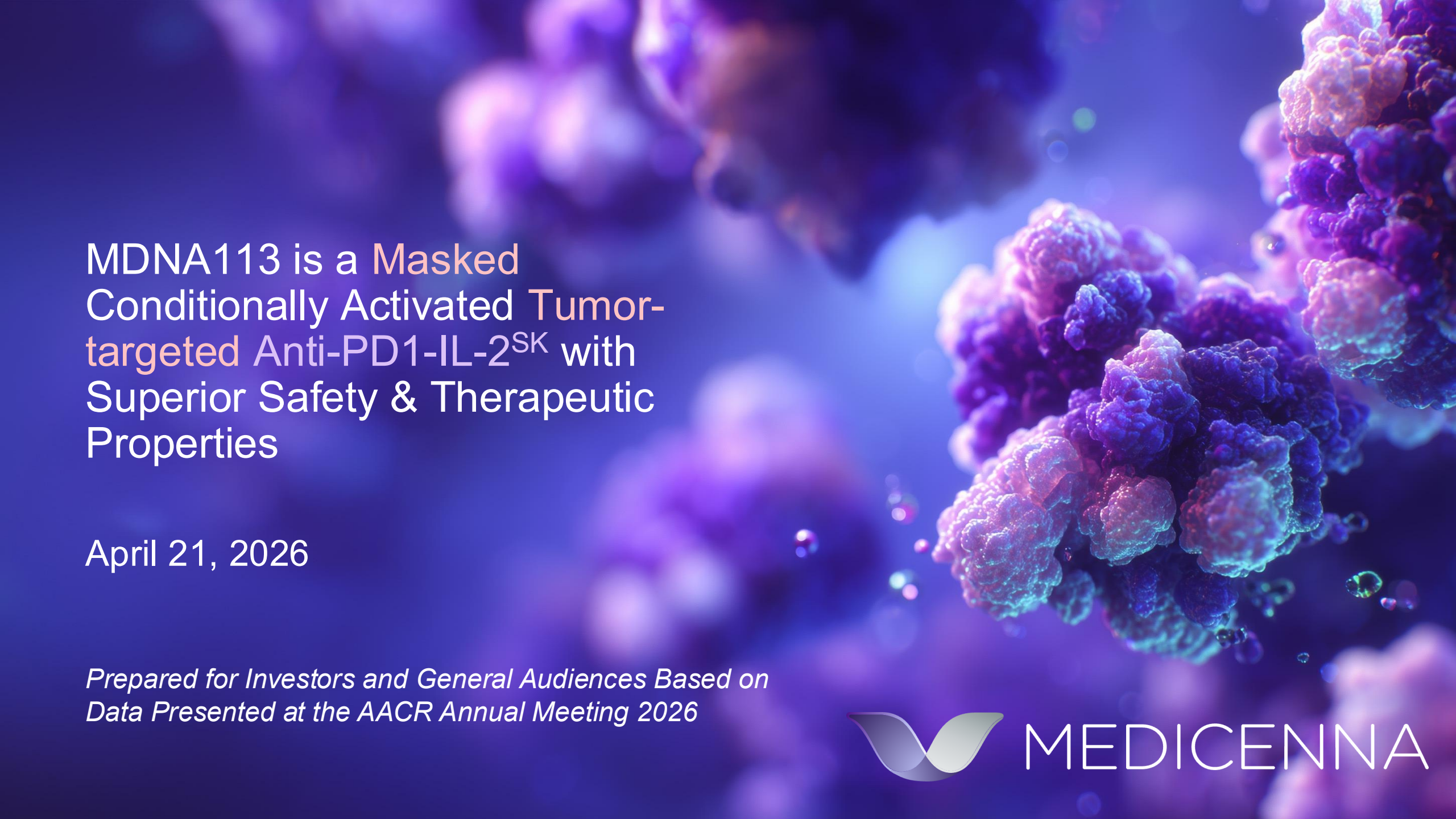
MDNA113 is a Masked Conditionally Activated Tumor-targeted Anti-PD1-IL-2^{SK} with Superior Safety & Therapeutic Properties

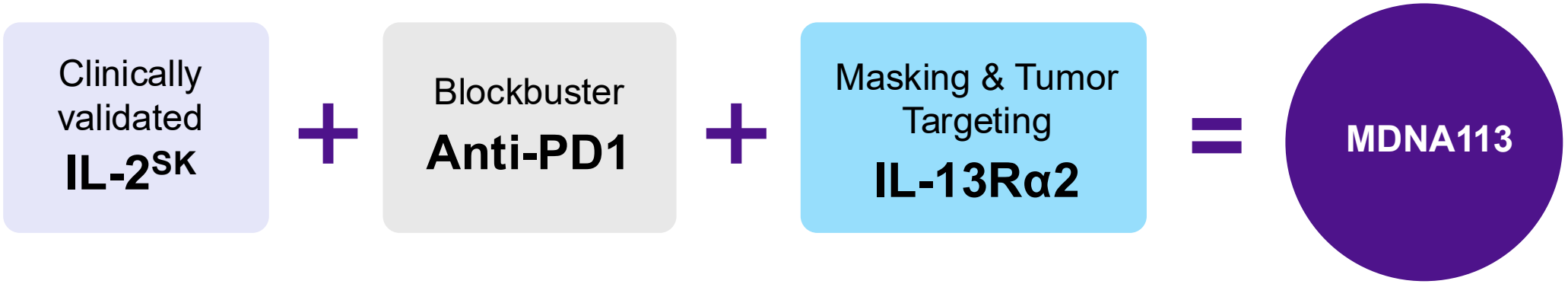
April 21, 2026

Prepared for Investors and General Audiences Based on Data Presented at the AACR Annual Meeting 2026



MEDICENNA

MDNA113: A Differentiated First-in-Class, Tumor Anchored Anti-PD1 x IL-2 Bi-functional Molecule

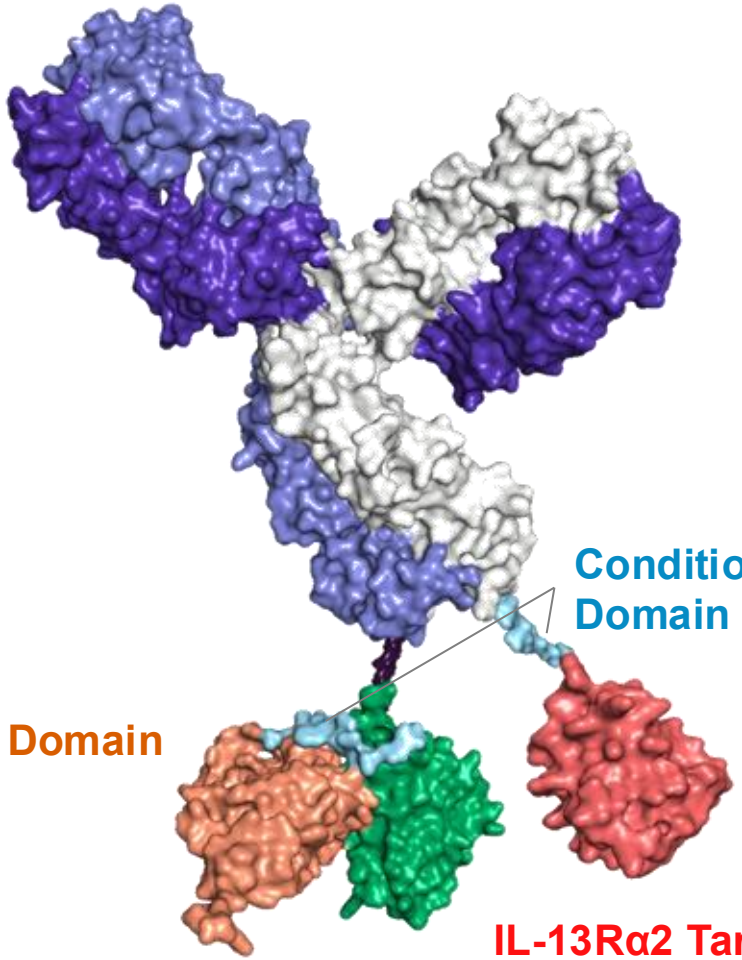


- **Differentiated** masking approach allows for saturation of PD-1 whilst unleashing IL-2^{SK} within the TME
- **Tumor targeting** to IL-13Rα2, **anchors** the PD-1 x IL-2 to the TME for a sustained period of time
- **MOA 1 for Activation:** activation by tumor specific proteases MMPs
- **MOA 2 for Activation:** *cis*-expression of PD-1 and IL-2R on target effector cells unmasks MDNA113

MDNA113 demonstrates:

- Exceptional tumor selectivity, localization, and potency with improved systemic tolerability
- Superior tolerability and significantly wider therapeutic window vs. PD-1 x IL-$2^{\alpha\text{-bias}}$ comparator
- Well tolerated up to 50 mg/kg in non-human primates

