Results from Monotherapy Dose Escalation of MDNA11, a Long-acting IL-2 Superkine, in a Phase 1/2 Trial Shows Evidence of Single-agent Activity in Advanced Solid Tumors

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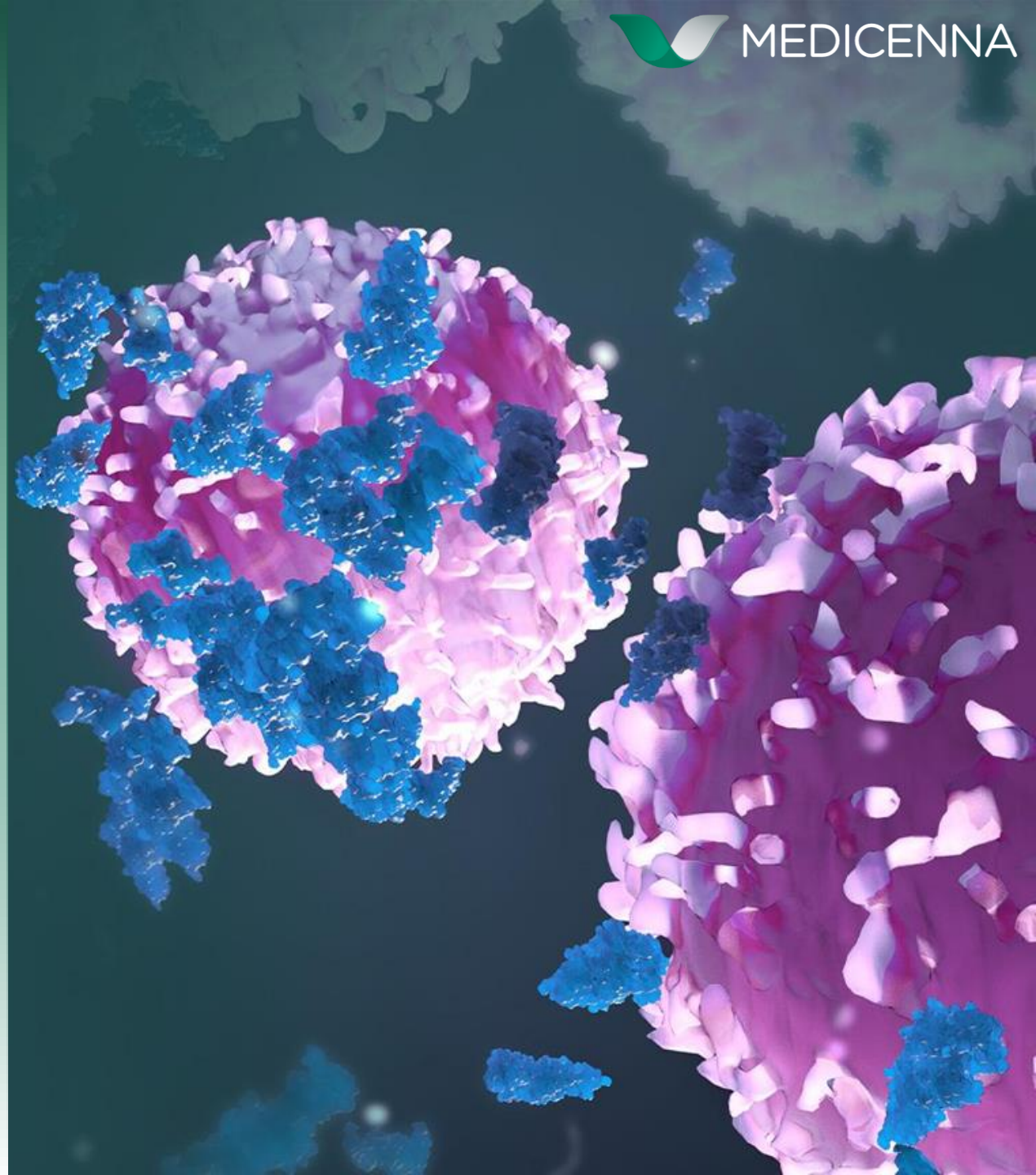
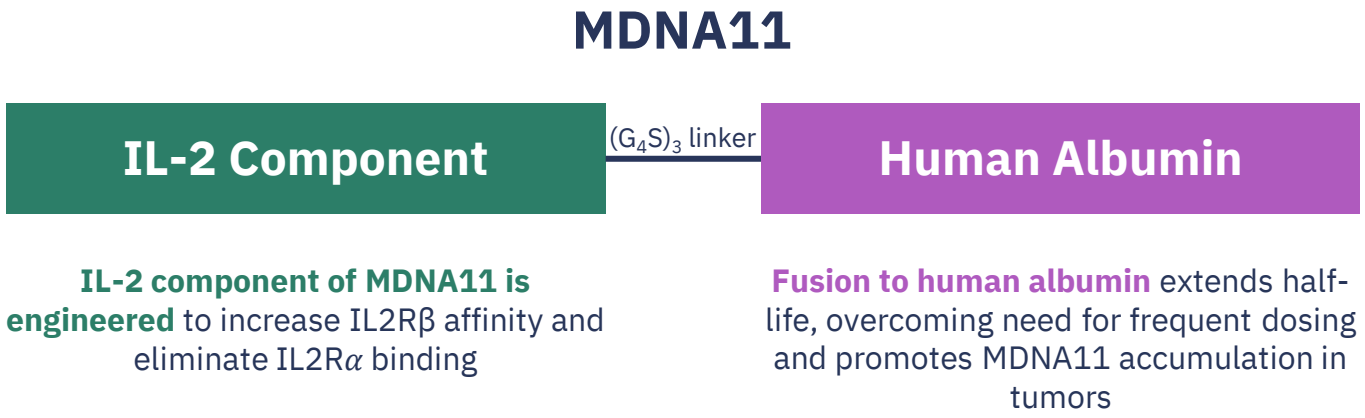
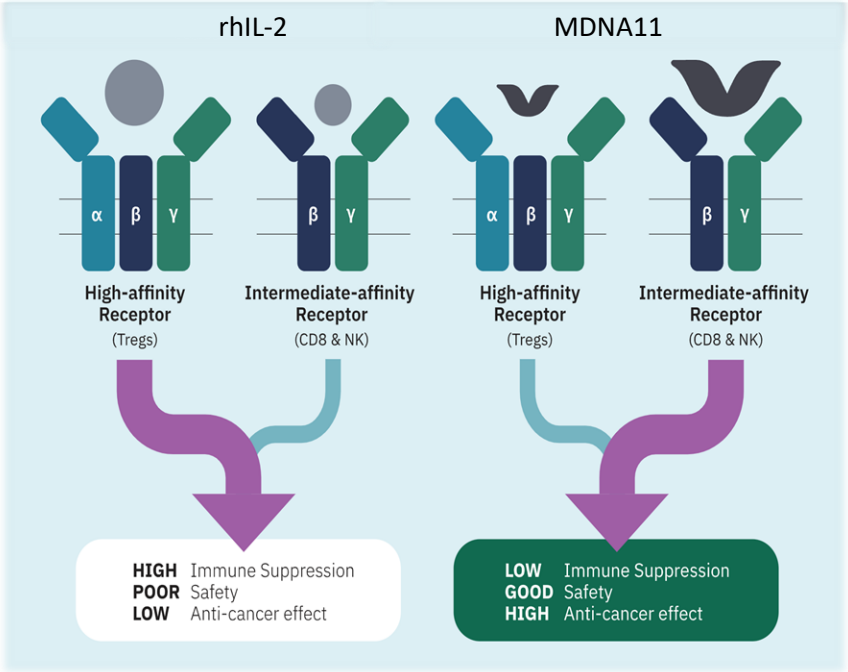


