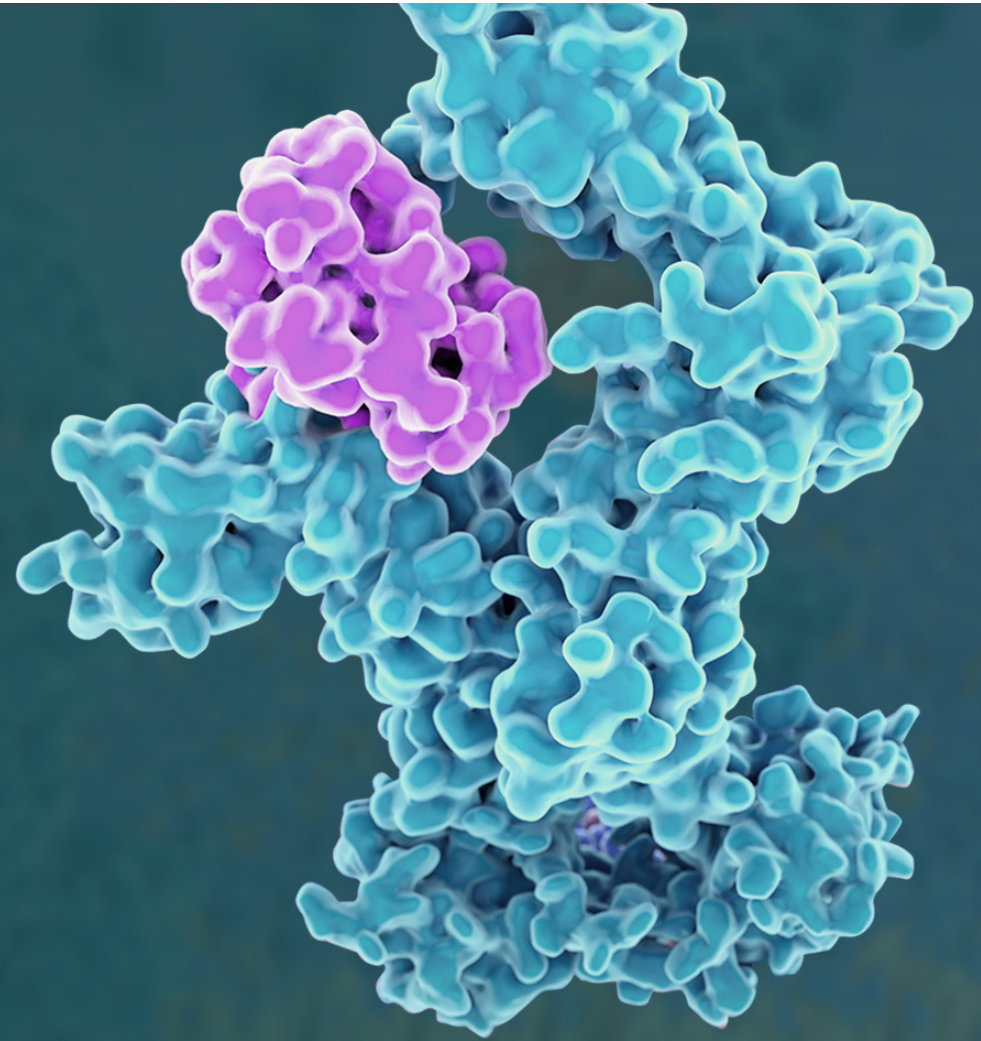


Q3, 2023

# Evolutionary Cytokines Revolutionary Medicines



MEDICENNA



Lorem ipsum dolor sit amet, consectetur adipiscing elit

# Disclaimer and Forward-Looking Statements

Certain statements in this presentation may constitute “forward-looking statements” under applicable securities laws. These forward-looking statements include, but are not limited to, information about possible or assumed future results of the Medicenna Therapeutics Corp’s (the “Company” or “Medicenna”) business, clinical trials, drug development, financial condition, results of operations, liquidity, plans and objectives. Further, any statements that express or involve discussions with respect to predictions, expectations, beliefs, plans, projections, objectives, assumptions or future events or performance (often, but not always, using words or phrases such as “expect”, “seek”, “endeavour”, “anticipate”, “plan”, “estimate”, “believe”, “intend”, or stating that certain actions, events or results may, could, would, might or will occur or be taken, or achieved) are not statements of historical fact and may be “forward-looking statements”.

Forward-looking statements are based on expectations, estimates and projections at the time the statements are made that involve a number of risks and uncertainties which would cause actual results or events to differ materially from those presently anticipated. Forward-looking statements are based on expectations, estimates and projections at the time the statements are made and involve significant known and unknown risks, uncertainties and assumptions. A number of factors could cause actual results, performance or achievements to be materially different from any future results, performance or achievements that may be expressed or implied by such forward-looking statements. These include, but are not limited to, the risk factors discussed in the public filings made by Medicenna with the applicable securities commissions and regulators in Canada and the United States, including, but not limited to, the Annual Report on Form 20F dated June 26, 2023 filed in Canada on SEDAR at [www.edgar.com](http://www.edgar.com) and in the United States with the United States Securities and Exchange Commission on Edgar at [www.sec.gov](http://www.sec.gov). Should one or more of these risks or uncertainties materialize, or should assumptions underlying the forward-looking statements prove incorrect, actual results, performance or achievements could vary materially from those expressed or implied by the forward-looking statements contained in this document. These factors should be considered carefully and prospective investors should not place undue reliance on these forward-looking statements.

Although the forward-looking statements contained in this document are based upon what Medicenna currently believes to be reasonable assumptions, Medicenna cannot assure prospective investors that actual results, performance or achievements will be consistent with these forward-looking statements. Furthermore, unless otherwise stated, the forward-looking statements contained in this presentation are made as of the date hereof. Except as required by law, Medicenna does not have any obligation to advise any person if it becomes aware of any inaccuracy in or omission from any forward-looking statement, nor does it intend, or assume any obligation, to update or revise these forward-looking statements to reflect new events, circumstances, information or changes.

## Legal Disclaimers

This presentation of Medicenna is for information only and does not, and is not intended to, constitute or form part of, and should not be construed as, an offer or invitation to buy, sell, issue or subscribe for, or the solicitation of an offer to buy, sell or issue, subscribe for or otherwise acquire any securities in any jurisdiction in which such offer, solicitation or sale would be unlawful, nor shall it or any part of it be relied upon in connection with or act as any inducement to enter into any contract or commitment or investment decision whatsoever.

Certain information contained in this presentation and statements made orally during this presentation relate to or are based on studies, publications and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources.



# Investment Highlights

## Multiple Significant Catalysts Are Expected in The Next Six Months



### Superkine Platform: Drug Discovery Engine

Directed evolution **enhances the desired properties** of IL-2, IL-4, & IL-13 to generate Superkines  
Protein fusion can **improve PK, add an MOA, or confer new capabilities** to Superkines  
IL-2, IL-4, & IL-13 are known to modulate immune activity against **2,000 different diseases**



### MDNA11: "Beta-only" & Long-acting IL-2 Super- agonist in Phase 1/2

Super-agonist against IL-2R, a **clinically validated anti-cancer target**  
Enhanced IL-2R $\beta$  binding and lack of IL-2R $\alpha$  affinity position MDNA11 to be **best-in-class**  
MDNA11 has **successfully completed** the dose escalation phase 1 with grade 1-2 AEs only  
MDNA11 **commences dose expansion** in Q3 2023 as monotherapy and Q4 with pembrolizumab



### MDNA55: Phase 3 Ready Empowered IL-4 Superkine

Targeting recurrent glioblastoma, the most aggressive form of brain cancer  
Phase 2b data show **~100% improvement in median OS** vs. a matched external control arm  
Pursuing a **partnership** to advance development



### BiSKIT Platform: Bifunctional SuperKines for ImmunoTherapy

Fusion of two Superkines or a Superkine and an antibody (e.g. a checkpoint inhibitor)  
Incorporate **two synergistic MOAs** into a single molecule





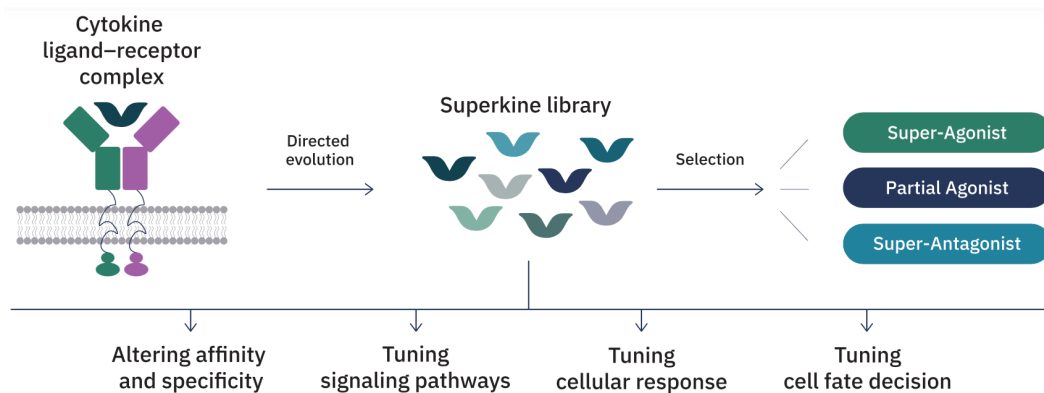
# Our Superkine Platform

Our scientific platform enables us to transform natural interleukins into Superkines, which are enhanced to combat a specific disease. For example, Superkines could alter the immunosuppressive tumor microenvironment, deliver cell-killing agents without harming healthy cells, or turn off destructive autoimmune processes.