MDNA113: Designed to be the Optimal PD-1 x IL-2 Bifunctional



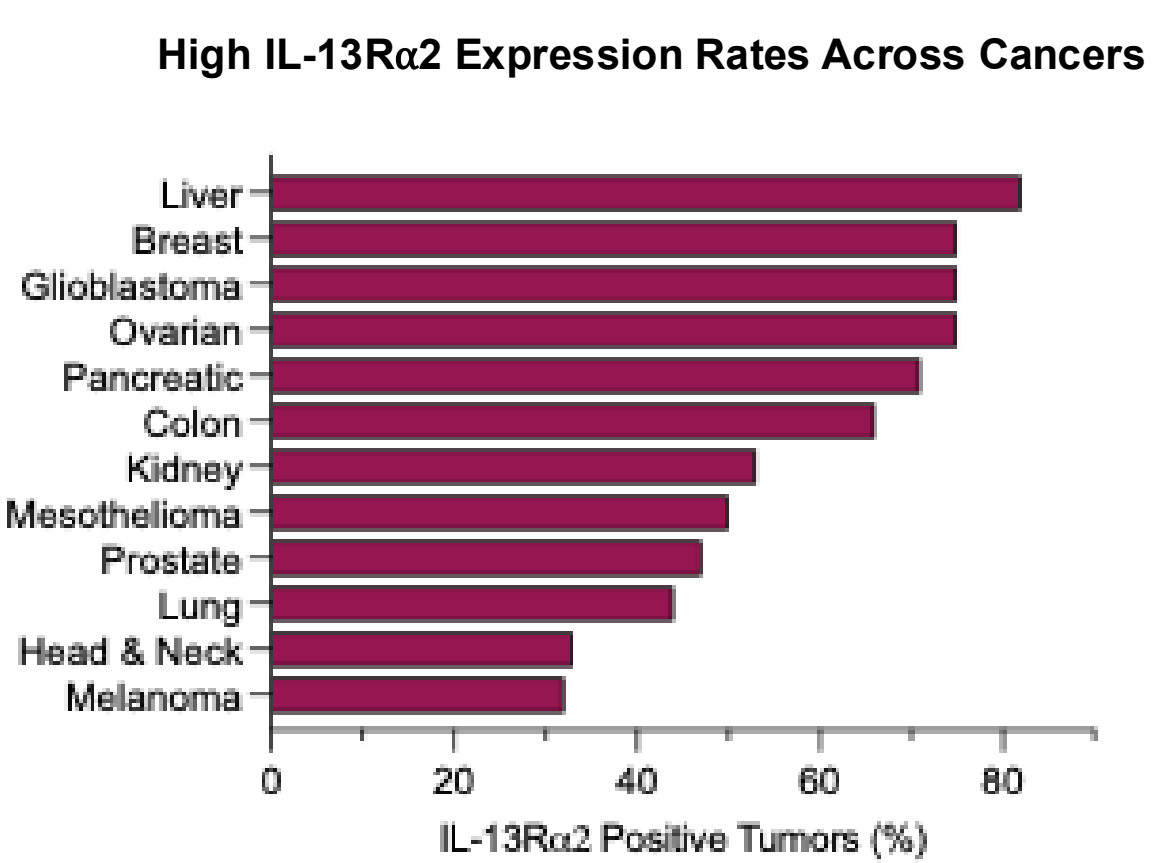
IL-2^{SK} Derived from MDNA11: demonstrating single agent activity in patients with checkpoint resistance

MDNA113: First-in-class

1. Delivering a commercially validated anti-PD-1 inhibitor
2. Supercharging PD-1 with a clinically validated IL-2 superkine
3. Masking IL-2 systemically such that 3 mg/kg Q2W can be administered to saturate PD-1
4. IL-13Rα2 Tumor Targeting: anchoring MDNA113 at the tumor
5. Ensuring activation at the TME by two unmasking mechanisms

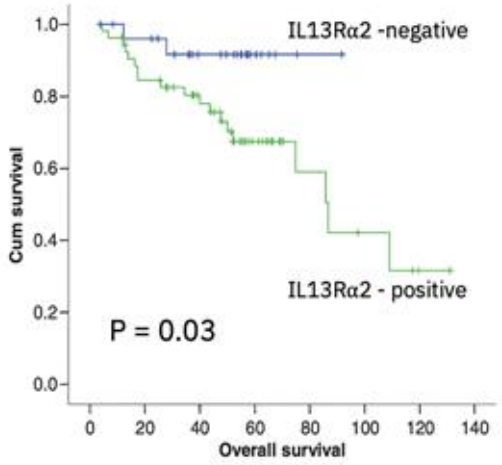
IL-13Rα2 is Expressed in Many Tumors Affecting 2M+ Patients Annually

Blockbuster potential: High IL-13Rα2 expression is associated with poor clinical outcomes, making it an ideal TAA target



