

MEDICENNA

MDNA11:2020 ASCO PRESENTATION
And Supplementary Results

Evolutionary Cytokines. Revolutionary Medicines.

TSX: **MDNA**
OTCQB: **MDNAF**

***In Vitro* and *In Vivo* Characteristics of MDNA11: A Long-Acting “Beta-only” IL-2 Superkine in Syngeneic Mice Tumor Models and Non-human Primates**

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BACKGROUND

Use of IL-2 (Proleukin) to treat cancer is limited by a short half-life, undesirable activation of Tregs, and adverse side effects.

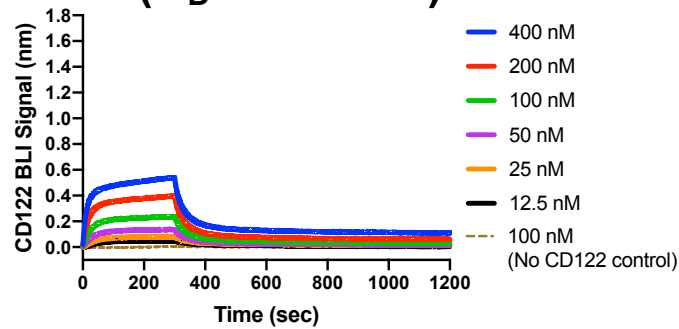
MDNA11 is an IL-2 Superkine with the following features:

- Core mutations to increase affinity to CD122 (expressed by CD8⁺ T and NK cells) and diminish binding to CD25 (expressed by Tregs)
 - Designed to enhance therapeutic efficacy.
- Extended half-life by fusion to an albumin scaffold, known to also allow accumulation at tumor sites.
 - Designed to overcome the need for frequent administration at a high dose.

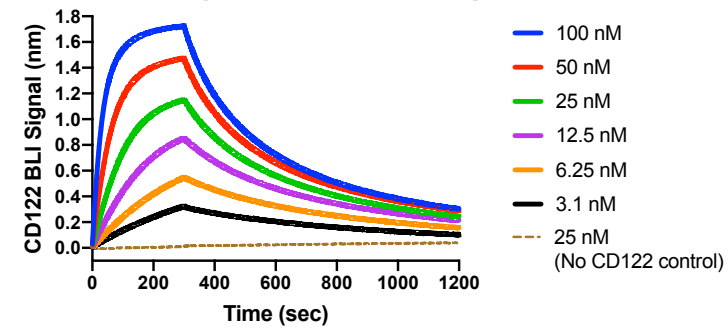
MDNA11: Enhanced Affinity for CD122; Does Not Bind CD25

CD122 Binding

rhIL-2
($K_D = 210$ nM)

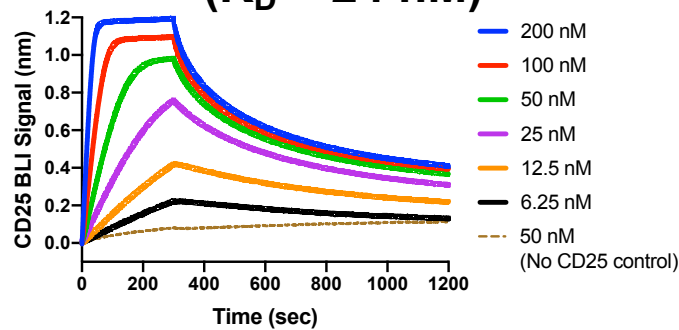


MDNA11
($K_D = 6.6$ nM)

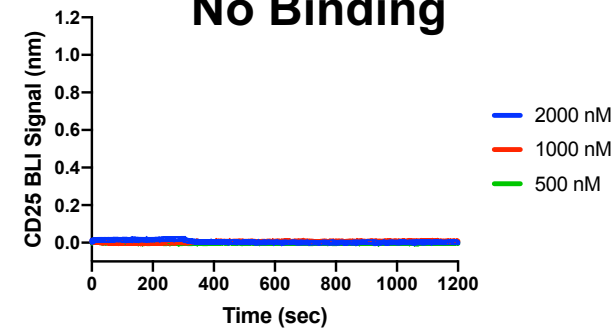


CD25 Binding

rhIL-2
($K_D = 24$ nM)



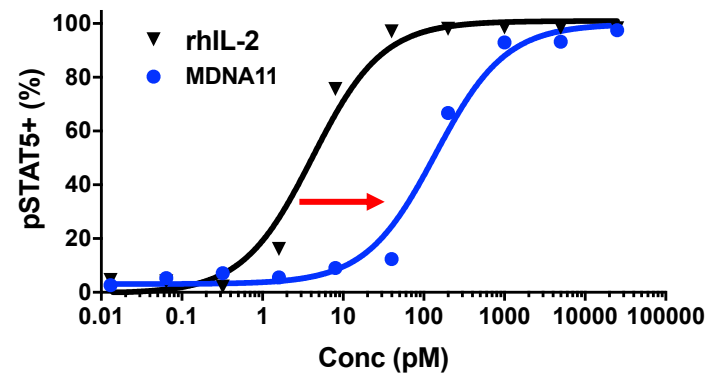
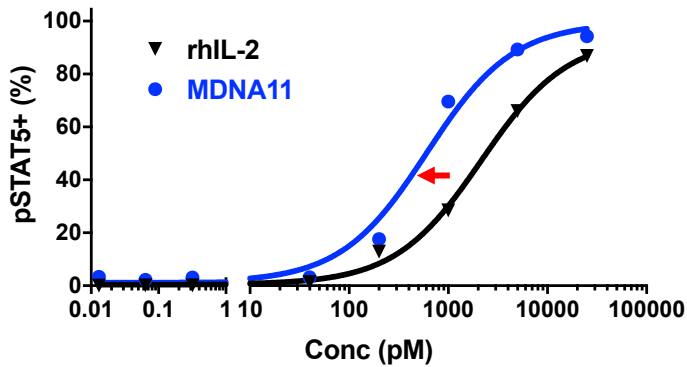
MDNA11
No Binding



