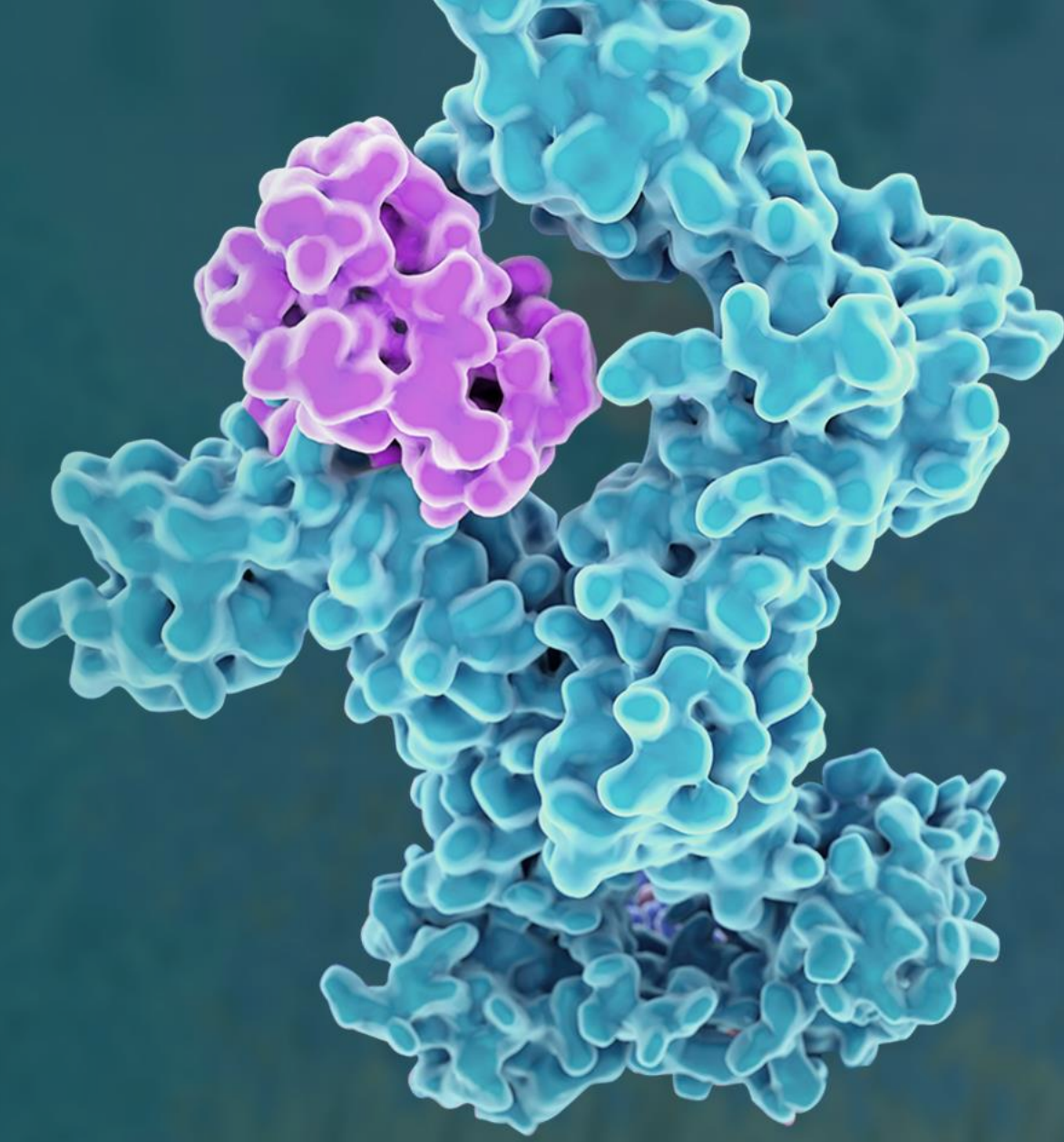
# Evolutionary Cytokines Revolutionary Medicines



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February 2024 | Corporate Overview | **TSX: MDNA** | **OTCQB: MDNAF**

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Toronto, CA
TSX: MDNA
OTCQB: MDNAF

## OUR MISSION

To leverage our **Superkine Platform** and design life-changing therapies that transform people's lives and deliver the best possible patient outcomes

## WHO WE ARE

MDNA is a clinical-stage immunotherapy company developing **Superkines** for the treatment of cancer and other diseases with serious unmet needs

## PIPELINE OF PROMISING ASSETS

| BiSKITs | MDNA11 | Bizaxofusp (MDNA55) |
|---|---|---|
| Pre-clinical | Phase 1/2 | Phase 3-ready |

## ANTICIPATED 2024 CATALYSTS

**MDNA11 Phase 1/2 Data**

Dose Escalation: Combination with KEYTRUDA®
Dose Expansion: Monotherapy, Combination

**Pursuing a Partnership for Bizaxofusp Phase 3**

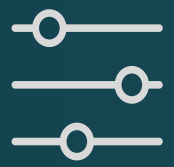
**MDNA11 | Lead Clinical Asset | Phase 1/2**

- a non-α, β-enhanced IL-2 Super Agonist
- stimulates the anti-cancer response (β)
- avoids stimulation of the immunosuppressive response (α)

**Bizaxofusp | Lead Clinical Asset | Ready for Phase 3**

- an IL-4 Agonist fused with a toxin
- *Trojan Horse* which targets IL-4R expressing tumors causing immunogenic cell death

# A Leading Clinical-Stage Immunotherapy Company with a Scalable Superkine Platform



## Drug Discovery Engine

### Superkine Platform

Directed evolution fine-tunes properties of IL-2, IL-4, IL-13 to generate Superkines

Protein fusion improves PK, adds MOA, and confers new capabilities

### BiSKITs*

Creates bi-specifics with Superkines, checkpoint inhibitors or antibodies

BiSKITs target cancers where other immunotherapies have failed

## Compelling Clinical Results

### MDNA11

A non-α, β-enhanced IL-2 Super Agonist with >20% single-agent response rate

Phase 1/2 ABILITY study: Monotherapy Dose Expansion, KEYTRUDA® Combination

### Bizaxofusp (MDNA55)

Phase 3-ready IL-4 fusion toxin for recurrent glioblastoma

Bizaxofusp doubled median overall survival in patients vs. matched external control arm in Phase 2b

## Anticipated 2024 Catalysts

### MDNA11 Phase 1/2

Preliminary Phase 1/2 Data:

Monotherapy Dose Expansion
Combination Dose Escalation
Combination Dose Expansion

### Bizaxofusp Phase 3

FDA-endorsed Phase 3 design, utilizing an ECA

Secure Breakthrough Designation

EMA Alignment for Phase 3 Trial

## Financial Stability

### Cash Runway

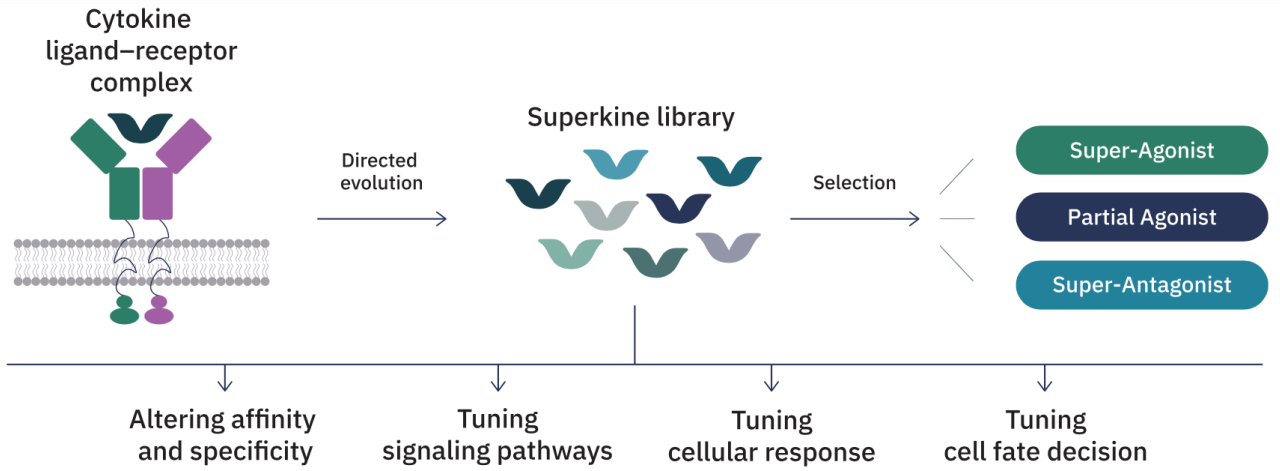
Cash and cash equivalents of $21.8M CAD *(as of 12/31/2023)* provides runway into Q2 2025

Disciplined, strategic capital allocation for our most promising assets

Substantial Insider Ownership (~24% *as of 12/31/2023*)