MDNA11 is a Long-acting "Beta-enhanced Not-alpha" IL-2

Distinctive Features of MDNA11

- **Highly Selective Anti-tumor Effector Immune Cell Activation:**
  - *"Beta-enhanced"* IL-2 agonist promoting selective activation of $CD8^+$ T and NK cells
  - *"Not-alpha"* binding with negligible to no expansion of Tregs
- **Improved Safety Profile Over High-dose rhIL-2:** No vascular leak syndrome or significant eosinophilia
- **Extended PK:** Albumin fusion prolongs half-life (given IV Q2W)
- **Tumor Accumulation:** Albumin promotes retention in tumor and tumor-draining lymph nodes



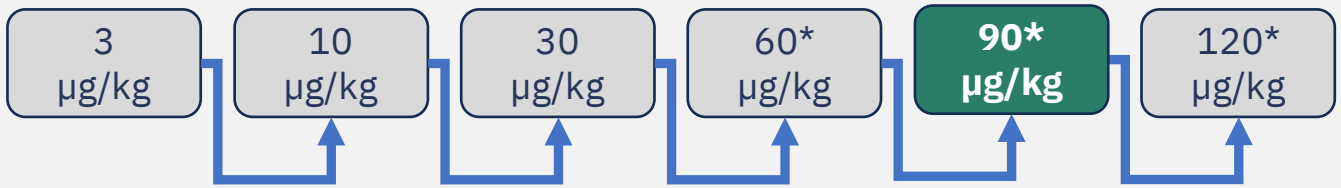


ABILITY-1: First-in-Human Trial of MDNA11 in Advanced Solid Tumors

(NCT05086692)

MDNA11 Monotherapy Dose Escalation (IV Q2W)

- Modified 3+3 design
- Intra-patient dose escalation & parallel backfill
- Identify monotherapy Recommended Dose for Expansion (RDE) @ 90 µg/kg



* Step-up dosing (SUD)

Monotherapy Dose Evaluation

- Optimize Step-up dosing (SUD) schedule

Monotherapy Dose Expansion (Phase 2)

- Melanoma (2° CPI Resistance)
- Non-melanoma skin cancer (1°/2° CPI Resistance)
  - cSCC, BCC, MCC
- MSI-H/dMMR tumors (1°/2° CPI Resistance)

MDNA11 (Q2W) + Pembrolizumab (Q6W) Dose Escalation

Select PD1/L1 refractory and CPI-naive indications

- Identify combination RDE (cRDE) for MDNA11
- Assess safety, tolerability and anti-tumor activity

MDNA11 + Pembrolizumab Dose Expansion (Phase 2)

