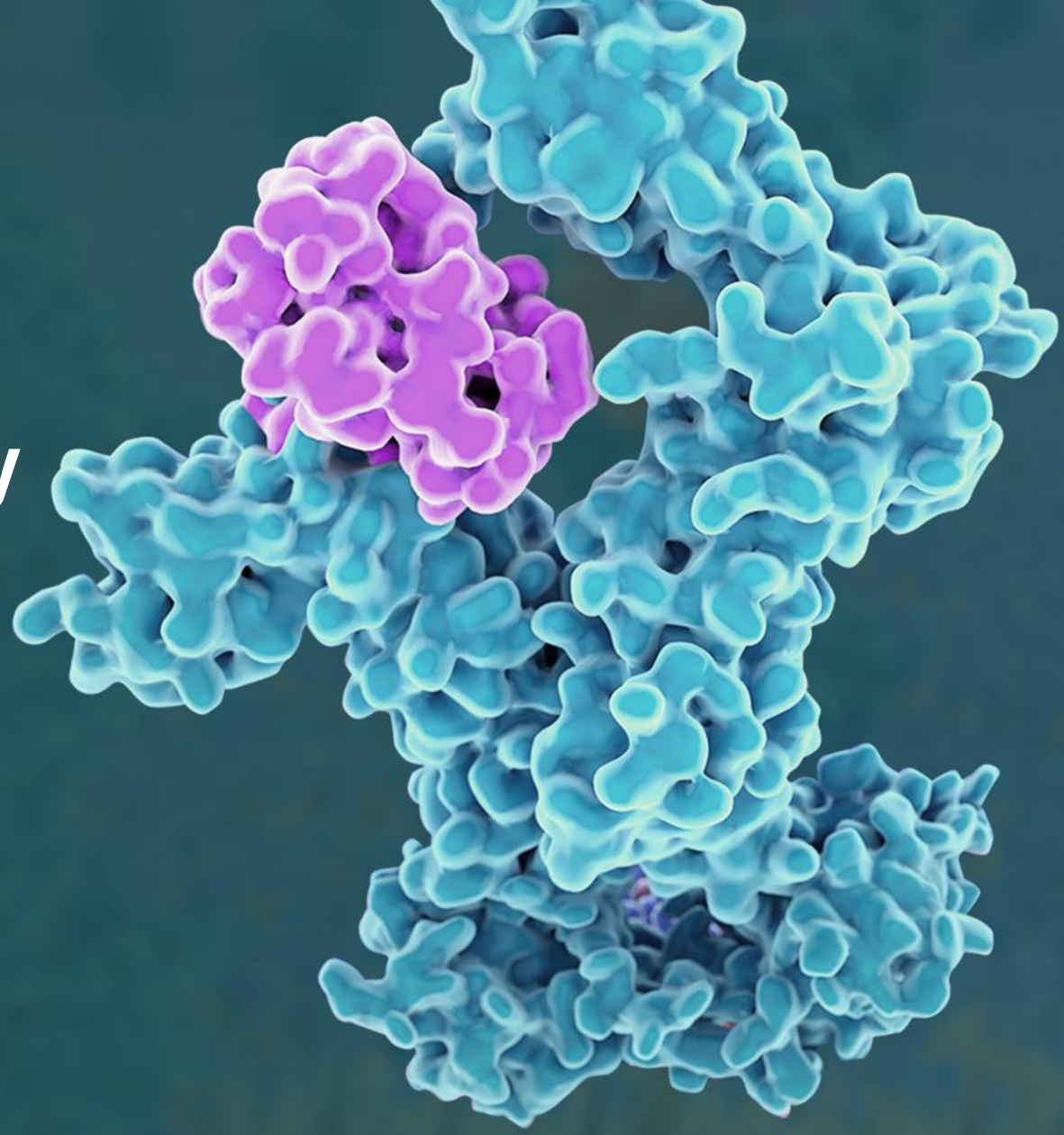
AACR Annual Meeting
8TH-13TH APRIL 2022

An ‘Anti-PD1-IL2 Beta-Only Super-Agonist’ Displays Potent Anti-Tumor Efficacy



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Senior Director
Pre-Clinical Research

