AACR-NCI-EORTC Virtual International Conference on
MOLECULAR TARGETS AND CANCER THERAPEUTICS
October 7-10, 2021

MDNA11 is a Long-Acting 'Beta-Only' IL-2 Agonist that Demonstrates Safe and Durable Anti-Tumor Immune Response

Minh D. To, Fahar Merchant, Ma'an Muhsin, Carole Galligan, L. Bruce Pearce, Peter Lloyd, and Rosemina Merchant

Medicenna Therapeutics Inc,
Toronto, Ontario, Canada

Minh D. To, PhD

I have the following financial relationships to disclose:

Consultant for: N/A

Speaker’s Bureau for: N/A

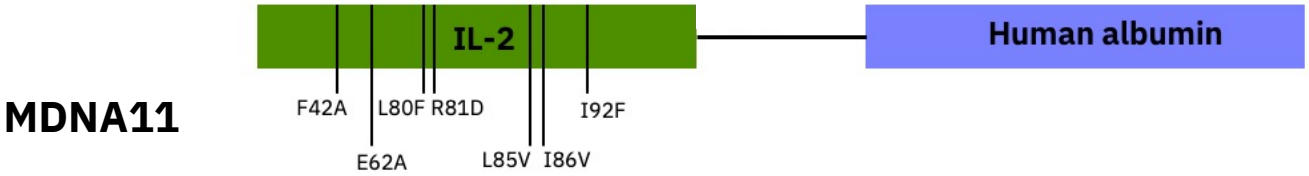
Grant/Research support from: N/A

Stockholder in: Medicenna Therapeutics Inc.

Employee of: Medicenna Therapeutics Inc.

Overview of MDNA11

A long-acting ‘beta-only’ IL-2 superkine with superior receptor selectivity: increases activation of effector immune cells, reduces Treg stimulation and reduces toxicities



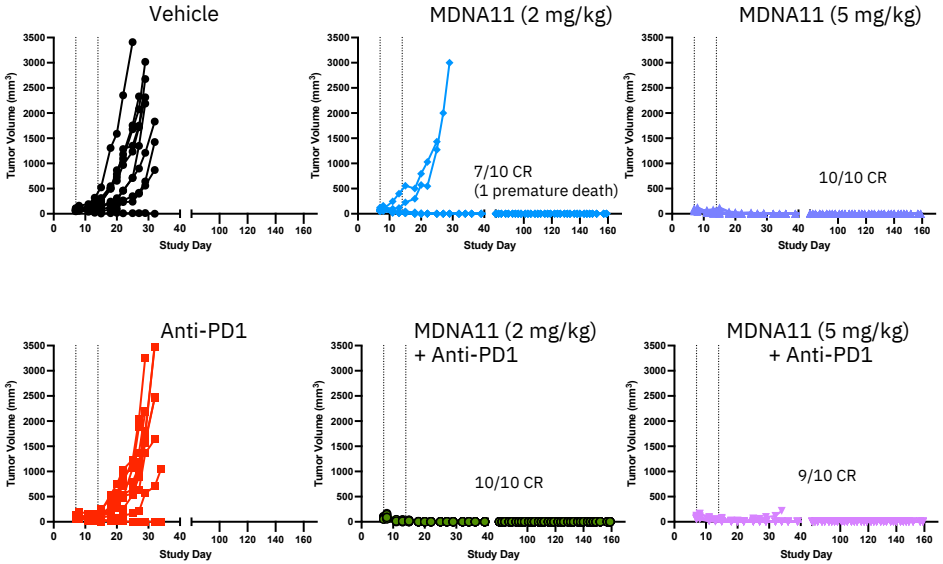
- Mutations to enhance affinity for CD122 and abrogate binding to CD25

BLI / Octet	Human		Non-Human Primate	
	CD122 K_D (nM)	CD25 K_D (nM)	CD122 K_D (nM)	CD25 K_D (nM)
rhIL-2	210	24	170	12
MDNA11	6.6	No binding	8.2	No binding

- Fusion to human albumin
  - Increases molecular weight to overcome renal filtration, extending in vivo half-life
  - Facilitates FcRn recycling, leading to further increase in half-life
  - Potential for enhanced therapeutic efficacy by accumulating in highly vascularized tissues (i.e. tumors, lymph nodes)

