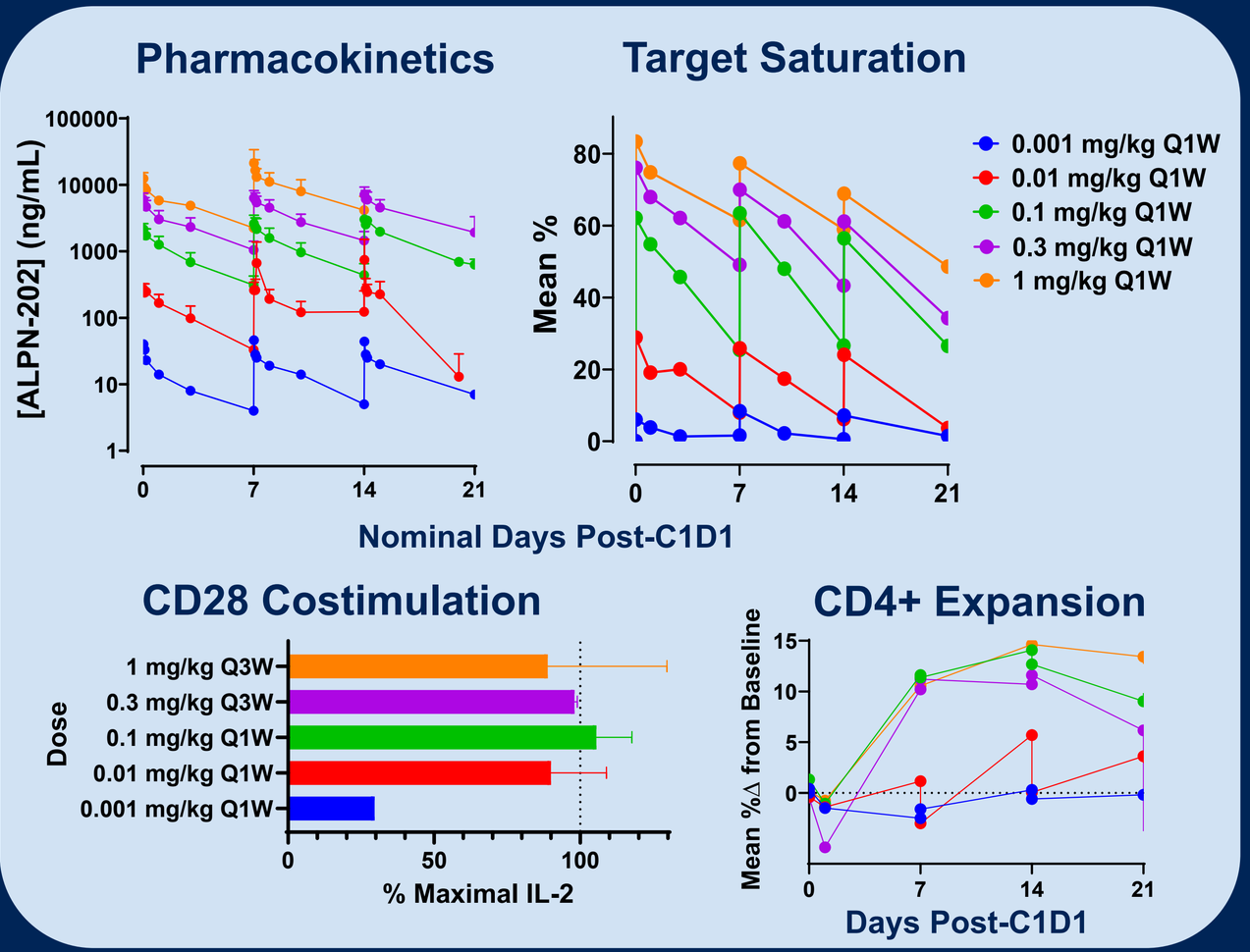
ALPN-202 Exhibits Well-Tolerated Dose-Related PK/PD, with Evidence of CD28 Engagement and T cell Expansion