# Superkine Platform Powers Drug Discovery Engine

Transforming IL-2, IL-4 and IL-13 into Druggable Superkines Using Directed Evolution



Our IL-2, IL-4 and IL-13 Superkines are known to modulate immune activity in many diseases, each providing “A Pipeline in a Product” opportunity

## Superkine Design and Development



### Generate Tunable Superkine Library

Transform interleukins using directed evolution to enhance desired properties



### Enhance via Protein Fusion

To improve PK, add a second MOA, or confer new capabilities



### Lead Selection & Development

Advance the most promising candidates towards clinical studies





# Our Diversified Pipeline Of Next-Generation Superkines

Candidate	Indication	Discovery	Preclinical	Phase 1	Phase 2	Pivotal
<b>Bizaxofusp</b> IL-4–Toxin Fusion	Recurrent Glioblastoma (GBM)					
<b>MDNA11</b> IL-2 Super Agonist	Various solid tumors (monotherapy & combo with pembrolizumab)					
<b>MDNA223</b> Anti PD-1-IL-2 BiSKIT	Various solid tumors					
<b>MDNA413</b> IL-4/13 Super Antagonist	Oncology and Th2-mediated diseases					
<b>MDNA209</b> IL-2 Super Antagonist	Autoimmune Diseases					
<b>MDNA213</b> IL-13Rα2 Selective Binder	Solid tumors expressing IL-13Rα2					





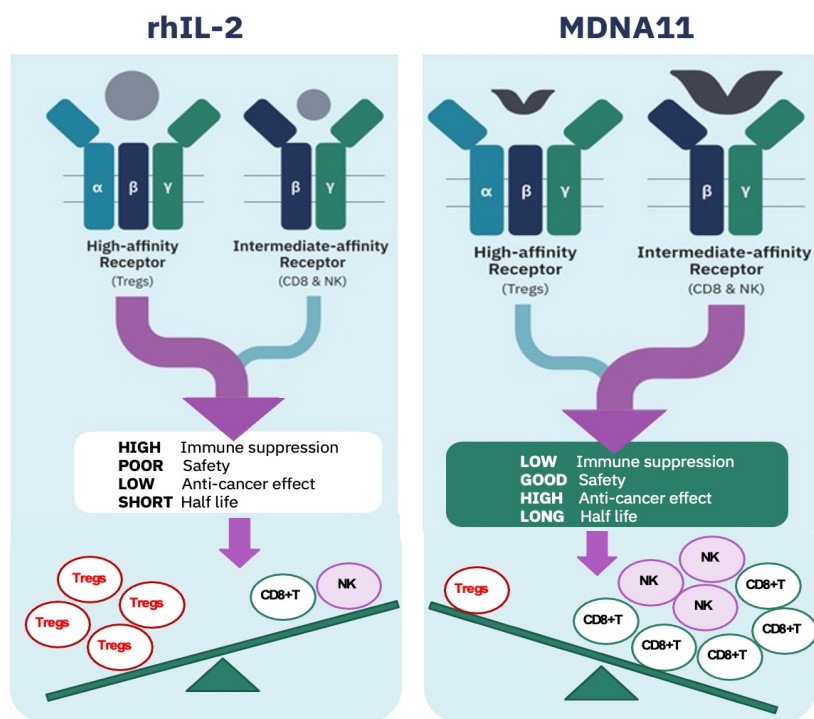
# MDNA11

“Beta-only” & Long-acting IL-2  
Super-Agonist for Solid Tumors



# Targeting IL-2 Receptor Subunits in Cancer Therapy

## IL-2 Receptor



The IL-2 receptor (IL-2R) consists of three subunits

- IL-2R $\alpha$  (CD25)
- IL-2R $\beta$  (CD122)
- IL-2R $\gamma$  (CD132)

### Stimulation of IL-2R $\beta$

- Key for the activation of cancer killing immune cells such as CD8+ T cells, naïve T cells, and NK cells.

### Stimulation of IL-2R $\alpha$

- Leads to activation of immunosuppressive Tregs, which abrogate the anti-tumor response
- Causes extreme toxicity

**Proleukin (recombinant human [rh] IL-2), which selectively stimulates IL-2R $\alpha$ , is approved by the FDA for the treatment of metastatic melanoma and renal cell carcinoma.**

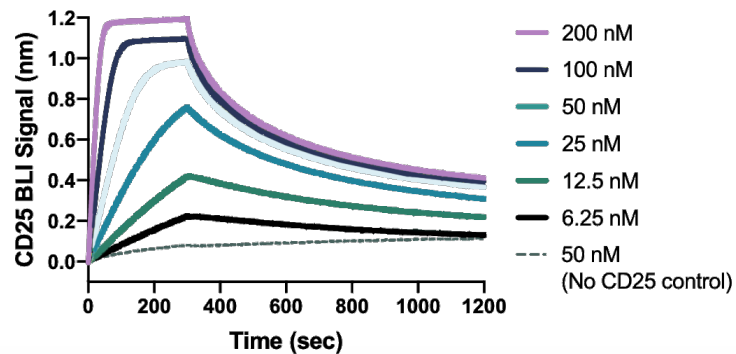




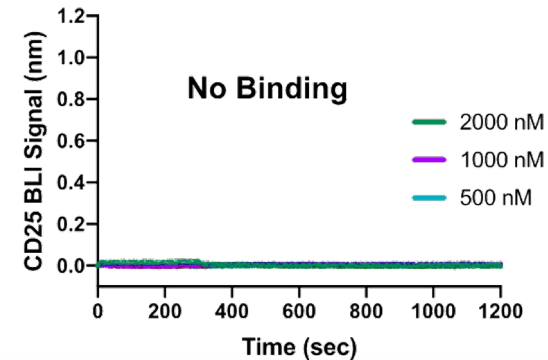
# MDNA11's IL-2 Binding is Highly Differentiated vs. Proleukin (rhIL-2)

No IL-2R $\alpha$  (CD25) Binding and Enhanced Affinity and Selectivity for IL-2R $\beta$  (CD122) Compared to rhIL-2