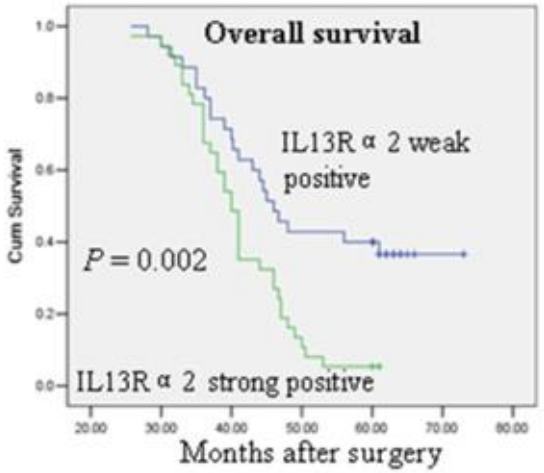
COLON CANCER

Barderas et al., Cancer Res, 2012



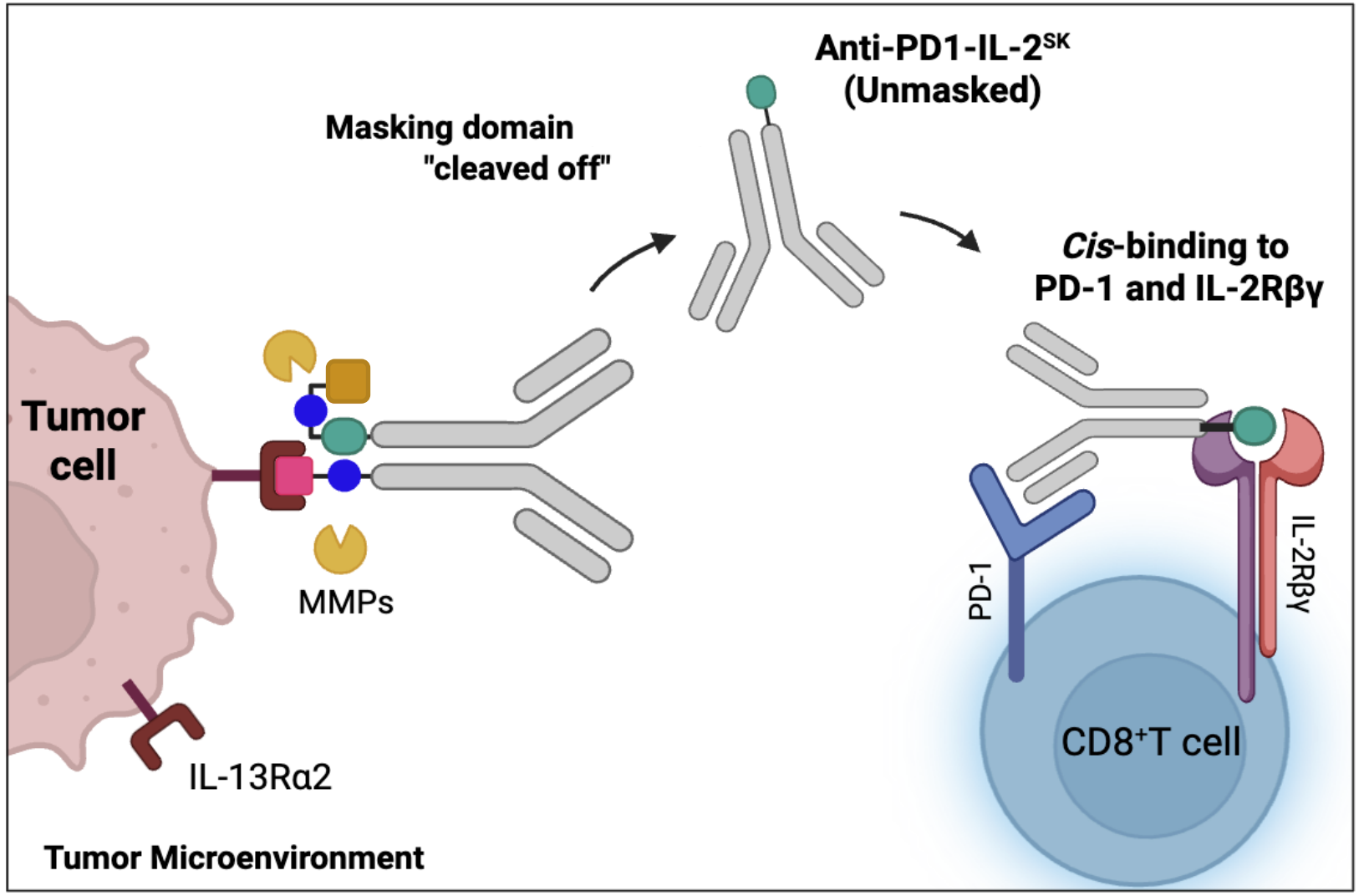
LUNG CANCER

Xie et. al. Oncotarget, 2015

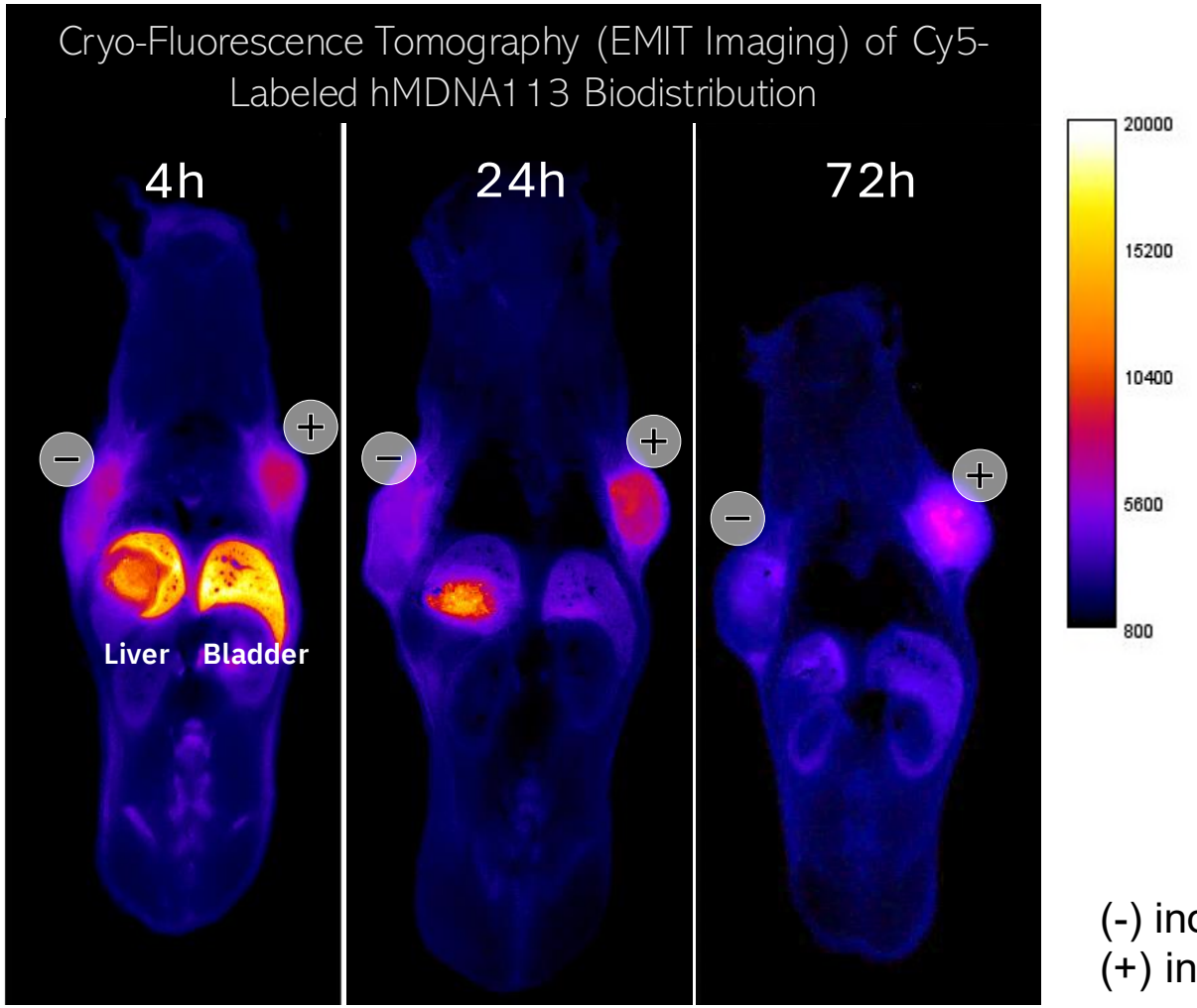


1. Hou et al., J Cancer Res & Clinical oncol (2009); 2. Papageorgis et al., Br Cancer Res (2015); 3. Joshi et al., Cancer Res (2000); 4. Kioi et al., Cancer (2006); 5. Shimamura et al., Clin Cancer Res (2010); 6. Barderas et al., Cancer Res (2012); 7. Kang et al., J Per Med (2021); 8. Oncomine Cancer MicroArray (OMCA Database); 9. Nagai et al., Cancer Reprots (2023); 10. Xiw et al., Oncotarget (2015); 11. Kawakami et al., Clin Cancer Res (2003); 12. Beardi et al., Clin Cancer Res (2013)

Mechanism 1: MDNA113 is Anchored to IL-13Rα2 and is then Activated in the TME via MMP Cleavage



Tumor-Anchoring: Preferential Tumor Localization and Retention of MDNA113 in IL-13Rα2 Expressing Tumors



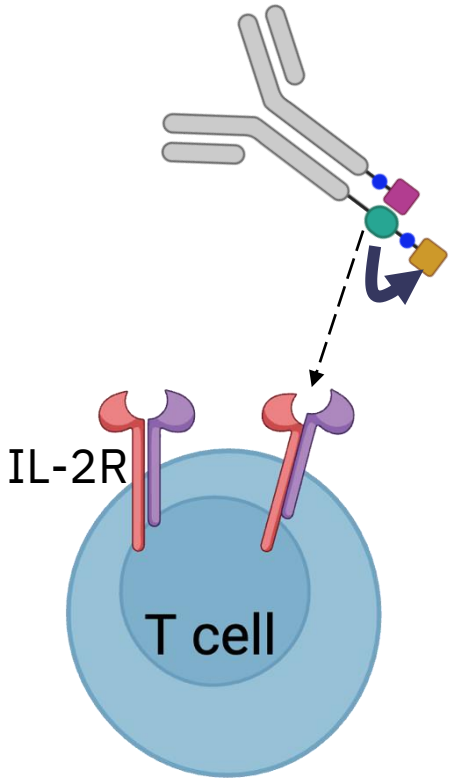
Delivering PD-1 and Unleashing IL-2^{SK}

- MDNA113 is localized to **IL-13Rα2$^{(+)}$ tumors** and anchored for conditional activation

(-) indicates IL-13Rα2-negative
(+) indicates IL-13Rα2-positive tumors

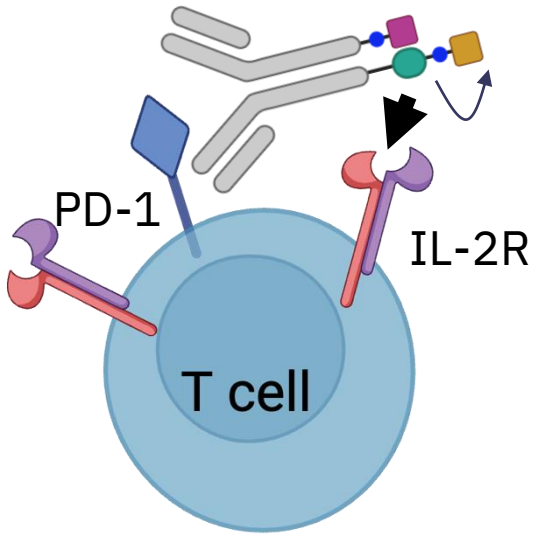
Mechanism 2: cis-Expression of PD-1 and IL-2R on Target Cells Unmasks MDNA113 Without Requirement for MMP Cleavage

Periphery: No PD-1 binding, IL-2 masking intact



PD1^{Neg} CD8^{+} T Cells
(predominantly in circulation)