# Superkine Platform

## 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

# Robust Pipeline of Next Generation Superkines

| Candidate | Indication | Discovery | Preclinical | Phase 1 | Phase 2 | Pivotal |
|---|---|---|---|---|---|---|
| **Bizaxofusp (MDNA55)** IL-4–Toxin Fusion | Recurrent Glioblastoma (GBM) | | | | | |
| **MDNA11** IL-2 Super Agonist monotherapy | Melanoma, cSCC, BCC Merkel cell, MSI-H/dMMR | | | | | |
| **MDNA11** IL-2 Super Agonist combo with KEYTRUDA® | Various solid tumors | | | | | |
| **MDNA113** Anti PD-1-IL-2 Masked BiSKIT | Various solid tumors expressing IL-13Rα2 | | | | | |
| **MDNA413** IL-4/13 Pathway Super Antagonist | Oncology and Th2-mediated diseases | | | | | |
| **MDNA209** IL-2/15 Pathway Super Antagonist | Autoimmune Diseases | | | | | |

# The Challenges with Other Cytokine Therapies vs. Our Approach

## Cytokine Therapy Challenges

**Off-target Toxicity**

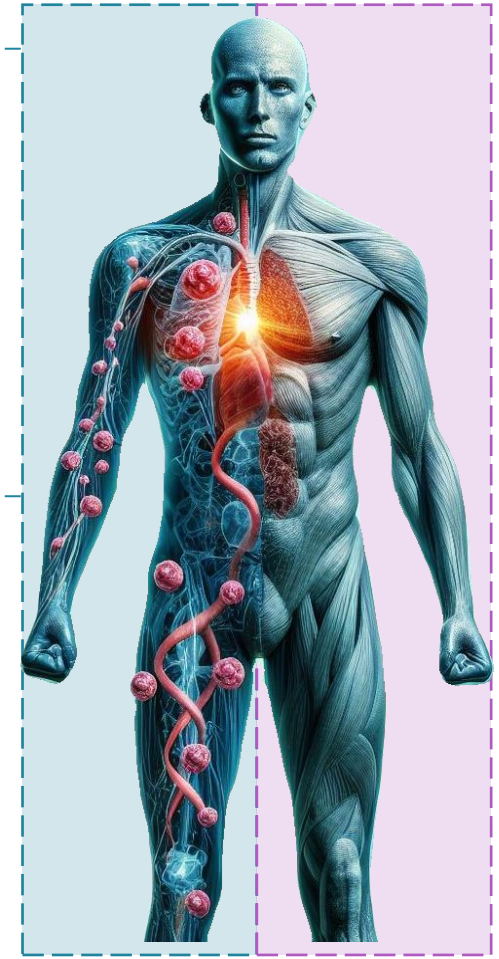
Heterogeneity of IL receptor expression on different immune cell populations and vasculature has posed significant challenges to mitigating severe systemic side effects

Lack of selectivity to receptor subtypes has been a major challenge for prior therapies

**Short Half-life**

Utility in other immunotherapies has been severely limited by short half-life, requiring frequent administration at a high dose to offset rapid clearance to achieve meaningful clinical response

High dose, frequent administration results in significant **systemic toxicity**



## The MDNA Way

**Tune | Enhance | Abolish**

Our therapies are engineered to be highly selective towards specific targets found within various tumors, the tumor microenvironment, and other desired cell populations

Abolishing binding to off-target pathways prevents toxicity

**↑Half-Life | Tumor Accumulation | Payloads**

Fusion of Superkines with other molecules can add new mechanisms of action, increase half-life, or enhance tumor accumulation

Fusion of Superkines with toxins allows our therapies to deliver toxic payloads directly to tumors

Clinical-Stage Asset in Phase 1/2
with a Monotherapy Treatment Arm and a
Combination Arm with KEYTRUDA®

# MDNA11

## MDNA11's Strong Anti-tumor Activity, Desirable Safety Profile and Convenient Outpatient Dosing Regimen Paves the Way for a Potential Best-in-Class Therapy With Significant Commercial Potential

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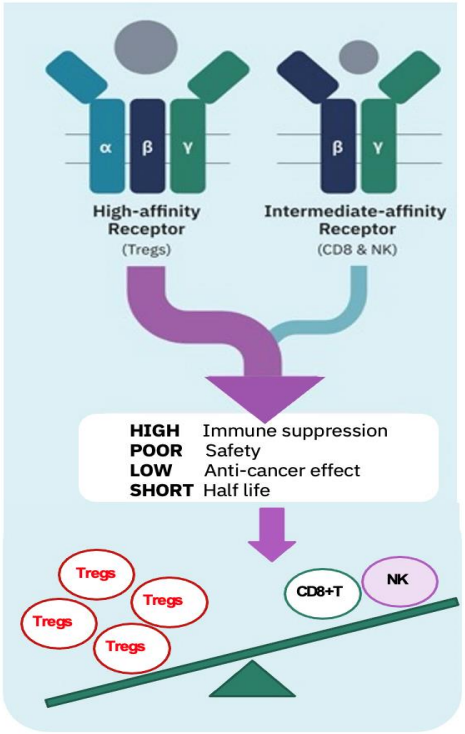
# MDNA11: A Non-α, Enhanced-β, IL-2 Super Agonist

## A Next Generation IL-2 Agonist Designed to Overcome Prior Challenges

rhIL-2

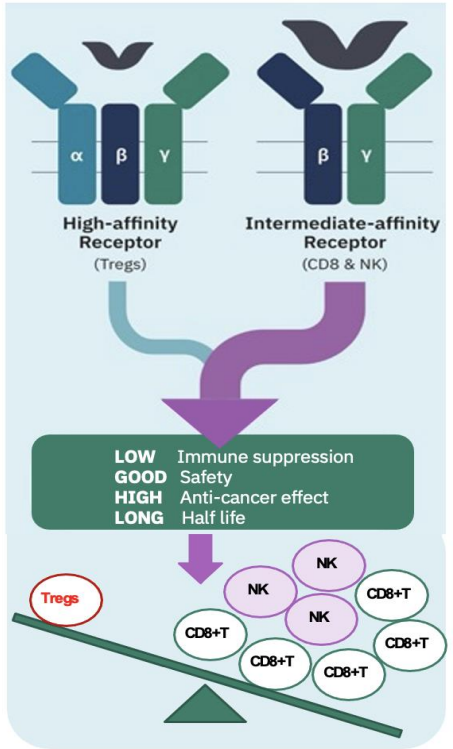



### Proleukin® (*Iovance*)

Approved in metastatic melanoma and renal cell carcinoma

- First approved cancer immunotherapy
- **Selectively stimulates IL-2Rα (toxic)**
- High systemic toxicity causing vascular leak syndrome due to expression of trimeric IL-2R in lungs and other vasculature
- Extremely Short half-life requiring IV administration every 8 hours for up to 5 days in an ICU setting

MDNA11




### MDNA11

Directed evolution via **Superkine Platform** to **selectively target IL-2Rβγ**

- Expand CD8+ T cells without Tregs
- Desirable Safety Profile
- Combined with albumin to extend half-life and enhance tumor-homing

**Superior selectivity**

**Engineered IL-2**

**Abolish α binding**

**Enhance β binding**

First-in-class

**Improved PK profile**

**Human Albumin**

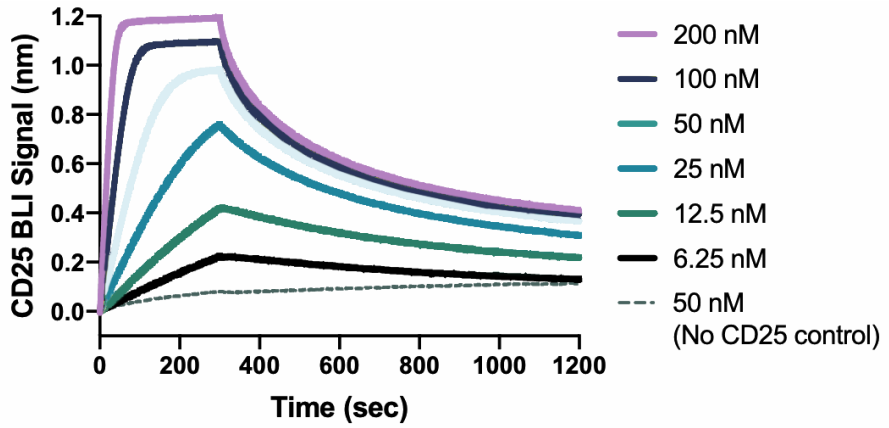
**↑ tumor accumulation**

**↑ half life**

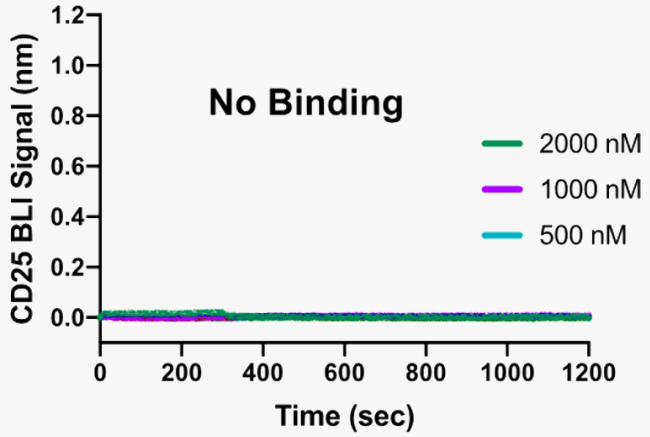
# MDNA11's IL-2R Binding is Highly Differentiated vs. Proleukin (rhIL-2)