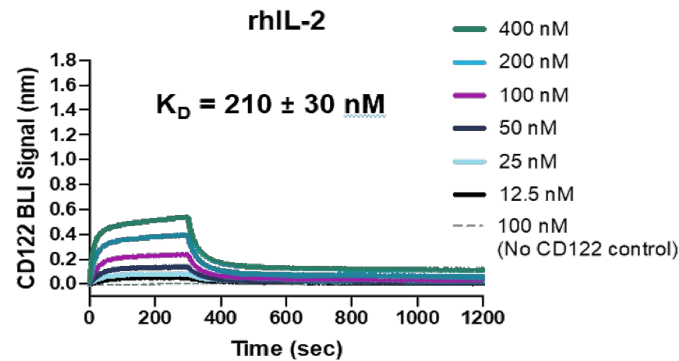
rhIL-2 – IL-2R $\alpha$  Binding



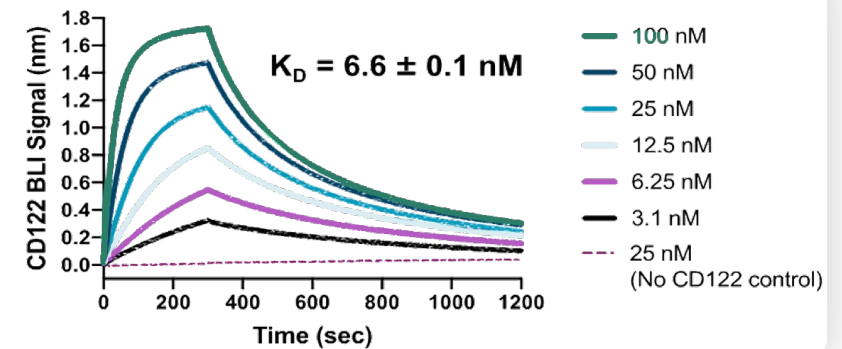
MDNA11 – IL-2R $\alpha$  Binding



rhIL-2 – IL-2R $\beta$  Binding

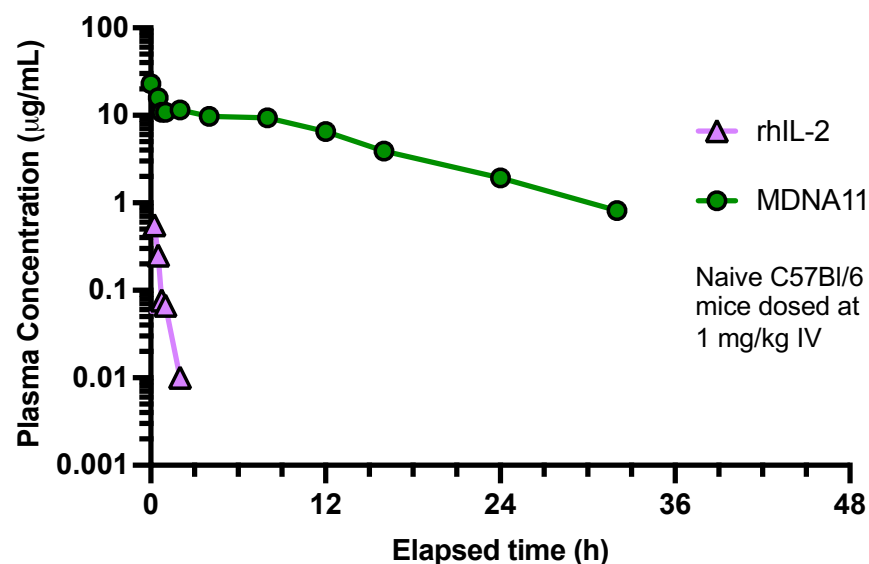


MDNA11 – IL-2R $\beta$  Binding



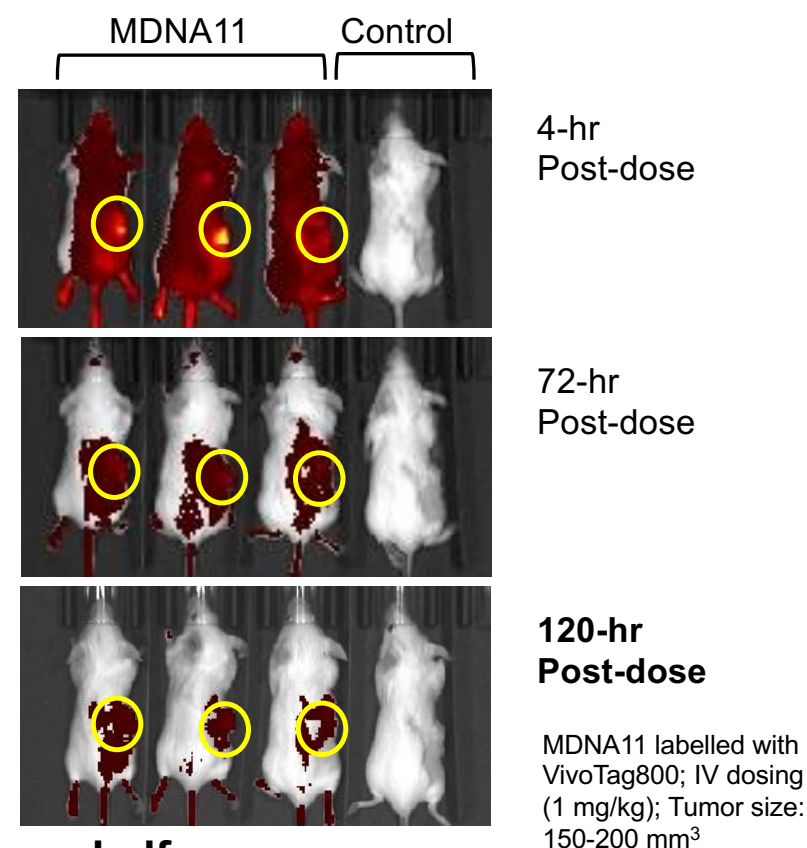
# MDNA11 Durably Accumulates In Solid Tumors In Vivo

PK Profile in Mice



	C <sub>max</sub> (µg/mL)	AUC (µg.hr/mL)	T <sub>half</sub> (hr)
rhIL-2	5.77	1.07	0.28
MDNA11	23.02	182.3	6.83










MDNA11 Imaging in CT26 Tumor Model



**Tumor exposure of MDNA11 is > 15x longer than its serum half-life**

# MDNA11 – Best in Class Potential

MDNA11's strong anti-tumor activity, well-tolerated safety profile and convenient outpatient dosing regimen paves the way for a potential best-in-class therapy with significant commercial potential

	 MDNA11	 Proleukin <sup>1</sup>	 NKTR-214	 SAR'245 <sup>2</sup>	 ALKS 4230 <sup>3</sup>	 WTX-124 <sup>5</sup>	 XTX202 <sup>6</sup>	 STK-012 <sup>7</sup>	 TransCon IL-2 $\beta/\gamma$ <sup>8</sup>
No binding to IL-2R $\alpha$	✓	X	X	✓	✓	X	✓	X	Minimal binding
Enhanced IL-2R $\beta\gamma$ Binding	✓	X	X	X	X	X	X	X	✓
QW, Q2W or Q3W Dosing	✓	X	✓	✓	X	Unknown	✓	✓	✓
Tumor Accumulation	✓	X	X	X	X	X	X	X	X
No Pegylation Liabilities	✓	✓	X	X	✓	✓	✓	X	✓
Pipeline Potential	✓	✓	X	X	X	X	X	✓	✓



# ABILITY: Phase 1/2 Dose Escalation & Expansion Study

## Monotherapy Dose Escalation

N = 20 patients with advanced, treatment-refractory solid tumors

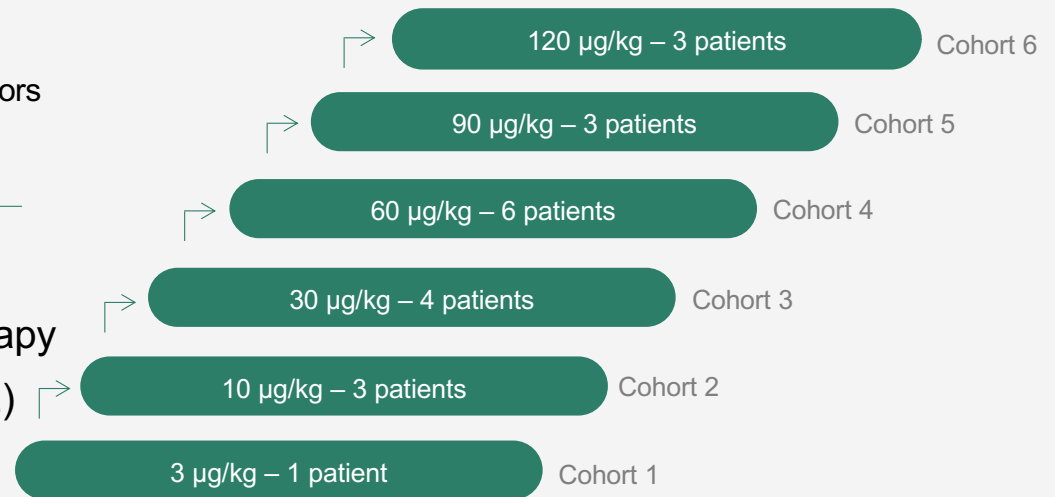
MDNA11 Q2W IV; cut-off date: June 20, 2023

Modified 3+3 design. Open-label

Assess safety & tolerability of MDNA11 monotherapy

Identify Recommended Dose for Expansion (RDE)

[NCT05086692](https://clinicaltrials.gov/ct2/show/study/NCT05086692)



## MDNA11 Monotherapy Dose Expansion

N≈40: Melanoma and other selected solid tumors

MDNA11 Q2W IV at RDE

Further evaluate safety and tolerability

Evaluate single-agent anti-tumor activity

## MDNA11 + Anti-PD-1 (Pembrolizumab) Dose Expansion

N≈40: Melanoma and other selected solid tumors

MDNA11 + anti-PD-1 (pembrolizumab)

