

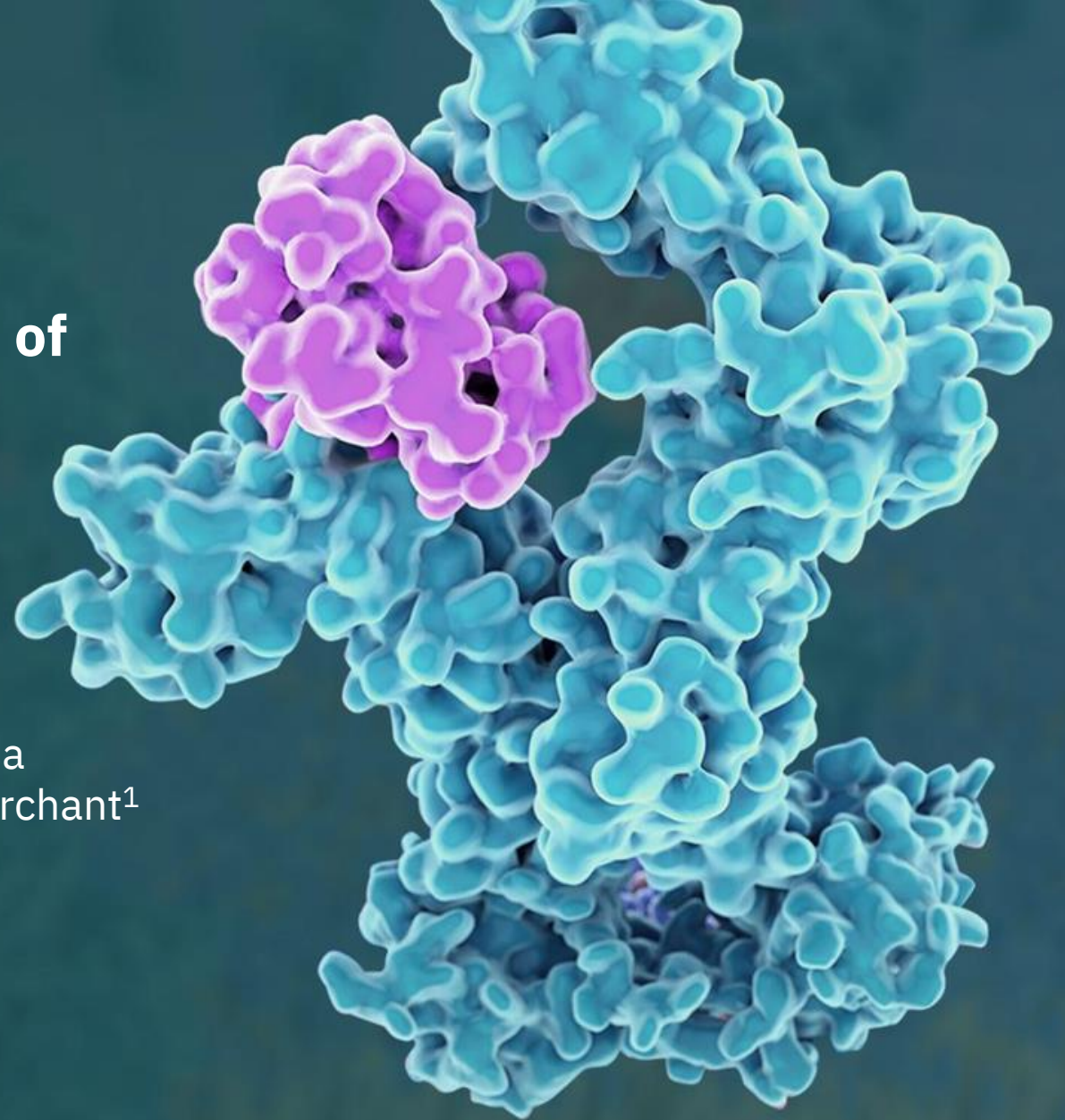
AACR IO 2025

Pharmacokinetics and Pharmacodynamics of MDNA11, a Long-acting IL-2 Superkine, as Single Agent and in Combination with Pembrolizumab in Patients with Advanced Solid Tumors