TME: PD-1 binding enables IL-2 x IL-2R engagement without need for cleavage

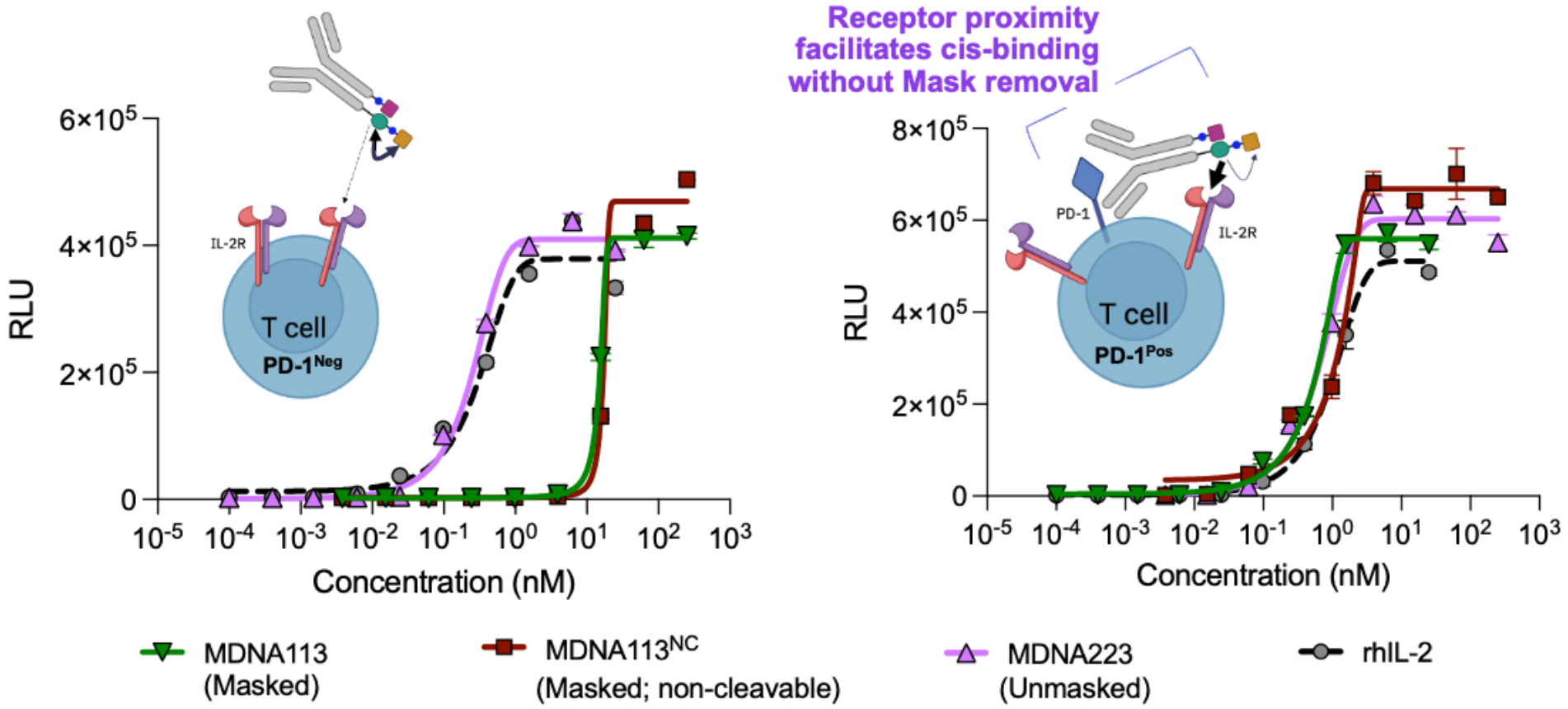


PD1^{Pos} CD8^{+} T Cells
(predominantly within TME)

Mechanism 2: cis-Expression of PD-1 and IL-2R on Target Cells Unmasks MDNA113 Without Requirement for MMP Cleavage

Periphery: No PD-1 binding, IL-2 masking intact

TME: PD-1 binding enables IL-2 x IL-2R engagement without need for cleavage

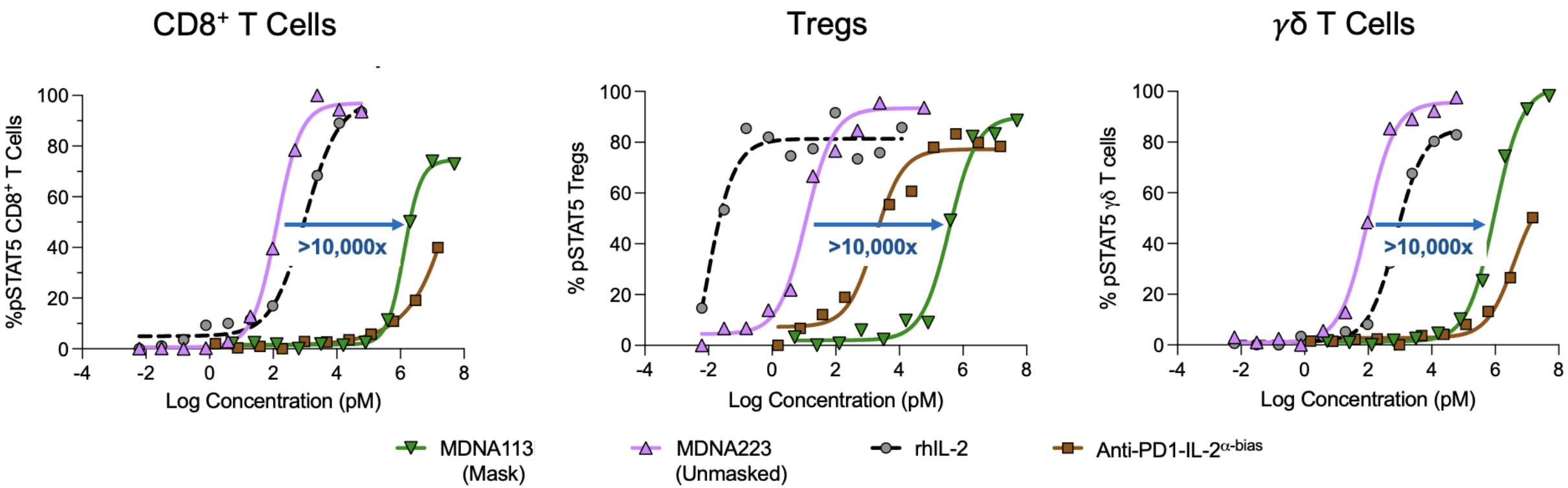


293T-STAT5-Luc2-IL2Rαβγ (left) and 293T-STAT5-Luc2-IL2Rαβγ-PD1 (right) reporter assays. Incubation at 37 °C for ~22 hours and measured relative luminescence unit (RLU)

Differentiation of MDNA113 to other Bifunctional Anti-PD-1-IL-2 Programs

KEY FEATURES	Medicenna MDNA113	Other IL2/anti-PD1 candidates
β-enhanced and not-α IL-2^{SK} (clinically validated)	✓	✗
Tumor Specific Targeting (IL-13Rα2)	✓	✗
Dual conditional activation mechanisms	✓	✗
PD-1/PD-L1 Blockade (clinically validated vs. novel)	✓	✓✗
Cis-binding (IL-2R/PD-1)	✓	✓✗
IL-2^{SK} attenuated in periphery	✓	✓✗
IL-2^{SK} activated in TME	✓	✓✗

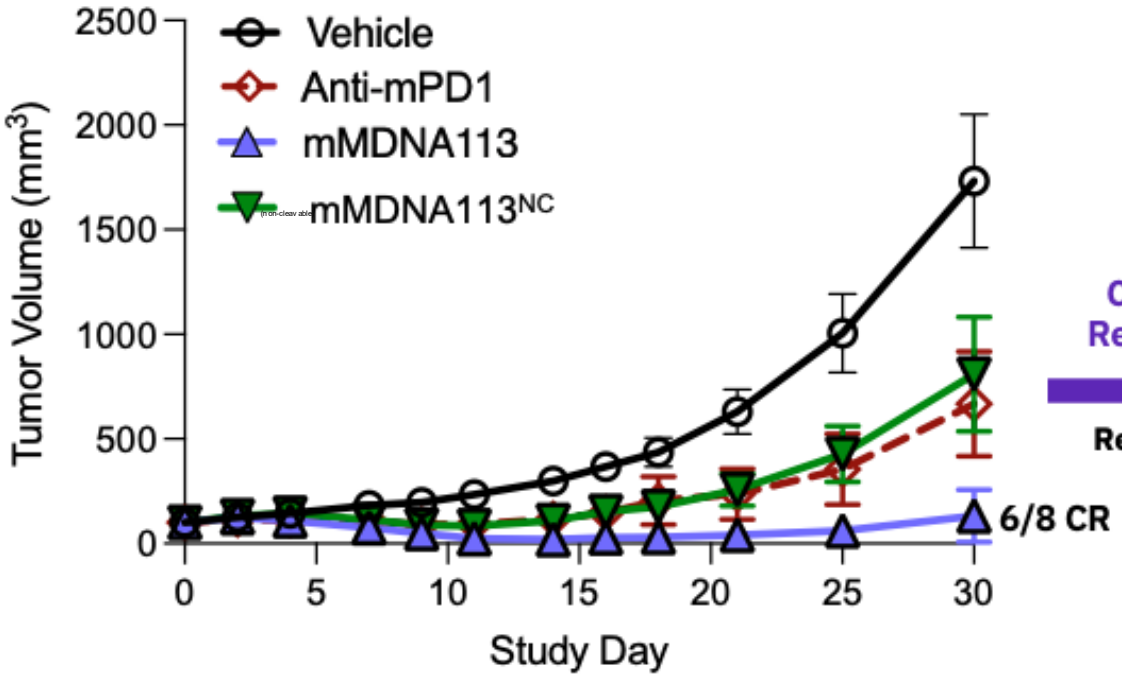
PBMC: 10,000-Fold Blockade of pSTAT5 Signaling in Human PBMCs Demonstrates Superior Masking Capacity