Evaluate safety and tolerability of MDNA11 / anti-PD-1 combination

Evaluate combination anti-tumor activity





# ABILITY: Patient Baseline Characteristics in Dose Escalation

## Demographics/Performance

Median age, years (range)	<b>61 (27-78)</b>
Male (%)	<b>16/20 (80%)</b>
ECOG 0	<b>14/20 (70%)</b>
ECOG 1	<b>6/20 (30%)</b>

## Prior Systemic Therapies

Prior Lines of Therapy: 1	<b>5/20 (25%)</b>
Prior Lines of Therapy: 2-4	<b>15/20 (75%)</b>
Prior Immunotherapy	<b>15/20 (75%)</b>
Prior Targeted Therapy	<b>5/20 (25%)</b>
Prior Chemotherapy	<b>9/20 (45%)</b>

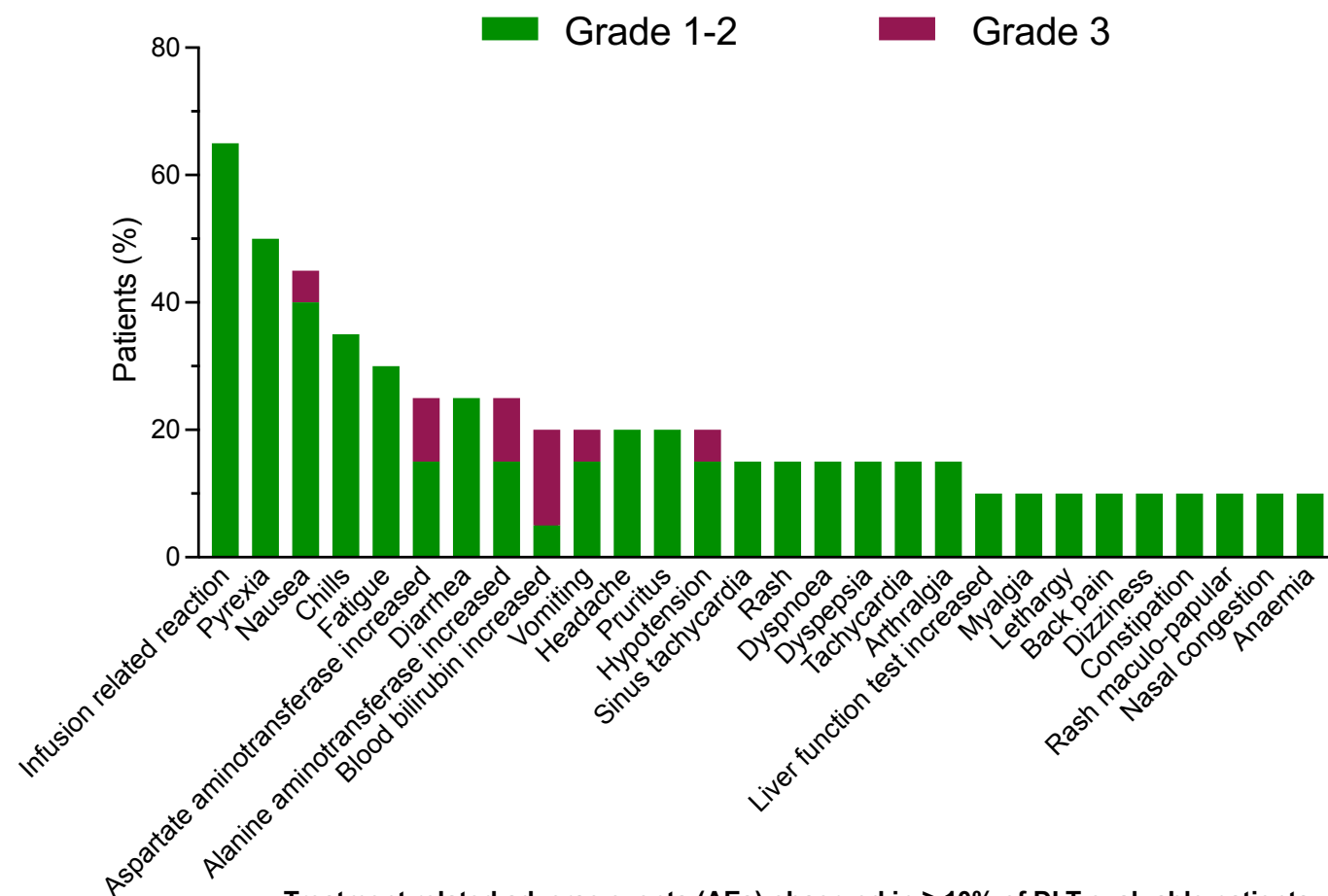
## Primary Cancer Diagnosis

Melanoma	<b>11/20 (55%)</b>
Renal Cell Carcinoma (non-clear cell)	<b>2/20 (10%)</b>
Pancreatic Ductal Adenocarcinoma (PDAC)	<b>2/20 (10%)</b>
Sarcoma	<b>2/20 (10%)</b>
Squamous Cell Carcinoma	<b>1/20 (5%)</b>
Gastro-esophageal Adenocarcinoma	<b>1/20 (5%)</b>
Lung Adenocarcinoma	<b>1/20 (5%)</b>

**Most patients received multiple prior lines of anti-cancer therapy, including immunotherapy**



# Single Agent Safety Profile Across all Dose Escalation Cohorts



No DLTs or MTD reached

No Grade 4/5 events

Majority of AEs Grade 1/2 and resolved within 1-2 days

Data cut-off: June 20, 2023

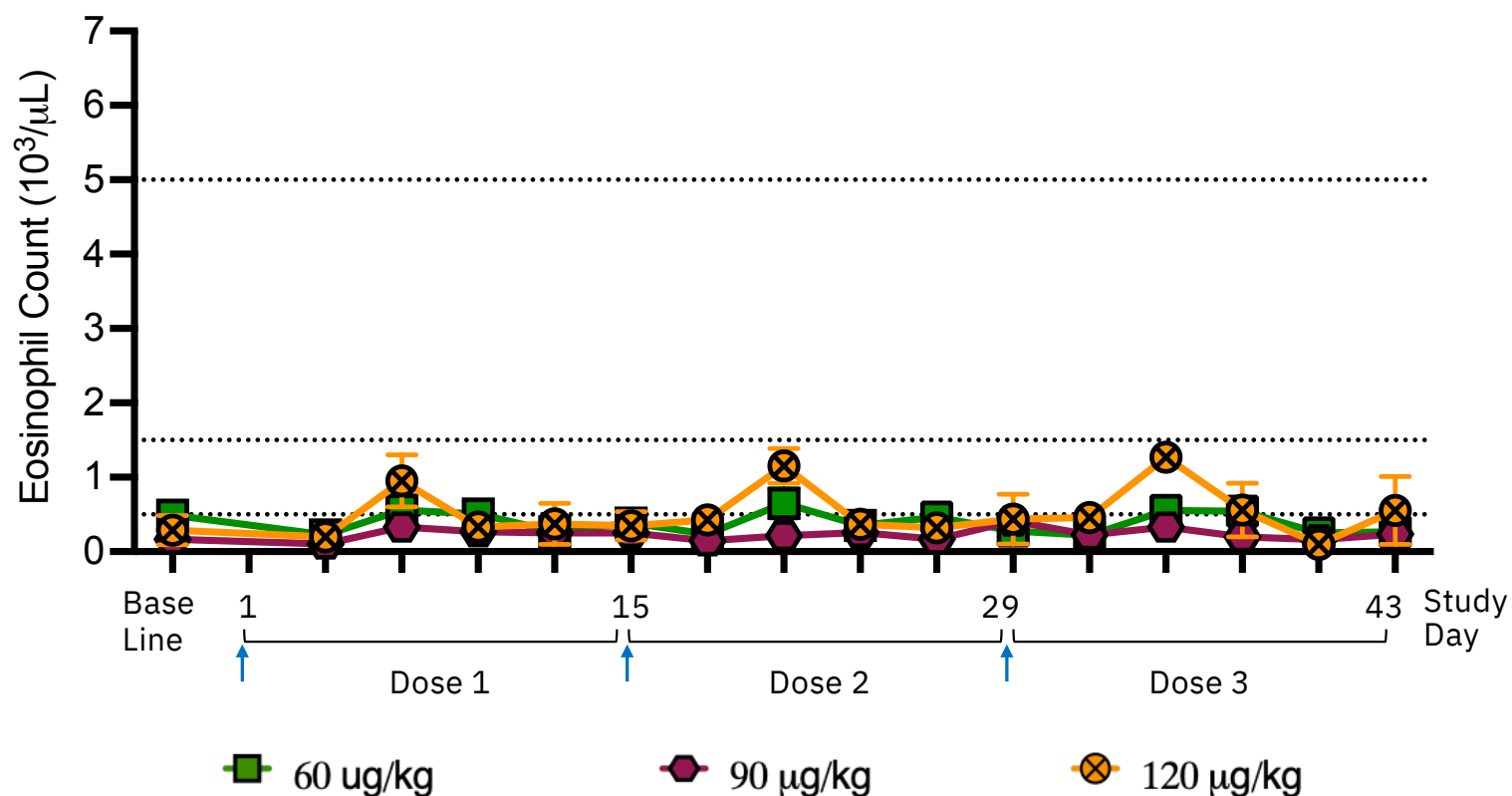
**MNDA11 generally well-tolerated across cohorts**