## No IL-2Rα Binding and Enhanced Affinity and Selectivity for IL-2Rβ (CD122) Compared to rhIL-2

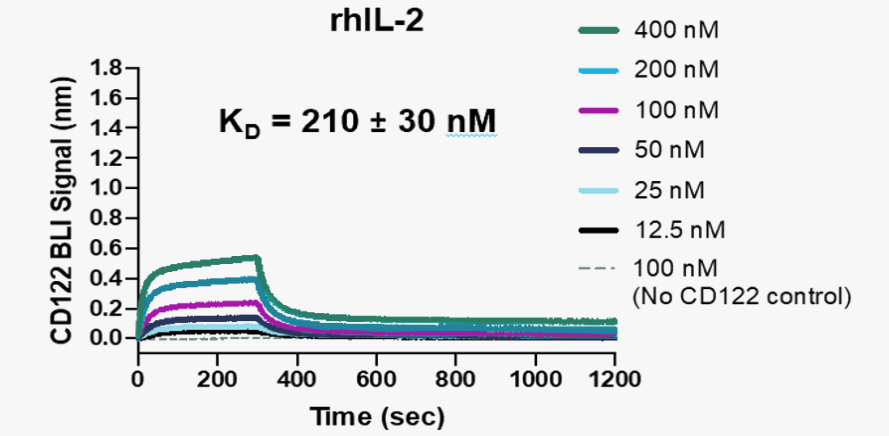
### rhIL-2 – IL-2Rα Binding



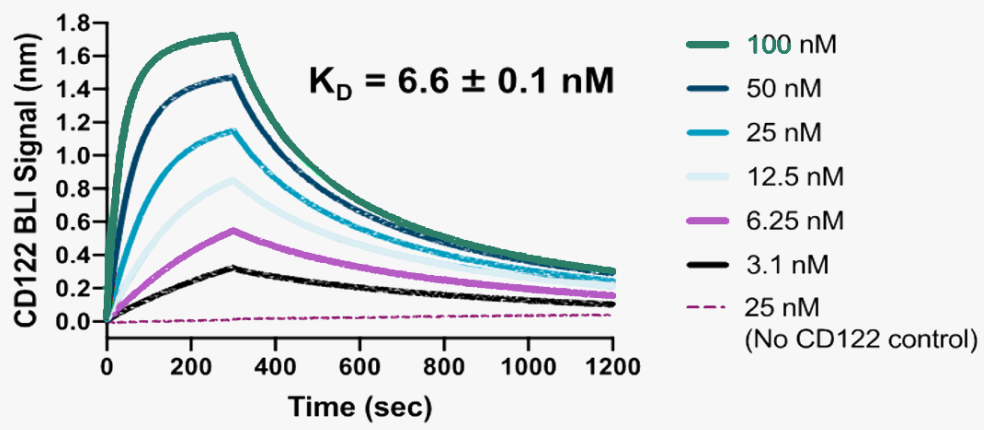

### MDNA11 – IL-2Rα Binding




### rhIL-2 – IL-2Rβ Binding

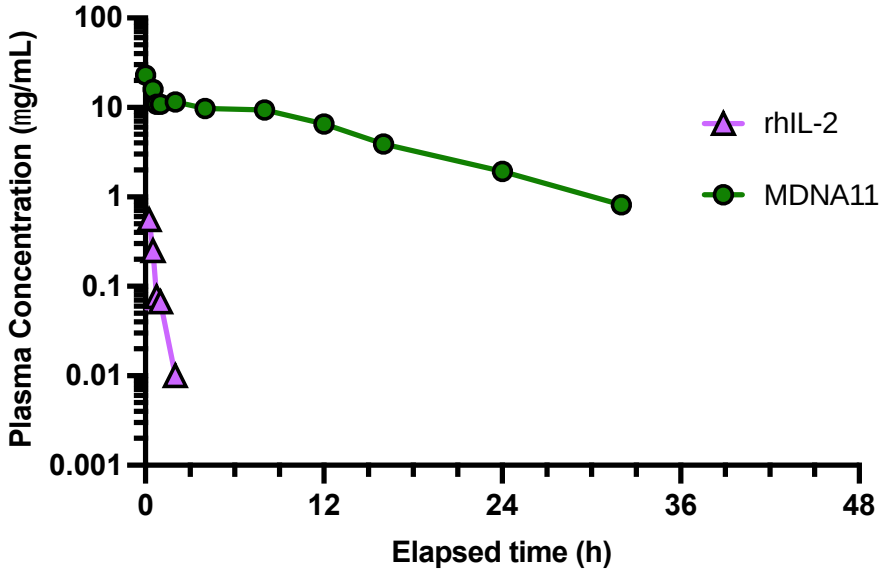



### MDNA11 – IL-2Rβ Binding



# Albumin Fusion Improves Half-life and Promotes Tumor Accumulation

## PK Profile in Mice

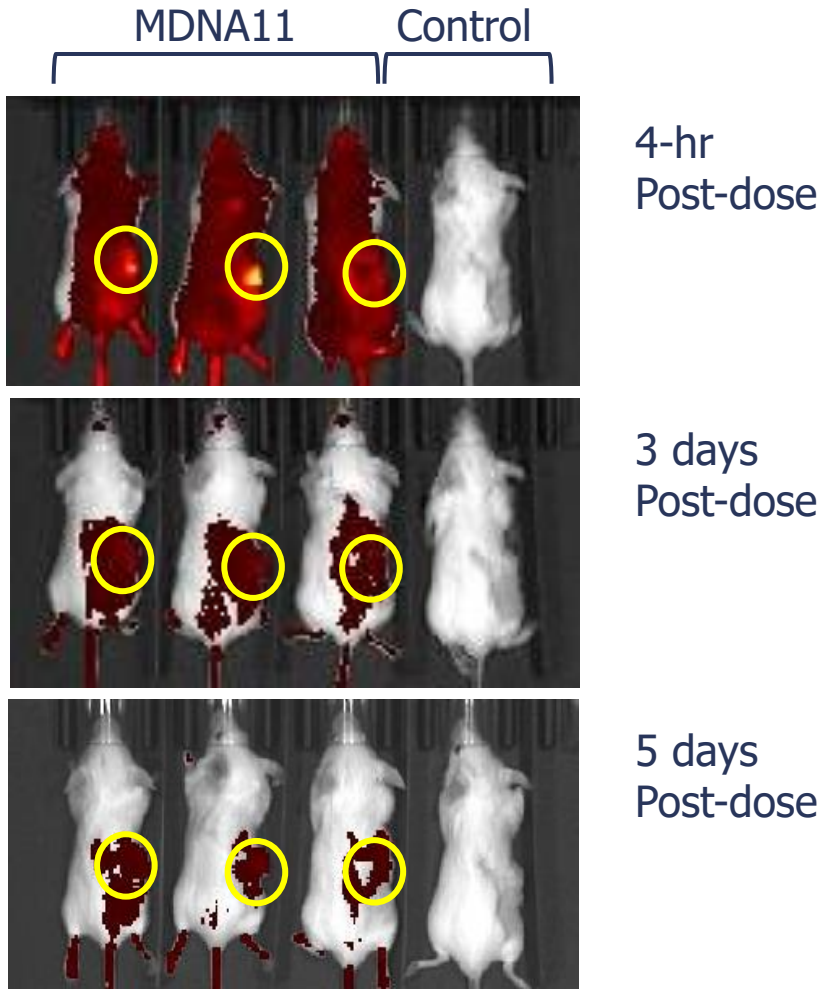



| | $C_{max}$ (µg/mL) | AUC (µg.hr/mL) | $T_{half}$ (hr) |
|---|---|---|---|
| rhIL-2 | 5.77 | 1.07 | 0.28 |
| MDNA11 | 23.02 | 182.3 | 6.83 |

Naive C57Bl/6 mice IV dosed at 1 mg/kg IV

- Albumin-bound paclitaxel (Abraxane) is used for treatment of cancers (Hoy, Drugs 2014; Blair and Deeks, Drugs 2015)