MEDICENNA

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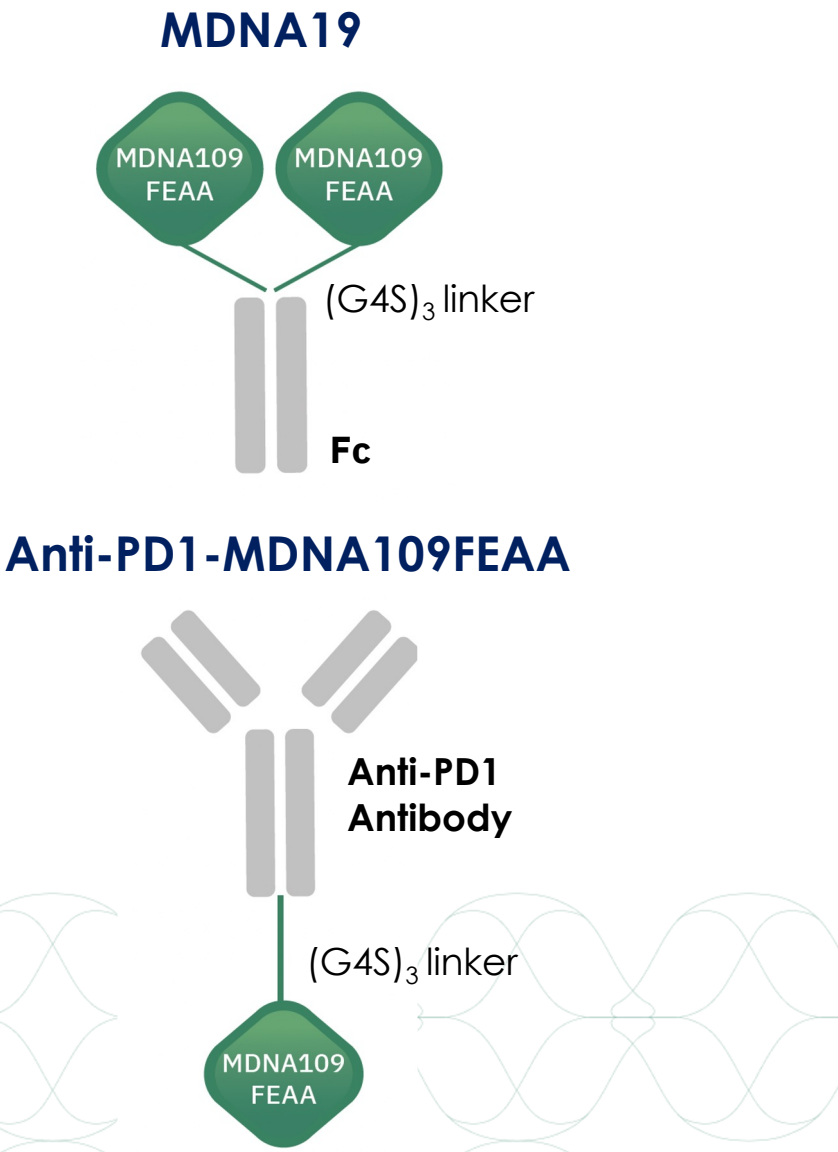
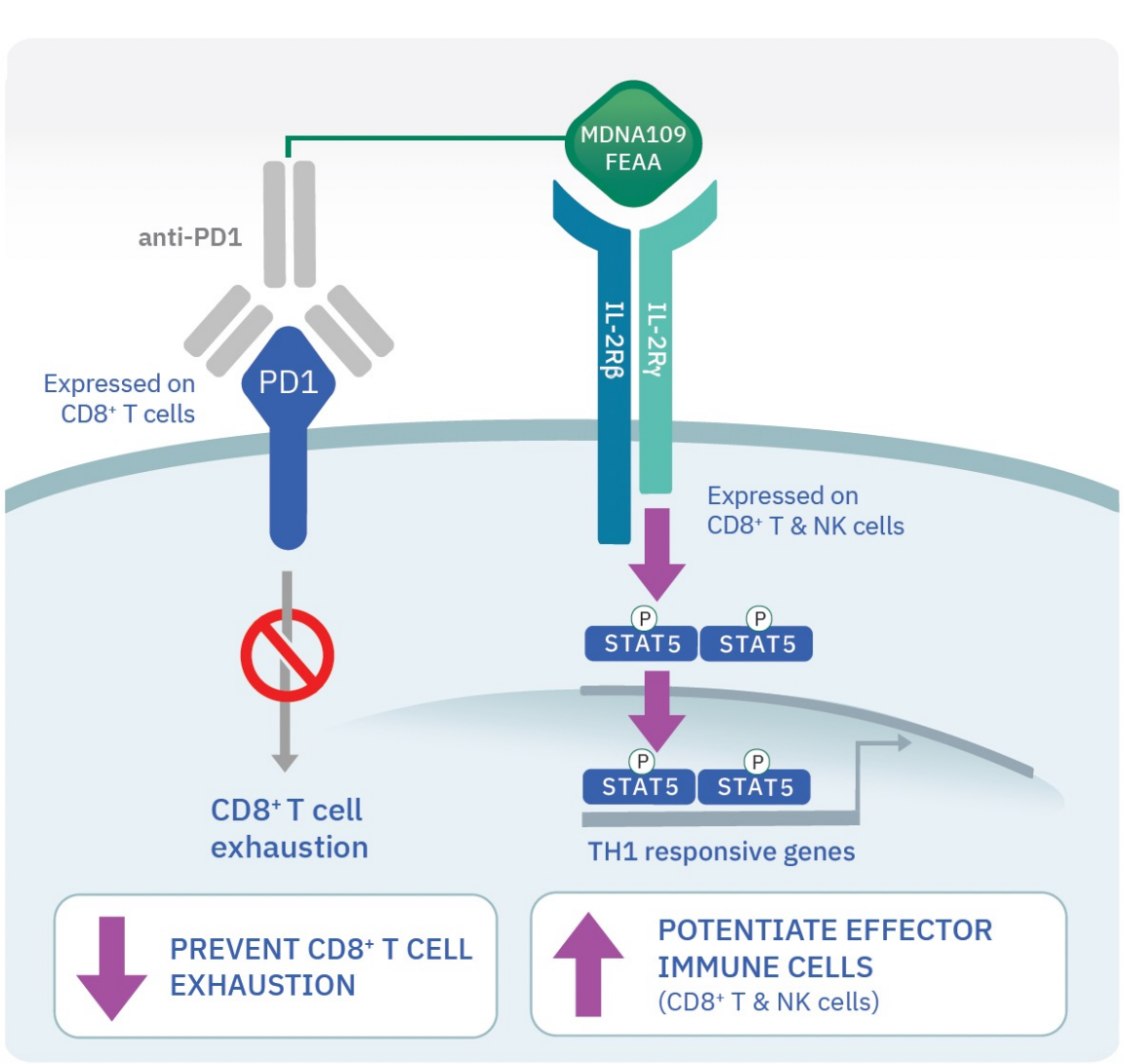
Overview of Anti-PD1-MDNA109FEAA

- MDNA19 (MDNA109FEAA-Fc) is a long-acting 'beta-only' IL-2 super-agonist with enhanced affinity for CD122 and does not bind CD25, designed to preferentially activate immune effector cells (i.e., CD8+ T and NK cells) over Tregs.

- Anti-PD1-MDNA109FEAA is a next-generation Bifunctional SuperKines for ImmunoTherapy (BiSKIT) designed to potentiate synergy between IL-2 agonism and PD1/PDL1 blockade by cis-binding to respective receptors.