Treatment related adverse events (AEs) observed in  $\geq 10\%$  of DLT evaluable patients



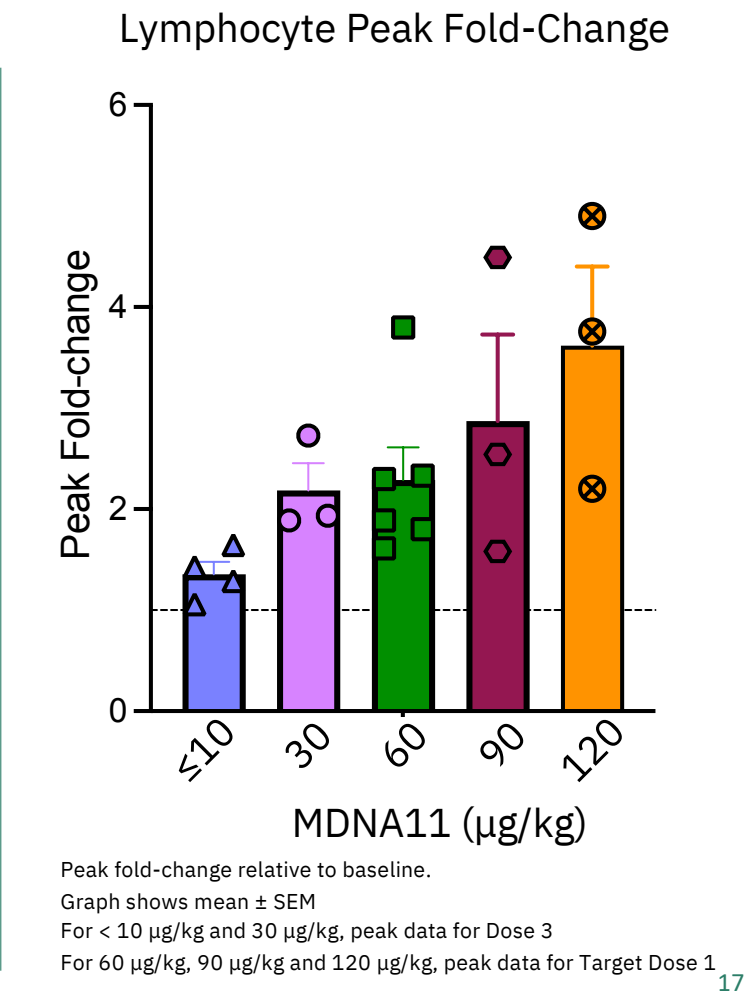
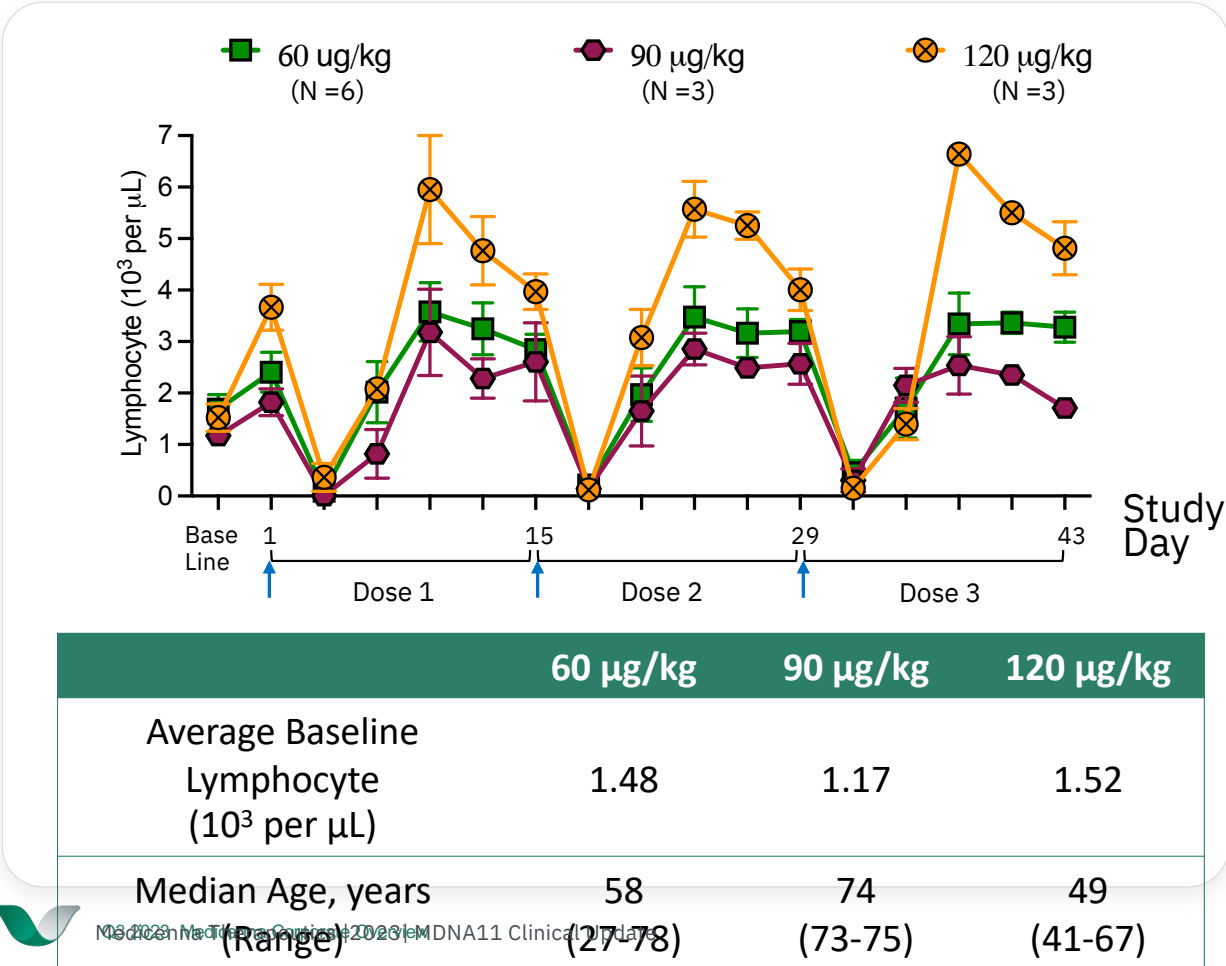
# No Significant Eosinophilia (Associated with VLS)

Vascular Leak Syndrome (VLS) is a hallmark dose-limiting toxicity of IL-2



# MDNA11-Induced Sustained Dose-Dependent Lymphocyte Expansion

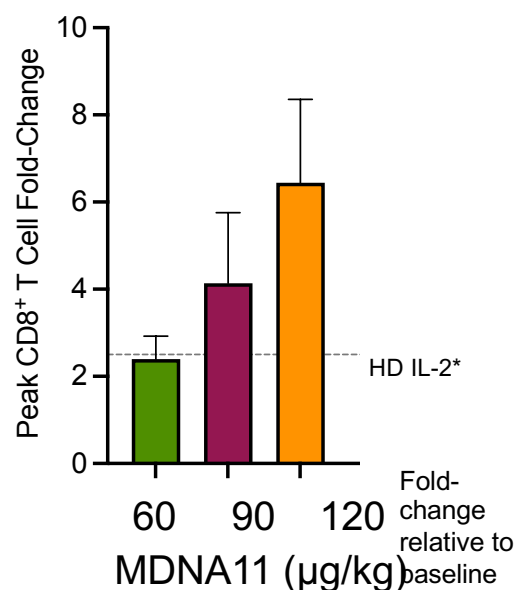
Expansion of cancer killing immune cells