## Imaging of CT26 Tumor Bearing Mice




MDNA11 labelled with VivoTag800
IV dose: 1 mg/kg
Tumor size: 150-200 $mm^3$

# ABILITY Phase 1/2 Study: Dose Expansion & Combination with Pembrolizumab

## Global, Multi-center, Open-label Study Underway

### Phase 1: Monotherapy Dose Escalation/Evaluation

MDNA11 IV (Q2W)
Advanced solid tumors
N ~ 30

- 120 µg/kg
- **RDE: 90 µg/kg**
- 60 µg/kg
- 30 µg/kg
- 10 µg/kg
- 3 µg/kg

### Phase 2: Monotherapy Dose Expansion

MDNA11 IV at 90 µg/kg (Q2W)

- Melanoma
- Non-melanoma skin cancer
- MSI high MMR deficient cancer

(N≈40)

**Objectives**

- Safety
- Anti-tumor activity

**Next steps:**

- Preliminary Data H2 2024

### Phase 1/2: Combo with Pembrolizumab

MDNA11 IV + anti-PD-1 (pembrolizumab)

- Melanoma
- TBD
- TBD

(N≈40)

**Objectives**

- Safety
- Anti-tumor activity
- cRDE

**Next steps:**

- Preliminary Data H1 and H2 2024



RDE, Recommended Dose for Expansion
cRDE, combination Recommended Dose for Expansion

# Baseline Characteristics of Patients in Monotherapy Dose Escalation

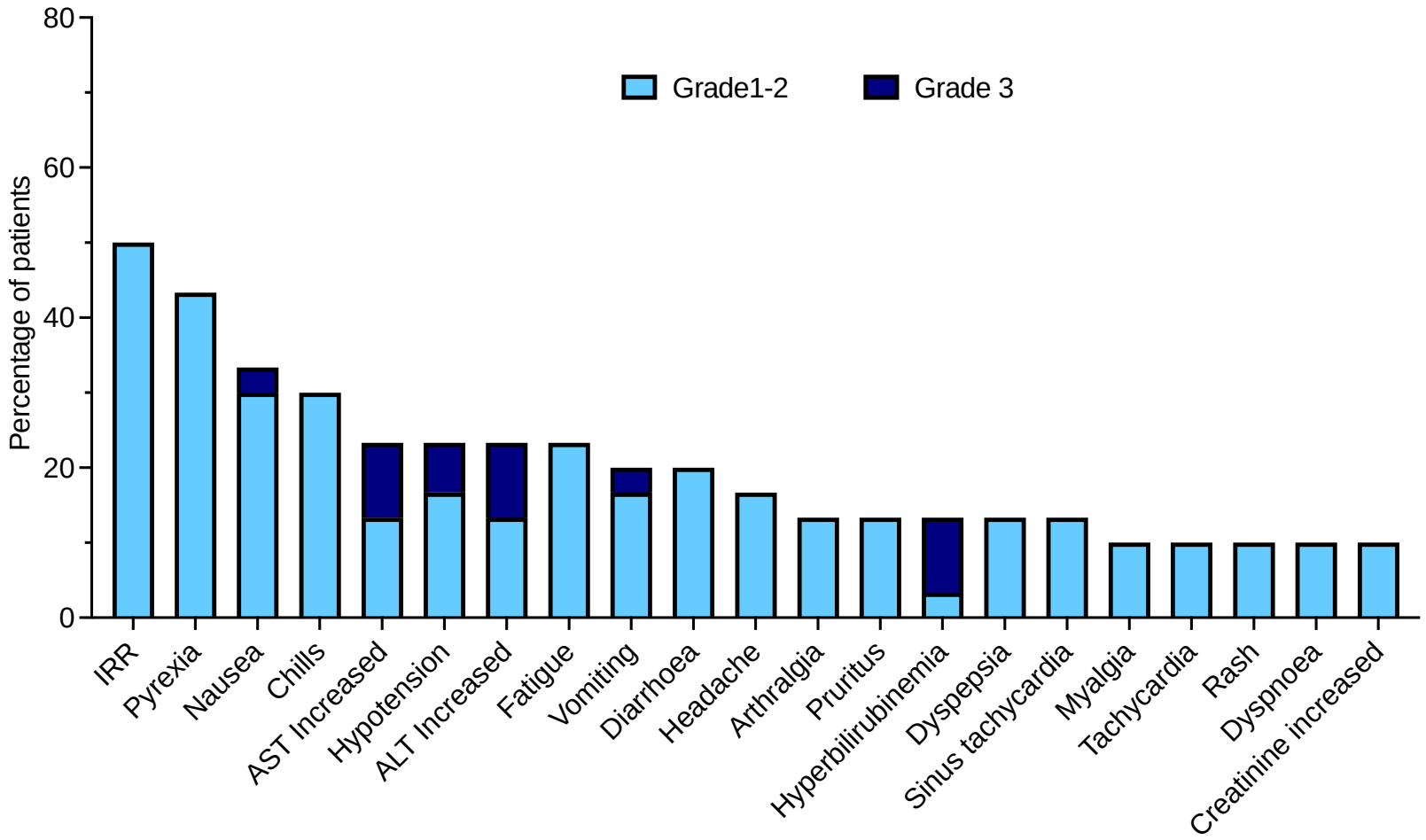
## All Patients Have Advanced Solid Tumors and Failed Prior Therapies

| Demographics/Performance | |
|---|---|
| Median age (range), years | **63 (27-78)** |
| Male (%) | **22/30 (73.3%)** |
| Baseline ECOG = 0 | **19/30 (63.3%)** |
| Baseline ECOG = 1 | **11/30 (36.6%)** |

| Prior Systemic Therapies | |
|---|---|
| Prior Lines of Therapy: 1-2 | **22/30 (73.3%)** |
| Prior Lines of Therapy: 3-4 | **8/30 (26.6%)** |
| Prior Use of Immunotherapy | **22/30 (73.3%)** |
| Prior Use of Targeted Therapy | **5/30 (16.6%)** |
| Prior Use of Chemotherapy | **15/30 (50%)** |

| Primary Cancer Diagnosis | |
|---|---|
| Melanoma (14 cutaneous, 1 mucosal; 1 acral) | **16/30 (53.3%)** |
| Non-small Cell Lung Cancer (NSCLC) | **3/30 (10%)** |
| Pancreatic Ductal Adenocarcinoma (PDAC) | **3/30 (10%)** |
| Renal Cell Carcinoma (RCC) | **2/30 (6.6%)** |
| Sarcoma (1 pleiomorphic; 1 leiomyosarcoma) | **2/30 (6.6%)** |
| Ovarian Cancer (Platinum-resistant) | **2/30 (6.6%)** |
| Tonsillar Squamous Cell Carcinoma | **1/30 (3.3%)** |
| Gastro-esophageal Adenocarcinoma | **1/30 (3.3%)** |

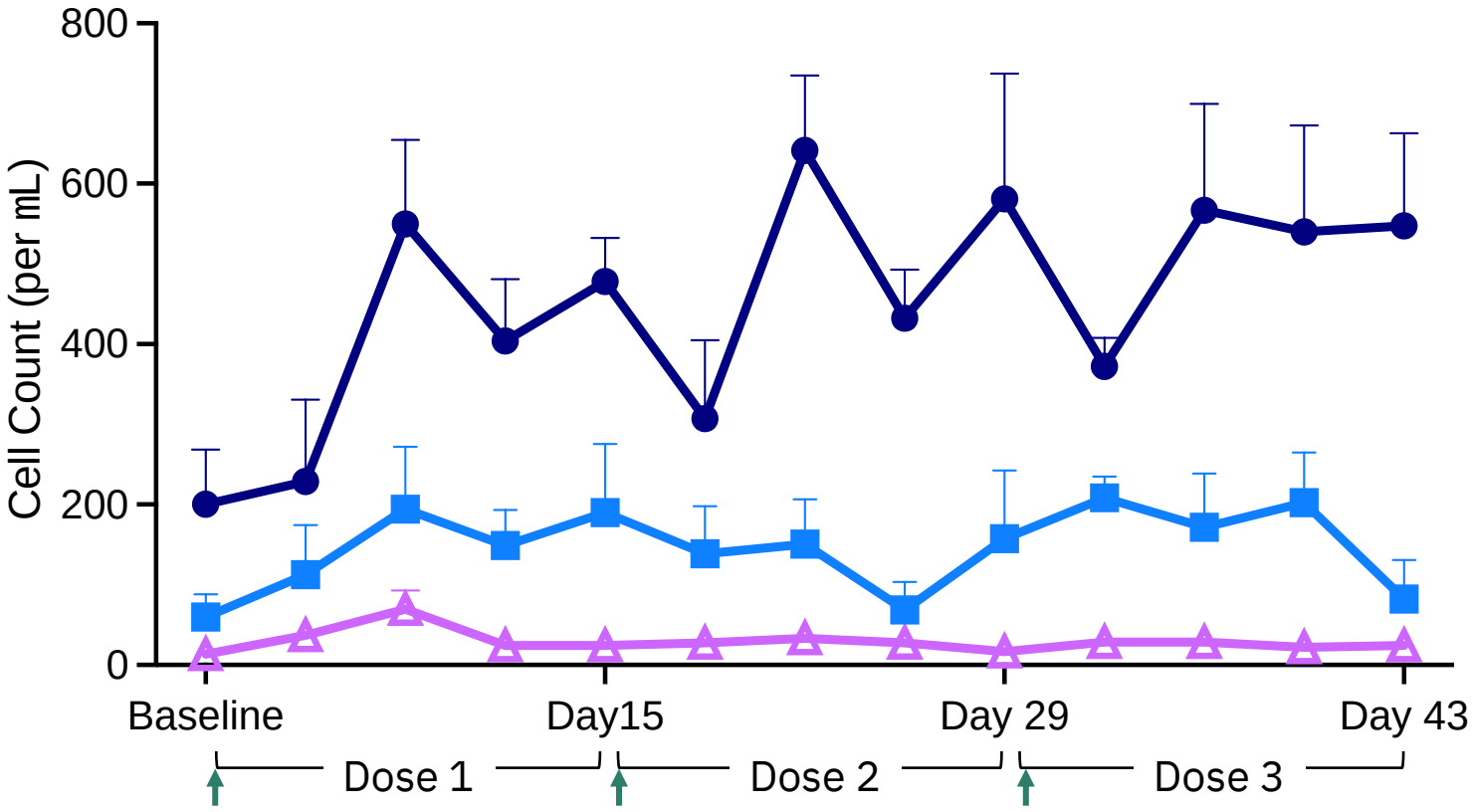
# MDNA11 Demonstrates Desirable Safety Profile Across All Doses