Adverse Events

Data: 22APR2021

Category	Subjects (N=32)
Any Related Adverse Event Gr ≥ 3	1 (3%)
Any Serious AE (SAE)	9 (28%)
Any Related SAE	1 (3%)
AE of Interest (AEI)	16 (50%)
• Infusion Related Reaction	6 (19%)
• Skin & Subcutaneous Disorders	9 (28%)
• Rash (macular, maculo-papular, or papular)	9 (28%)
• Pruritis	1 (3%)
• Rosacea	1 (3%)
• Hyper- or hypothyroidism	3 (9%)
• Acute Kidney Injury (SAE)	1 (3%)
• Testicular Pain (SAE)	1 (3%)
Dose-limiting toxicity	0
Cytokine release syndrome	0

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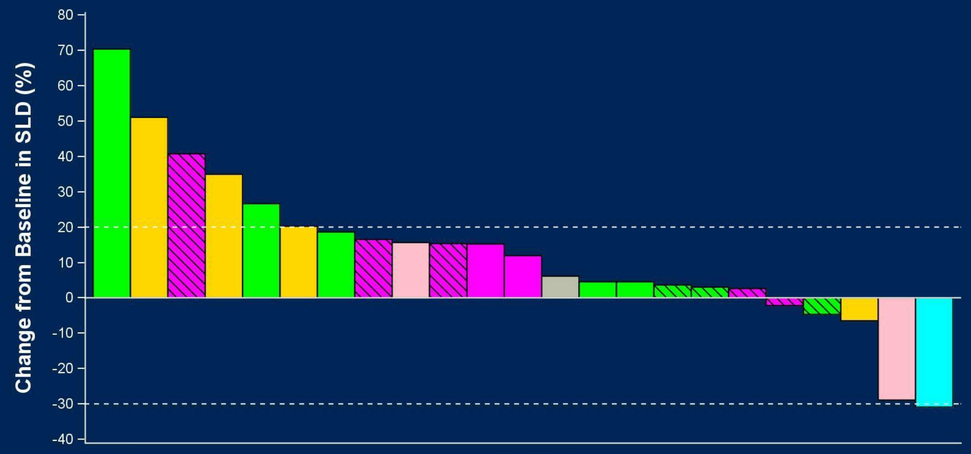
ALPN-202 Shows Early Potential for Clinical Benefit