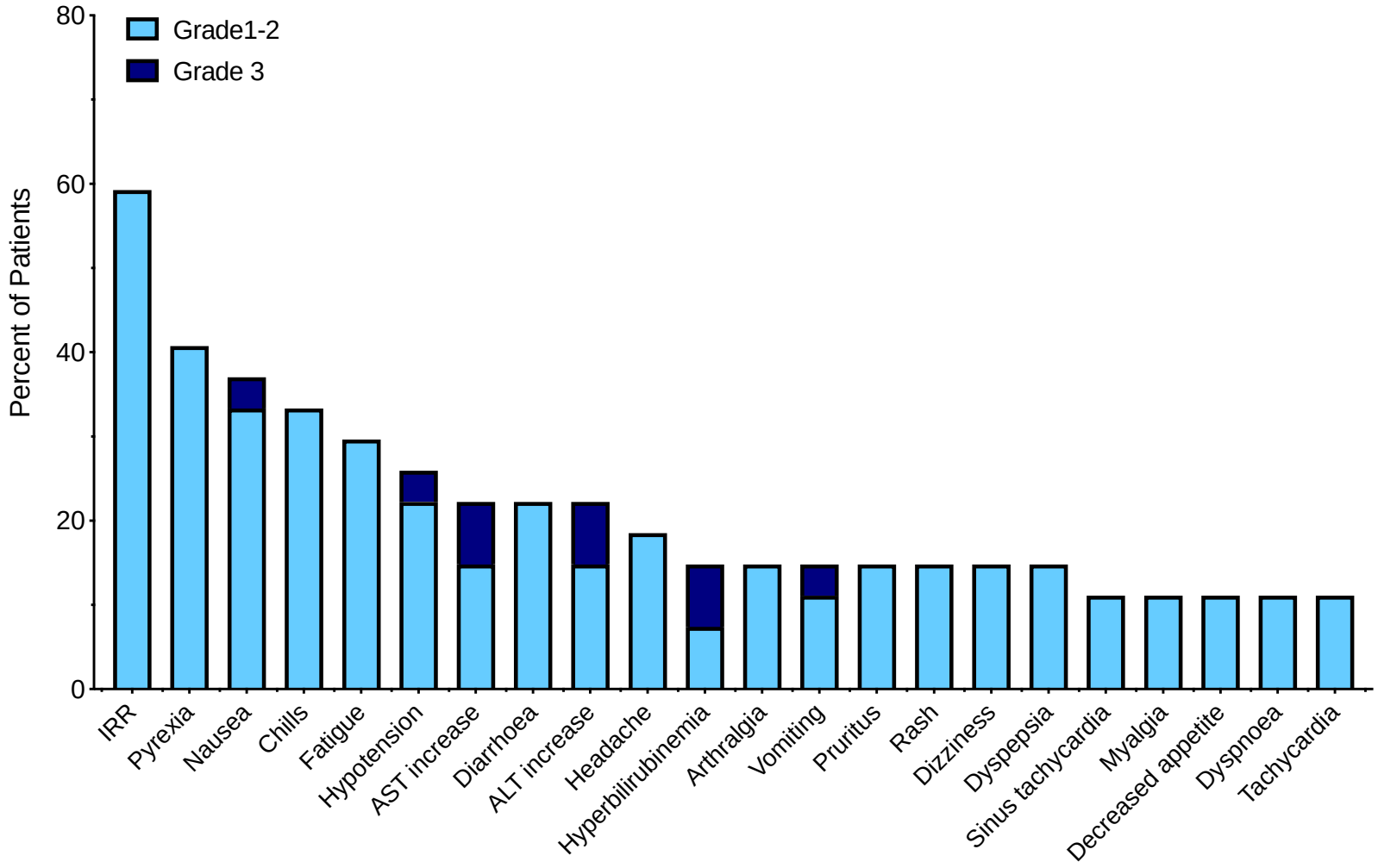
- MDNA11(Q2W, cRDE) + Pembrolizumab (Q6W)
- Assess safety, tolerability and anti-tumor activity

Baseline Patient and Tumor Characteristics

Baseline characteristics *(as of 22-Mar-2024)*	**Escalation/Evaluation (N=30)** *Completed*	**Expansion (N=8)** *Enrolling*
Age, years: median (range)	63 (27-78)	65.5 (49-85)
Male, N (%)	22 (73.3%)	4 (50%)
Baseline ECOG = 0, N (%)	19 (63.3%)	5 (62.5%)
Baseline ECOG = 1, N (%)	11 (36.6%)	3(37.5%)
Primary Tumor Type	**N (%)**	**N (%)**
Melanoma (16 Cutaneous, 1 Mucosal and 2 Acral)	16 (53.3 %)	3 (37.5%)
Non-small Cell Lung Cancer (NSCLC)	3 (10%)	
Pancreatic Ductal Adenocarcinoma (PDAC)	3 (10%)	
Renal Cell Carcinoma (Non-Clear Cell)	2 (6.6%)	
Sarcoma (1 Pleiomorphic sarcoma and 1 Leiomyosarcoma)	2 (6.6%)	
Ovarian Cancer	2(6.6%)	
Cutaneous Squamous Cell Carcinoma		2 (25%)
Basal Cell Carcinoma		1 (12.5%)
Tonsillar Squamous Cell Carcinoma	1 (3.3%)	
Small Bowel Cancer		1 (12.5%)
Gastro-esophageal/Gastric Adenocarcinoma	1 (3.3%)	1 (12.5%)
Prior Systemic Therapies	**N (%)**	**N (%)**
Prior Lines of Therapy: 1-2	22 (73.3%)	6 (75%)
Prior Lines of Therapy: 3-4	8 (26.6%)	2 (23%)
Immunotherapy	22 (73.3%)	8 (100%)
Targeted Therapy	5 (16.6%)	1 (12.5%)
Chemotherapy	15 (50 %)	2 (25%)