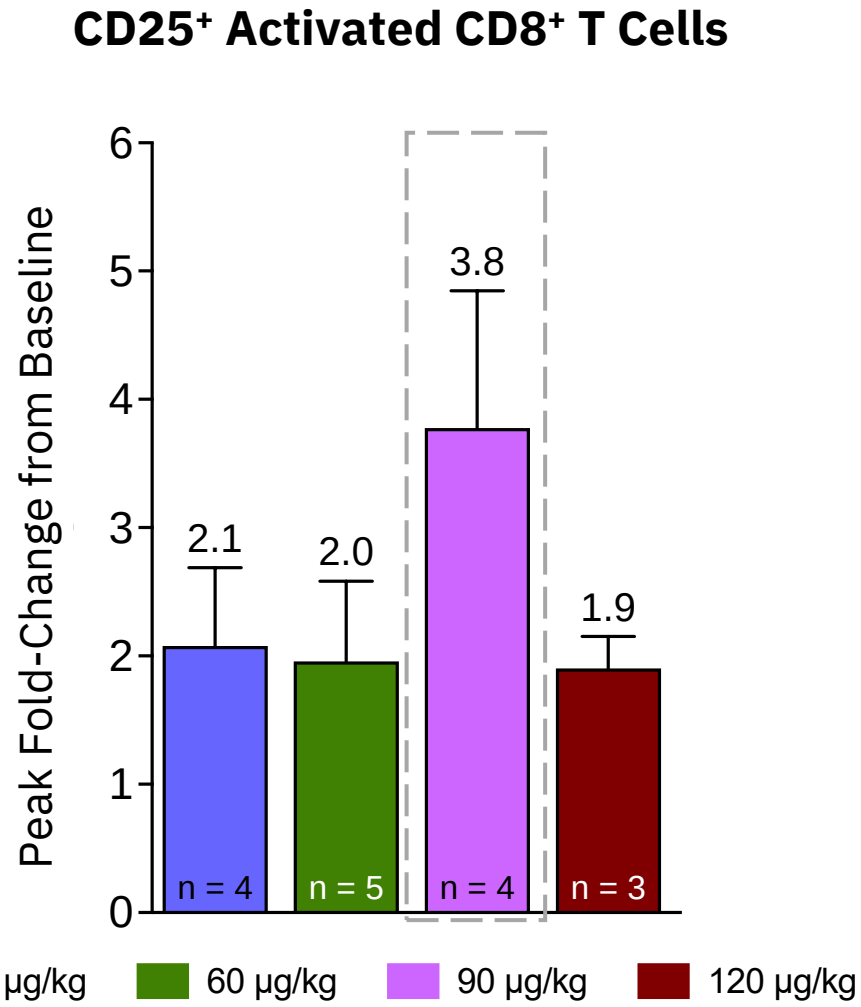



**95% of AEs were Grade 1-2**

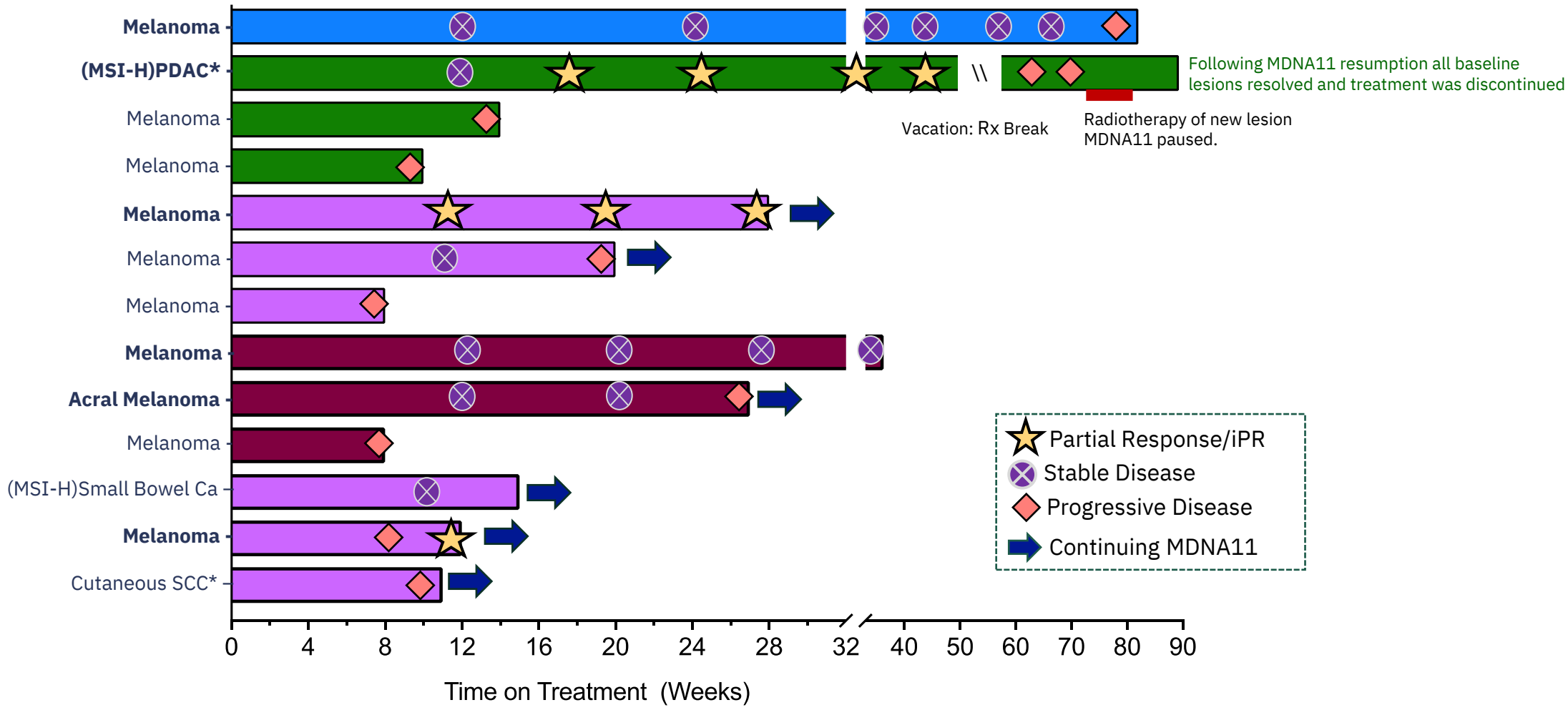
# Robust CD8+ T Cell Expansion and Activation at RDE (90 µg/kg)

## Preferential CD8+ T Cell Expansion and Activation Provides Antigen-specific Tumor Cell Killing and Promotes Memory Response