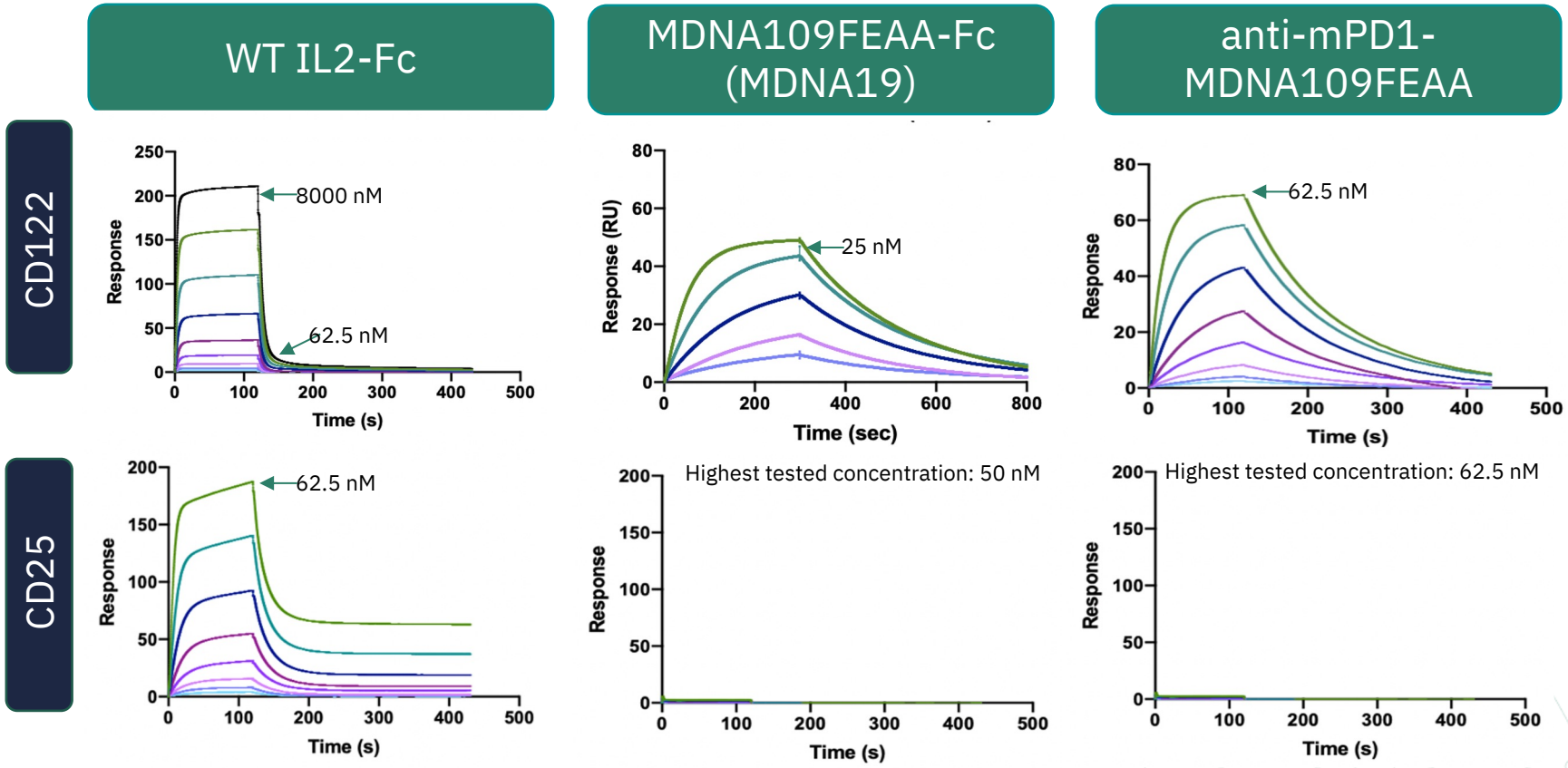


Proposed MOA Anti-PD1-MDNA109FEAA



Anti-PD1-MDNA109FEAA Retains Preferential Affinity to CD122

Anti-mPD1-MDNA109FEAA retains selective binding to human CD122 and no binding to CD25

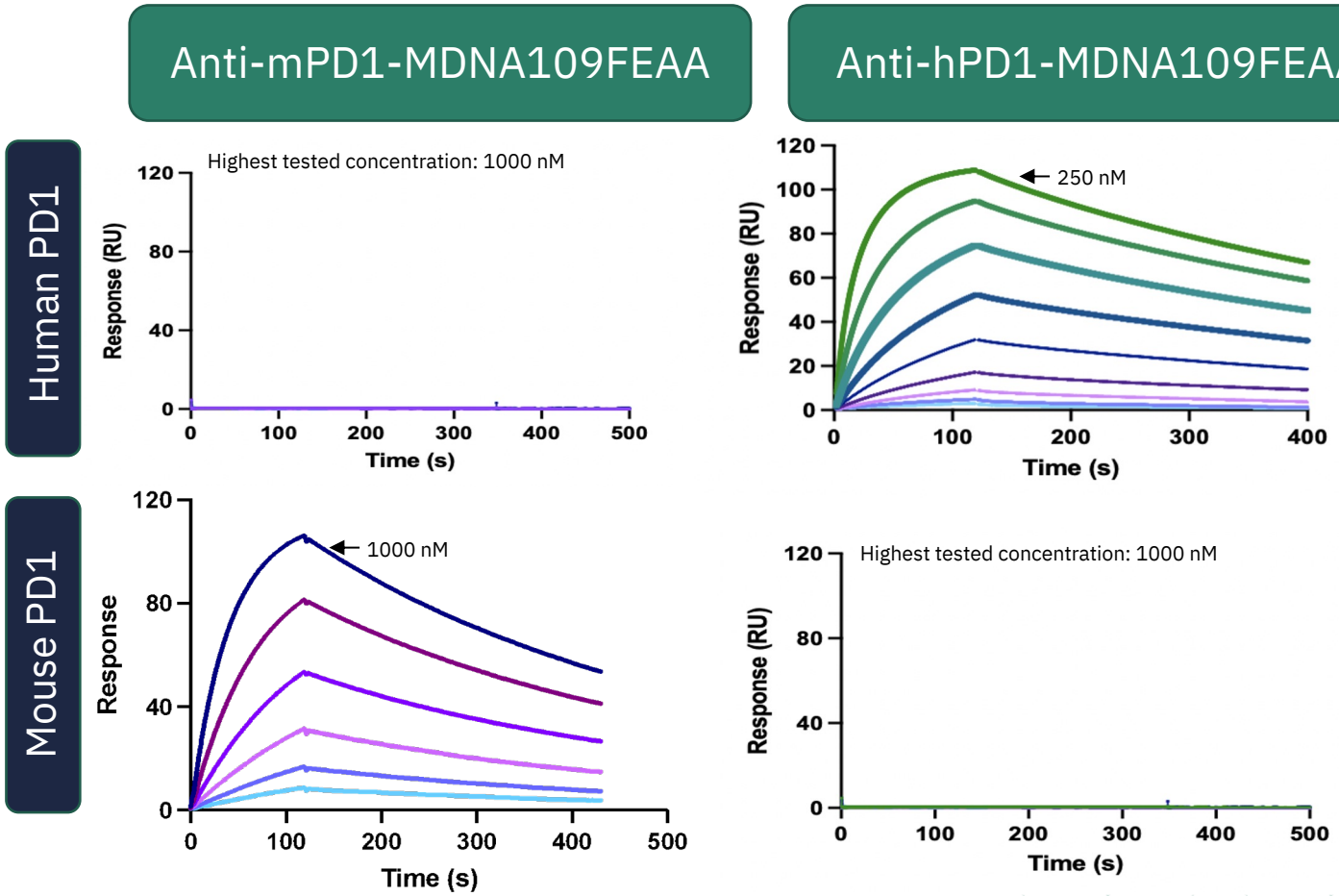


K_D (nM)	hIL-2α (CD25)	hIL-2Rβ (CD122)
WT IL2-Fc	32	3540
MDNA109FEAA-Fc (MDNA19)	No binding	6.28
anti-mPD1-MDNA109FEAA	No binding	11.3