MDNA11 Demonstrates Favorable Safety Profile Across All Doses

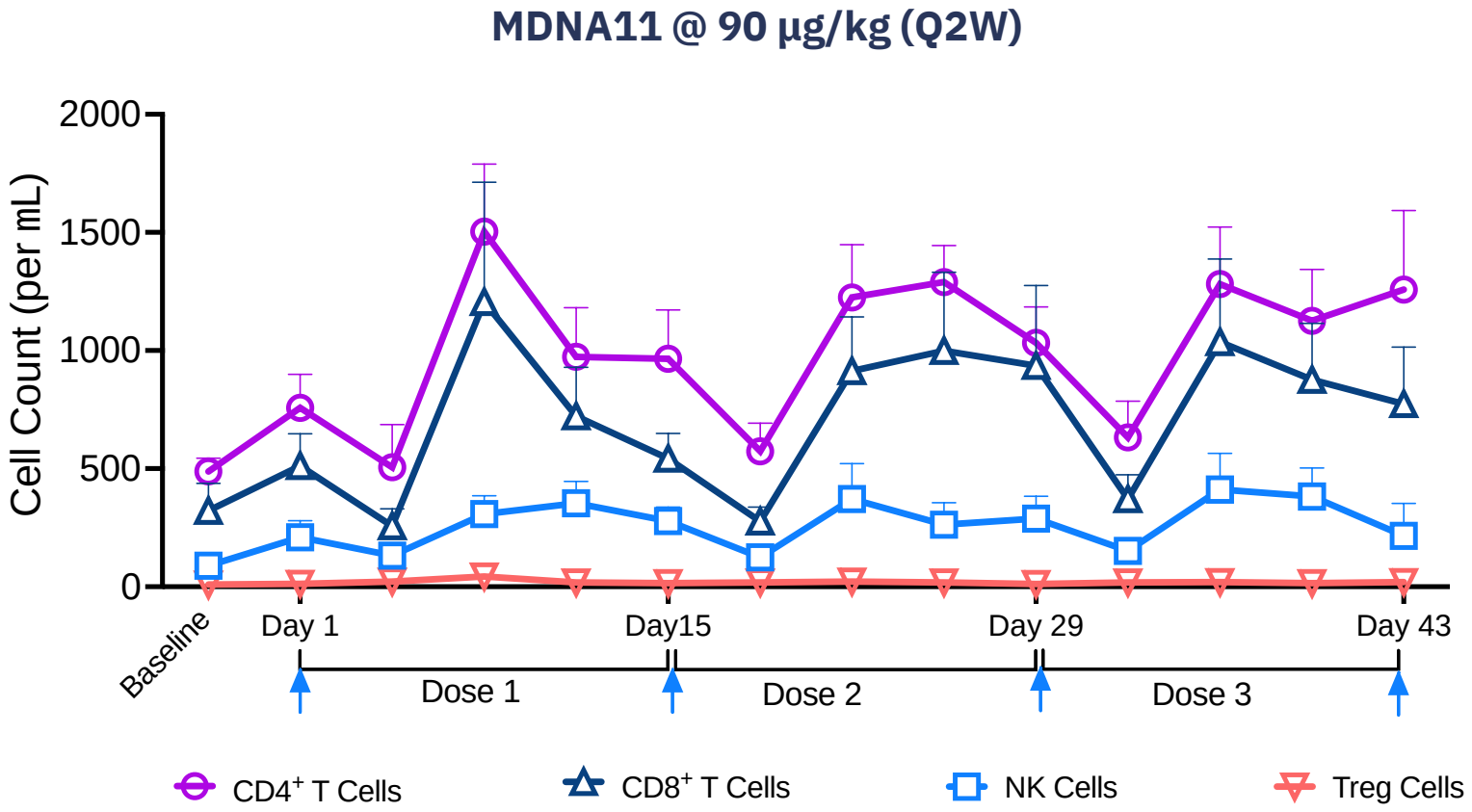
Most Common Treatment Related Adverse Events (TRAEs in ≥10% of Patients)



- No dose limiting toxicity (DLT)
- No grade 4 or 5 TRAE
- 95% of TRAEs were grade 1-2; majority resolved within 48 hours
- Grade 3 LFT elevations were asymptomatic and transient; resolved prior to next scheduled dose