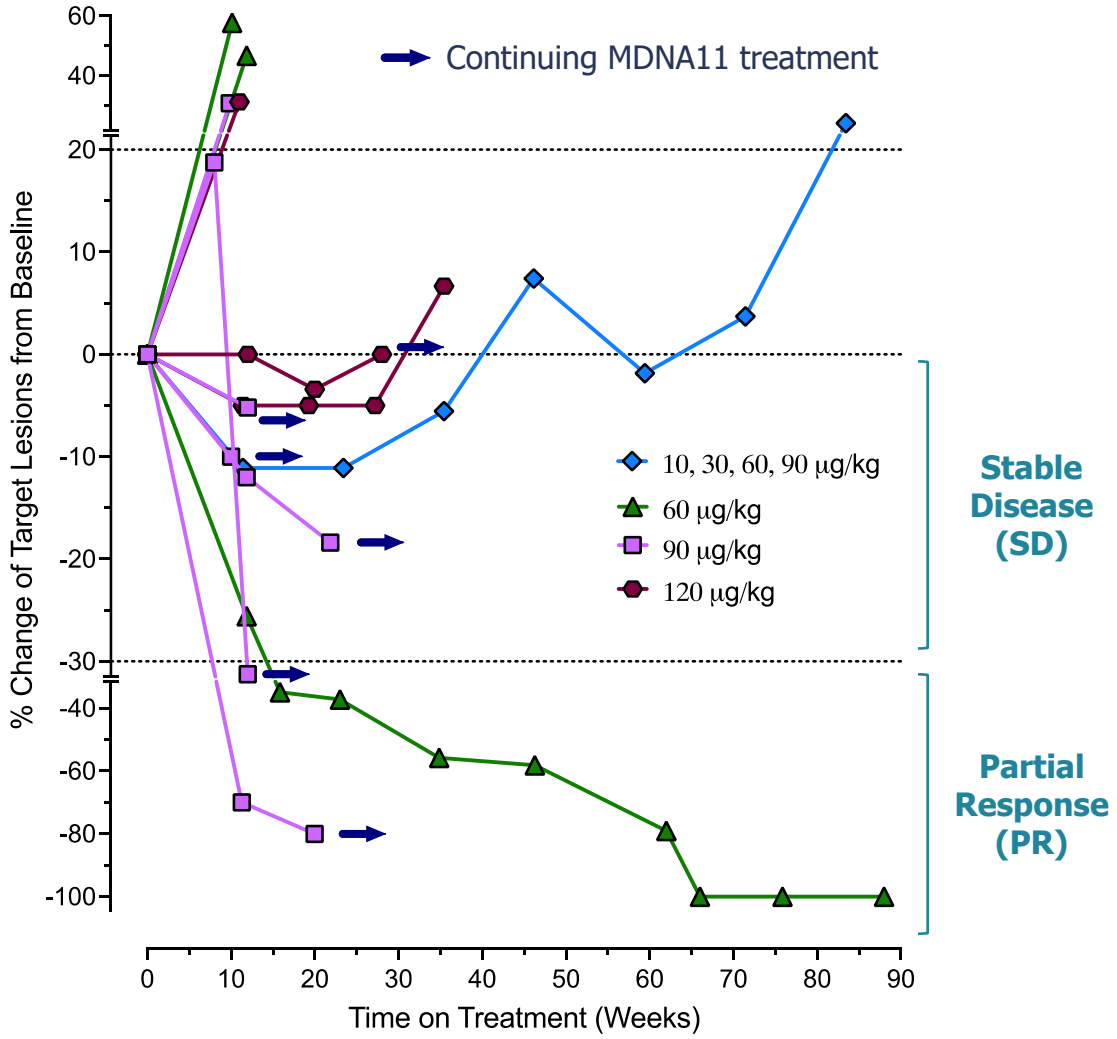
# MDNA11 Monotherapy: Shows Durable Tumor Response in High-Dose (≥60 µg/kg) Phase-2 Eligible Patients with Checkpoint Resistance

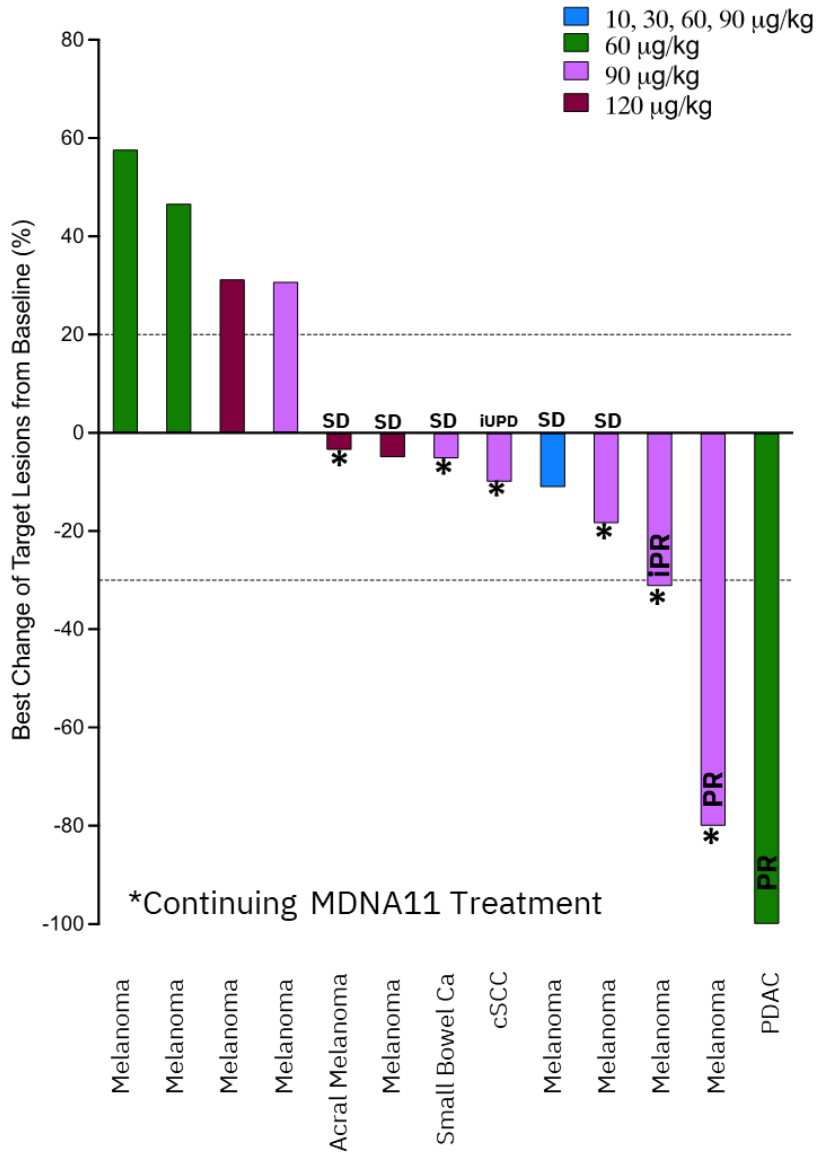




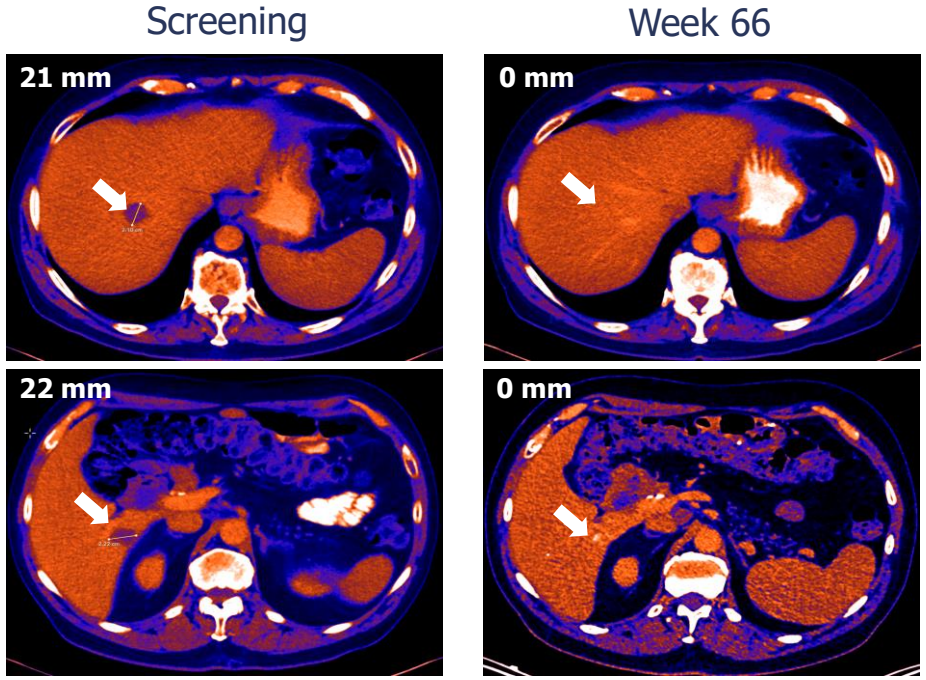

*Primary resistant to check point inhibitors

# Monotherapy: 23% Response Rate (3 PR) and 69% Tumor Control Rate (3 PR, 6 SD) in High-Dose (≥60 µg/kg) Phase-2 Eligible Patients