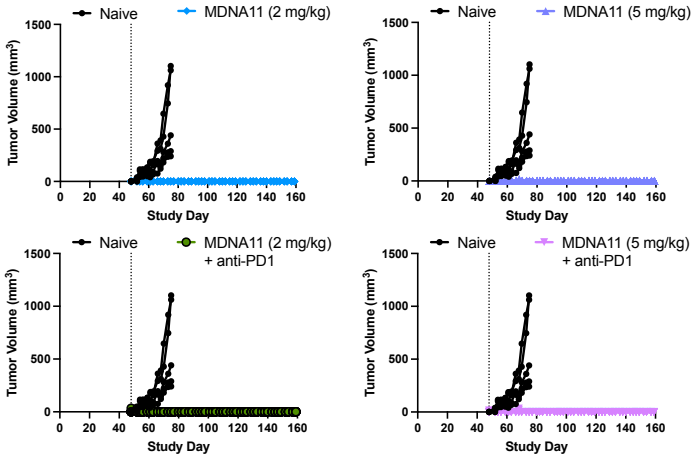
MDNA11 +/- Anti-PD1: Inhibit Tumor Growth & Induce Memory and Antigen Specific CD8⁺ T-Cells

Primary MC38 Tumors

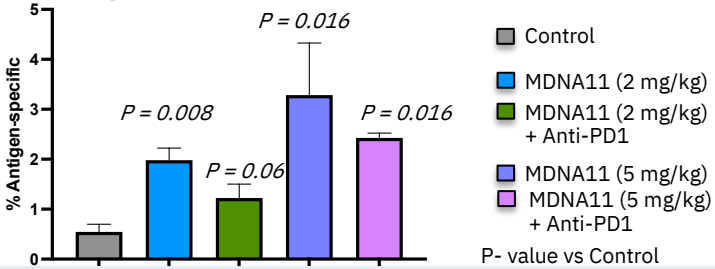


MDNA11: IP QWx2
Anti-PD1 (RMP1-14; 10 mg/kg): IP BIWx3, IP
Average size at initiation of dosing ~ 75 mm³
Study in C57Bl/6 mice.
Antigen-specific CD8 T-cells by flow cytometry using H-2K MuLV p15E tetramer
All mice boosted with MC38 5 days prior to flow cytometry analysis

MC38 Re-challenge



Antigen-Specific Effector CD8⁺ T-Cells



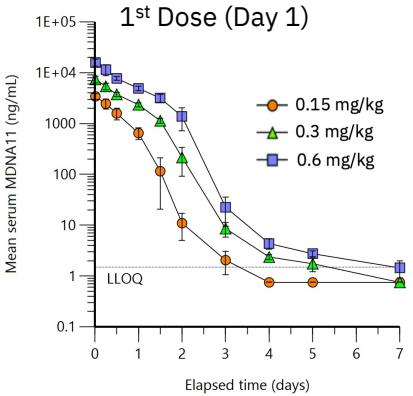
MDNA11 Exhibits a Favorable Safety Profile in NHP
Summary of GLP Toxicology Study in NHP

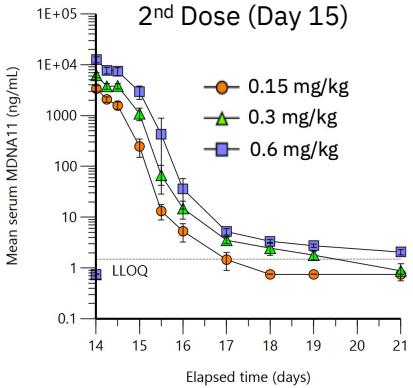
Male and female cynomolgus monkeys received 3 doses of MDNA11 (0.15, 0.3 and 0.6 mg/kg) by IV infusion 14-days apart

Key Findings:

- Main observations in cynomolgus monkeys were transient loss of appetite, reduced activity and diarrhea
  - More common in the high dose group (0.6 mg/kg); all animals recovered
  - Mostly observed after the 1st dose; lower incidence rate or not observed after 2nd and 3rd dose
- No cytokine release syndrome in cynomolgus monkeys
- No ADA in cynomolgus monkeys
- No histological evidence of pulmonary edema or VLS in cynomolgus monkeys