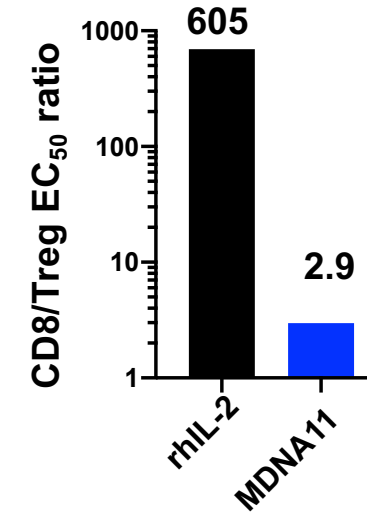
MDNA11: Enhanced Potency on CD8⁺ T and NK Cells; Reduced Activity on Tregs

Signaling in Naïve CD8⁺ T Cell

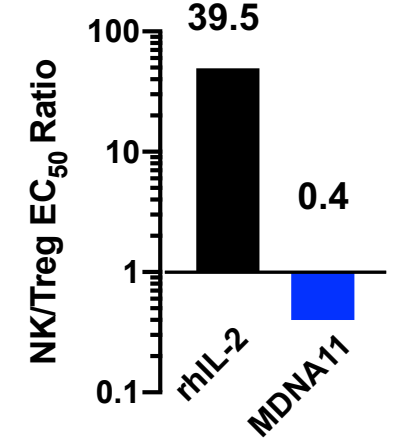
Signaling in Tregs



CD8/Treg Ratio



NK/Treg Ratio



	Naïve CD8 ⁺ T cells (EC ₅₀ , pM)	Treg (EC ₅₀ , pM)
rhIL-2	3390	5.6
MDNA11	460	160

pSTAT5 signaling in human PBMC. PBMC treated with increasing doses of rhIL-2 or MDNA11; pSTAT5 signals in different immune populations detected by flow cytometry.

MDNA11 Has Longer Half-Life than MDNA19 In Mice and Non-human Primates

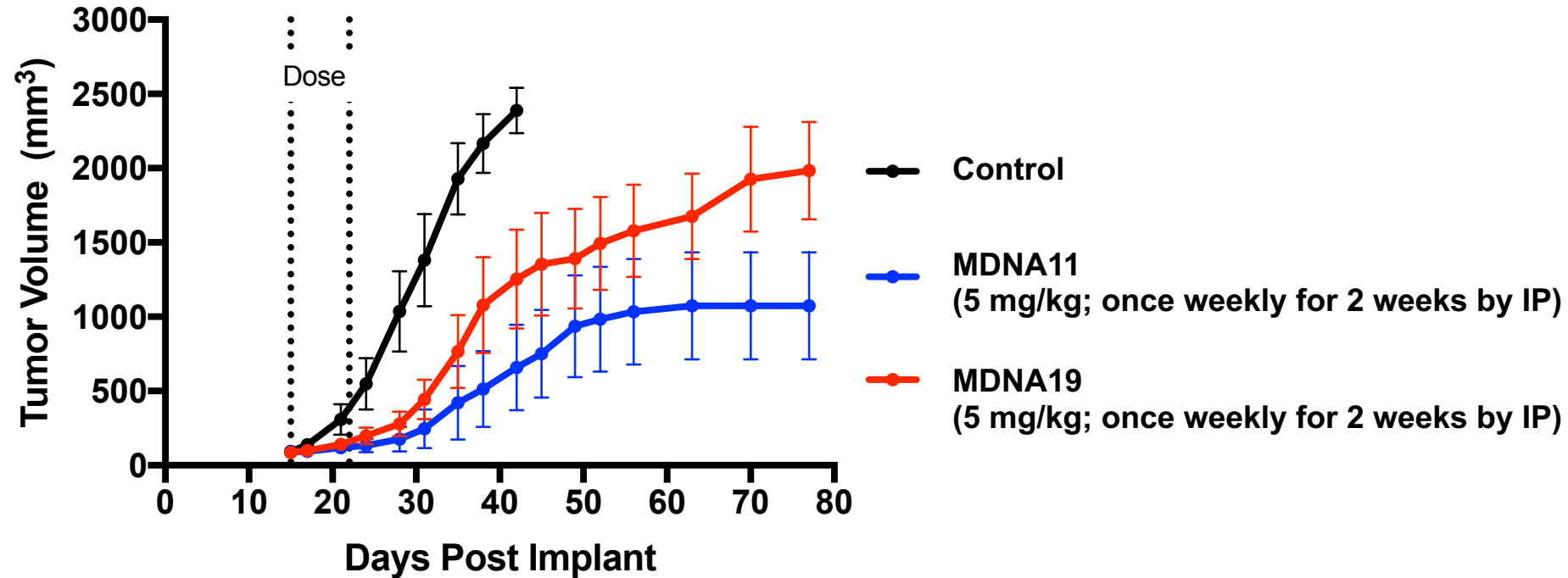
	$T_{1/2}$ in Mice (h)	$T_{1/2}$ in NHP (h)	C_{max} in NHP (ng/mL)	AUC in NHP (h.ng/mL)
rhIL-2	0.28	1.4 ^(a)		
MDNA11	6.83	12.8 – 24.7 ^(b)	3,446 ^(c)	76,297 ^(c)
MDNA19	6.08	7.3 – 9.1 ^(b)	7,091 ^(c)	70,807 ^(c)