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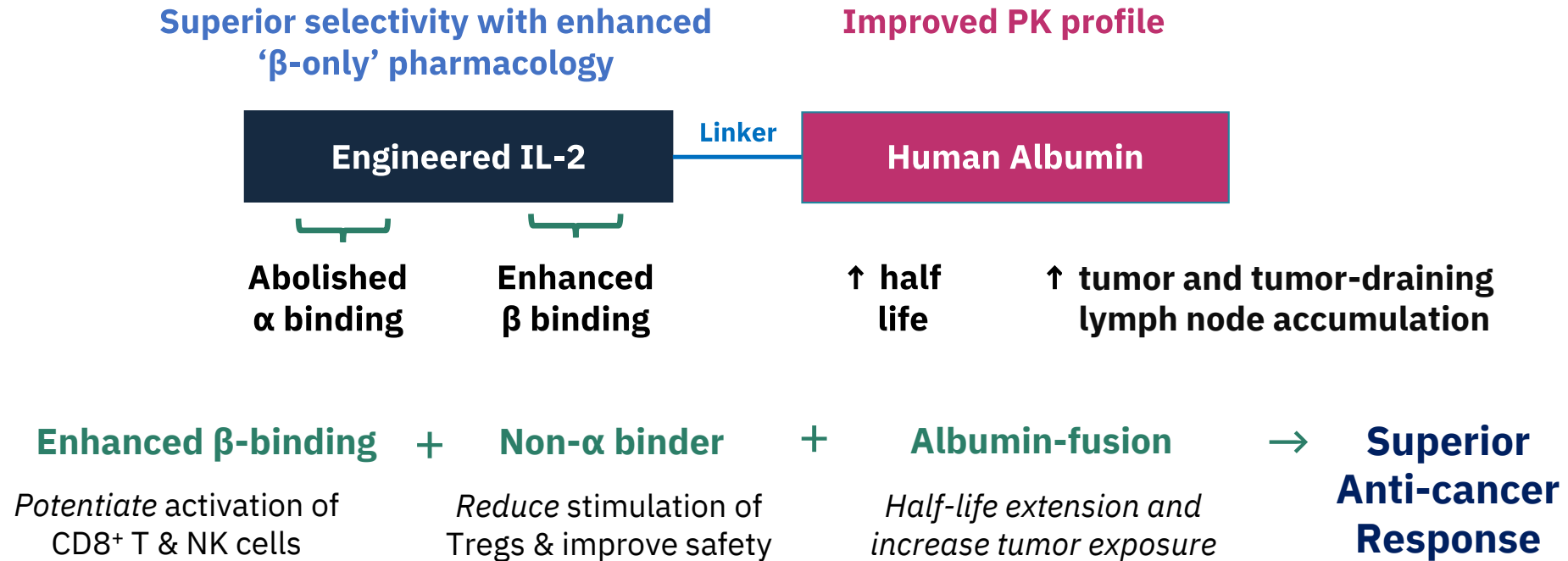
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MDNA11: A Long-acting 'β-enhanced Not-α' IL-2 Superkine

Engineered to overcome key limitations of high dose IL-2



MDNA11 demonstrated a favorable safety profile and promising anti-tumor activity as a single agent and in combination with pembrolizumab

(Yavari et al., Melanoma Bridge 2024; To et al., SITC 2024)



ABILITY-1: FIH Trial of MDNA11 in Advanced Solid Tumors

ABILITY-1: **A** Beta-only **IL-2** Immuno**T**herap**Y** Study (NCT05086692)

Parts 1 and 2: MDNA11 Dose Escalation/Evaluation (Phase 1)

Part 1

Monotherapy in advanced solid tumors progressed on SoC

Solid tumors:

- Melanoma
- NSCLC
- PDAC
- Ovarian cancer
- Tonsillar SCC
- GEJ Adenocarcinoma

3-30 µg/kg cohorts

no DLT, Q2W

60 µg/kg cohort*

no DLT, Q2W

90 µg/kg cohort

no DLT, Q2W **RDE**

120 µg/kg cohort

no DLT Q2W/Q3W

Part 2

Combination with pembrolizumab in advanced solid tumors

Solid tumors:

- Endometrial
- NSCLC
- SCC
- Ovarian cancer
- Pleural mesothelioma
- TNBC
- Esophageal cancer
- Gastric
- Testicular

60 µg/kg cohort*

no DLT, Q2W

90 µg/kg cohort

no DLT, Q2W

120 µg/kg cohort

no DLT, Q2W/Q3W

Enrolling at 120 µg/kg Q3W in Monotherapy & Combination

*lowest dose with observed objective response

Part 3 and 4: MDNA11 Dose Expansion (Phase 2)

Part 3

Monotherapy in advanced solid tumors progressed on SoC

Solid tumors:

- Melanoma
- MSI-H cancer
- Non-melanoma skin cancers

MSI-H / dMMR Cohort

TMB-H Cohort

Cutaneous Melanoma Cohort

anti-PD(L)1 experienced

Virally Associated Tumor Cohort

Part 4

Combination with pembrolizumab in advanced solid tumors

Anticipated to start in H1/2025

MSI-H / dMMR Cohort

TMB-H Cohort

Cutaneous Melanoma Cohort

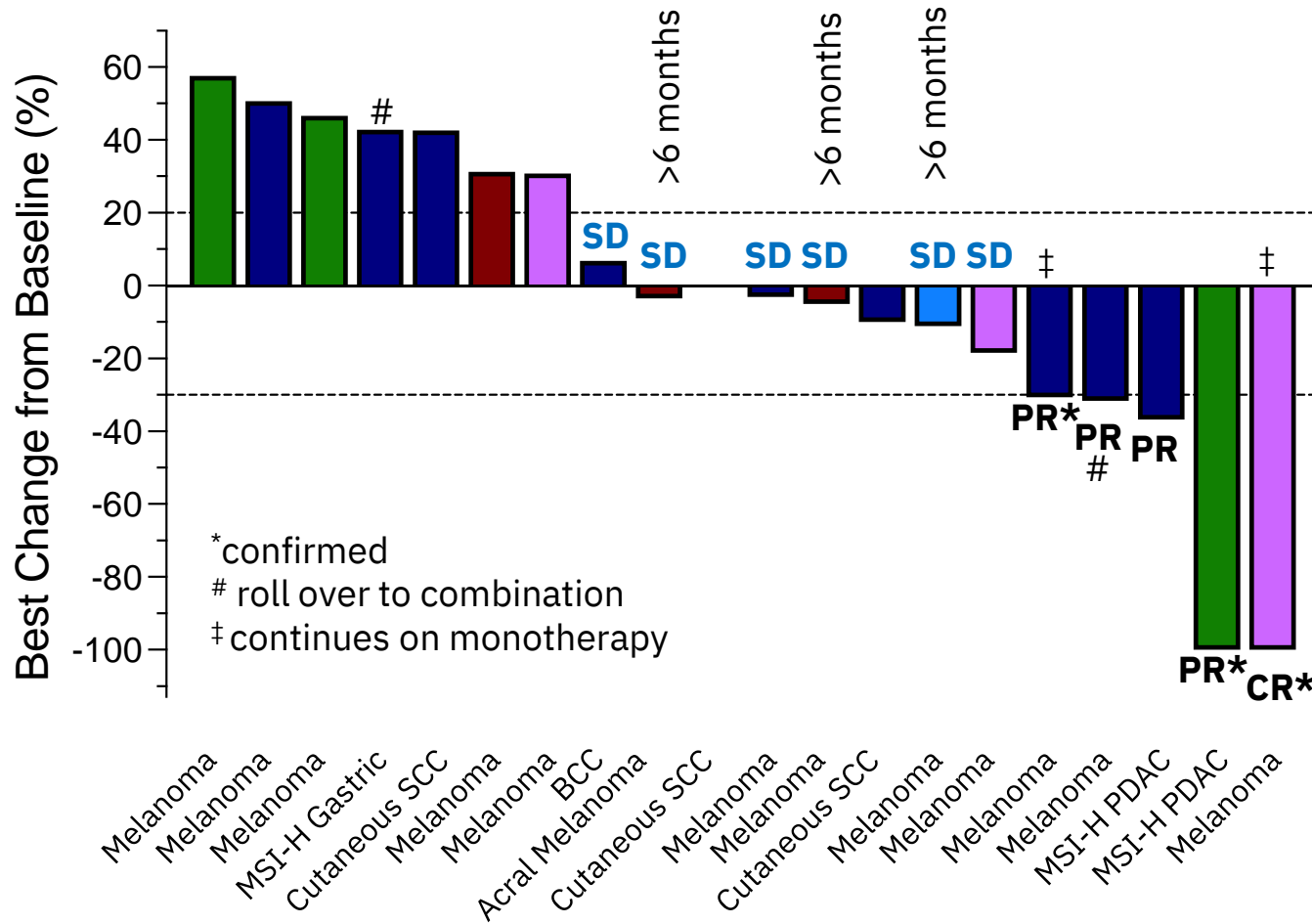
anti-PD(L)1 experienced

Gynecological Cancer Cohort



MDNA11 Shows Monotherapy Clinical Activity in Patients Refractory to CPI

Best response on Phase 2 Eligible, CPI resistant Patients Treated with MDNA11 \geq 60 μ g/kg



Objective Response Rate (ORR):

- 5/20 (25%) [95% CI: 6-44]
 - 1 Complete Response
 - 4 Partial Responses

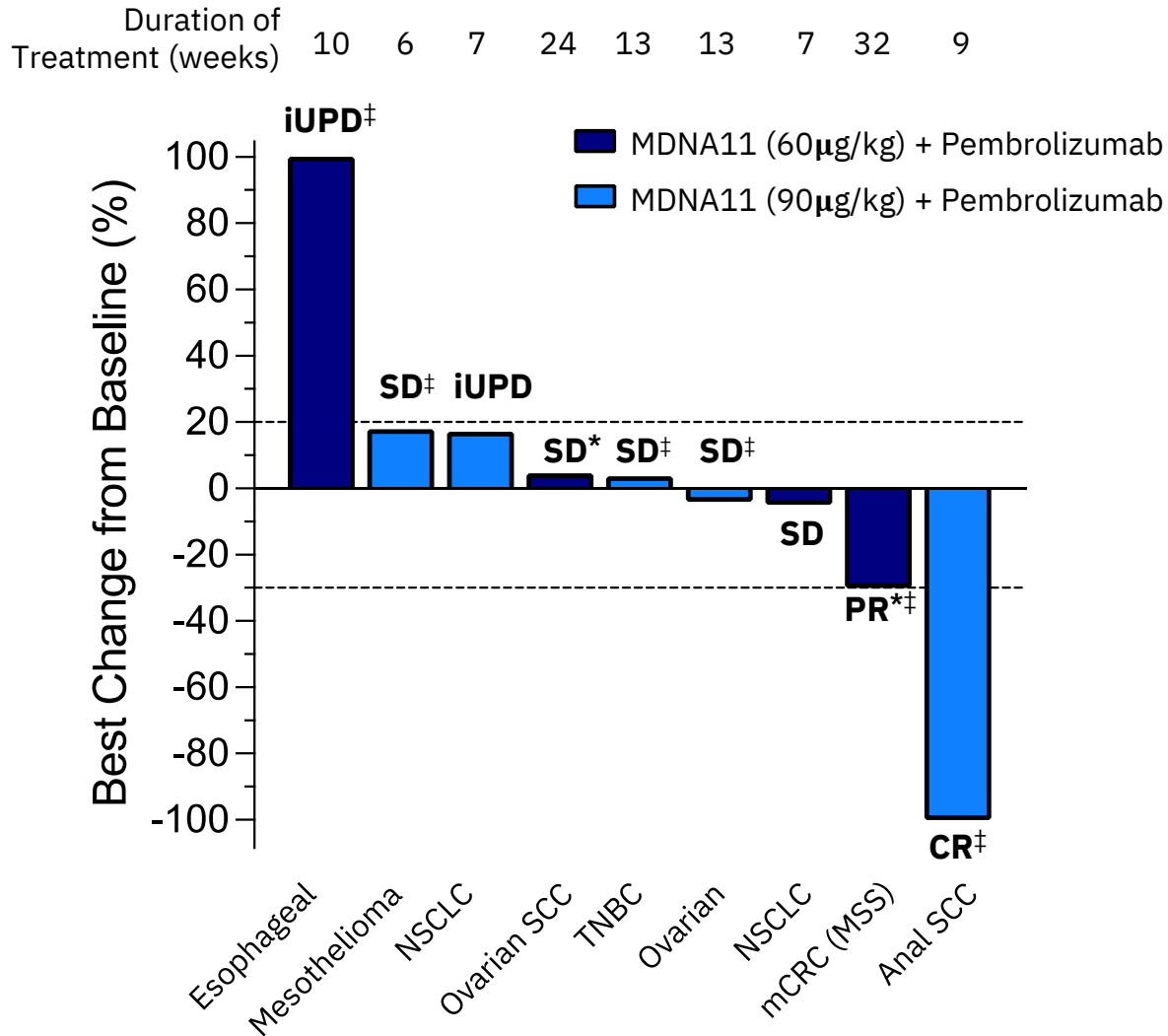
Clinical Benefit Rate:

- 8/20 (40%)
 - 1 Complete Response
 - 4 Partial Responses
 - 6 Stable Disease, including 3 for > 6 months

- Monotherapy expansion (90 μ g/kg)
- 120 μ g/kg
- 90 μ g/kg
- 60 μ g/kg
- 10, 30, 60, 90 μ g/kg (intra-patient dose escalation)



MDNA11 + Pembrolizumab Shows Clinical Activity in Less Immunologically Responsive Tumor Types



➤ CR in 70 yr M with anal SCC

- Progressed on 2 prior lines of treatment (1L capecitabine/mitomycin + radiation; 2L carboplatin/paclitaxel)

➤ Confirmed PR in 52 yr F with MSS mCRC

- Progressed on 2 prior lines of chemotherapy (1L folinate/fluorouracil/oxaliplatin; 2L capecitabine)

➤ Combination dose escalation continues

MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W

*confirmed; ‡ continues treatment

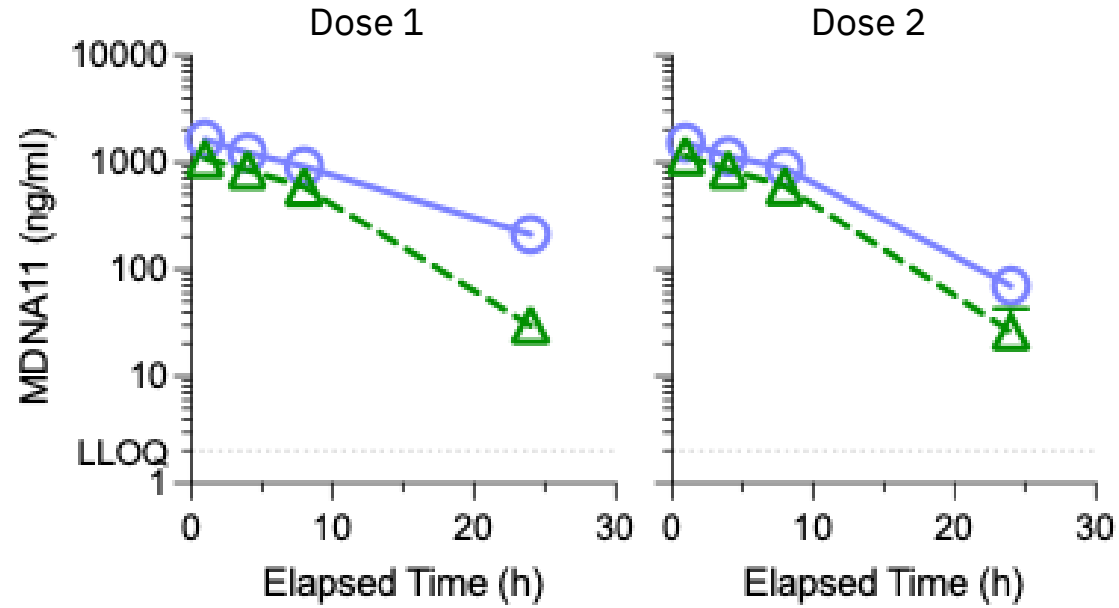
Data cut-off: November 18, 2024

This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.



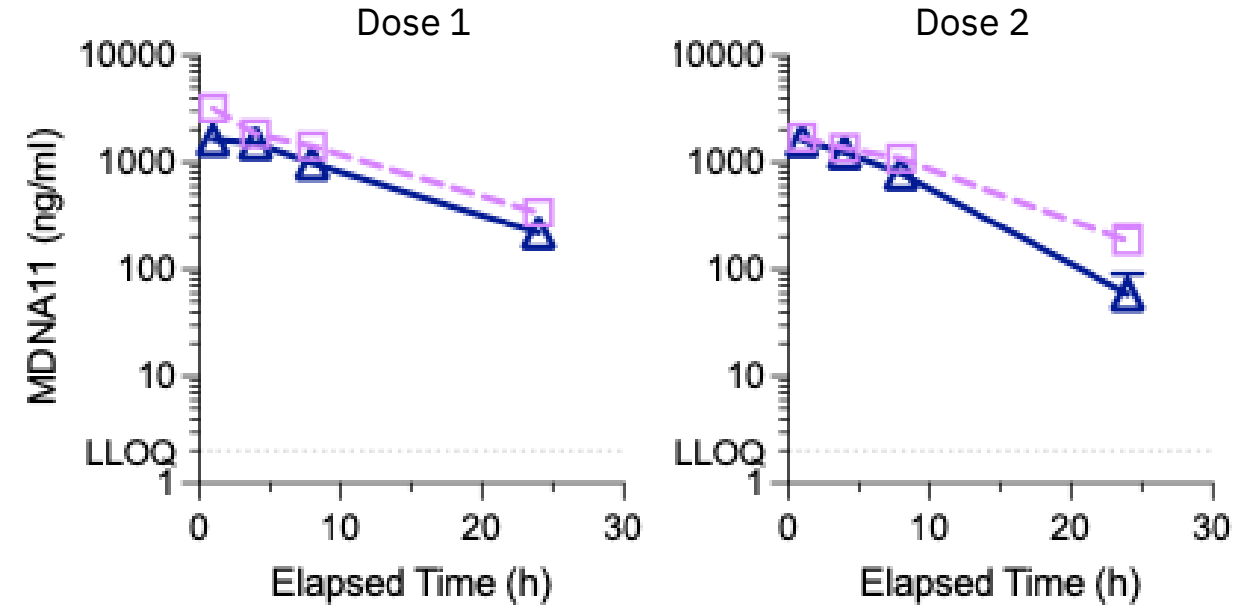
MDNA11 PK Profiles Are Consistent Across Repeated Dosing