Data from representative normal human PBMC donor. Analysis by flow cytometry; normalized pSTAT5 signal shown

In vivo: MDNA113 Inhibits IL-13Rα2-Expressing MC38 Tumors and Promotes Memory Response Against Tumor Rechallenge

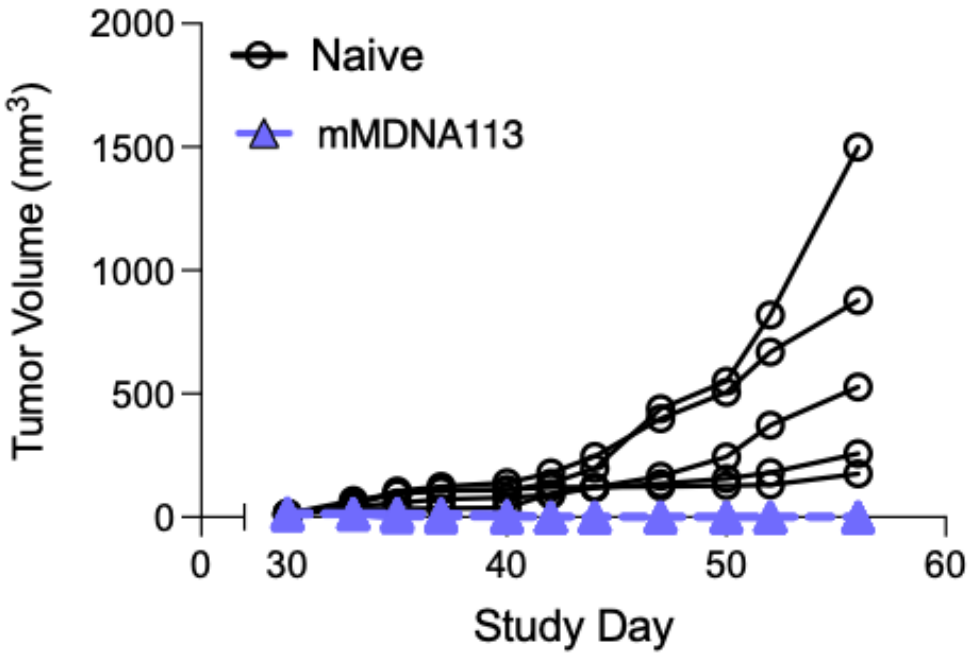
MC38-IL-13Rα2 Colon Tumor Model



Complete Responders

Re-challenge

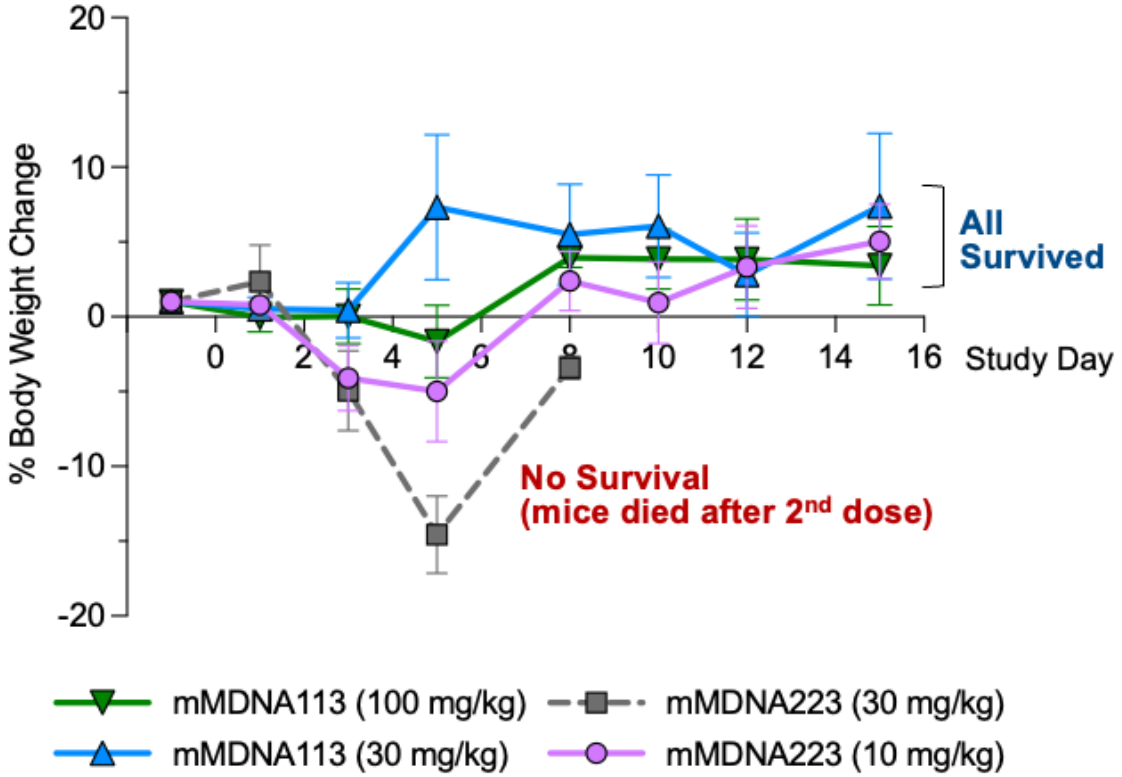
Memory Response



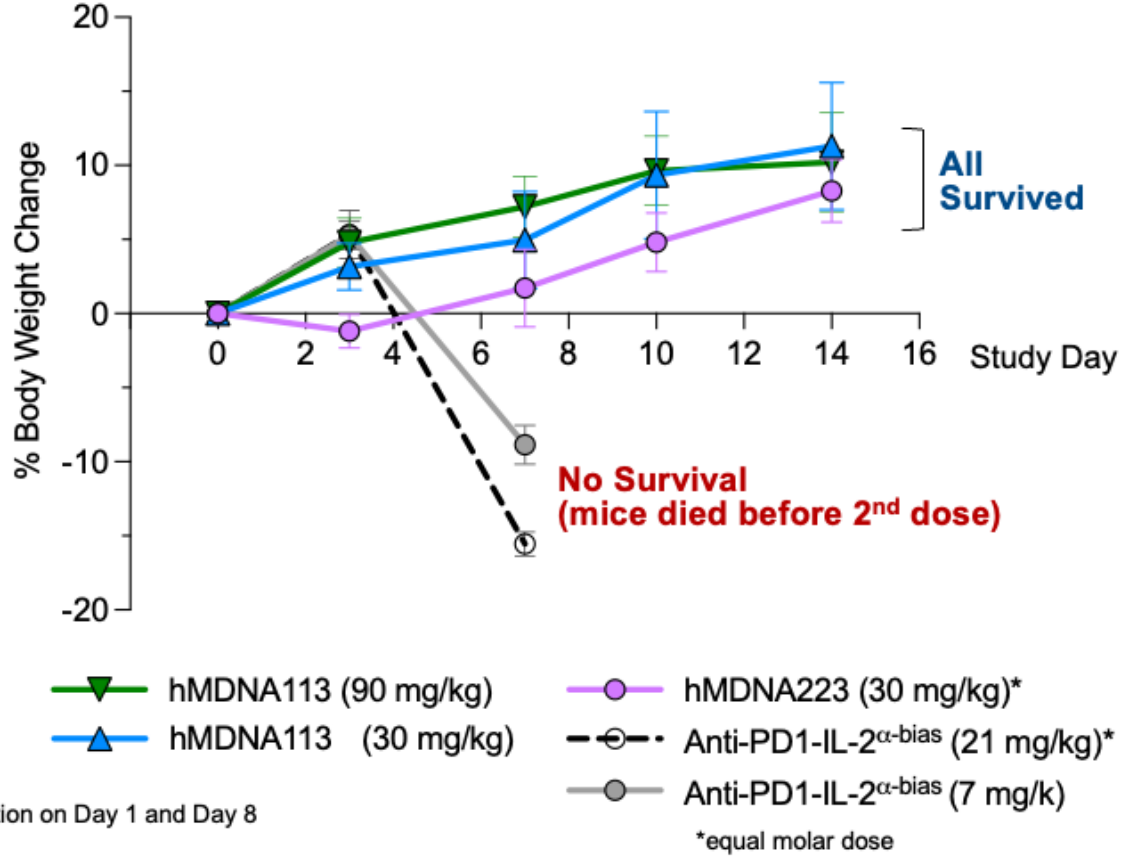
In vivo: MDNA113 was Well Tolerated in Mice up to At least 100 mg/kg