MDNA11 PK Profile in NHP



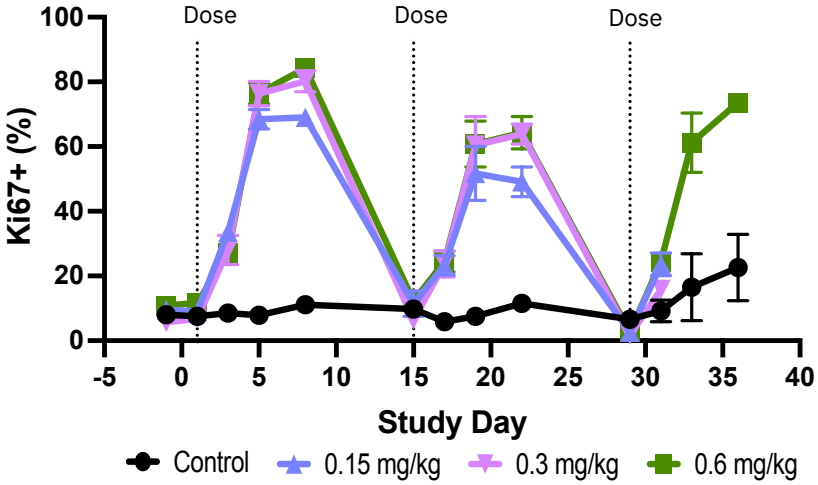


- MDNA11 shows initial slow loss of exposure followed by a more rapid decline, suggestive of a saturable clearance process often referred to as target-mediated drug disposition (TMDD)
- Dose proportional increase in Cmax and AUC
- Evidence of increase clearance following the second dose, possibly due to immune cell expansion

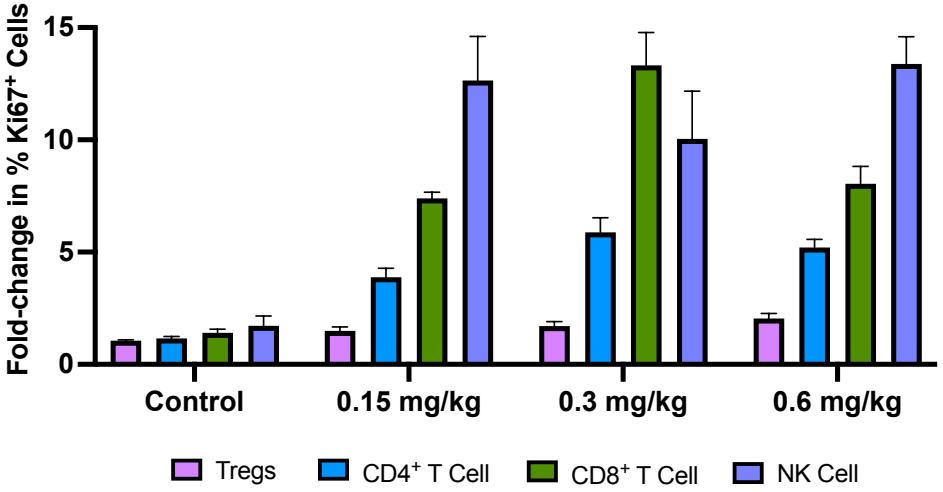
Dose (mg/kg)	Study Day	Cmax (ng/mL)	AUClast (h.ng/mL)
0.15	1	3,430	48,800
	15	3,380	40,200
0.3	1	7,400	135,000
	15	6,220	90,300
0.6	1	16,000	310,000
	15	12,700	193,000

MDNA11 Induces Effector Immune Cell Proliferation with Limited Effect on Tregs

CD8⁺ T-Cell Proliferation (Ki67 Expression)