SPR performed on immobilized ligands with receptors as flow analytes

Anti-PD1-MDNA109FEAA Retains Specificity to PD1

Human and mouse anti-PD1 BiSKITs show species specific binding to PD1 as expected



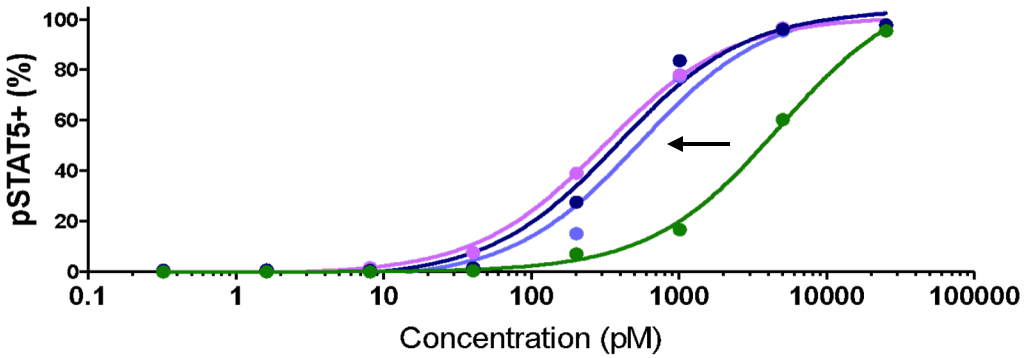
K_D (nM)	Anti-hPD1-MDNA109FEAA	Anti-mPD1-MDNA109FEAA
Human PD1	9.4	No binding
Mouse PD1	No binding	102

SPR performed on immobilized ligands with constructs as flow analytes

Preferential Stimulation of CD8+ T cells over Tregs

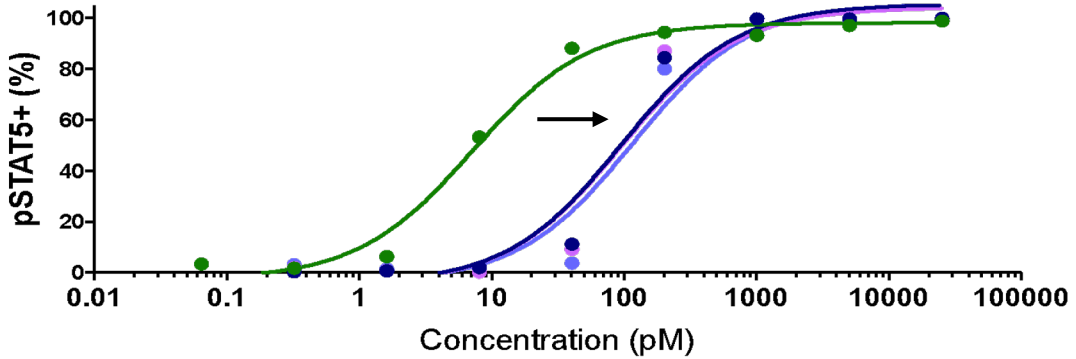
Enhanced signaling in CD8+ T cells

Naïve CD8 T cells



Diminished signaling in Tregs

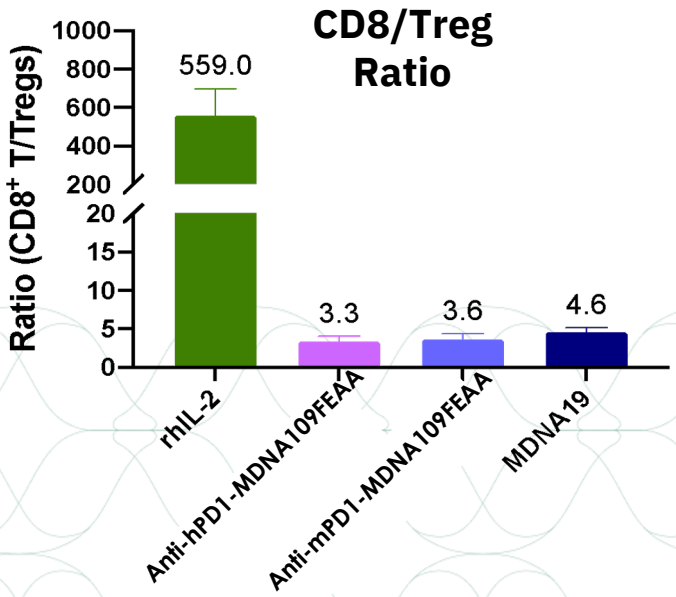
Tregs



IL-2 MDNA109FEAA-Fc Anti-hPD1-MDNA109FEAA Anti-mPD1-MDNA109FEAA

Human PBMC pSTAT5 (EC_{50} pM)	rh IL-2	MDNA109FEAA-Fc (MDNA19)	Anti-hPD1-MDNA109FEAA	Anti-mPD1-MDNA109FEAA
Naïve CD8 T cells	2972	858.7	635.5	909
Tregs	4.0	201.7	244.3	370.5

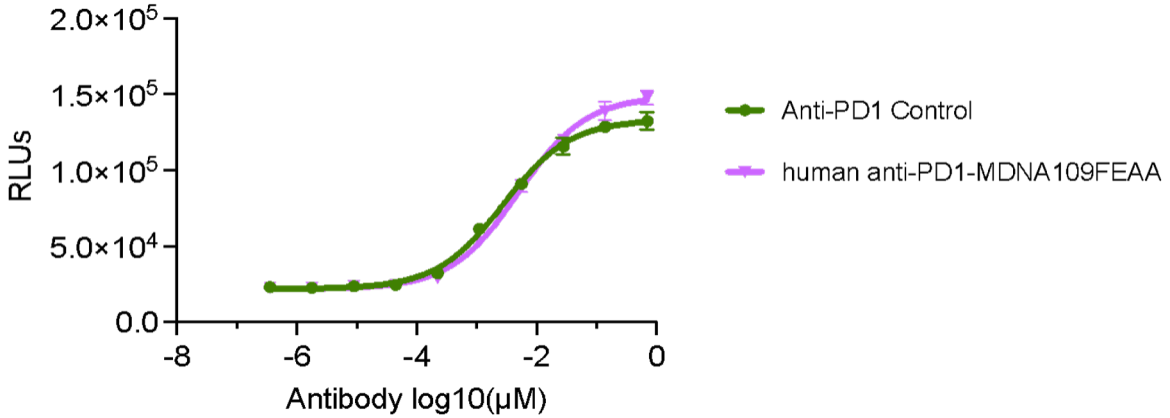
PBMCs allowed to rest in complete media, and then stimulated for 15 min with indicated agents. Samples analyzed by flow cytometry after intracellular staining for phosphorylated STAT5 (pSTAT5) in immune subsets