(a) Measured in human

(b) Data from repeat dosing (14-days apart) over the range of 0.01-0.6 mg/kg

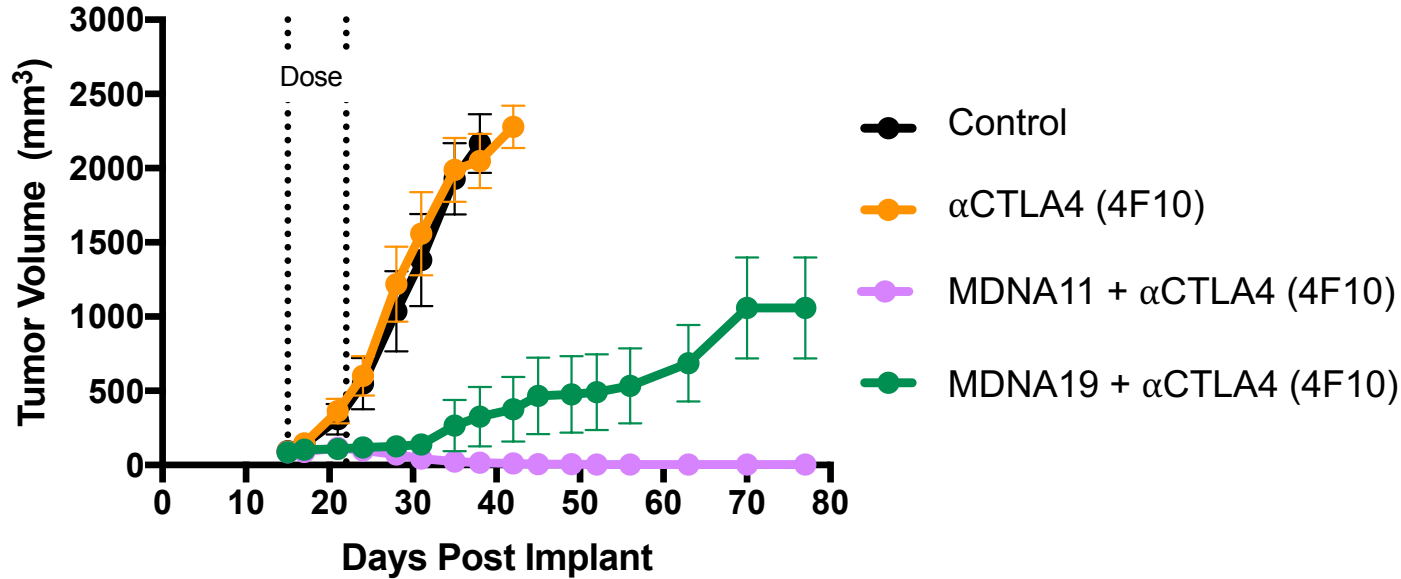
(c) Data based on first dosing at 0.3 mg/kg

MDNA11 Exhibits Superior Therapeutic Efficacy As Monotherapy Compared to MDNA19 in CT26 Tumor Model

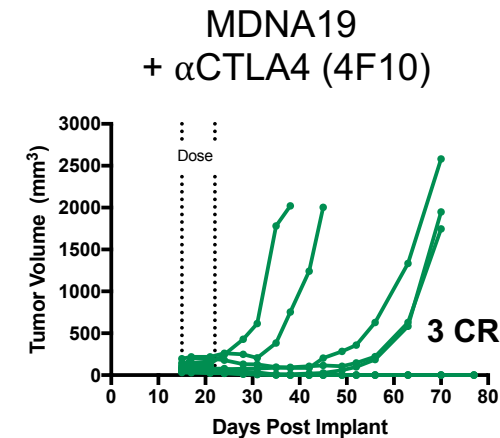
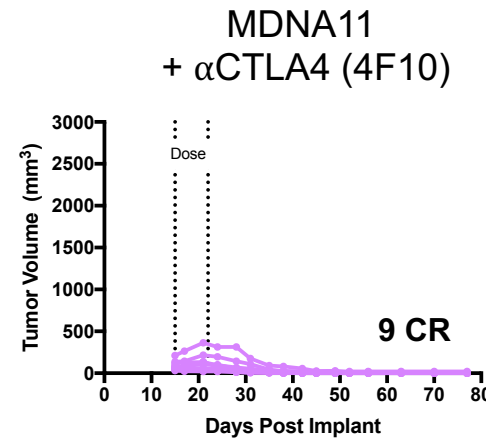
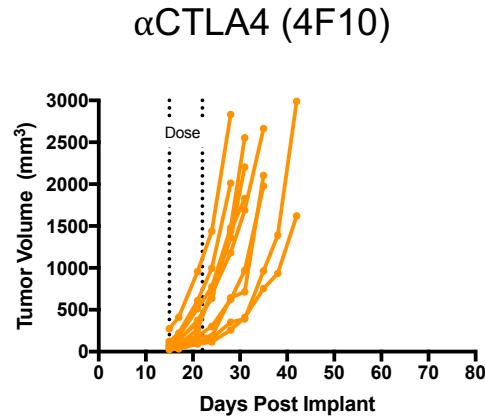
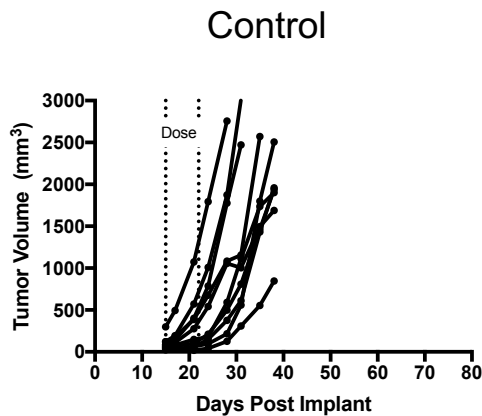