IRR: Infusion Related Reaction

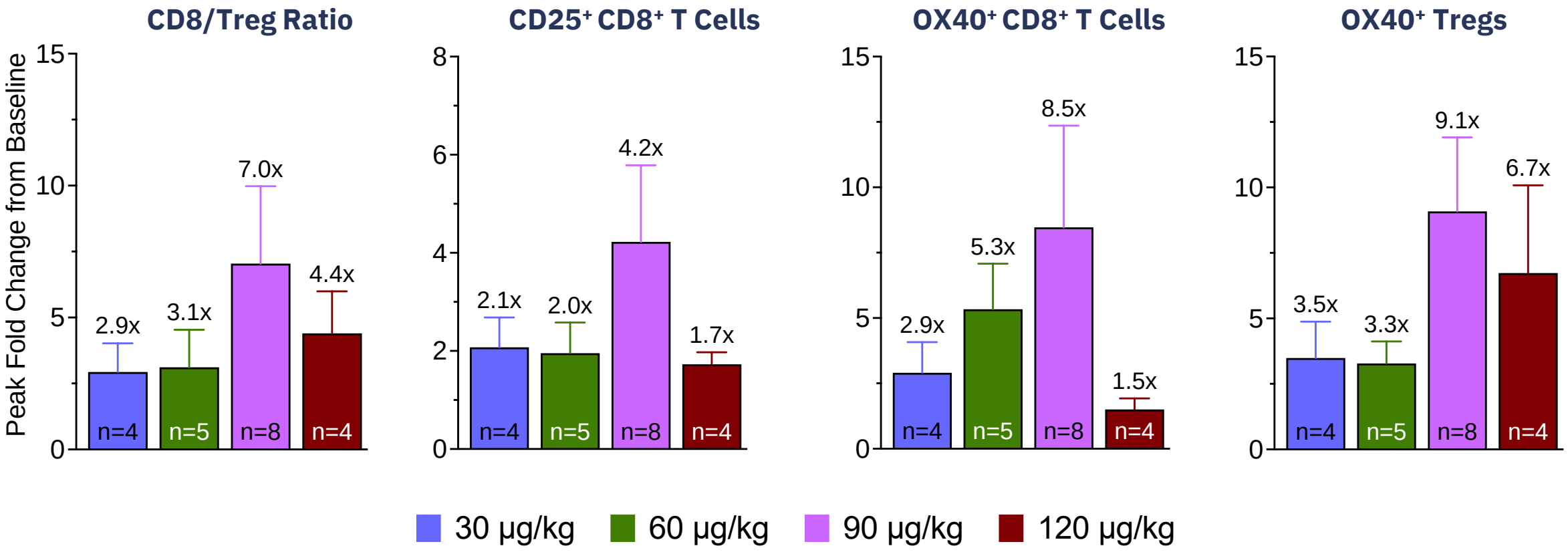
Sustained Immune Effector Cell Expansion with Repeat Dosing



N=8, patients received two priming doses (Q2W) prior to 90 µg/kg target dose.
Data for target dose are shown. Measurements on Day 1, 15 and 29 are prior to dose administration.
Baseline is prior to any MDNA11 exposure.

Virtually No Expansion of Regulatory T cells

Potent Effector Immune Cell Profile at MDNA11 RDE (90 µg/kg)