60µg/kg MDNA11 Cohorts



- MDNA11 (n=6)
- MDNA11 + Pembrolizumab (n=4)

90µg/kg MDNA11 Cohorts



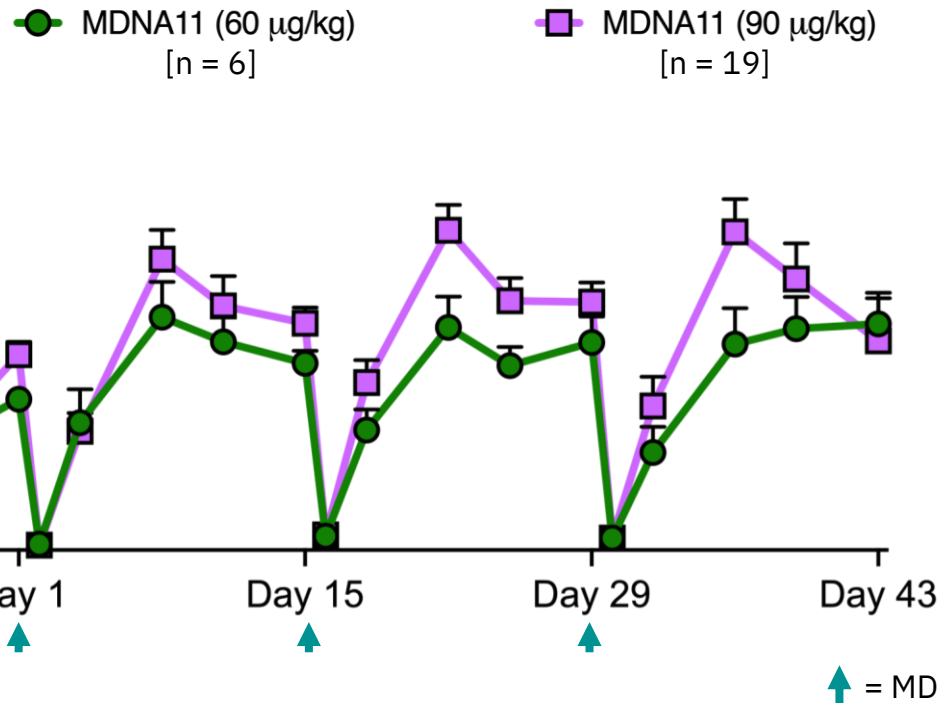
- MDNA11 (n=8)
- MDNA11 + Pembrolizumab (n=4)

Data shown for MDNA11 target Dose cycle 1&2 and represents Mean ± SEM
MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W