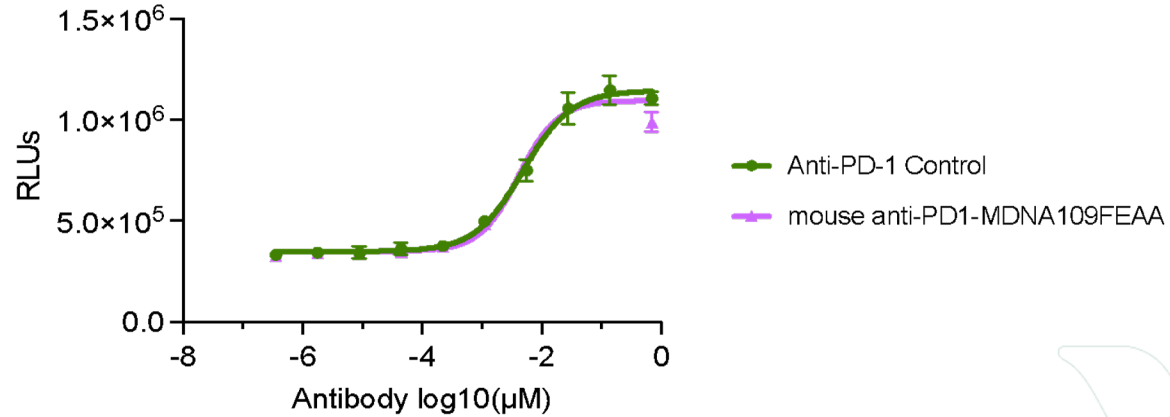
Blockade of PD-1/PDL-1 Retained

Similar PD-1/PDL-1 blockade by Anti-PD1-MDNA109FEAA BiSKIT and anti-PD1 antibody

Human PD-1/PDL-1 Blockade Assay



Mouse PD-1/PDL-1 Blockade Assay



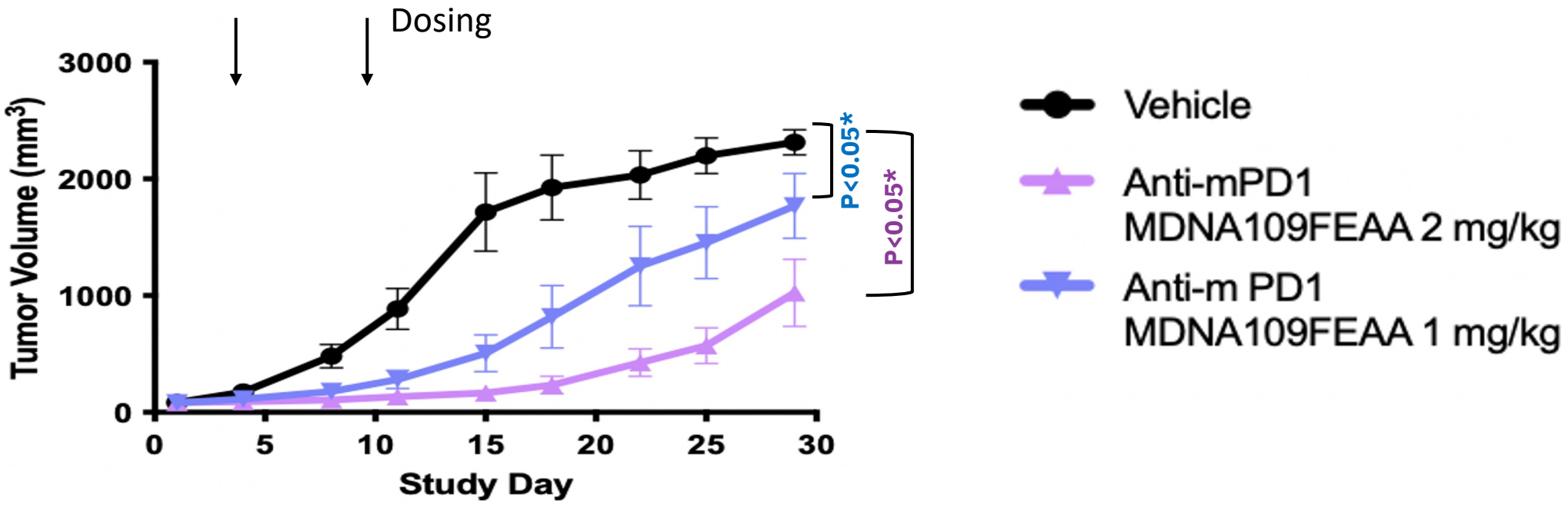
	EC_{50} (nM) Human Assay	EC_{50} (nM) Mouse assay
Anti-PD1 Control	2.7	4.7
Anti-hPD1-MDNA109FEAA	4.9	-
Anti-mPD1-MDNA109FEAA	-	4.1

PD1/PDL1 Bioassay kit from Promega was used. Target cells were treated with indicated reagents and luminescence was detected using Bio-Glow™ reagent

Anti-PD1 Control is Parent anti-PD1 antibody;
human anti-PD1 is nivolumab based ;
mouse anti-PD1 is RMP1-14 based