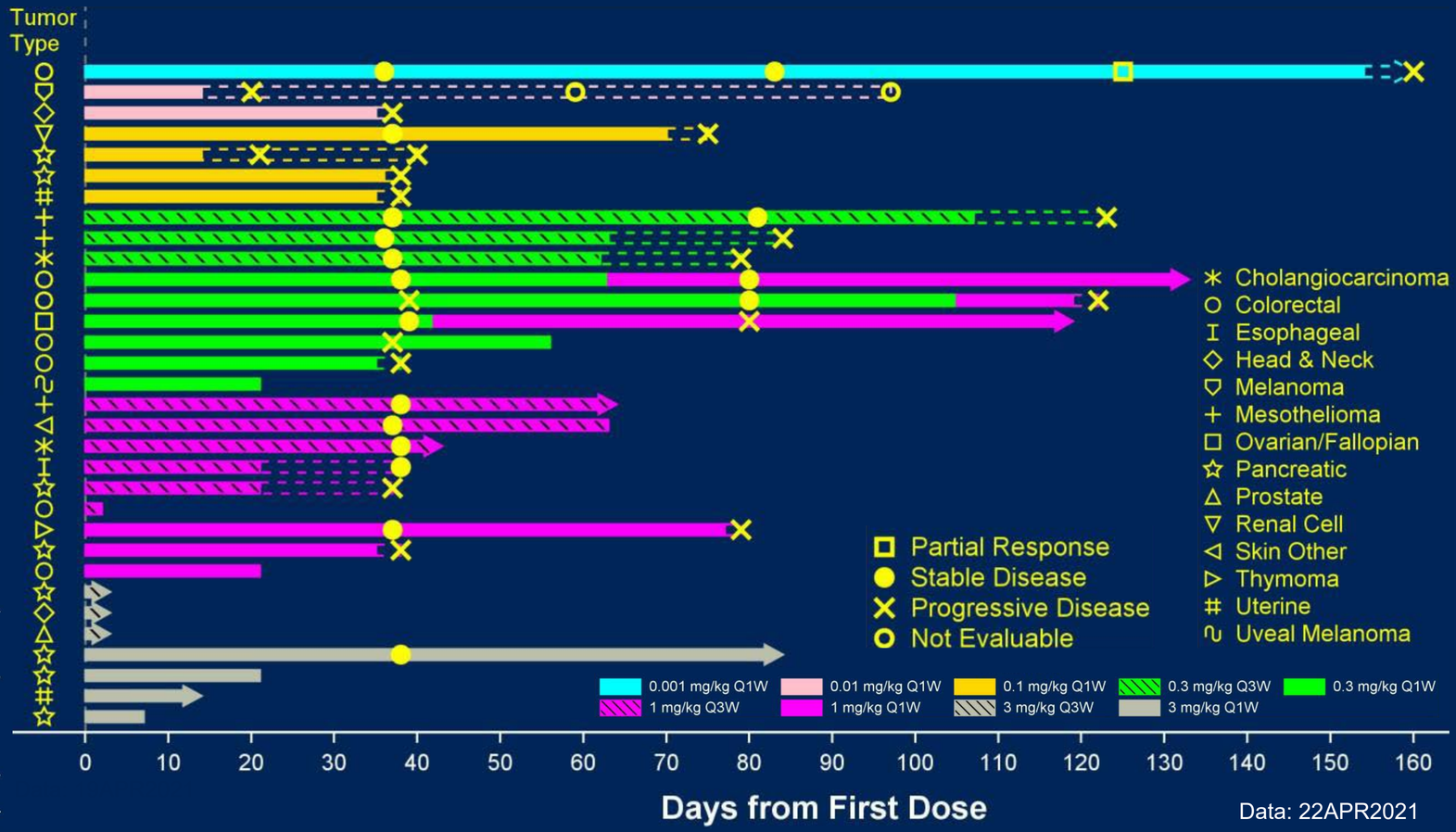
Best Responses

Best Response	Evaluable (N=23)
Partial Response	1 (4%)
Stable Disease	13 (57%)
Progressive Disease	9 (39%)