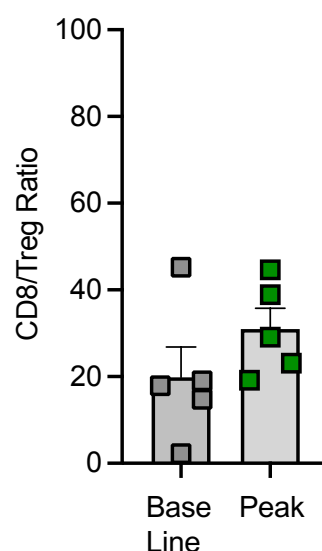
# MDNA11 Preferentially Induced CD8<sup>+</sup> T Cell Expansion Over Tregs

## Peak Increase: CD8<sup>+</sup> T Cell

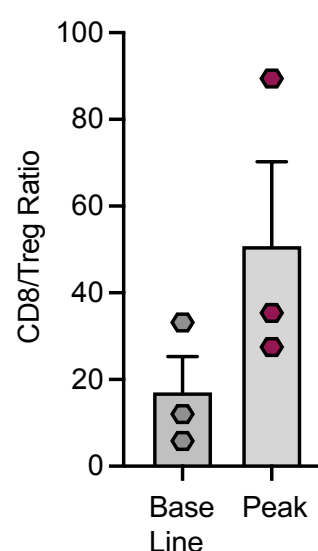


## Peak Increase: CD8<sup>+</sup>/Treg Ratio

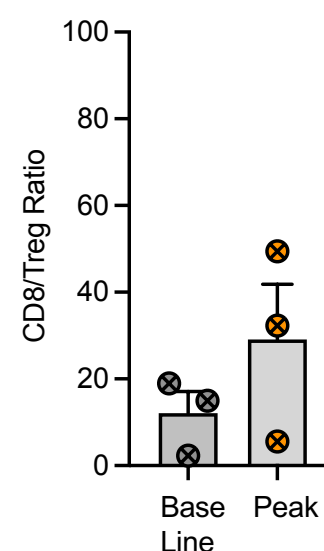
MDNA11: 60 µg/kg



90 µg/kg



120 µg/kg

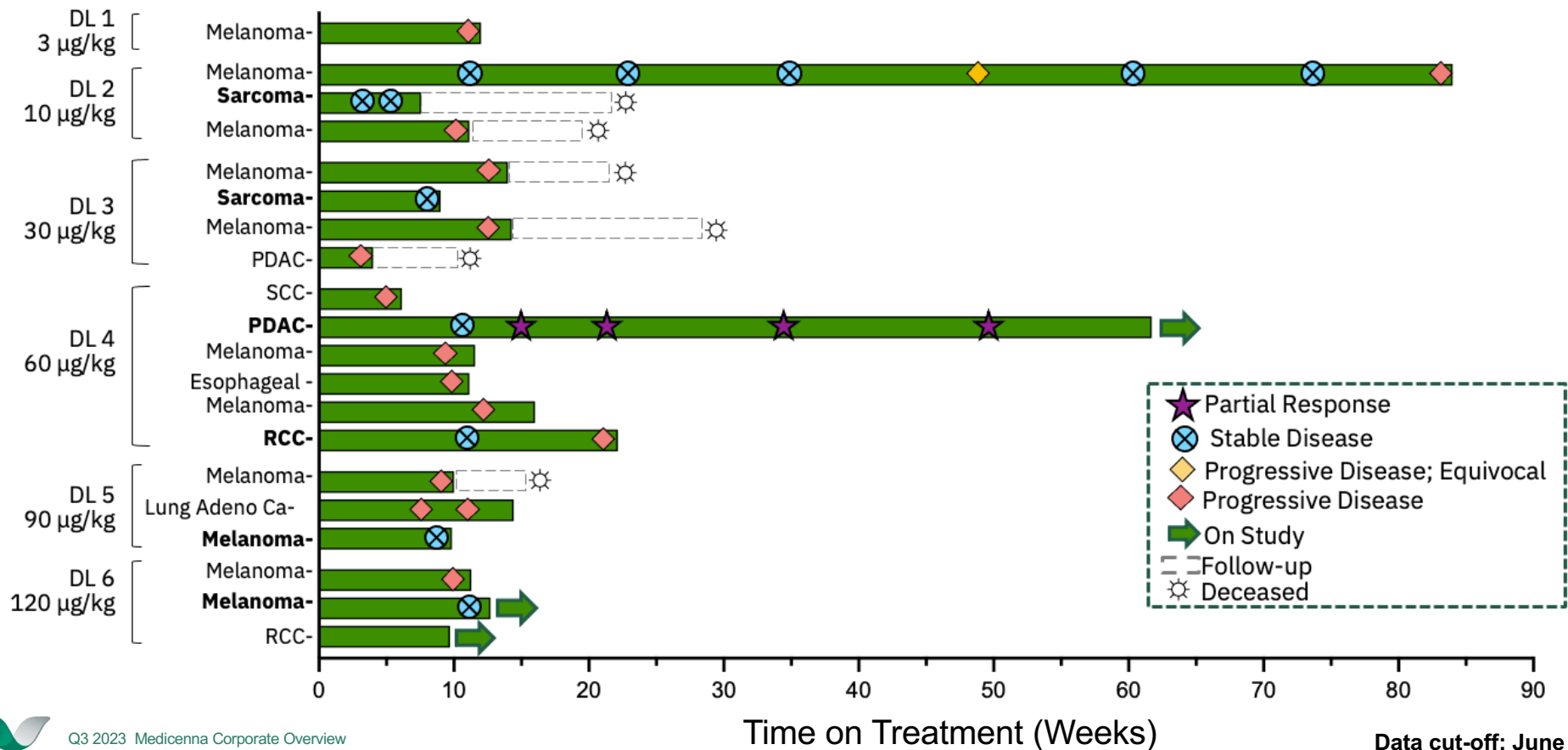


**CD8<sup>+</sup> T cells are powerful effectors of the anti-cancer immune response**

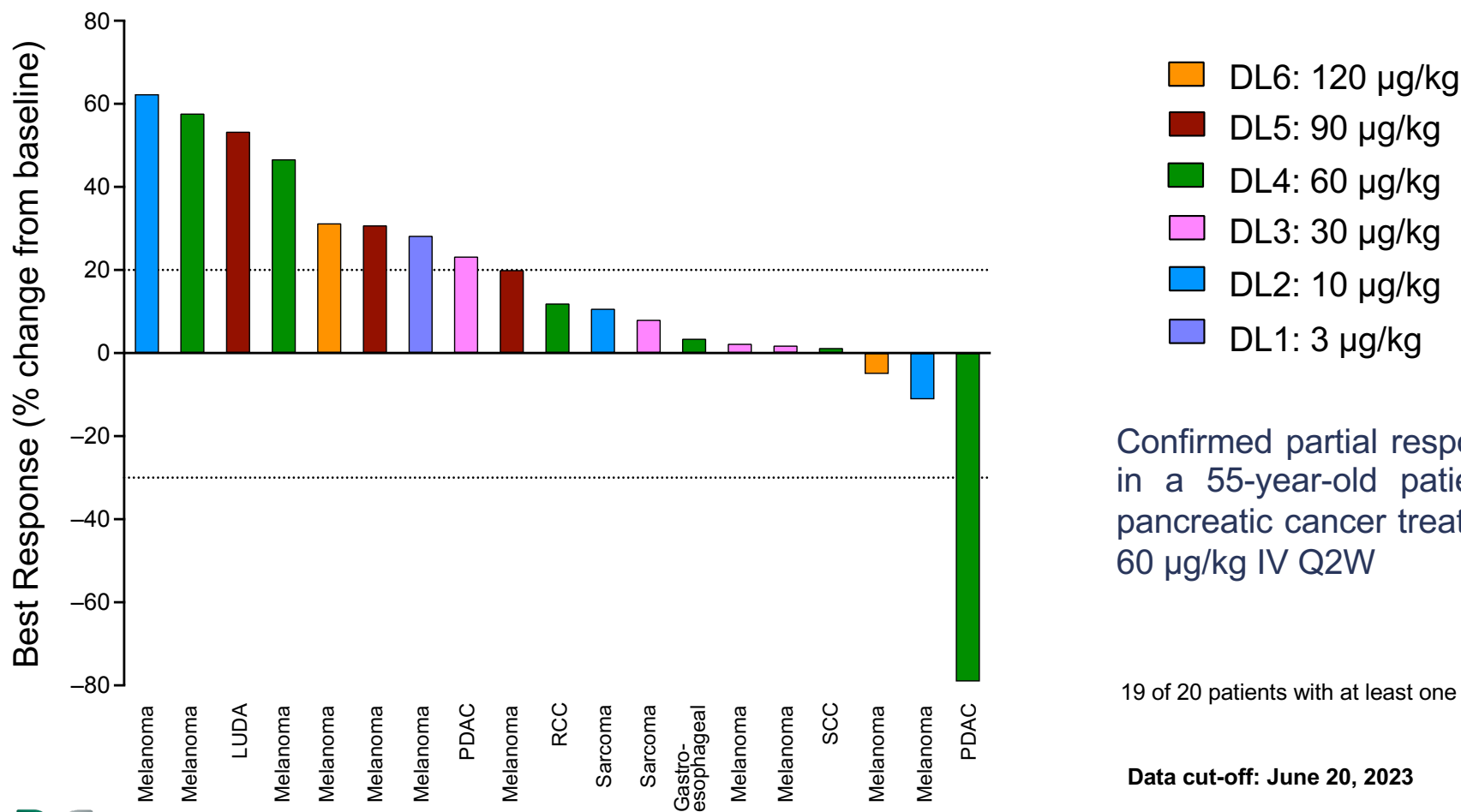


# Durable Responses Observed During Dose Escalation

SD lasting ~18 months in 71-year-old patient with metastatic melanoma treated with 2 prior lines of IO



# MDNA11 Shows Single Agent Clinical Activity



Confirmed partial response (PR) achieved in a 55-year-old patient with metastatic pancreatic cancer treated with MDNA11 at 60 µg/kg IV Q2W