Anti-PD1-MDNA109FEAA Shows Dose Dependent Tumor Growth Inhibition

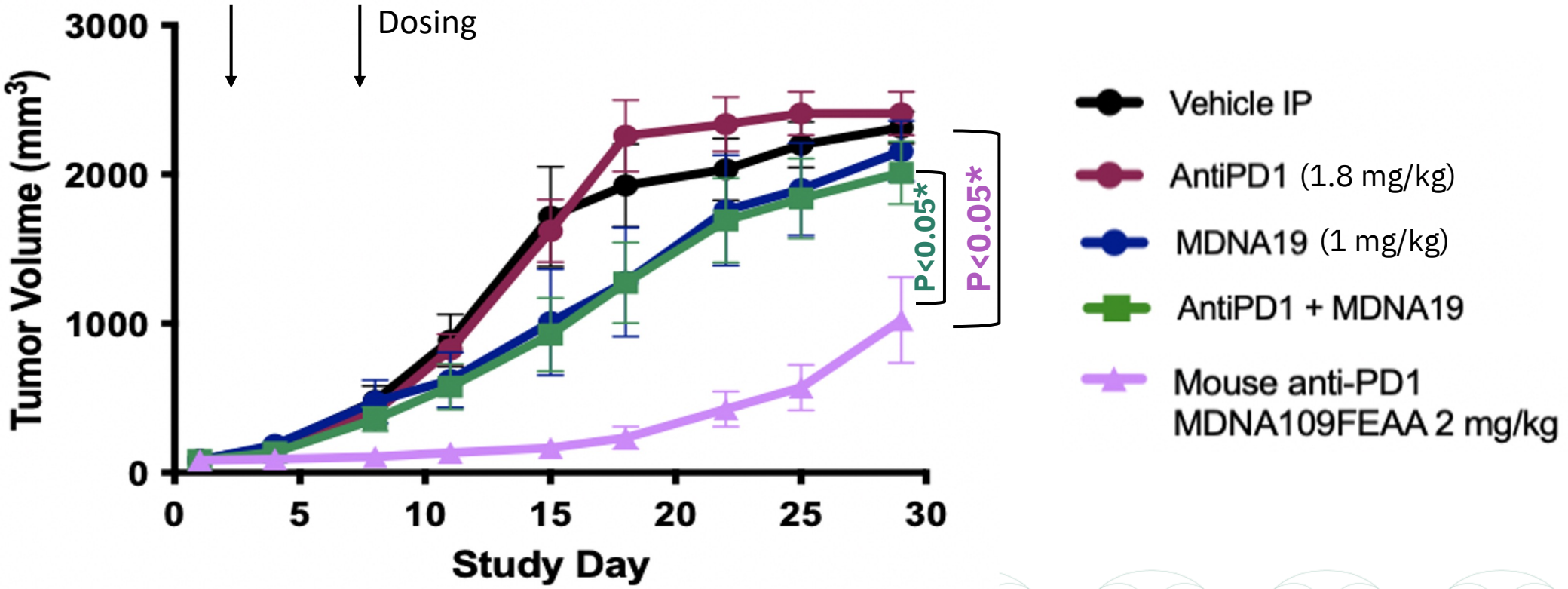
CT26 Colon Carcinoma



Tumor bearing mice were treated with anti-PD1-MDNA109FEAA IP once weeklyX2
Avg tumor size at initiation of dosing: 127 mm^3
*P value for t-test on day 30 data

Anti-PD1-MDNA109FEAA BiSKIT Is More Efficacious than Co-administration of Anti-PD1 + MDNA19

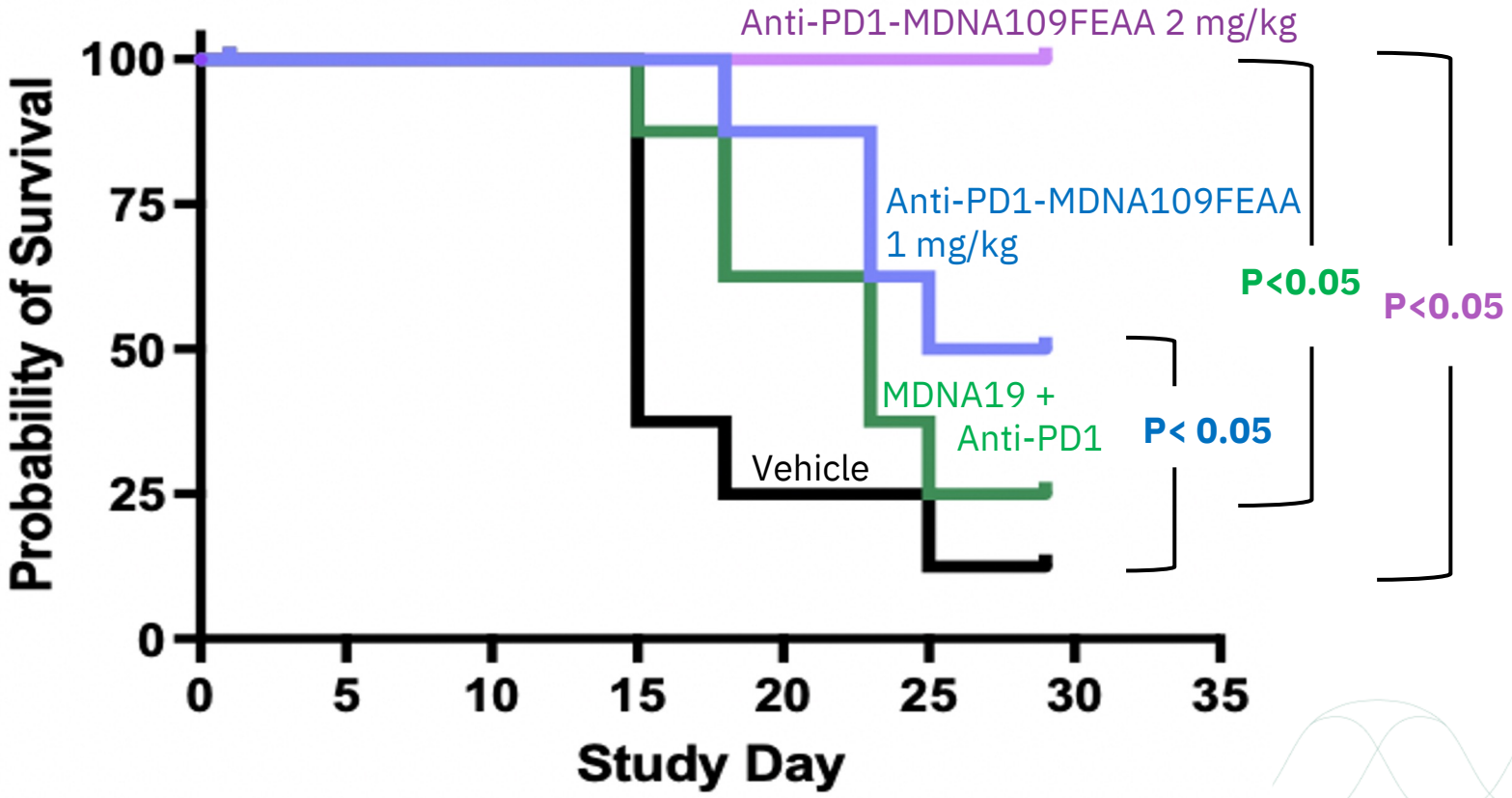
CT26 Colon Carcinoma



Treatment with molar equivalent doses of anti-PD1, MDNA109FEAA-Fc or anti-PD1-MDNA109FEAA IP QWX2.
Avg tumor size at initiation of dosing: 127 mm^3. *P value for t-test on day 30 data