- Mice implanted SQ with CT26 tumor cells and treatment initiated on Day 14
- Average tumor size at initiation of dosing = 90 mm³

MDNA11 Synergizes with Anti-CTLA4 to Induce 100% CT26 Tumor Regression



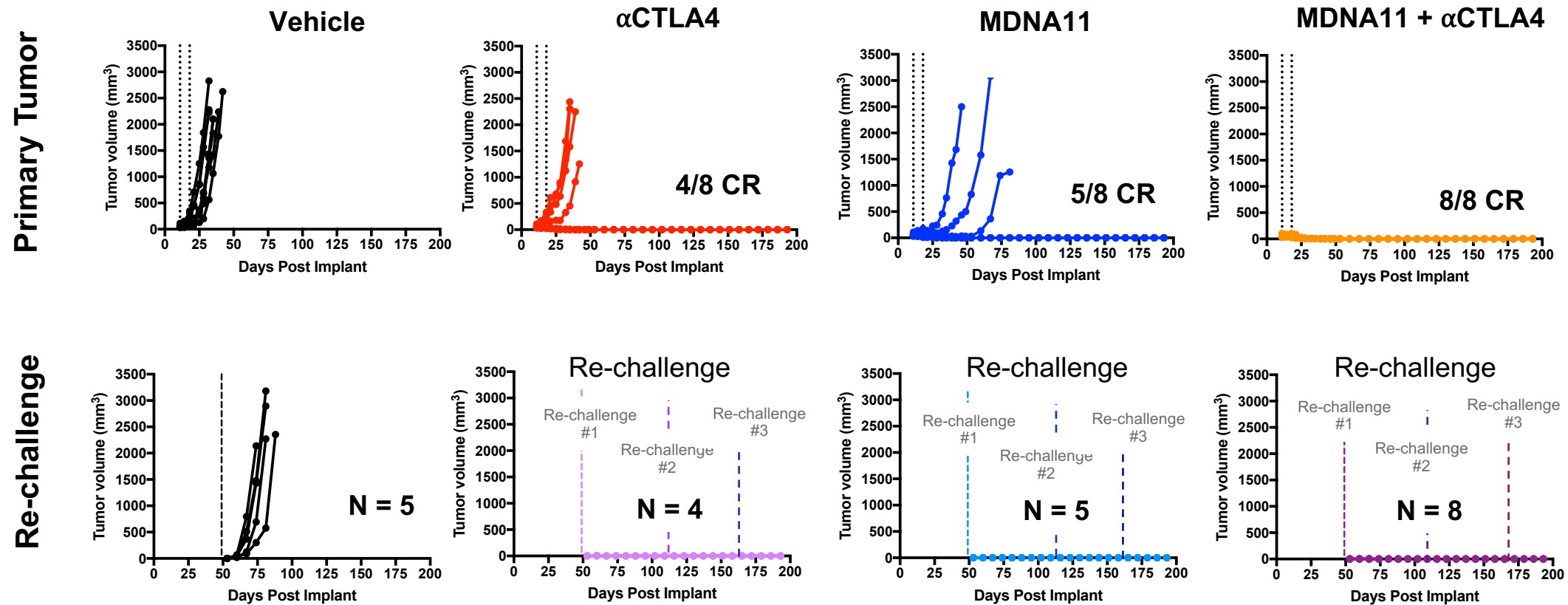
- Mice implanted SQ with CT26 tumor cells and treatment initiated on Day 14
- Average tumor size at initiation of dosing = 90 mm³
- MDNA11 & MDNA19: 5 mg/kg, 1x/wk for 2wks, IP
- αCTLA4 (4F10): 100 μg, 2x/wk for 2wks, IP



CR = Complete Regression

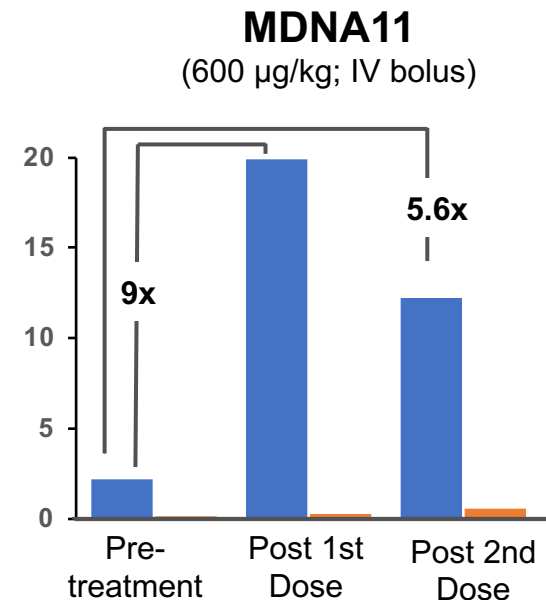
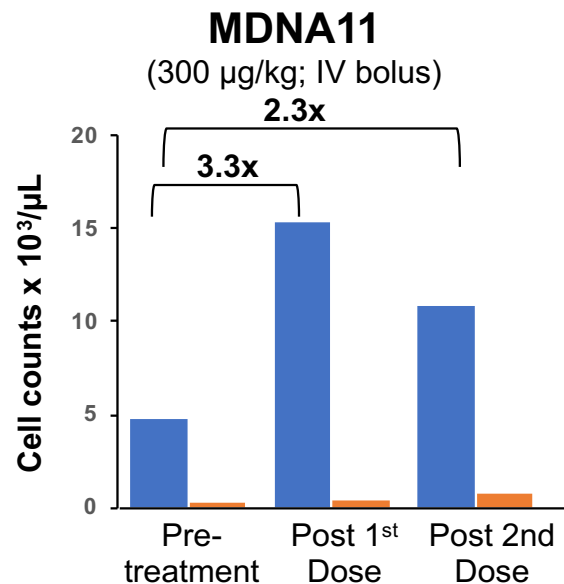
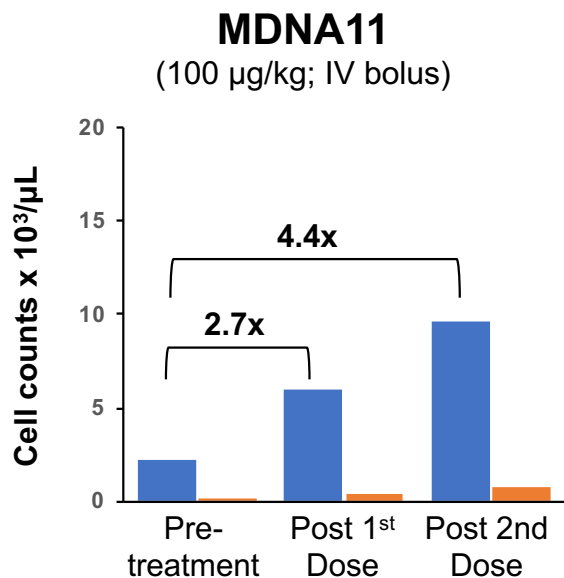