19 of 20 patients with at least one follow-up assessment

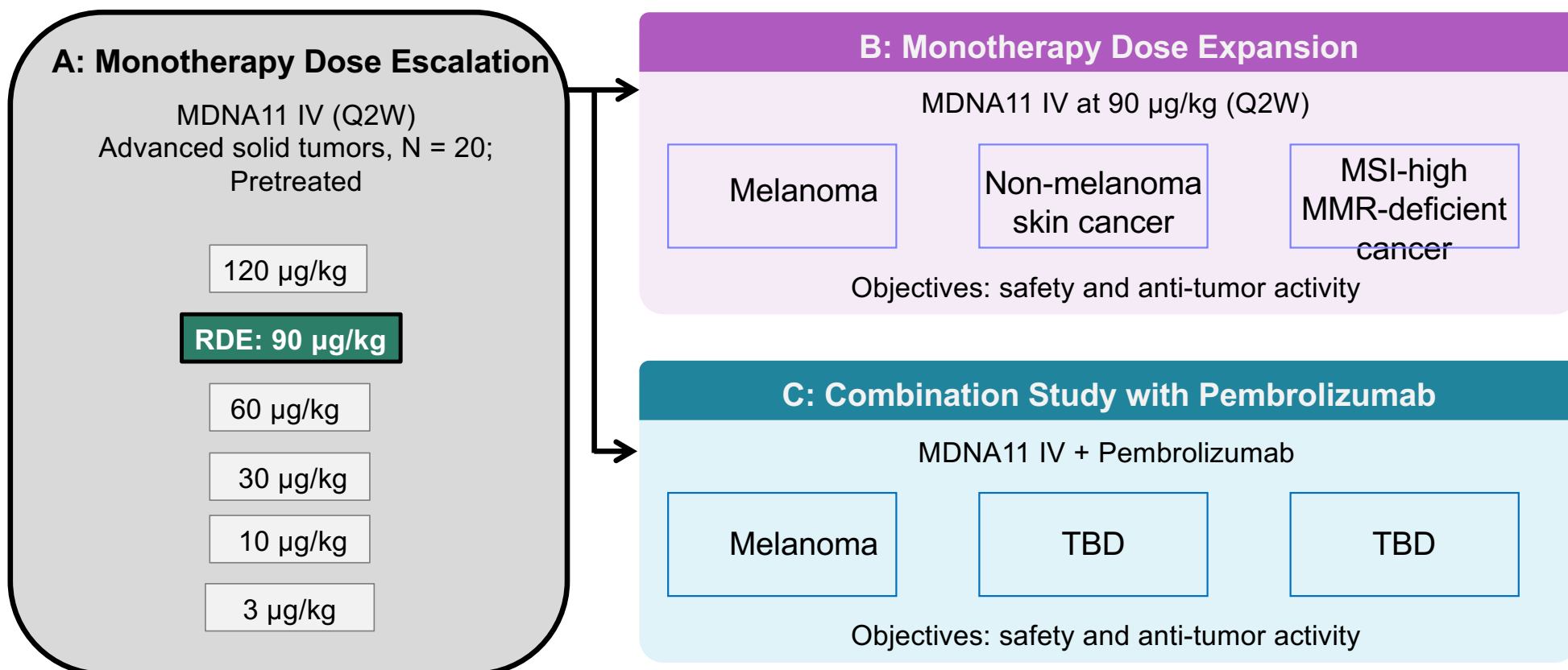
Data cut-off: June 20, 2023




# ABILITY Study Plan – Dose Expansion & Combination Phase

Global, multi-center, open-label Phase 1/2 study

Monotherapy dose escalation and expansion; combination with Pembrolizumab





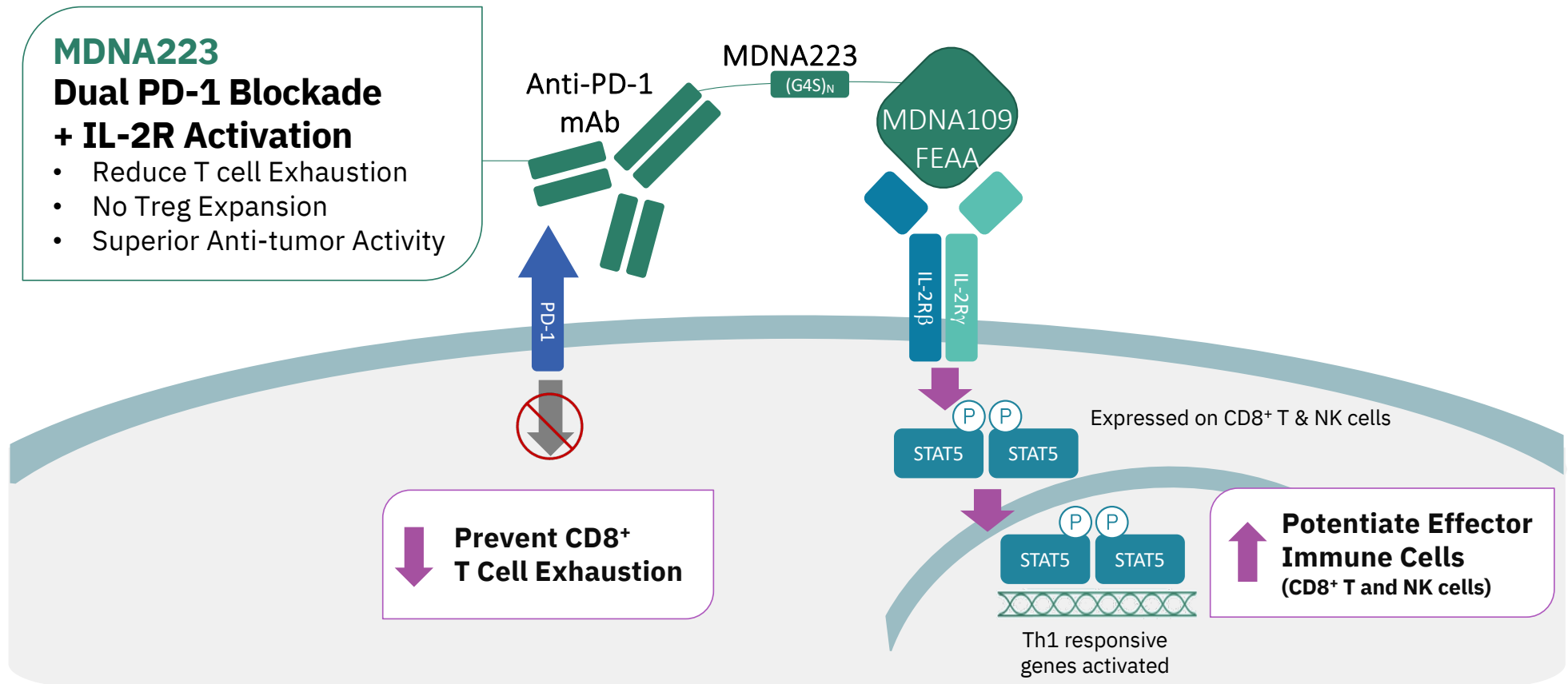


# Bifunctional SuperKines for ImmunoTherapy (BiSKIT)



# MDNA223: Anti-PD1-IL-2 Superkine BiSKIT

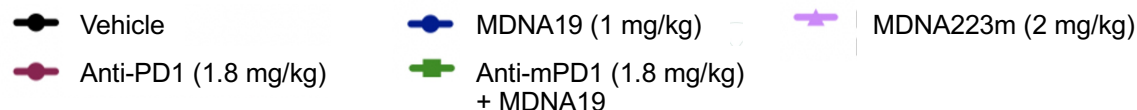
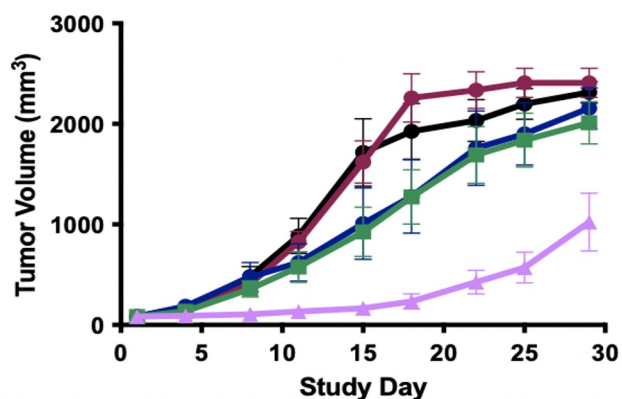
Synchronized cis-binding for PD-1 blockade and IL-2R activation on same CD8<sup>+</sup> T or NK cell



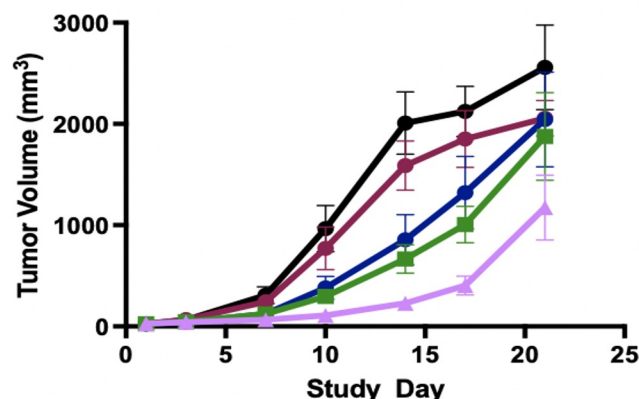
# MDNA223m Demonstrated Superior Anti-Tumor Activity

MDNA223m showed higher levels of anti-tumor activity than co-administration in pre-clinical studies

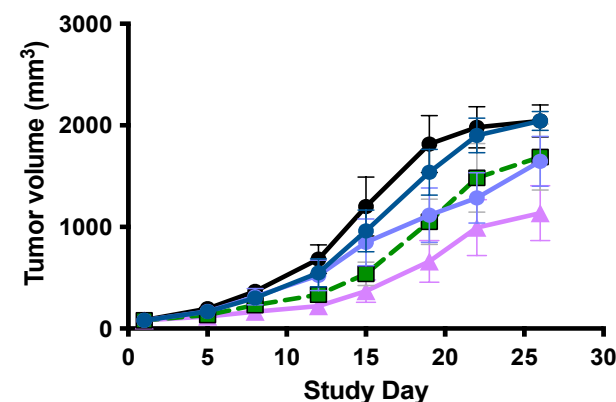
## CT26 Colon Tumor Model



## B16F10 Melanoma Model



## E0771 Breast Tumor Model



Treatment with molar equivalent doses of anti-PD1 (150 Kda), MDNA19 (83 Kda) or MDNA223m (165 Kda).  
 IP treatment QWx2 (CT26 and E0771) and QWx3 (B16F10)  
 Avg tumor size at initiation of dosing: 127 mm<sup>3</sup> (CT26), 80 mm<sup>3</sup> (E0771) or 30 mm<sup>3</sup> (B16F10)







# MDNA55

Empowered IL-4  
Superkine Targeting  
Glioblastoma





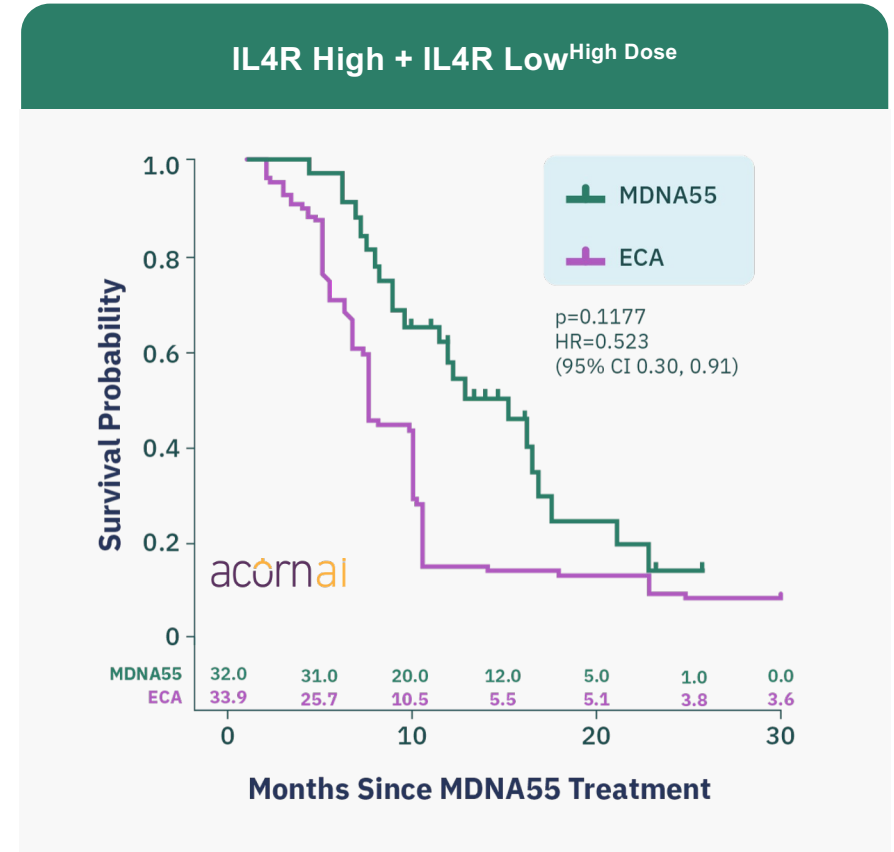
# Improvement of ~ 100% in mOS vs External Control Arm (ECA)

## Results\*

**Weighted IL4R High + IL4R Low<sup>High Dose</sup> (n=32)**  
mOS is 15.7 months vs 7.2 months in ECA