Isolated effect of IL-2R demonstrated poor tolerability of Anti-PD-1-IL-2$^{\alpha\text{-bias}}$ vs. Unmasked MDNA113

mMDNA113 (with anti-mPD1):
(effect of PD1/PDL-1 and IL-2R)



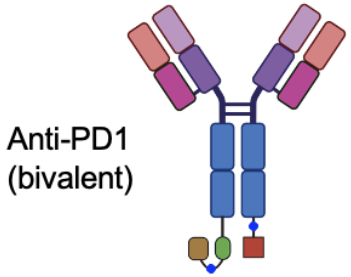
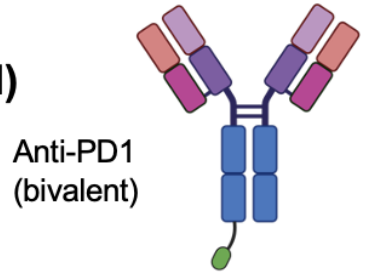
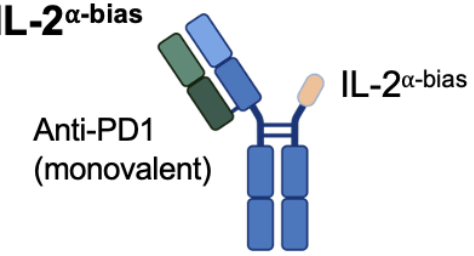
MDNA113 (with anti-hPD1):
(effect of IL-2R only)



Female C57Bl/6 mice treated by IV injection on Day 1 and Day 8

NHP: MDNA113 Was Well-tolerated at Doses up to 50 mg/kg

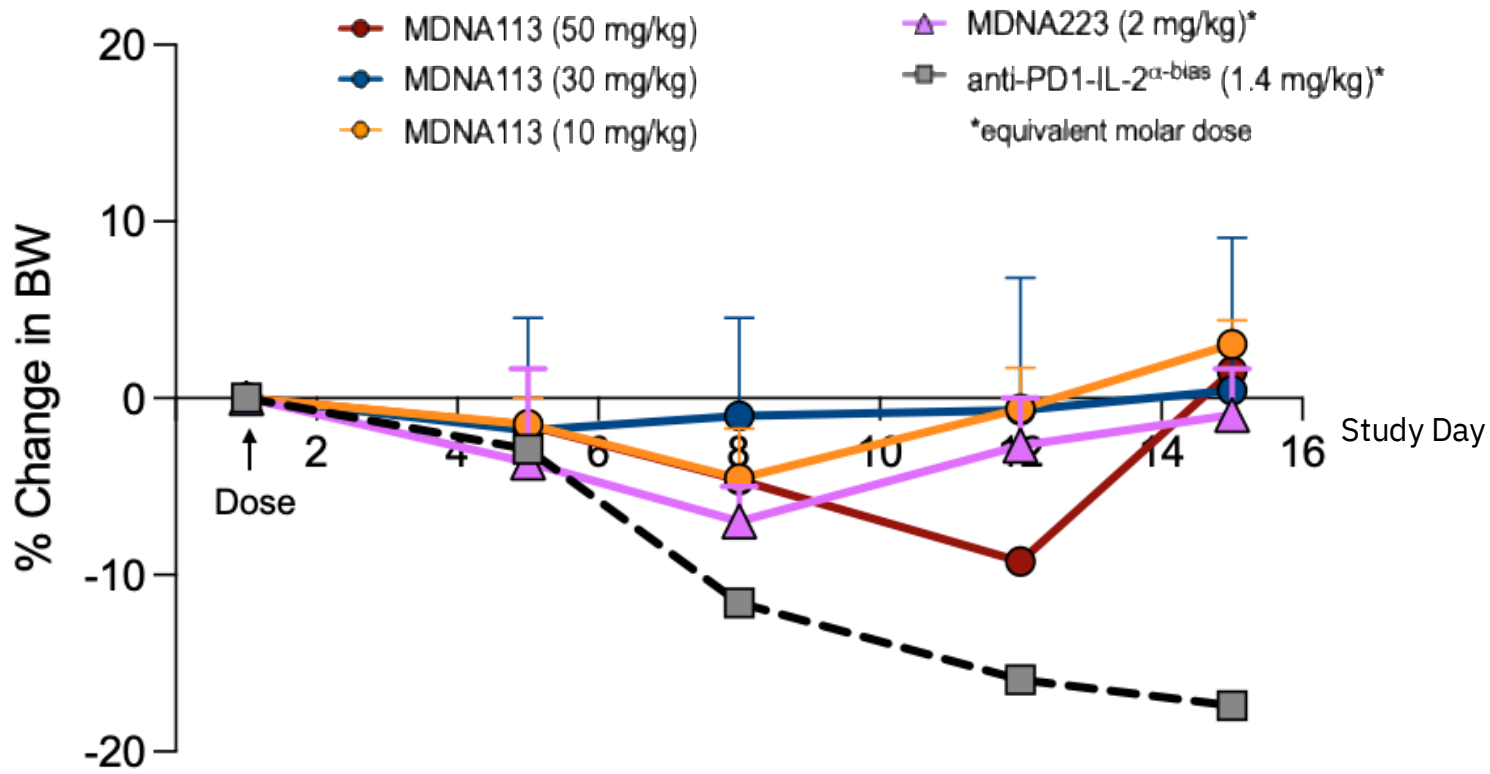
Head-to-Head: Unmasked MDN113 was Better Tolerated vs. Anti-PD-1-IL-2$^{\alpha\text{-bias}}$

Test Construct	Dose	Clinical Observations
MDNA113 (Masked) 	10 mg/kg (n = 2)	1 of 2 monkeys experienced diarrhea (7 days)
	30 mg/kg (n = 2)	No abnormal findings
	50 mg/kg (n = 1)	Monkey experienced diarrhea (7 days)
MDNA223 (Unmasked) 	2 mg/kg (n = 2)	1 of 2 monkeys experienced diarrhea (5 days)
Anti-PD1-IL-2$^{\alpha\text{-bias}}$ 	1.4 mg/kg (n = 1) Equivalent molar dose as MDNA223	Skin erythema in eye and inguinal regions (> 9 days) Decreased appetite (> 9 days) Decreased activity (7 days)

Naive cynomolgus monkeys; IV infusion

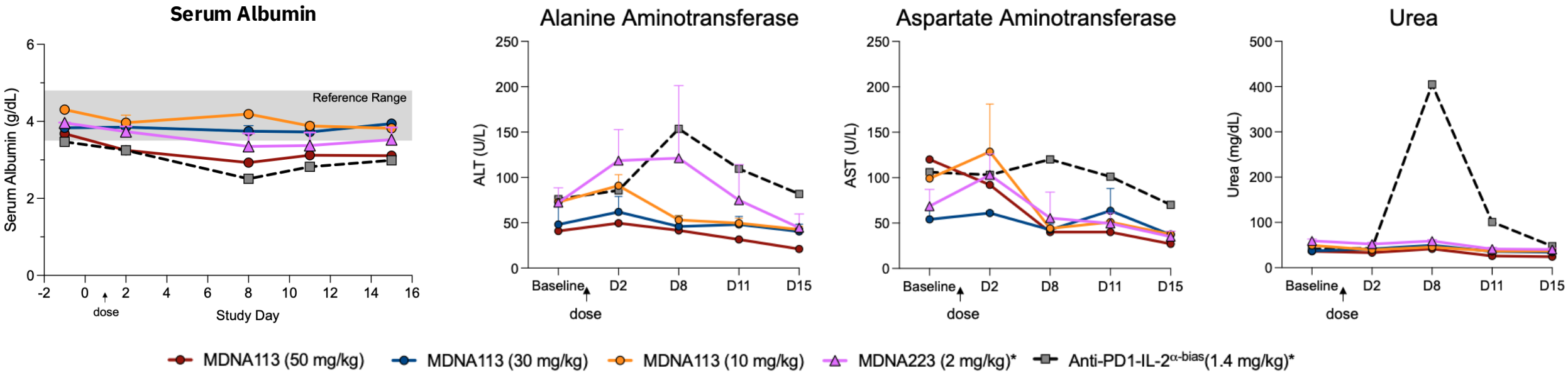
NHP: Body Weight in NHP Maintained with High Dose MDNA113