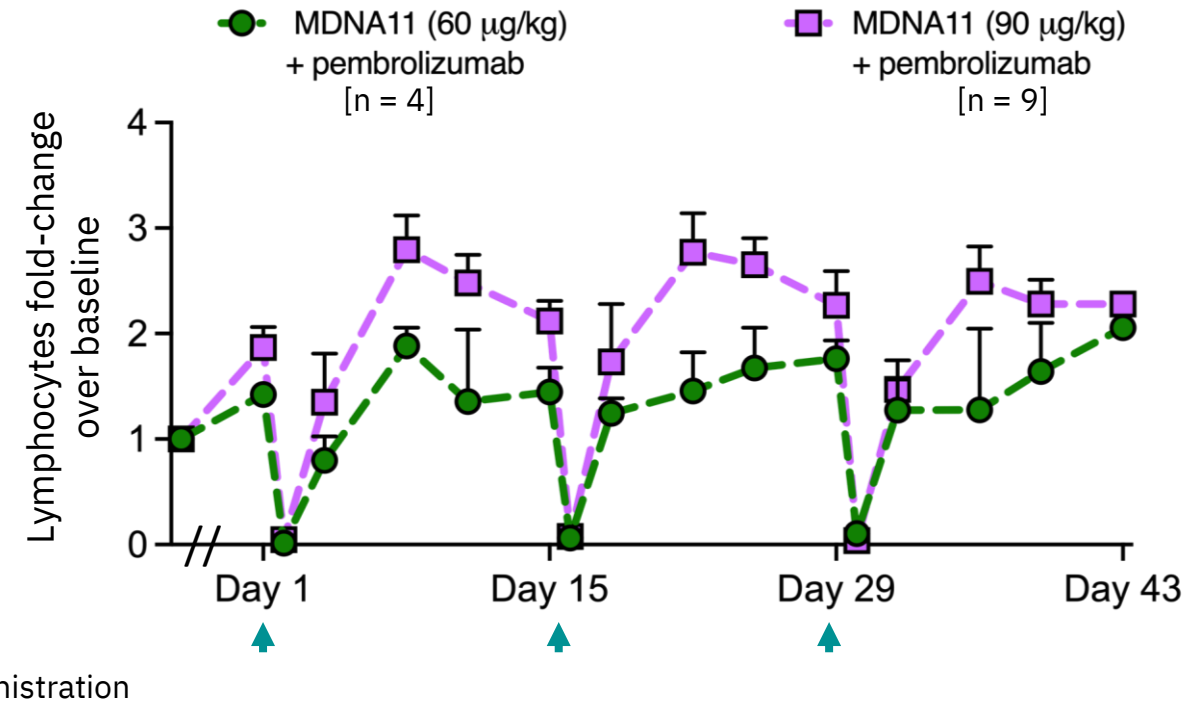


Dose-dependent Lymphocyte Expansion Sustained with Repeat Dosing

MDNA11 Monotherapy



MDNA11 + Pembrolizumab



Lymphocyte counts elevated above baseline for >14 d after each MDNA11 dose whether given as single agent or in combination with pembrolizumab