Peak Fold-change in Ki67 Expression



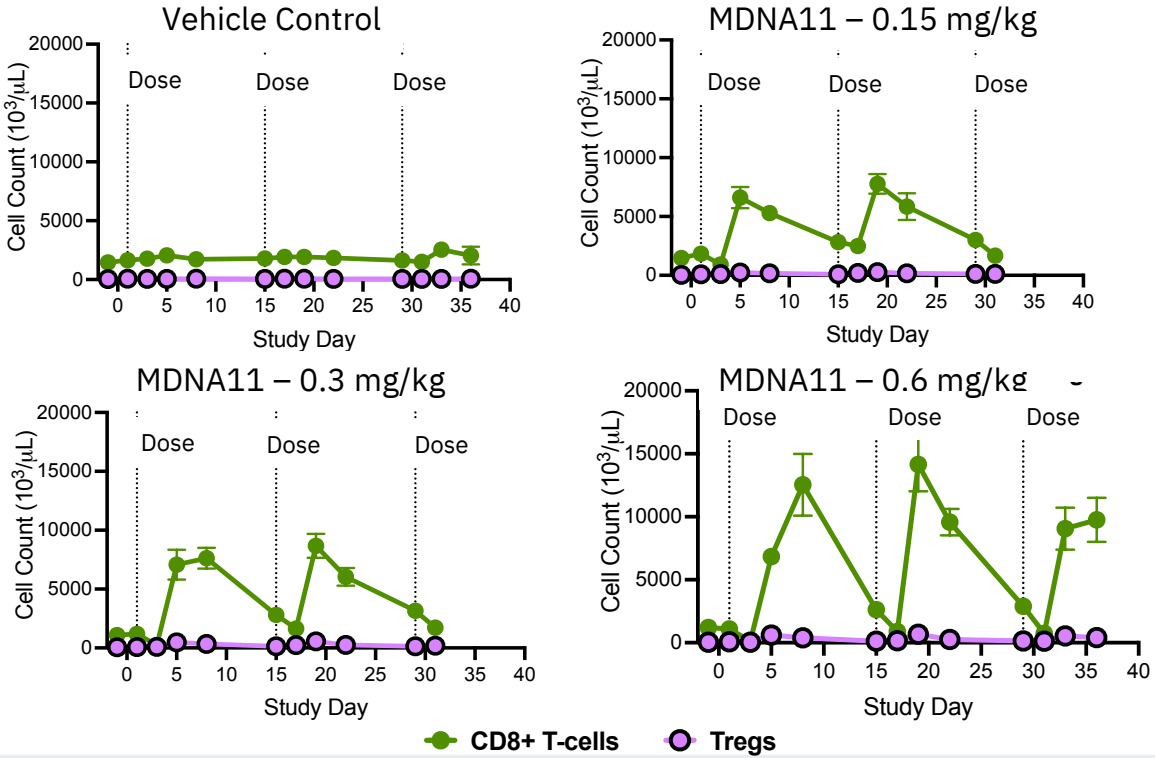
PD response response significantly more durable than exposure = Extended PD Effect

Ki67 expression by immune cell quantified by flow cytometry analysis of blood samples

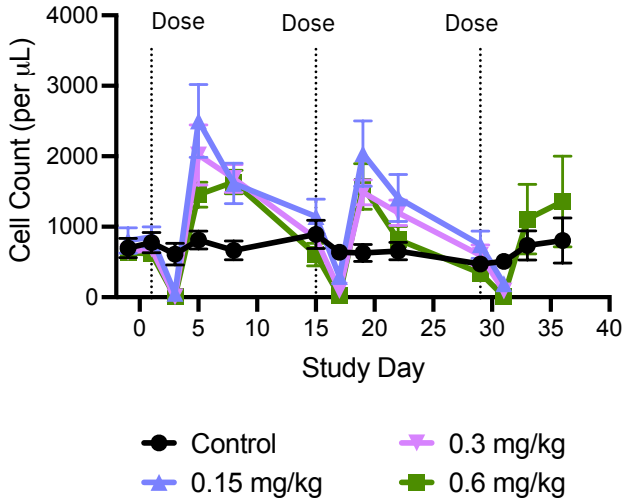
Fold-change relative to baseline (pre-dose) value