MDNA11 Inhibits Tumor Growth and Induces A Strong Memory Response As Monotherapy & In Combination with α CTLA4 in CT26 Tumor Model

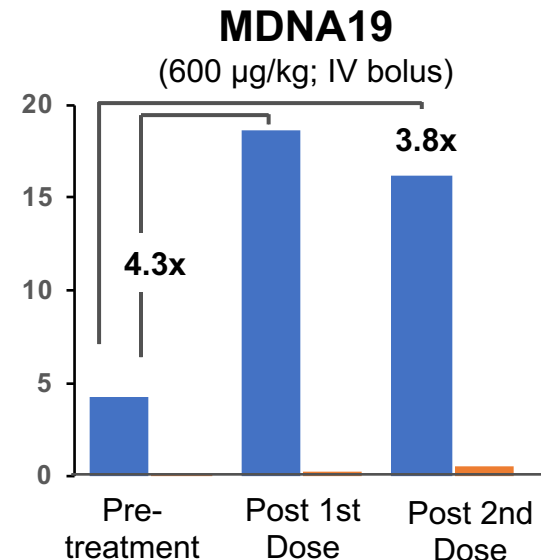
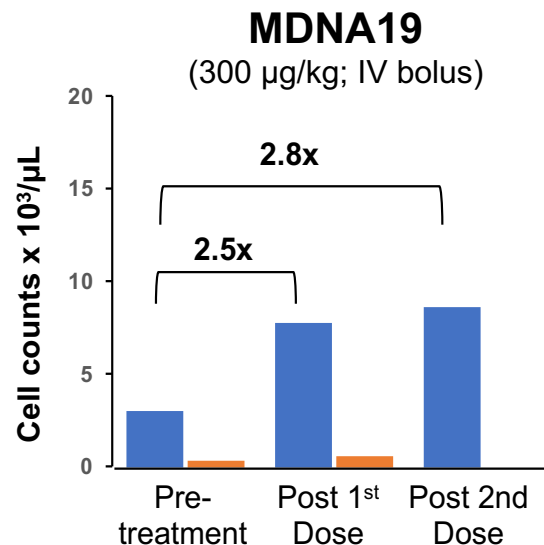
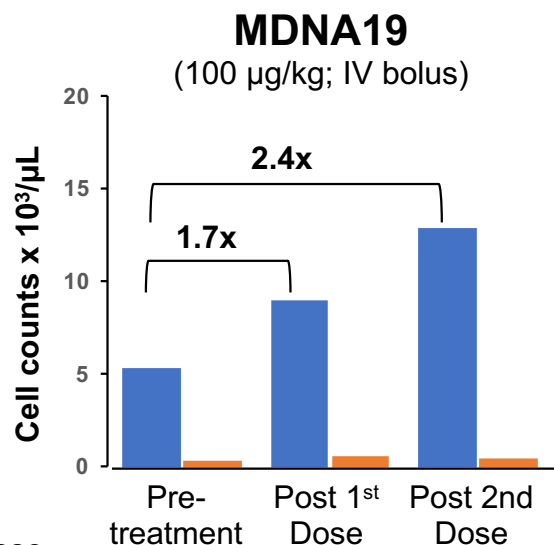


CT26 tumor (~60 mm³) bearing Balb/c mice were treated with MDNA11 (5 mg/kg 1x/week, 2 weeks) or Anti-CTLA4 (200 μ g 2x/week, 2 weeks) by IP injection. Re-challenge experiment performed by implanting 2 x 10⁶ CT26 cells in opposite flank (Day 49, Day 116 and Day 165), without further treatment.