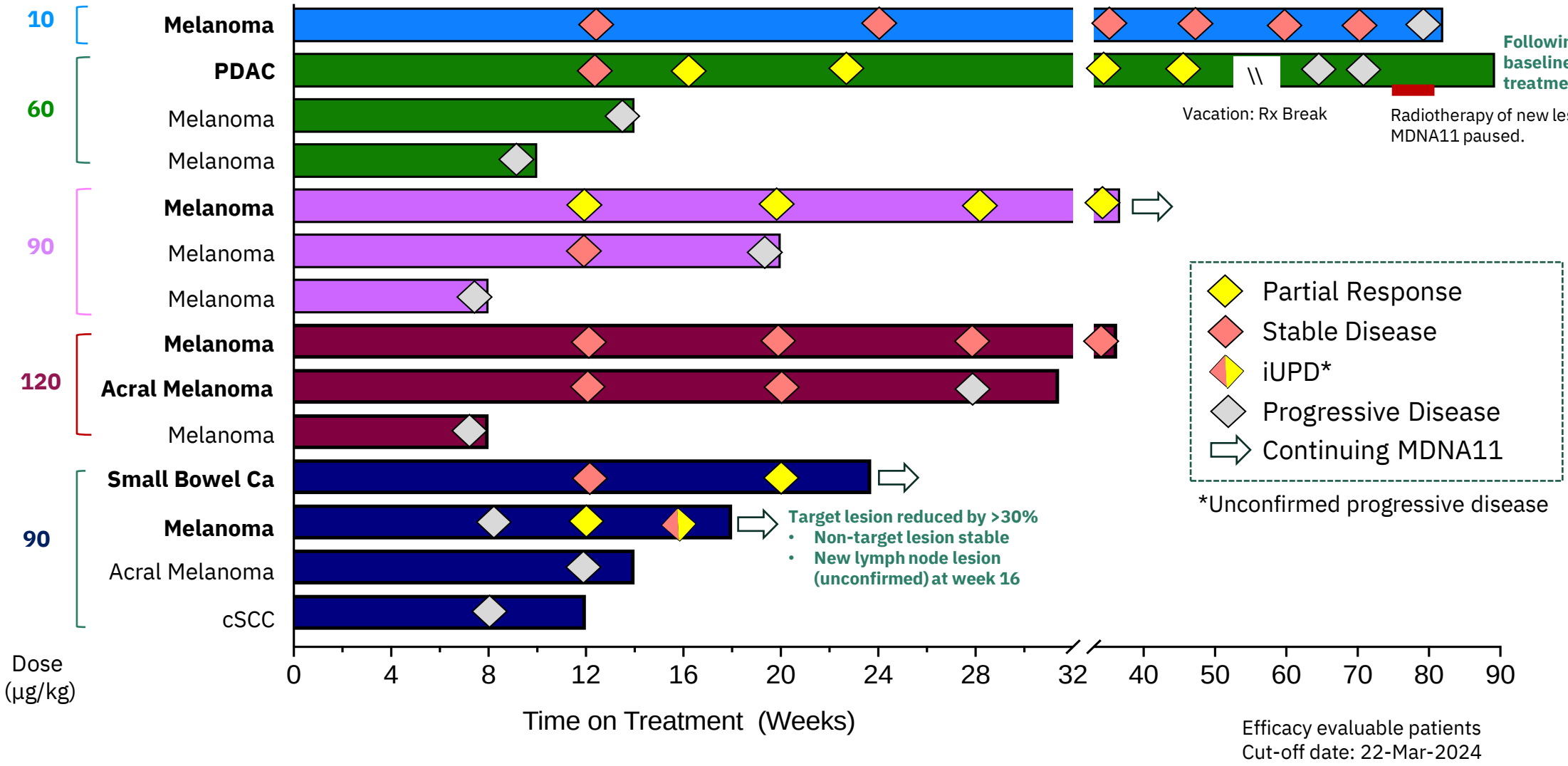


Superior expansion and activation of CD8⁺ T cells at RDE

OX40 positivity stimulates CD8⁺ T cells while impairing Tregs

Single Agent Efficacy of MDNA11 (≥60µg/kg) in Phase 2 Eligible Patients

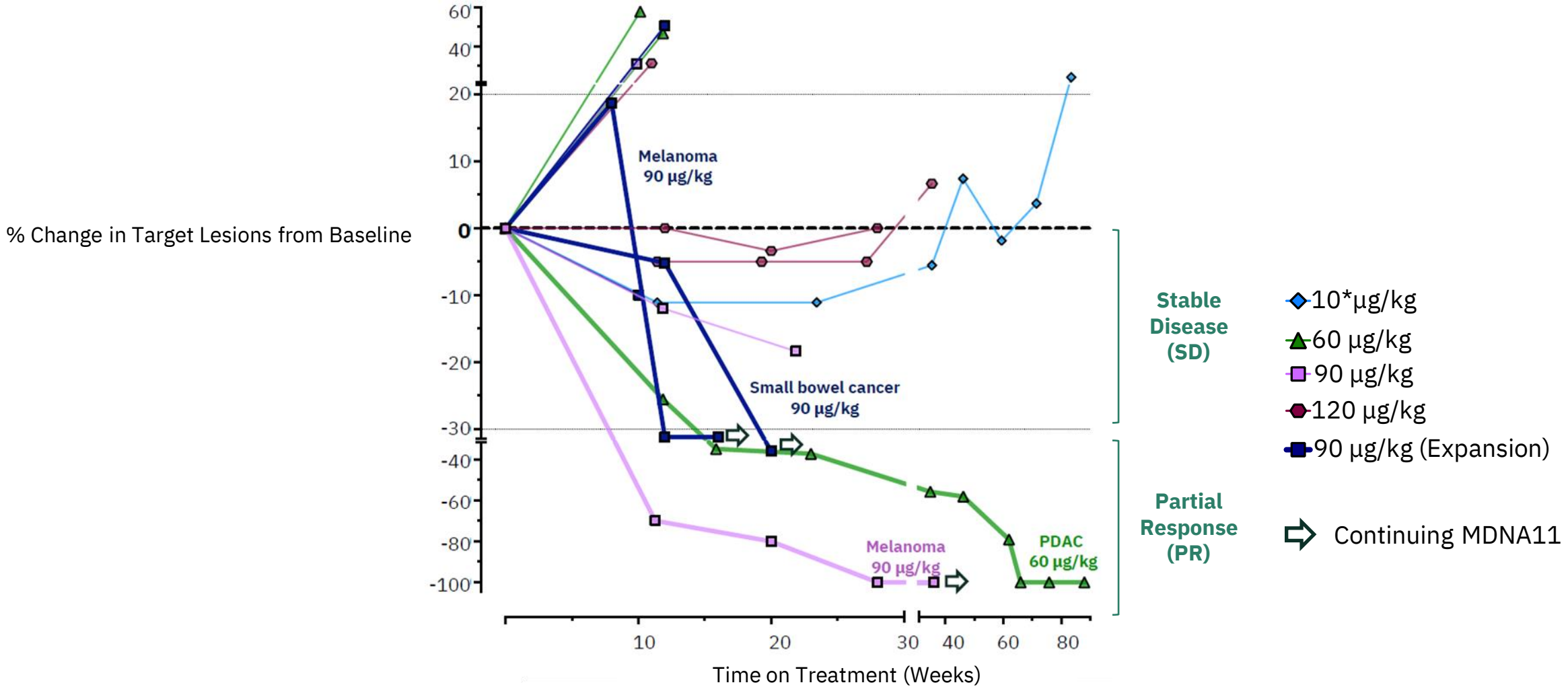
Response Rate (4PR) : 28.6% | Clinical Benefit Rate (4PR + 3SD >24 weeks): 50%



Efficacy evaluable patients
Cut-off date: 22-Mar-2024

Phase 2 Eligible Patients: 4 Partial Responses and 100% Reduction of Target Lesions in One Pancreatic Patient and One Melanoma Patient

2 of 4 evaluable dose expansion Patients (90 µg/kg) have had a PR



*Intra patient dose escalation:10,30, 60 & 90 µg/kg

MDNA11 Achieves Objective Response in Anti-PD-1 Resistant MSI-H

Pancreatic Ductal Adenocarcinoma (MSI-H)

PR
100% resolution of all target lesions (60 µg/kg)