Best Change in Tumor Size



Time on Treatment



Data: 22APR2021

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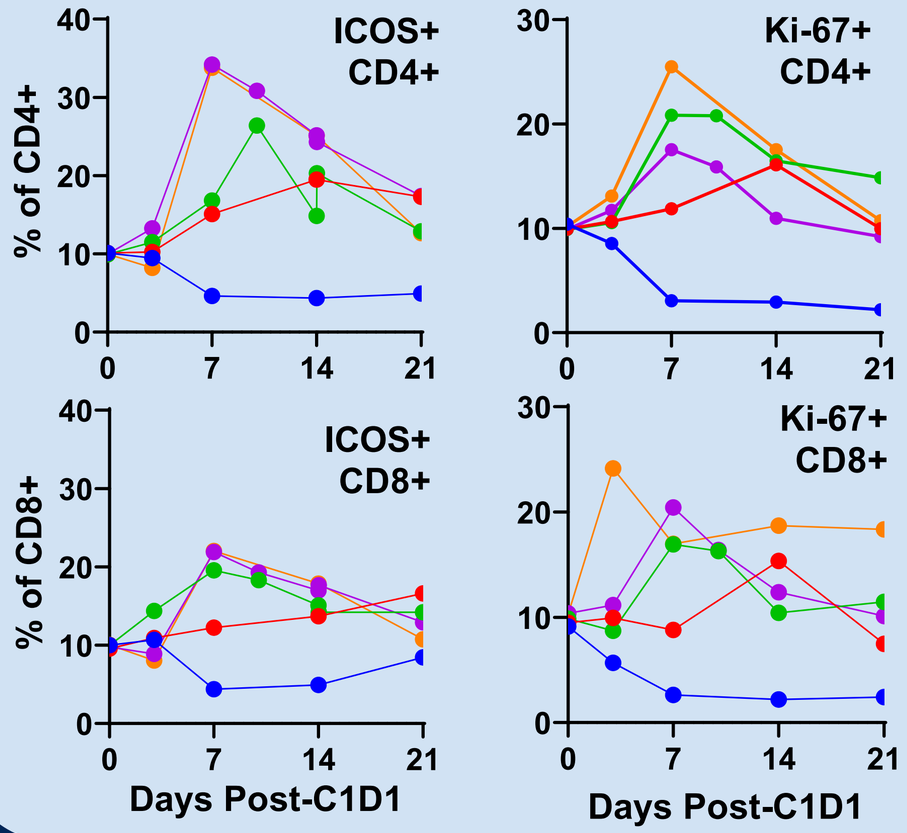
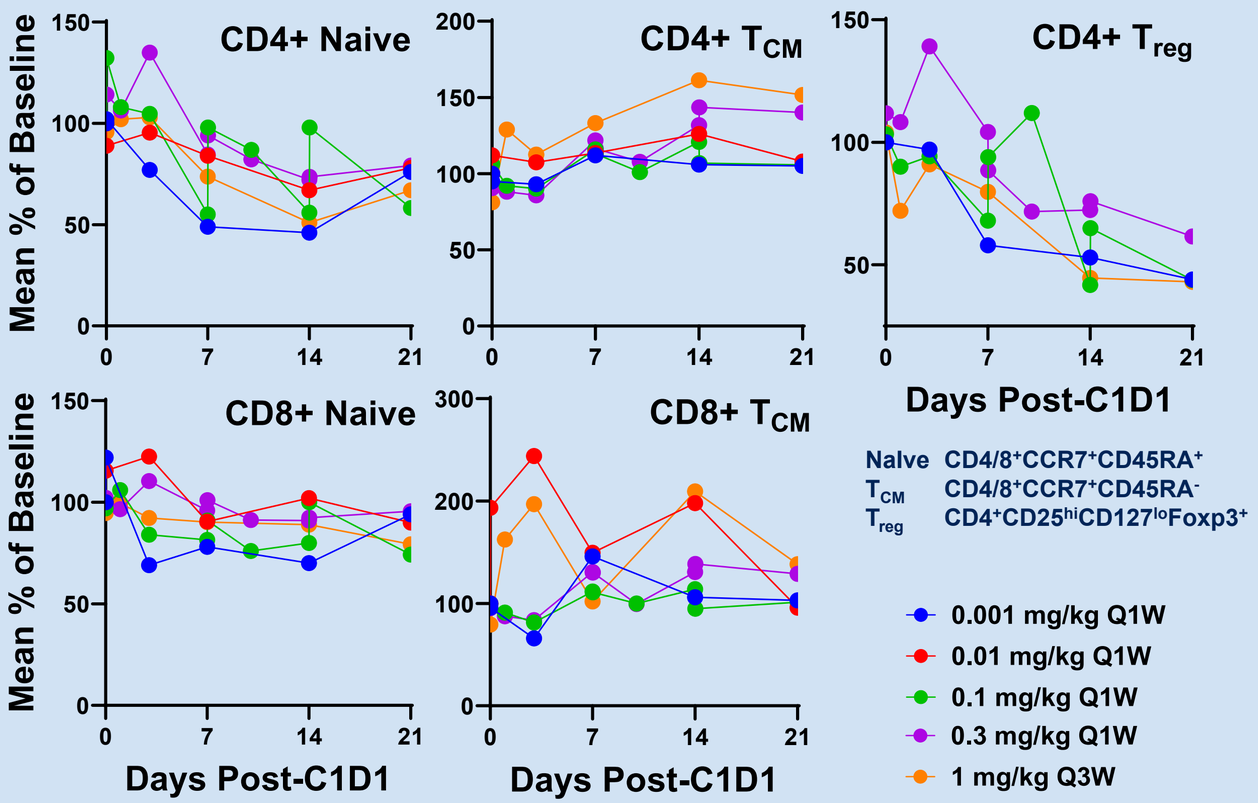
ALPN-202 Promotes T Cell Activation and Proliferation

T Cell Activation and Proliferation



T_{CM} Expansion and T_{reg} Reduction



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SUMMARY / CONCLUSIONS

- ALPN-202 is a first-in-class variant CD80 Fc fusion designed to overcome CPI resistance by focusing CD28 costimulation to the TME, while inhibiting PD-L1 and CTLA-4.
- In advanced tumors, ALPN-202 has been well-tolerated, with dose-dependent PK/PD.
- Early clinical benefit is suggested in some cancers not traditionally responsive to I/O.
- Peripheral immunological analyses demonstrate evidence of CD28 costimulation and relevant immune activation, including ↑ICOS, ↑Ki-67, ↑T_{CM} and ↓T_{reg}.
- Ongoing development of ALPN-202 is warranted to finalize a biologically-optimal dose. Additional cohorts and/or studies with specific tumors, and/or in combination with other therapies, are under consideration.
- **To our knowledge, this is the first demonstration that clinical CD28 agonism may be safely achieved for cancer immunotherapy.**