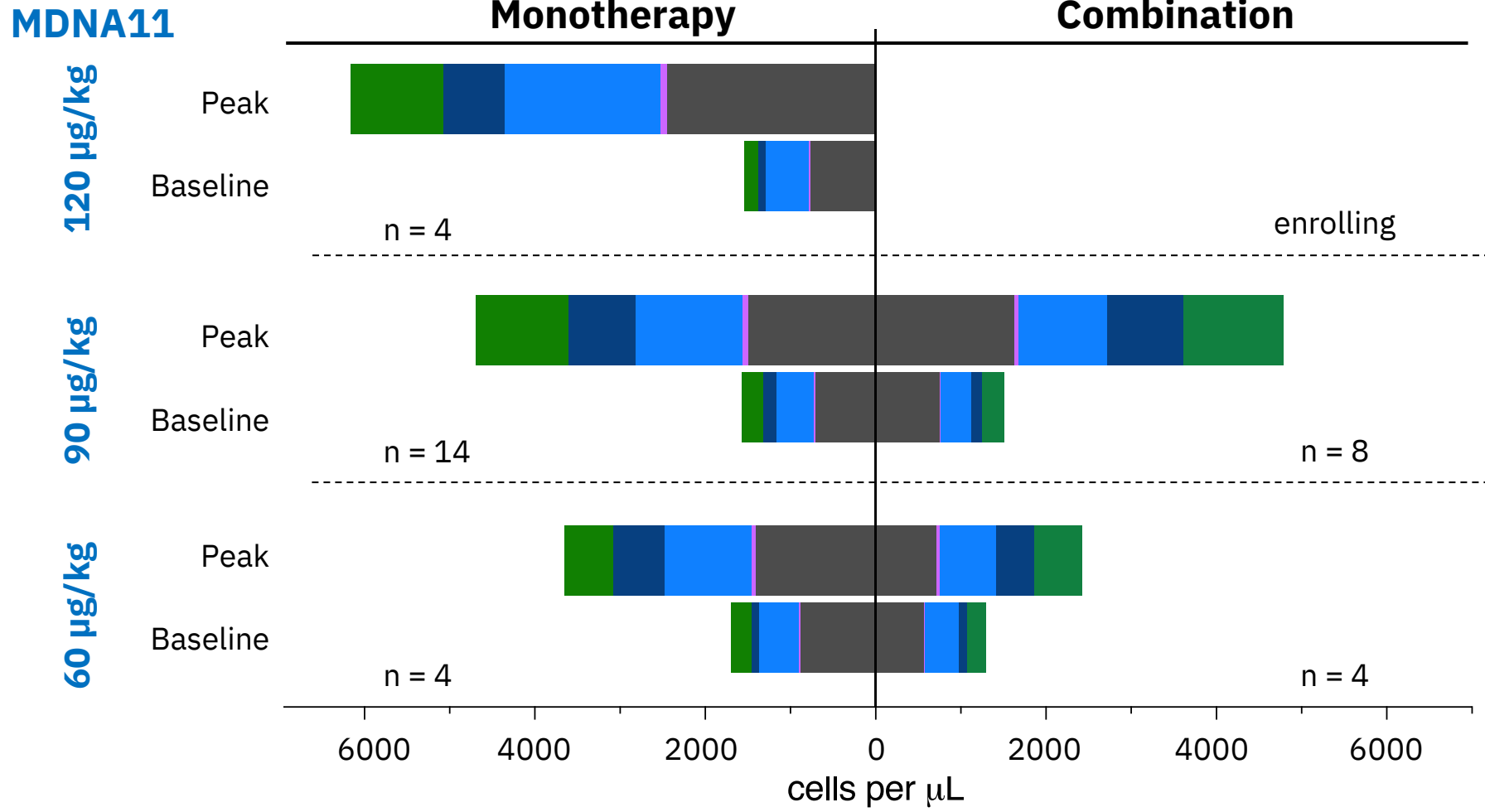
Data represents Mean ± SEM

MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W



Dose-Dependent Expansion of CD8+ T and NK cells

■ CD8+ T Cells
 ■ NK Cells
 ■ Tregs
 ■ CD4+ T Cells
 ■ Other CD45+ Cells



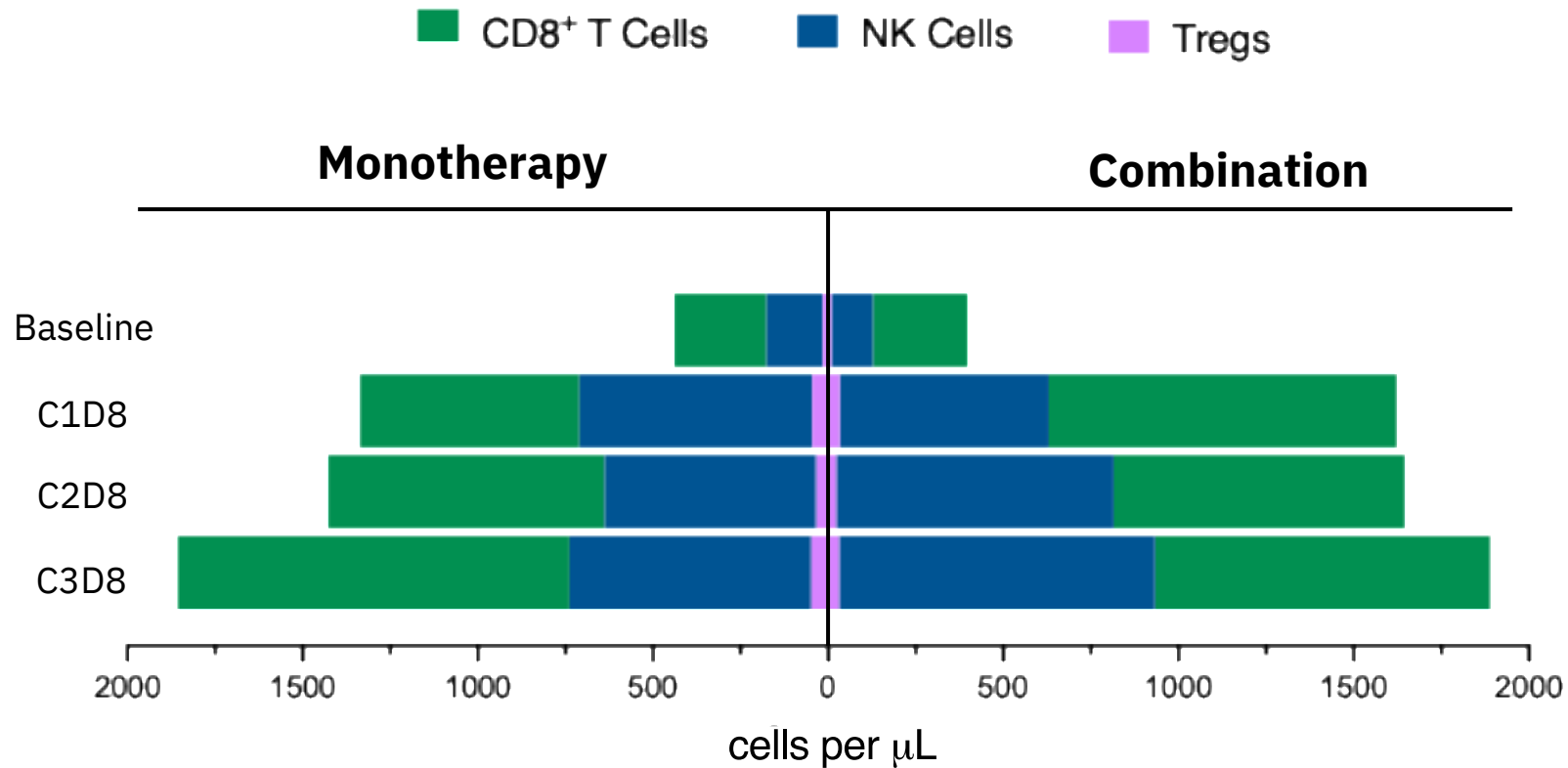
MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W



Sustained Expansion of CD8+ T and NK cells Over Multiple Cycles

MDNA11

90 µg/kg



C1D8 = Cycle 1 Day 8; C2D8 = Cycle 2 Day 8; C3D8 = Cycle 3 Day 8

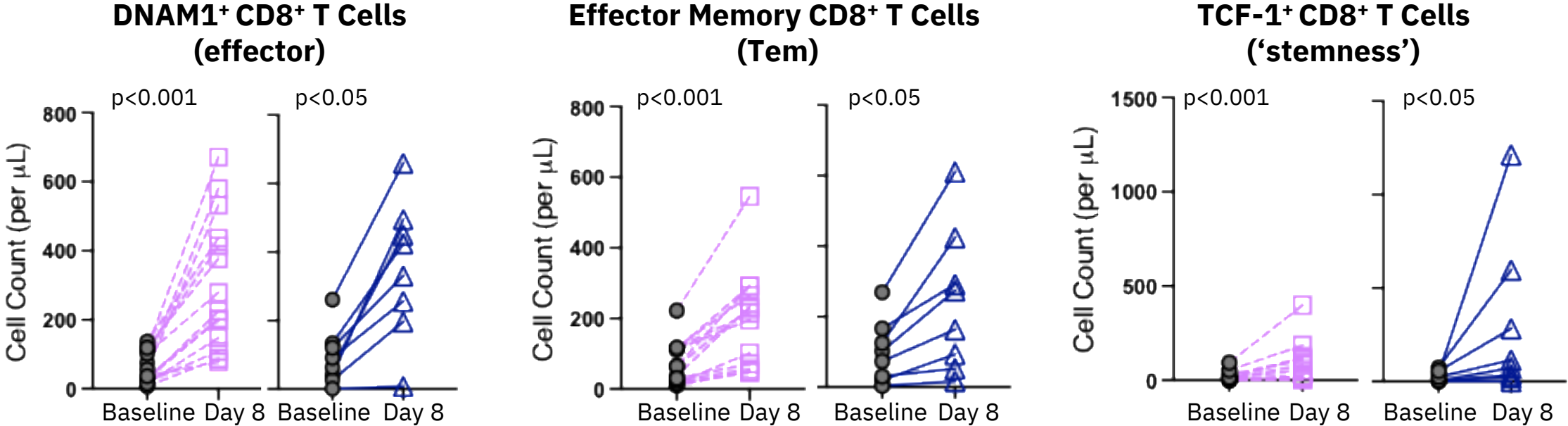
Monotherapy: Baseline (n = 12), C1D8 (n = 12), C2D8 (n = 8), C3D8 (n = 6)