# First Reported IL-2 Therapy Showing Single Agent Response in PDAC




**PR observed at Week 16 (60 µg/kg)**

- Pancreatic ductal adenocarcinoma (PDAC, MSI-H) treated with two prior lines:
  - Whipple procedure + Adjunctive FOLFIRINOX
  - 1L: Gemcitabine + nab-Paclitaxel
  - 2L: Pembrolizumab (PD-primary resistant)
- PR first observed at week 16

**100% reduction of 2 target and 1 non-target lesions on MDNA11 alone:**

- Patient developed a single new lesion while on treatment break (vacation)
- New lesion received radiotherapy and MDNA11 was resumed
- Following resumption, all baseline lesions were resolved, and treatment was discontinued after Week 88

Treatment Break: Patient Vacation (Week 55 – 62)

Treatment Break: Radiotherapy for New Lesion from Vacation Break (Week 67-73)

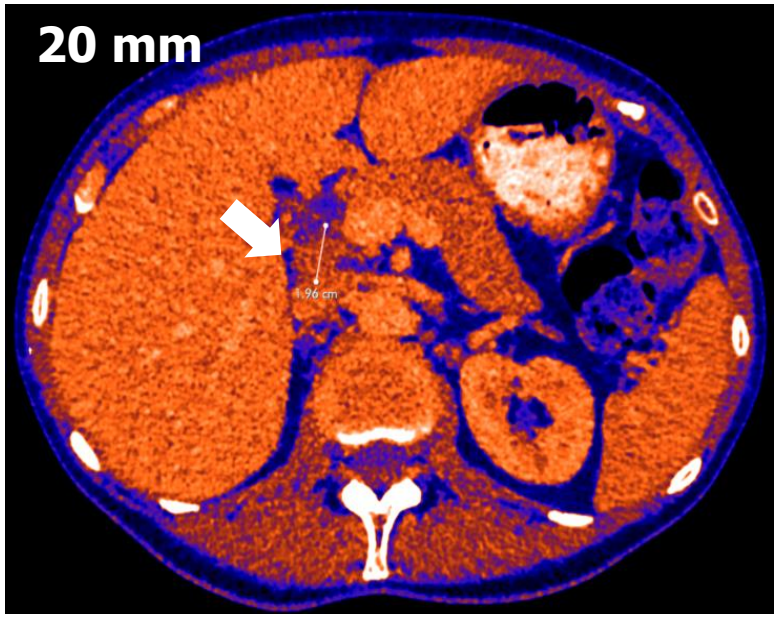
| | Baseline | Week 12 | Week 16 | Week 23 | Week 35 | Week 46 | Week 62 | Week 66 | Week 76 | Week 88 |
|---|---|---|---|---|---|---|---|---|---|---|
| Target lesions (Sum of diameters) | 43 mm | 32 mm | 28 mm | 27 mm | 19 mm | 18 mm | 9 mm | **0 mm** | 0 mm | 0 mm |
| Non-Target lesion | Present | Present | Present | Present | **Absent** | Absent | Absent | Absent | Absent | Absent |
| New lesion | None | None | None | None | None | None | 17 mm | 19 mm | 12 mm | 8 mm# |
| Overall response | | SD | **PR** | **PR** | **PR** | **PR** | PD | PD | *Not Evaluable | *Not Evaluable |

*Not evaluable as new lesion has received radiotherapy | # Lymph nodes <10 mm are considered normal as per RECIST 1.1
SD, stable disease | PR, partial response | PD, progressive disease

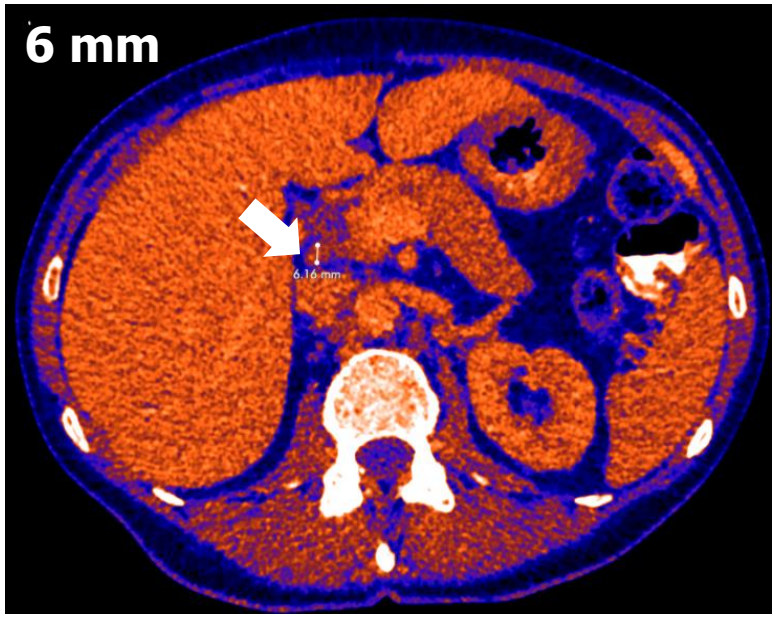
# PR at First On-Study Evaluation Scan in Metastatic Melanoma

Target Lesion

Screening




Week 12




**PR at Week 12 (90 µg/kg):**

- Cutaneous melanoma progressed on prior line of dual checkpoint inhibitors (Nivolumab + Ipilimumab)
- 70% reduction of the target lesion at week 12
- Deepening Tumor Response of 80% week 20
- Patient continues to receive MDNA11

| | Baseline | Week 12 | Week 20 |
|---|---|---|---|
| Target Lesion | 20 mm | 6 mm | 4 mm |
| Non-Target lesions | Present | Present | Present |
| Overall response | | **PR** | **PR** |

→ Continuing MDNA11 treatment

# MDNA11: an IL-2 Superkine with Single Agent Clinical Activity

| | |
|---|---|
| **Not Alpha, Beta-Enhanced IL-2 Super Agonist** | • Engineered as a long-acting potentiator of $CD8^+$ effector T cells and NK cells but limit Treg expansion compared to native IL-2 |
| **Extended Half-Life and Tumor-Homing** | • Convenient Q2W dosing with albumin scaffold extends half-life via FcRn recycling, lowers kidney clearance, and enhances homing to tumor sites and draining lymph nodes |
| **Desirable Safety Profile in Clinic** | • Acceptable toxicity with no DLTs, no evidence of cytokine release syndrome or vascular leak syndrome in ongoing monotherapy portion of Phase 1/2 ABILITY study |
| **Single Agent Activity in Ongoing Phase 1/2 Study** | • **Response Rate of 23%** (3/13), Clinical Benefit Rate of 46% (6/13) and **Tumor Control Rate of 69%** (9/13) in high-dose (≥60 µg/kg), Phase-2 eligible **patients with resistance to immune checkpoint therapies** |
| **Combination Trial with Checkpoint Inhibitor Initiated** | • Preclinical studies show a strong memory response, low immunogenicity and complete tumor regression when MDNA11 is combined with anti-CTLA4 or anti-PD1 therapies |

# Bizaxofusp (MDNA55)

## A Phase 3-Ready Asset with Orphan Drug Status and an FDA-Endorsed Pivotal Phase 3 Trial Design

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# Bizaxofusp (MDNA55): A Molecular Intratumoral Trojan Horse