→ Survival time more than doubled in the IL4R High + IL4R Low<sup>High Dose</sup> group compared to ECA

**Bisaxofusp (MDNA55) is Phase 3 ready  
in recurrent glioblastoma**



\*Survival was calculated from time of relapse



# Next Milestones



# Upcoming Anticipated Milestones & Financial Summary

ABILITY Study Fully Funded – Cash Runway Through Q3 2024

## Anticipated Milestones

Start of ABILITY monotherapy expansion	Q3 2023
--	---------

Update from ABILITY monotherapy expansion	Q4 2023
---	---------

Commence combination phase of ABILITY with MDNA11 & pembrolizumab	Q4 2023
---	---------

Update from ABILITY mono- and combination phases	Q1 2024
--	---------

## Financial Highlights

Nasdaq/TSX	MDNA
------------	------

Headquarters	Toronto, CA
--------------	-------------

Cash	CDN \$29.6M*
------	--------------

Debt	\$0
------	-----

Preferred Shares	None
------------------	------

Issued and Outstanding	~70 Million*
------------------------	--------------

Fully Diluted	~92 Million*
---------------	--------------

\* As of June 30, 2023.



# Thank you

**Fahar Merchant, PhD** / President and CEO  
[fmerchant@medicenna.com](mailto:fmerchant@medicenna.com)

**Delphine Davan, MSc, MBA** / VP Investor Relations  
[ddavan@medicenna.com](mailto:ddavan@medicenna.com)

**Medicenna Therapeutics:** TSX, NASDAQ: MDNA  
Toronto, Houston, Boston  
[www.medicenna.com](http://www.medicenna.com)