Anti-PD1-MDNA109FEAA BiSKIT Significantly Prolongs Survival in Mouse Tumor Models

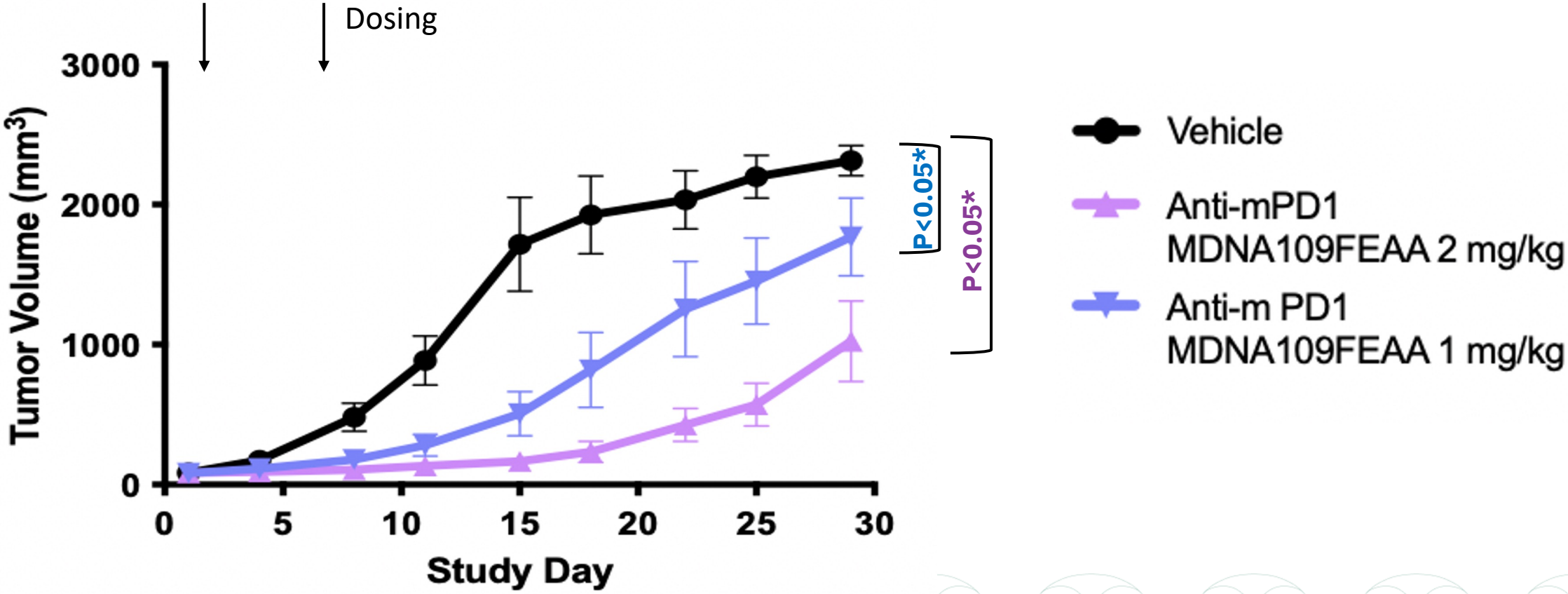
CT26 Colon Carcinoma



Group	% Survival at Study End
Vehicle	10
Anti-PD1 + MDNA19	25
Anti-mPD1-MDNA109FEAA (2 mg/kg)	100

Anti-PD1-MDNA109FEAA BiSKIT Shows Dose Dependent Tumor Growth Inhibition

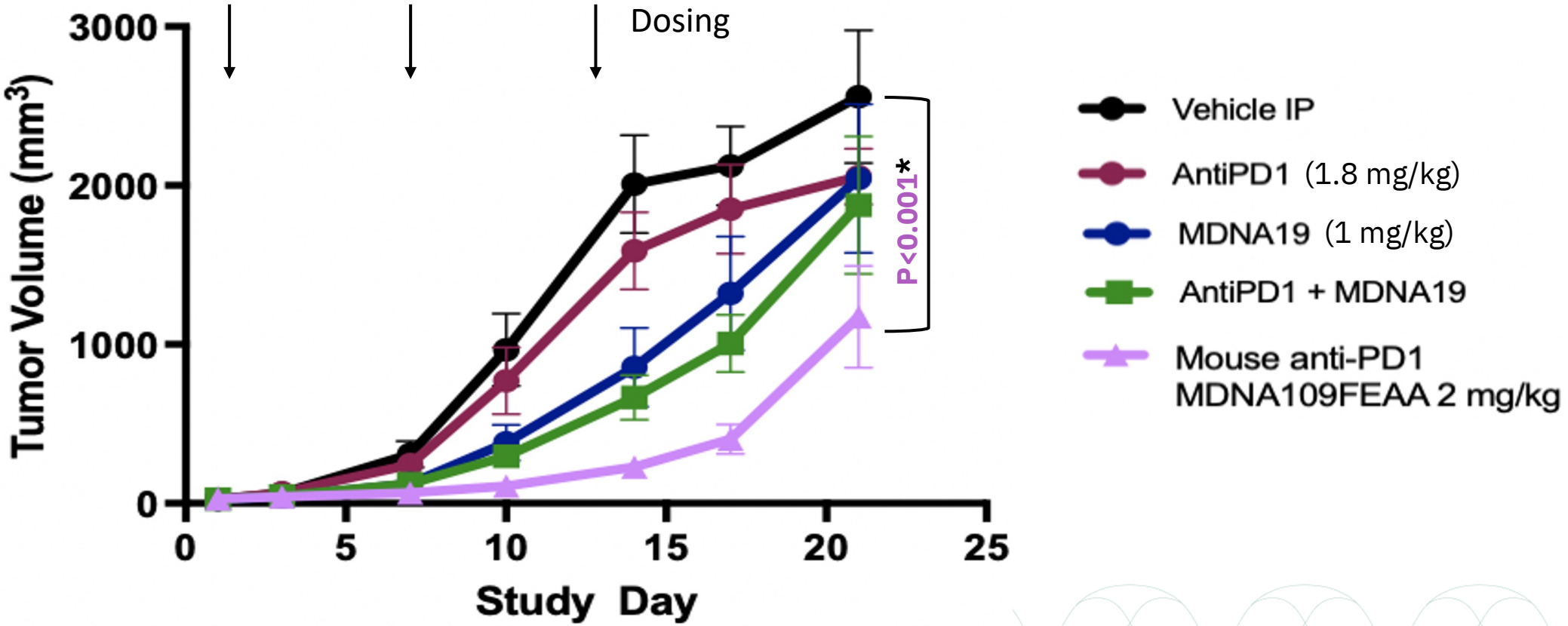
B16F10 Melanoma



Treatment with anti-PD1-MDNA109FEAA IP QWX3.
Avg tumor size at initiation of dosing: 30 mm^3. *P value for t-test on day 21 data