Combination: Baseline (n = 8), C1D8 (n = 8), C2D8 (n = 7), C3D8 (n = 5)

MDNA11 is dosed at Q2W ; 400mg of pembrolizumab is administered Q6W



MDNA11 ± Pembrolizumab Expands Effector, Memory and ‘Stem-like’ CD8+ T Cells



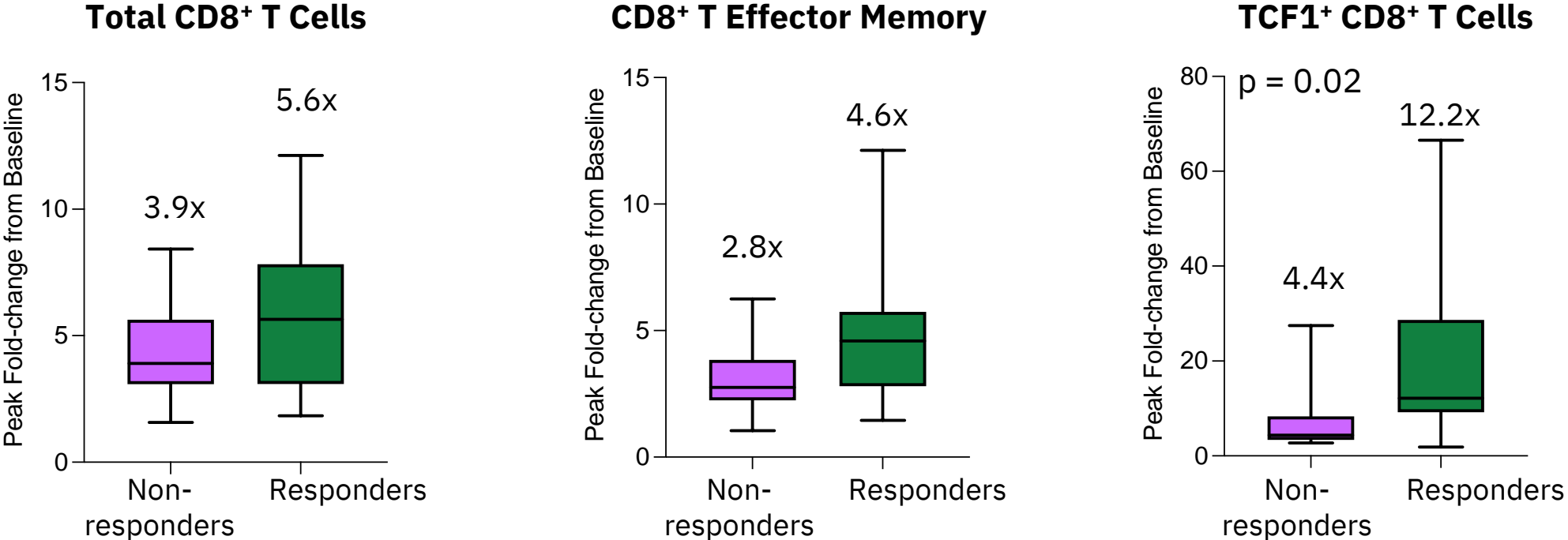
MDNA11, both as single agent and combined with pembrolizumab, promotes expansion of CD8+ T cell subsets which have been associated with durable anti-tumor immunity

- MDNA11 (90µg/kg; Q2W) [N=14]
- △ MDNA11 (90µg/kg; Q2W) + pembrolizumab (400mg; Q6W) [N=8]

p-values based on paired non-parametric Wilcoxon test



Clinical Benefit is Associated with Significant Increase in CD8+ T Cell ‘Stemness’



Efficacy evaluable patients in MDNA11 monotherapy and combination cohorts (60 and 90 µg/kg)
Responders: CR + PR + SD > 6 months (n = 9); Non-responders: PD (n = 14)
Median peak-fold change indicated
p-value by Mann-Whitney test



Summary

- MDNA11 is a next-generation, long-acting, 'β-enhanced not-α' IL-2 superkine
- MDNA11 shows compelling single-agent activity in CPI-resistant tumors
- MDNA11 in combination with pembrolizumab demonstrated clinical activity in tumor types that do not typically respond to CPI
- Serum exposure of MDNA11 is consistent across repeated dosing cycles in combination with pembrolizumab
- Consistent with its design, MDNA11 induces dose-dependent, sustained expansion of CD8⁺ T and NK cells with minimal Treg expansion, as monotherapy & combined with pembrolizumab
- MDNA11 promotes increases in effector and memory CD8⁺ T cells subsets, providing the potential for enhanced tumor killing and durable anti-tumor responses
- MDNA11 drives stem-like CD8⁺ T cell expansion resulting in clinical benefit



Acknowledgements

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