Head-to-Head: Unmasked MDNA113 was Better Tolerated vs. Anti-PD-1-IL-2$^{\alpha\text{-bias}}$



NHP: MDNA113 has Minimal Effect on Serum Albumin, Liver Enzymes and Urea

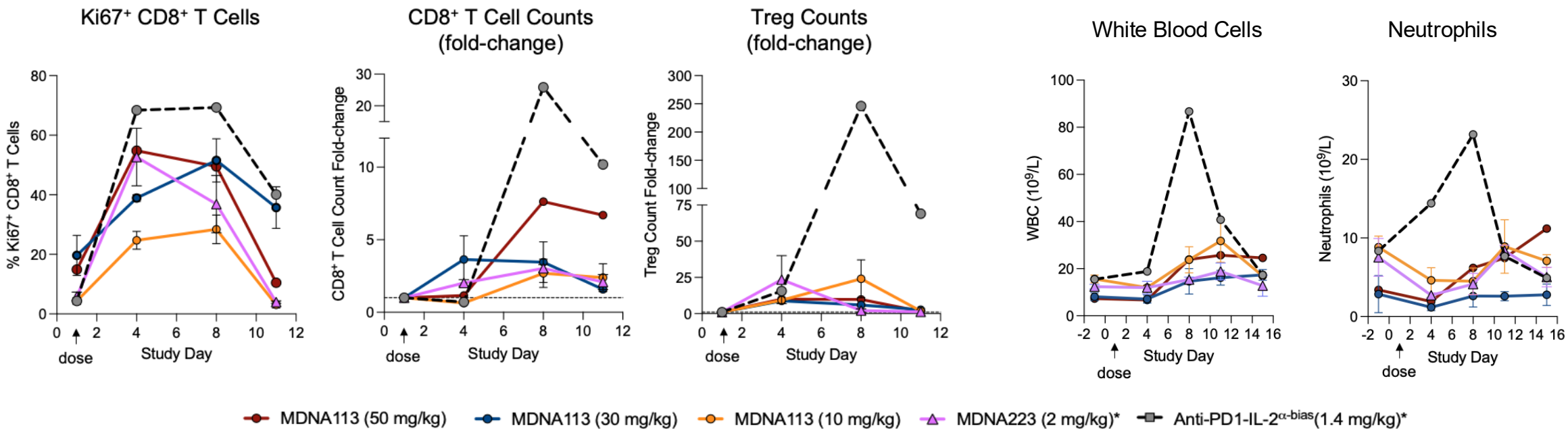
Head-to-Head: Anti-PD-1-IL-2$^{\alpha\text{-bias}}$ Demonstrates Impact on Renal Function



*equal molar dose

NHP Masking: Dampened Systemic Immune Activation in NHP with MDNA113

Head-to-Head: Anti-PD-1-IL-2α-bias Demonstrated Peripheral Activation of Tregs



*equal molar dose

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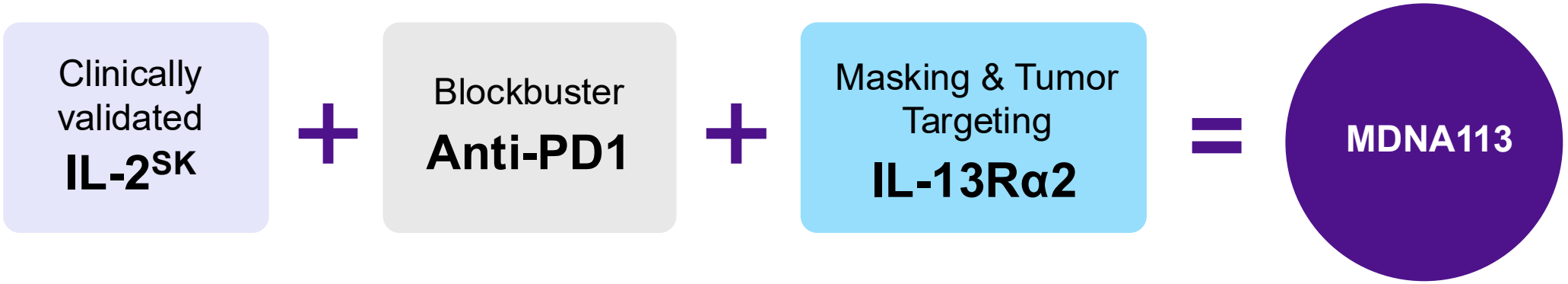

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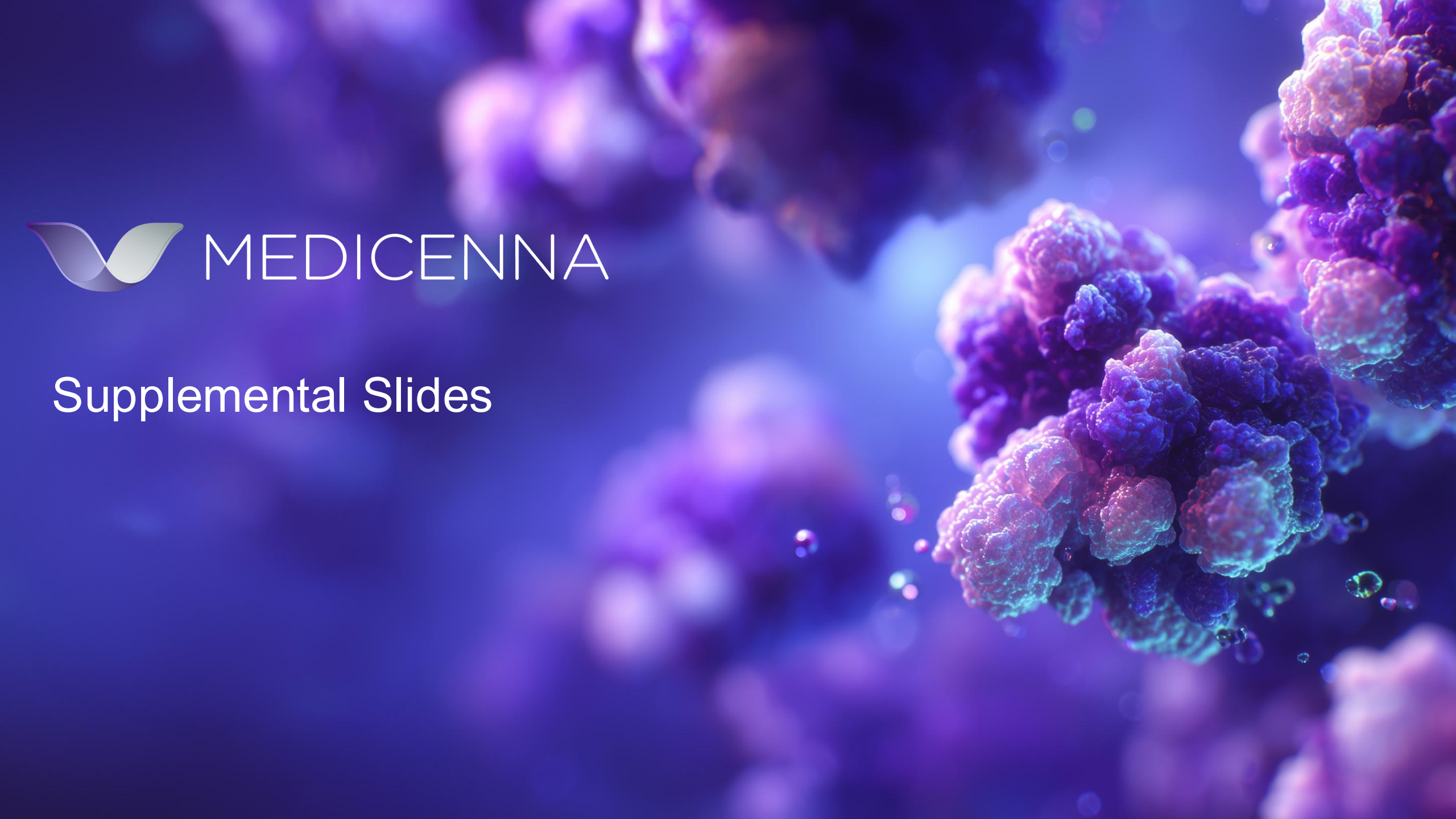
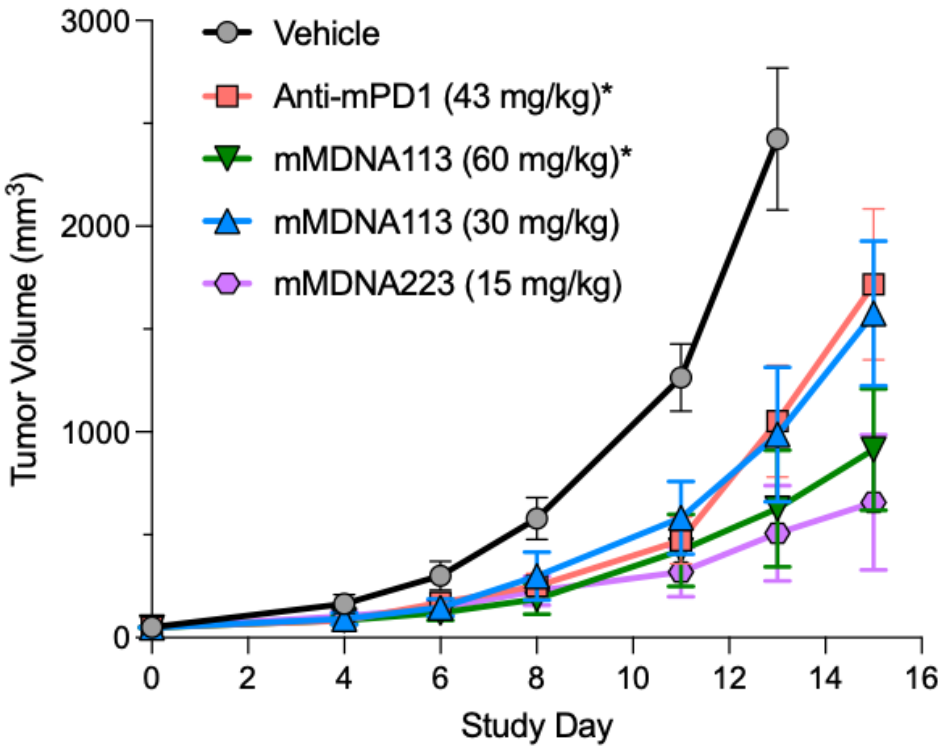