MDNA11 Has Stronger Effect On Lymphocyte Expansion Than MDNA19 In NHP



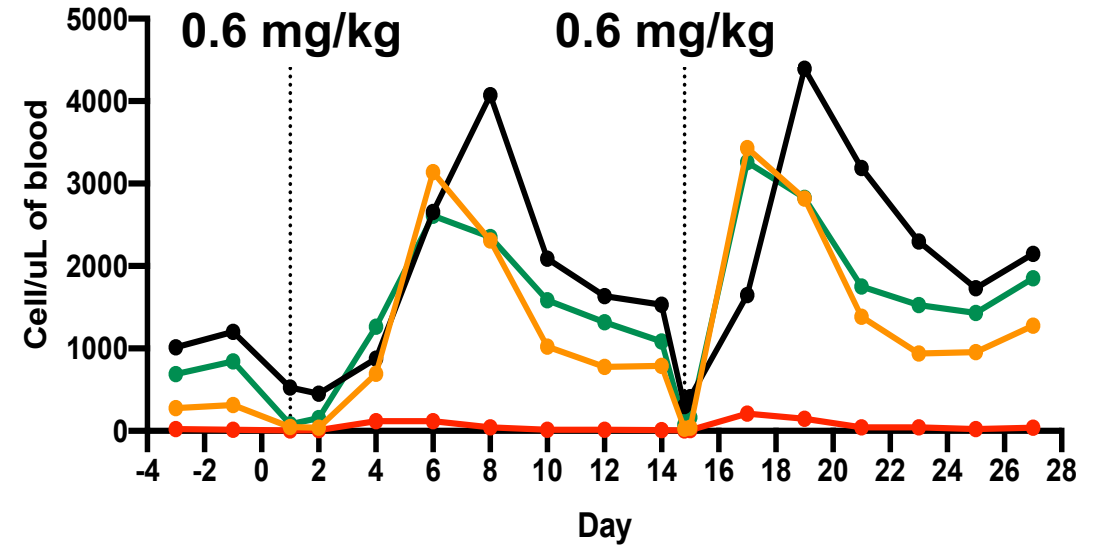
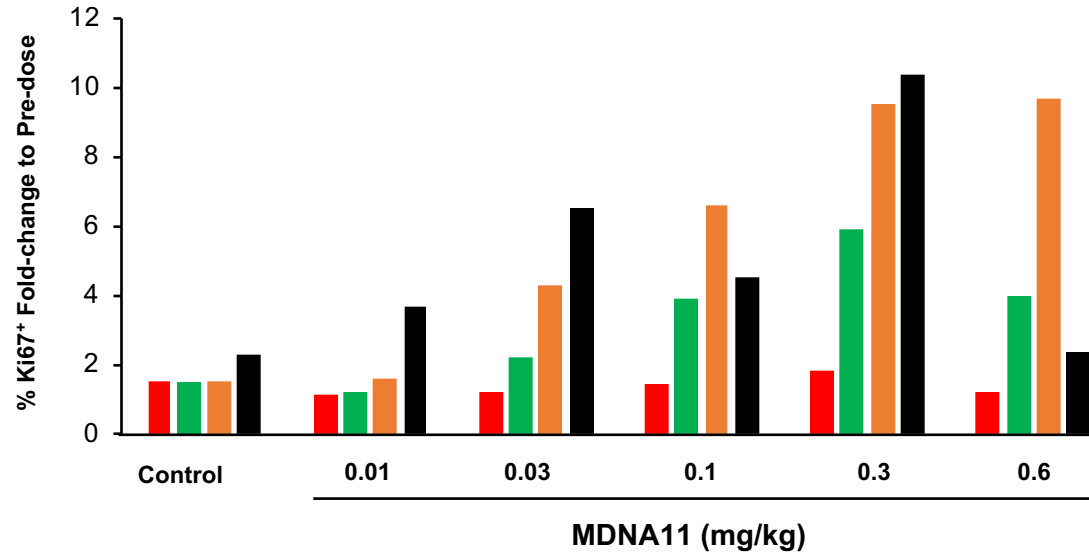
- Fold increase in lymphocytes compared to pre-treatment.
- No expansion of eosinophils, responsible for VLS.



■ Lymphocytes
■ Eosinophils

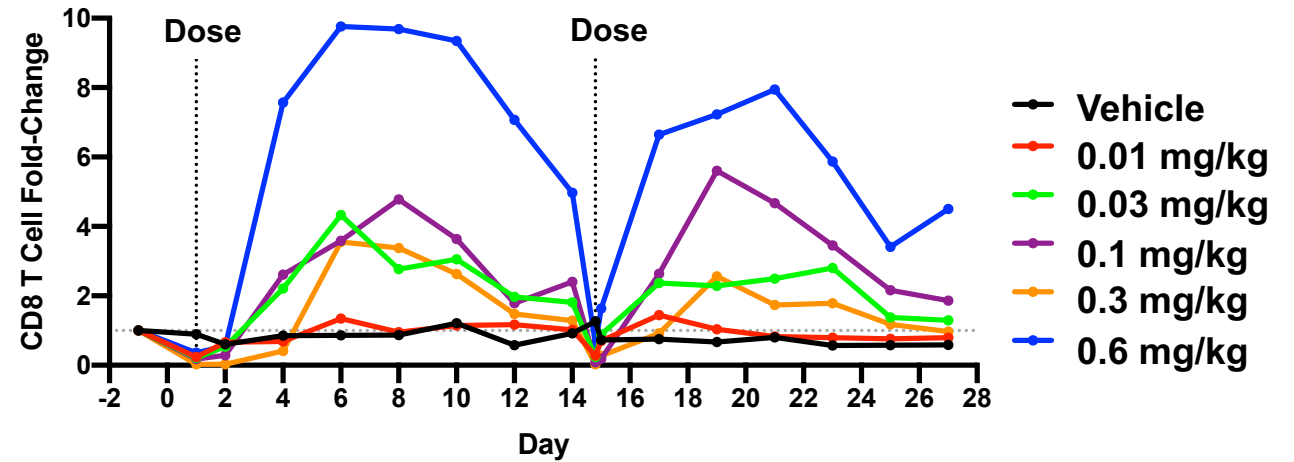
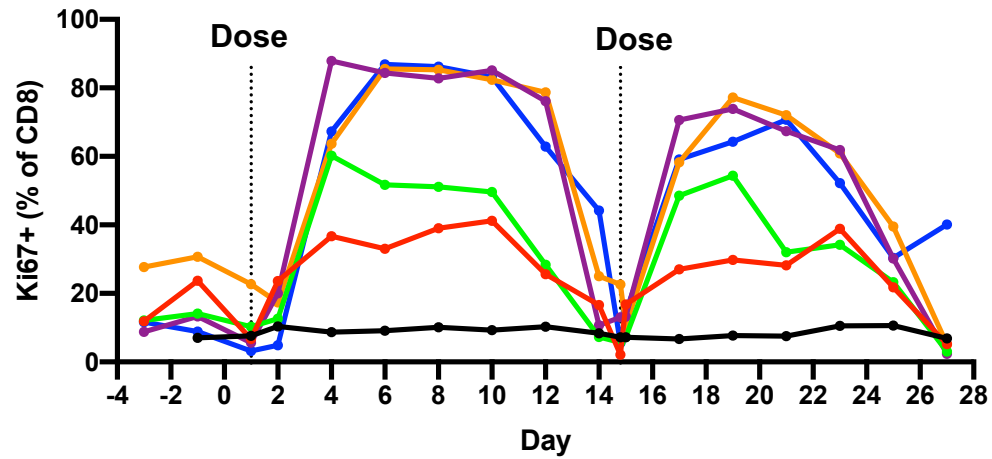
N = 1 per dose