- 55 Y/M PDAC:
  - Whipple procedure + Adjuvant FOLFIRINOX
  - 1L: Gemcitabine + nab-Paclitaxel
  - 2L: Pembrolizumab (PD; primary resistance)
- PR at week 16 of MDNA11 treatment
- A new lymph node (LN) lesion developed during treatment break (vacation; week 55-62)
- 100% regression of all baseline lesions (week 66) prior to radiotherapy
- New LN lesion (18 mm) treated with radiotherapy (week 67-73); MDNA11 resumed at week 73
- LN lesion reduced to < 10 mm; **MDNA11 treatment ended at week 90 with 100% regression of baseline target and non-target lesions originally in the liver**

Small Bowel Cancer (MSI-H)

PR

- 85 Y/F small bowel cancer:
  - Treated with pembrolizumab (confirmed progression; secondary resistance)
- PR at week 20 (90 µg/kg)
- Week 20 scan on MDNA11 showed 37% reduction in target lesions
- Continuing on MDNA11

MDNA11 Achieves Objective Response in Anti-PD-1 Resistant Melanoma

Cutaneous Melanoma

PR
100% resolution of target lesion (90 µg/kg)

- 63 Y/F cutaneous melanoma patient:
  - Progressed on prior line of dual checkpoint inhibitors (Nivolumab + Ipilimumab)
- PR at week 12 with target lesion reduced by 70%
- **Deepening of response with 100% reduction of target lesion (week 28, 36) and decreasing non-target lesions**
- Continuing on MDNA11

Cutaneous Melanoma

iPR following pseudo-progression (90 µg/kg)

- 56 Y/F cutaneous melanoma:
  - Treated with nivolumab (& rechallenge) (confirmed PD; secondary resistance)
- Developed a new lesion at week 8 and 18.75% increase in target lesion (pseudo-progression)
- iPR at week 12 confirmatory scan: marked reduction in target lesion (31.25% from baseline) and new lesion remained stable.
- New lymph node lesion at week 16; all baseline lesions and previous new lesion (week 8) were stable or decreased
- Continuing on MDNA11

Conclusions

RDE

- Dose of 90 µg/kg selected as monotherapy RDE

SAFETY

- MDNA11 is well-tolerated with no DLTs observed at all dose levels up to 120 µg/kg IV Q2W

PHARMACODYNAMICS

- MDNA11 shows robust increase in $CD8^+$ T and NK cells with activation markers peaking at 90 µg/kg

EFFICACY

- Compelling evidence of single-agent anti-tumor activity in checkpoint inhibitor refractory disease including tumor types not normally responsive to other IL-2 immunotherapies
  - 4 Partial Responses (1 PDAC, 1 small bowel cancer, and 2 cutaneous melanoma)
  - 3 Durable Stable Disease of 24 – 82 weeks in melanoma (2 cutaneous, 1 acral)
- **Single Agent Response Rate of 28.6% and Clinical Benefit Rate of 50% in Phase 2 Eligible Patients (MDNA11 ≥60 µg/kg) who all have failed checkpoint inhibitor therapies**