Supplemental Slides

In vivo: MDNA113 Enhances Infiltration of Functionally Active CD8⁺ T Cells in the B16F10/IL-13Rα2 Melanoma Model

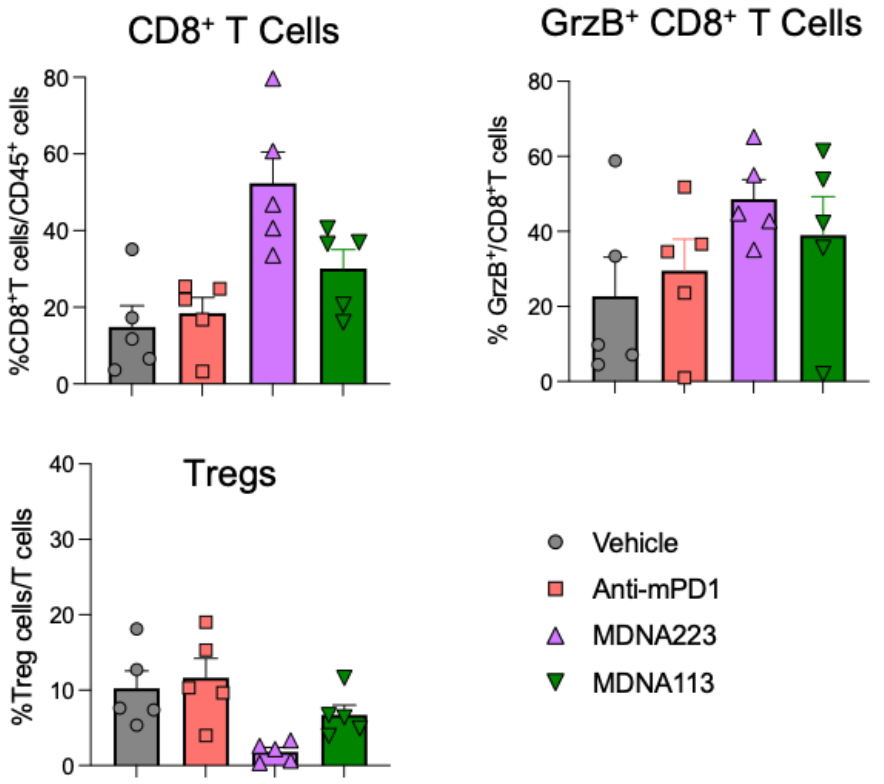
No Increase in Tregs

B16F10 Melanoma Model



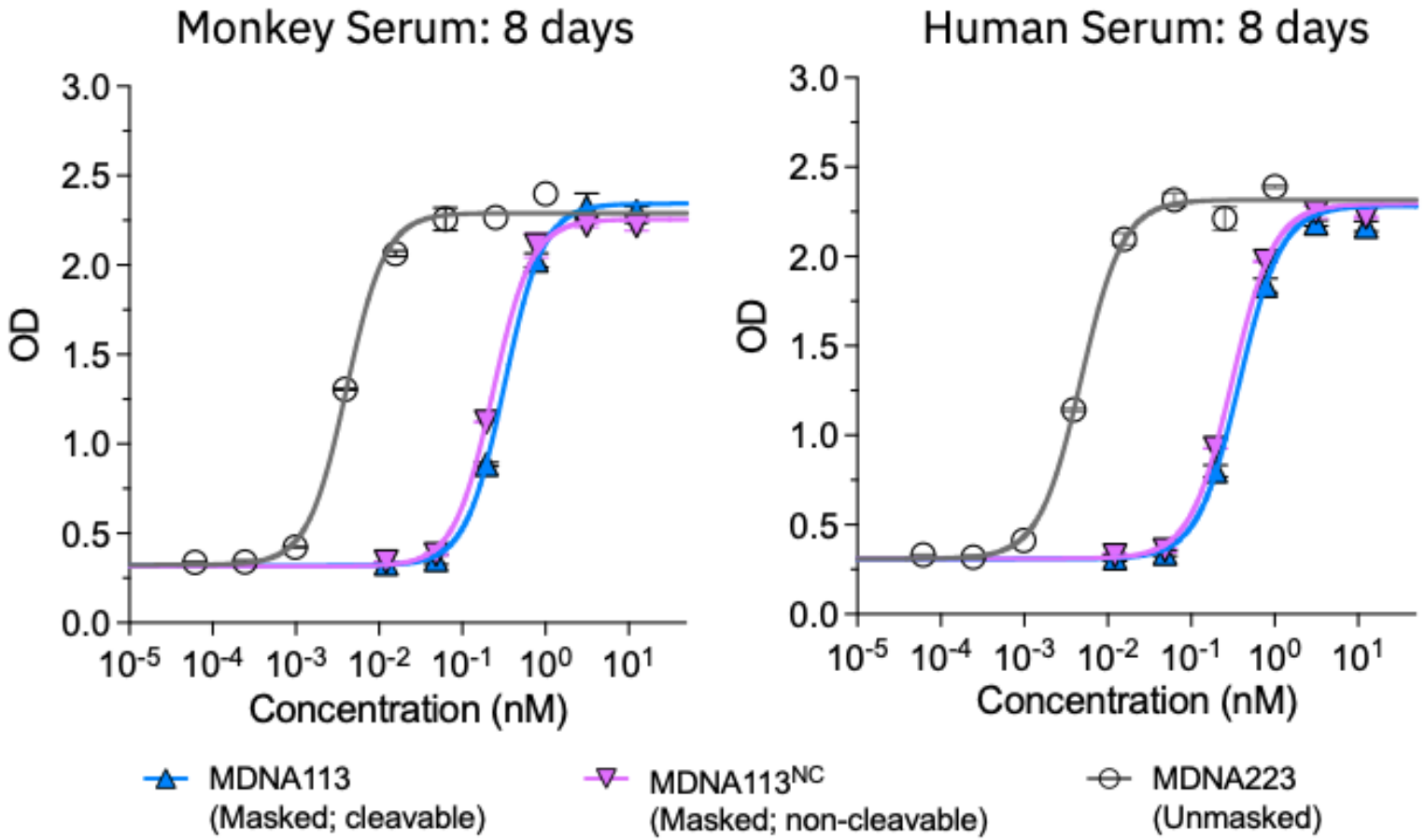
B16F10 tumor size of 70 mm³ at start of treatment; IV (Day 1 & 8)
*Equal molar dose of test articles used

Tumor Infiltrating Immune Cells



Mice with B16F10/IL-13Rα2 tumors (150 mm³) received 1 dose by IP injection.
Molar-equivalent dose of 10 mg/kg. Tumors harvested on Day 8 for flow cytometry

Masking: No Linker Cleavage Following Prolonged Incubation in Normal Sera



Constructs incubated in pooled normal serum at **37 ºC for 8 days** and evaluated for JAK-STAT activation in HEK-Blue IL-2Rαβγ reporter cells.

MDNA113 Pharmacokinetics Consistent with Approved Anti-PD-1 Therapies