MDNA11 Induces Proliferation & Expansion of CD4⁺ T, CD8⁺ T and NK Cells But Not Tregs in NHP

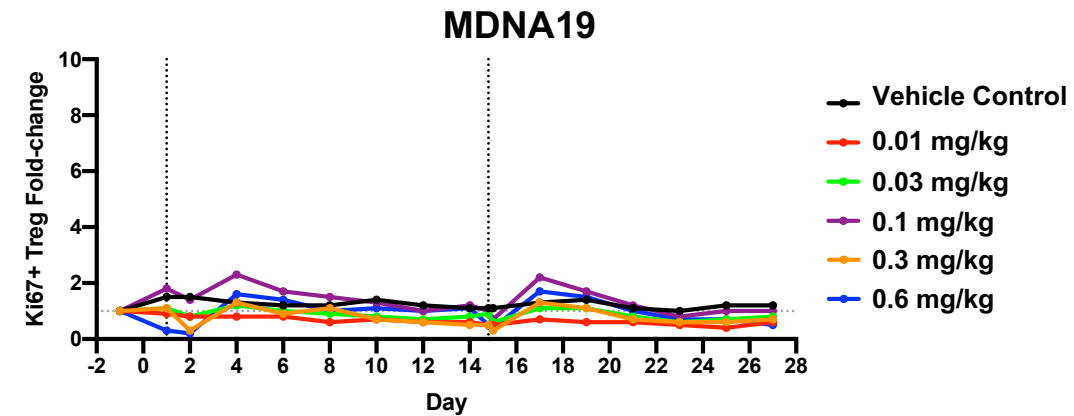
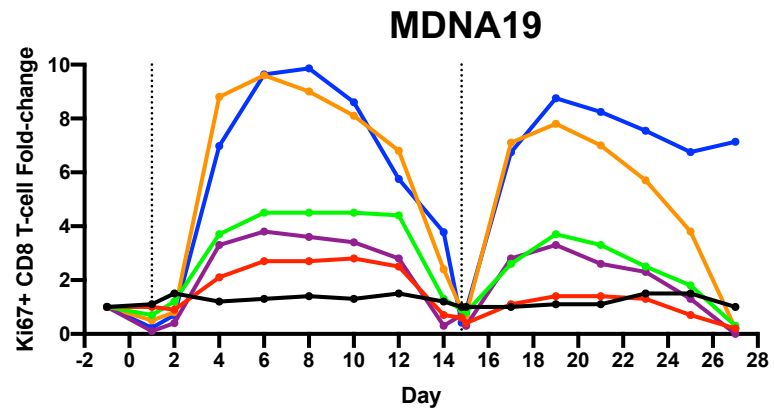
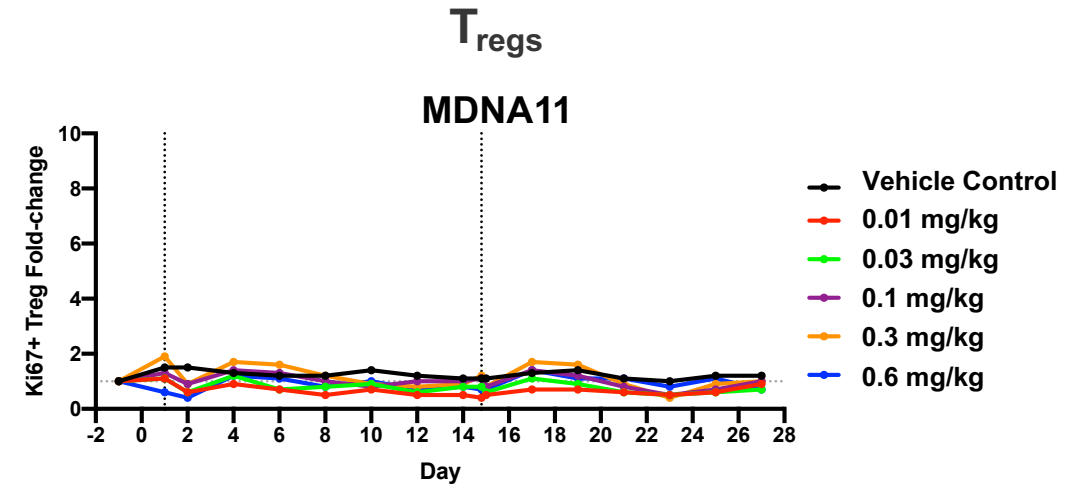
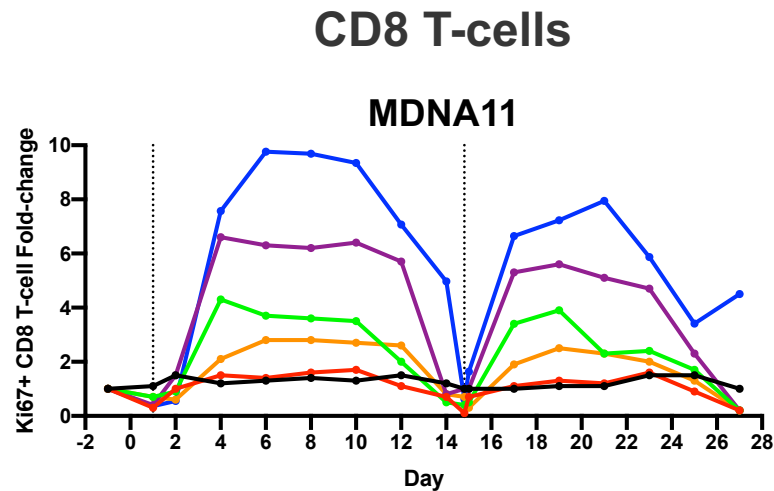