Anti-PD1-MDNA109FEAA BiSKIT Is More Efficacious than Co-administration of Anti-PD1 + MDNA19

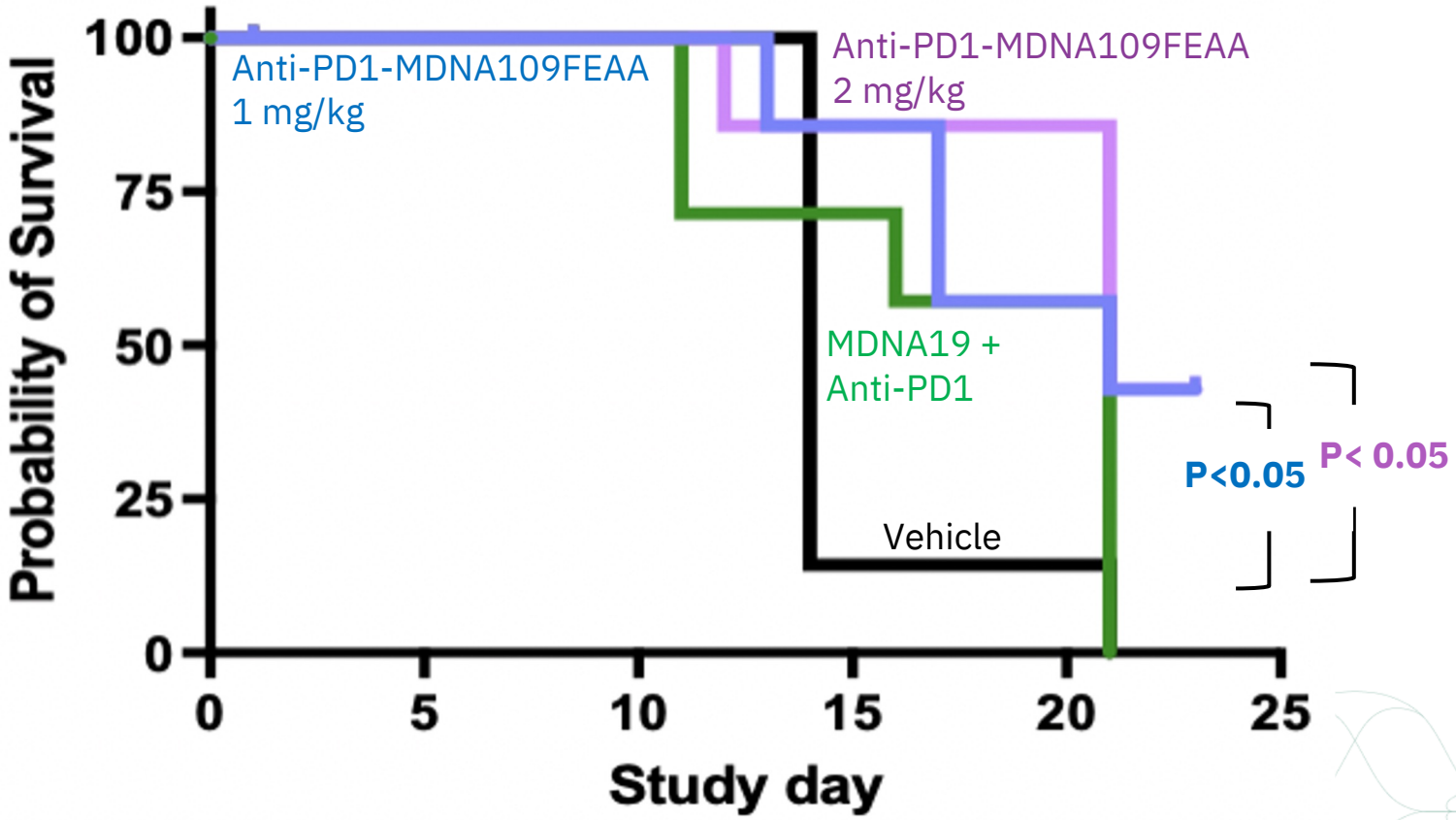
B16F10 Melanoma



Treatment with molar equivalent doses of anti-PD1, MDNA109FEAA-Fc or anti-PD1-MDNA109FEAA IP QWX3. Avg tumor size at initiation of dosing: 30 mm^3. *P value for t-test on day 21 data

Anti-PD1-MDNA109FEAA BiSKIT Significantly Prolongs Survival in Mouse Tumor Models

B16F10 Melanoma



Group	% Survival at Study End
Vehicle	0
Anti-PD1 + MDNA19	0
Anti-mPD1-MDNA109FEAA (1 & 2 mg/kg)	43

Conclusions

- **In Vitro Analysis of BiSKIT Anti-PD1-MDNA109FEAA shows:**
  - Enhanced CD122 affinity and no binding to CD25
  - Similar potency on immune cells as mono-specific MDNA19; preferential $CD8^+$ T cell stimulation over Tregs
  - Similar potency on PD1/PDL1 blockade as control anti-PD1 antibody
- **In Vivo Analysis of BiSKIT Anti-PD1-MDNA109FEAA shows:**
  - Dose dependent tumor growth inhibition and significant extension of survival in both CT26 colon carcinoma model and B16F10 melanoma model
  - Therapeutic efficacy of anti-PD1-MDNA109FEAA was significantly more efficacious than co-administration of MDNA19 + anti-PD1, highlighting therapeutic potential of cis binding to both target receptors
- **These data underscore the versatility of superkine platform and demonstrate that BiSKIT results in a strong potentiation of T cell response and antitumor efficacy as compared to co-administration of PD-1 checkpoint inhibition and IL-2 agonist**.
- **The presented preclinical data establish BiSKIT as a promising Next Generation IL-2 for Cancer Immunotherapy**.