MDNA11 Induces Preferential Expansion of Effector Immune Cells Over Tregs

Preferential Expansion of CD8+ T-Cells over Tregs

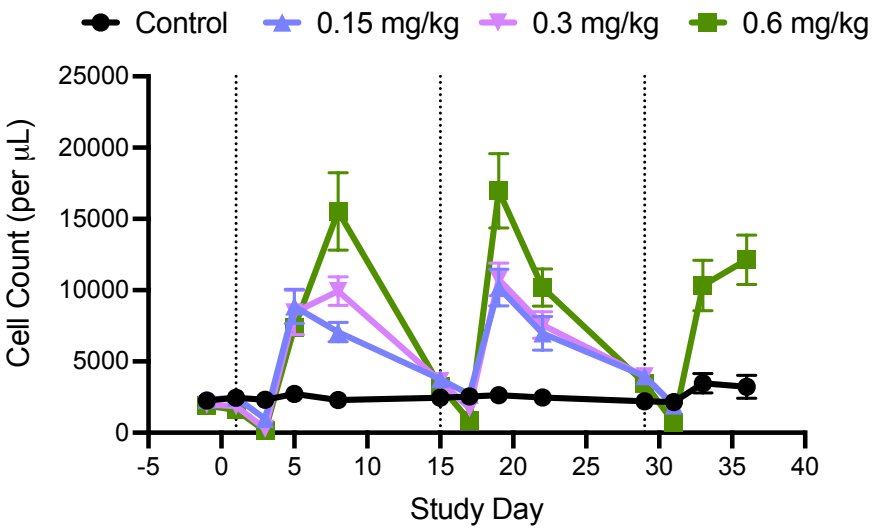


MDNA11 Induces NK Cell Expansion

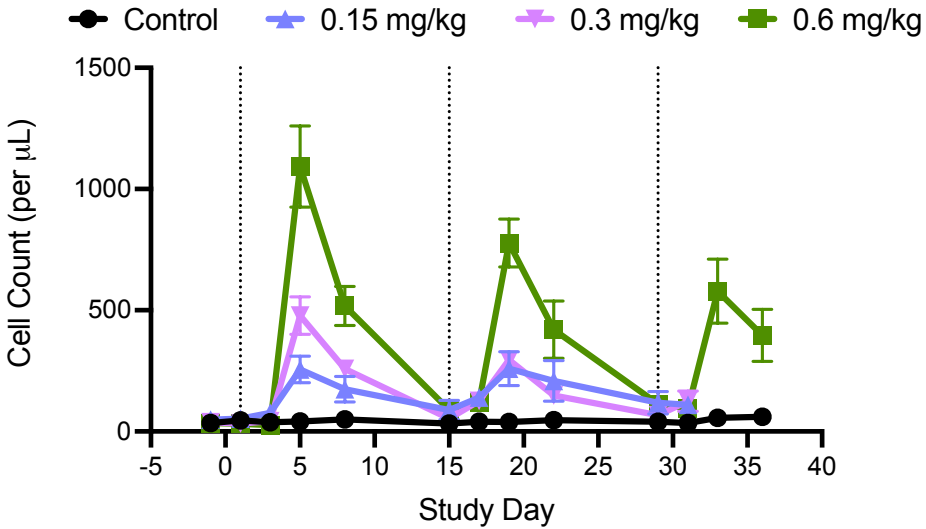


MDNA11 Induces Expansion of Naïve & Activated CD8⁺ T-Cells

Naïve (CD25⁻) CD8⁺ T-cells



Activated (CD25⁺) CD8⁺ T-cells



Summary

- MDNA11 is a long-acting ‘Beta-Only’ IL-2 agonist with enhanced CD122 binding that potentiates activation of effector immune cells (CD8$^+$ T-cells and NK cells) with reduced activity on Tregs
- MDNA11 demonstrates potent efficacy as monotherapy and in combination with immune check-point inhibitors in multiple mouse syngeneic tumor models including tumor clearance, protection against re-challenges, and promotion of durable antigen specific CD8$^+$ T-cells
- In NHP, MDNA11 induces durable proliferation and expansion of effector immune cells (CD4$^+$ T-cells, CD8$^+$ T-cells and NK cells) with limited effect on Tregs
- MDNA11 exhibits a favorable safety profile in cynomolgus monkeys: no ADA, no cytokine release syndrome and no pulmonary edema and VLS

Contact: Minh D. To, PhD (minh.to@medicenna.com)