■ Tregs
 ■ CD4⁺ T Cell
 ■ CD8⁺ T Cell
 ■ NK Cell

MDNA11 Induces Durable Proliferation and Expansion of CD8⁺ T Cells in NHP

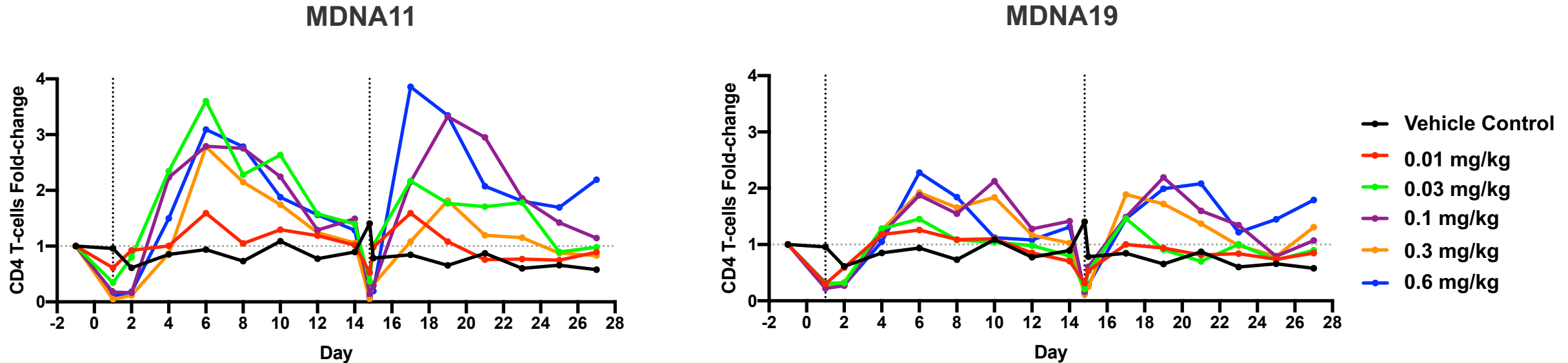


MDNA11 & MDNA19 Induce CD8 T-cell Proliferation But Not Tregs in NHP



- Adult male cynomolgus monkeys (8-12 years) received repeat dose (14 days apart) of MDNA11 or MDNA19 by slow IV bolus.
- Percentage of Ki67-positive circulating CD8 T-cells at different time points were quantified by flow cytometry.
- N = 1 per dose level.

MDNA11 Exhibits a Stronger Effect on Non-Treg CD4 T-cell Expansion than MDNA19



- Adult male cynomolgus monkeys (8-12 years) received repeat dose (14 days apart) of MDNA11 or MDNA19 by slow IV bolus.
- Circulating CD4 T-cells at different time points were quantified by flow cytometry.
- Post-dose data were normalized to base-line (Day -1)
- N = 1 per dose level.

MDNA11 and MDNA19 Compared

Phenotype/Parameter	Comparison
Activity in Human PBMC P-STAT5 Assay	MDNA11 ~ MDNA19
Receptor Selectivity Based on Affinity Studies	MDNA11 ~ MDNA19
Efficacy: Monotherapy in CT26 Tumor Model	MDNA11 > MDNA19
Efficacy: Combination with Anti-CTLA4 in CT26 Tumor Model	MDNA11 >> MDNA19
Half-Life in Mice	MDNA11 ≥ MDNA19
Half-Life in NHP	MDNA11 >> MDNA19
Effect on Lymphocyte Expansion in NHP	MDNA11 ≥ MDNA19
Effect on CD8 T-cell vs. Treg Proliferation in NHP	MDNA11 ~ MDNA19
Effect on CD4 T-cell Expansion in NHP	MDNA11 ≥ MDNA19
Low Immunogenicity (ADA response) in NHP	MDNA11 ~ MDNA19
Overall Safety Profile in NHP	MDNA11 ~ MDNA19

SUMMARY & CONCLUSIONS

Key Features of **MDNA11**:

- Increased affinity to CD122; no binding to CD25
- Increased potency towards CD8⁺ T cells with diminishing activity on Tregs
- Potential to accumulate in tumor micro-environment
- Enhanced PK in mice and NHP
- Potent and durable tumor control as monotherapy with strong memory response in mouse CT26 model; strong synergy with anti-CTLA4
- In NHP:
 - Induces expansion of lymphocytes and not eosinophils (associated with VLS)
 - Induces durable proliferation and expansion of CD8⁺ T and NK cells but not Tregs
 - Transient weight loss and diarrhea at higher dose (0.3 - 0.6 mg/kg).
 - Safety profile: No cytokine storm; No ADA response; No change in liver and kidney function; No hypotension; No VLS