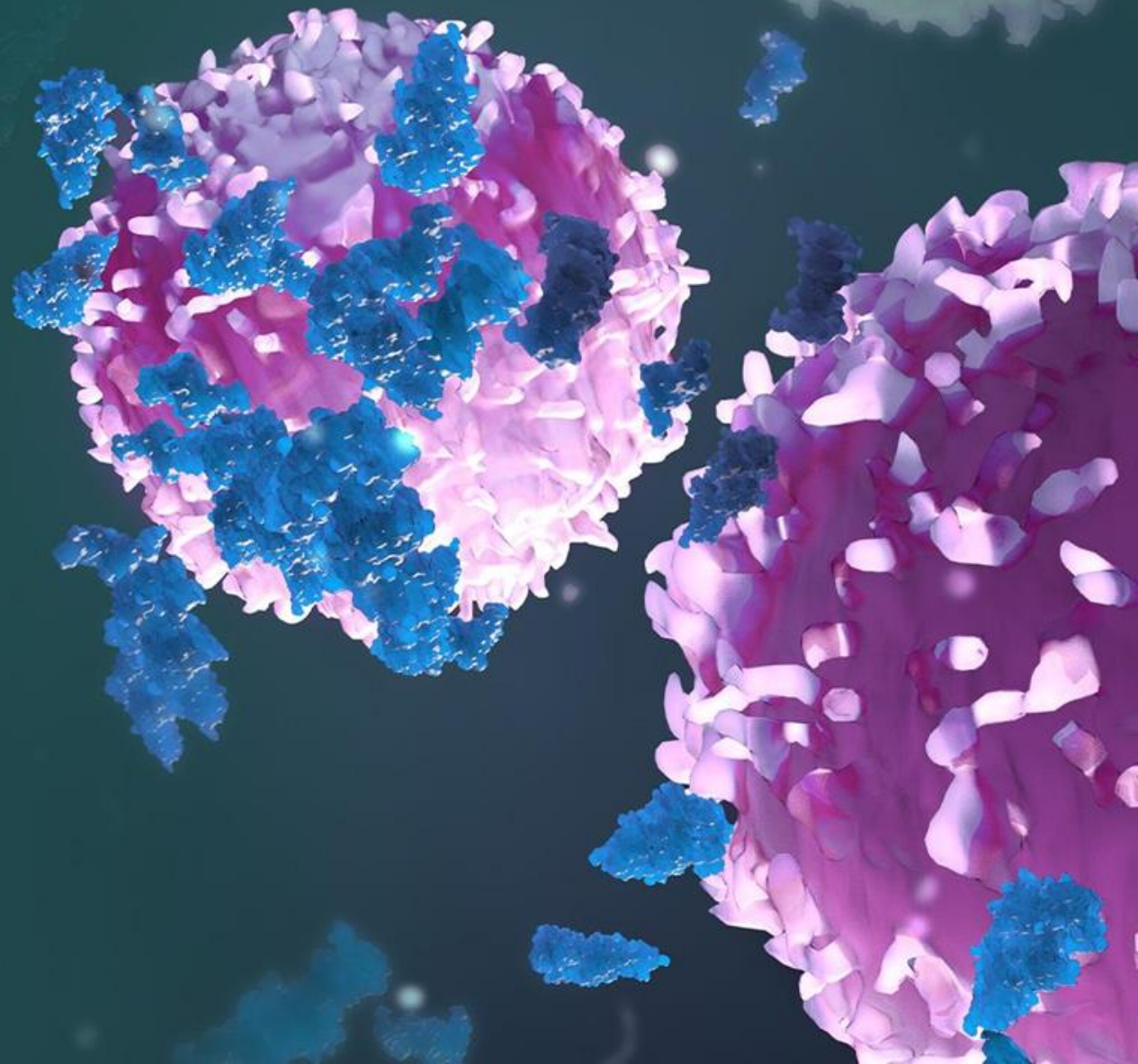
ENROLLMENT

- Monotherapy dose expansion and combination dose escalation with pembrolizumab are continuing to enroll

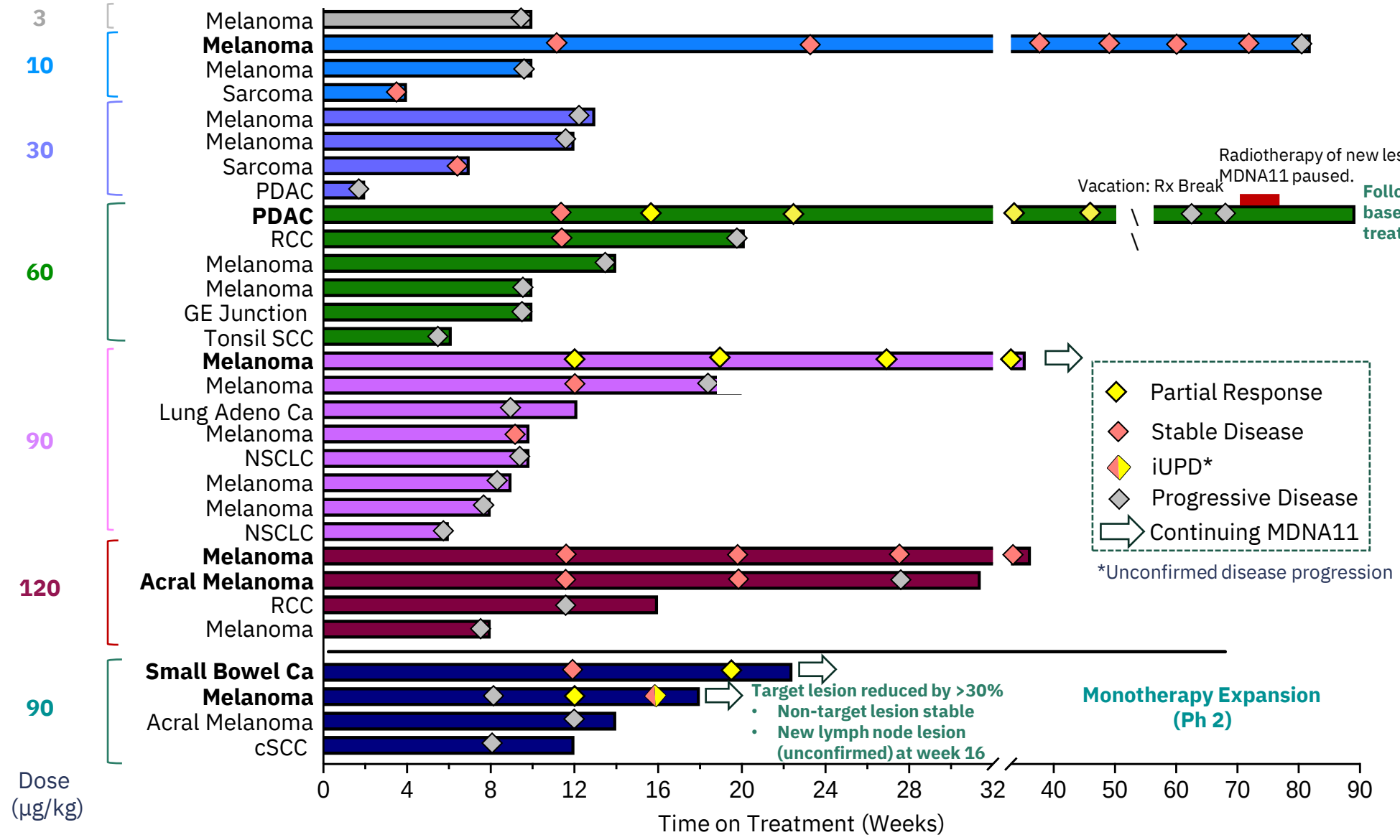
Acknowledgements

- The patients who have participated in the ABILITY trial and the families of the patients
- The investigators and all clinical and support trial staff at each of the study sites for their investment of time and effort into the trial
- The ABILITY-1 Trial is funded and sponsored by Medicenna Therapeutics

Appendix



MDNA11 Monotherapy: Duration of Treatment & Response



Efficacy evaluable patients
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