## A first-in-class Phase 3-ready Empowered IL-4 Superkine for recurrent glioblastoma (rGBM)

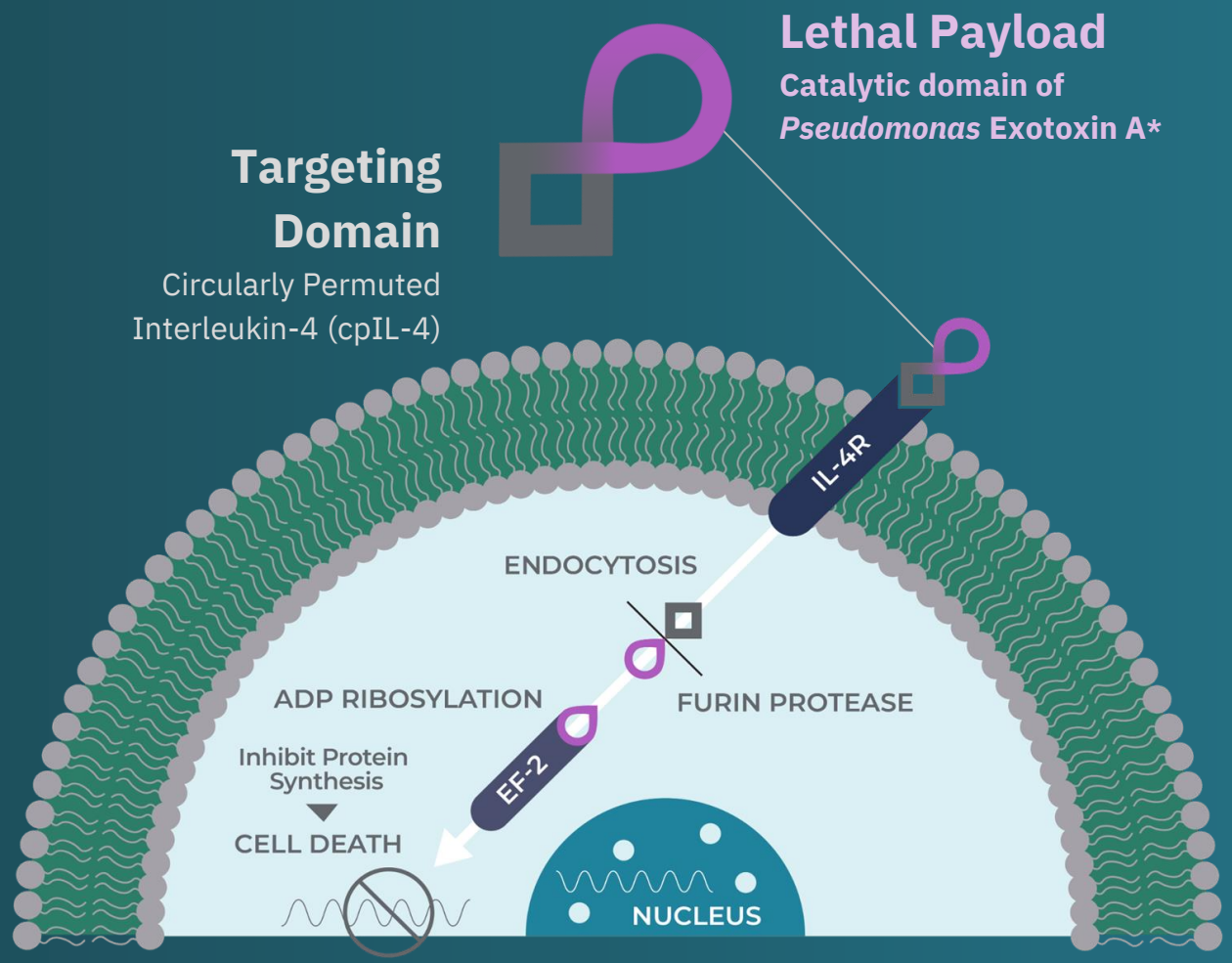
**Approach By-Passes BBB**
Single intra-tumoral CED infusion **avoids systemic toxicity** and achieves tumor control

**Targets IL-4R**
Receptor is expressed in brain tumors and immunosuppressive, non-malignant TME, but not in healthy brain cells

**Highly Selective**
Avoids off-target toxicity

**Disrupts the TME**
Targets IL-4R positive MDSCs in GBM unblinds the immunosuppressive TME

**Causes Immunogenic Cell Death**
Sustained anti-tumor immunity remains after clearance of bizaxofusp




BBB, blood-brain barrier; CED, convection enhanced delivery; TME, tumor microenvironment; MDSCs, myeloid-derived suppressor cells

# Bizaxofusp: The Better Option to ADCs for Brain Cancer

## Bizaxofusp

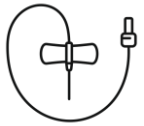
GBM is the most aggressive primary brain tumor; 100% of patients relapse following SOC

rGBM is uniformly fatal with median OS (mOS) of 6-9 months

**IL-4R**:
overexpressed in GBM and TME but not healthy brain tissue

Bizaxofusp only targets IL-4R expressing tumors causing immunogenic cell death

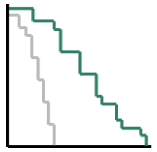
## Compelling Results



Single intra-tumoral treatment

By-passes the blood brain barrier

No systemic toxicity



**Bizaxofusp doubled mOS to 14.5 months vs matched external control arm (ECA)**

Strict inclusion criteria:
*de novo* GBM, 1st or 2nd relapse
non-resectable tumors
IDH wild-type only

## Phase 3 Ready

FDA-endorsed Phase 3 design, utilizing an ECA

Preparing for Phase 3

Pursuing a Partnership

Potential for Breakthrough Therapy Designation

Has FDA Fast-Track Designation

FDA's Project Orbis allows for swift international adoption

## $4B Opportunity

**$800M Market Opportunity (US/EU)**

Follow-on applications upwards of **$4B:**
1st line for non-resectable GBM
IL-4R expressing metastatic brain tumors

**Market Exclusivity**

**Orphan Drug Status** from EMA and FDA provides up to 11 years of market exclusivity

Patent Protection Projected to 2040



ADC, antibody drug conjugate; SOC, standard of care; OS, overall survival

# Bizaxofusp: Localized "One and Done" Delivery By-Passes the BBB

## Next Generation High-flow Convection Enhanced Delivery (CED) Achieves Uniform Distribution to Tumoral & Peritumoral Areas

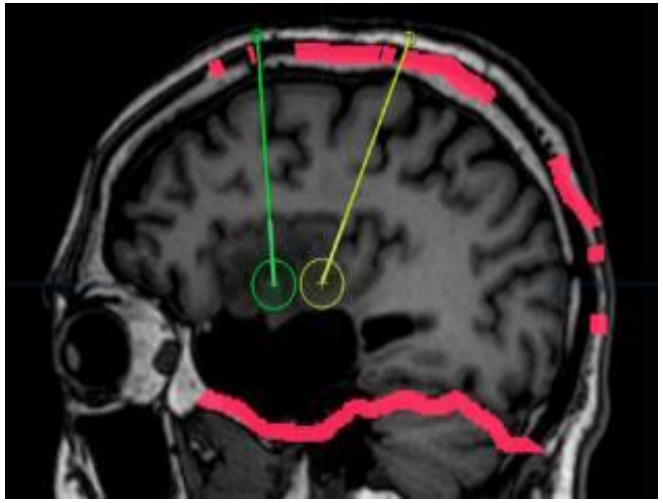
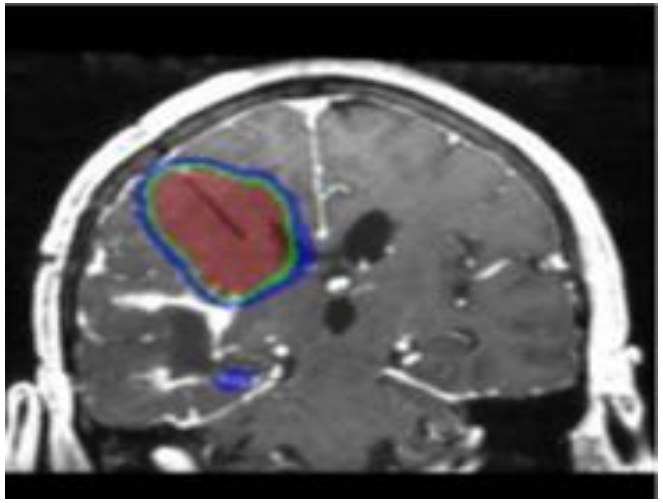
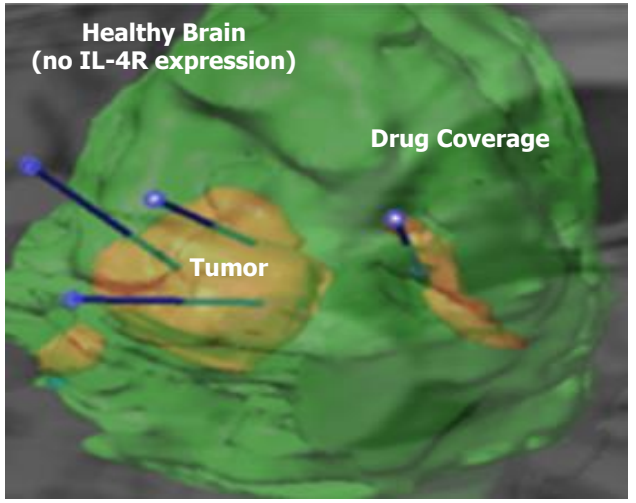


Image guided catheter placement to identify the **ideal catheter trajectory**



Unique catheter stepped design to **prevent backflow**




**Novel delivery** improves tumor coverage

**One-time treatment | Repeat administration has been shown to be safe**
Minimally invasive CED techniques for catheter placement are similar to those used used for brain tumor biopsies

# Bizaxofusp has Demonstrated Favorable Safety in 118 Patients

## No Signs of Systemic Toxicity at any Dose in Phase 1/Phase 2/Phase 2b Trials

| STUDY | PATIENT | DOSE (µg) |
|---|---|---|
| NIH-sponsored Investigator Initiated (U.S.) | Recurrent GBM (n=9) | 6 - 720 |
| Multi-Center (U.S./Germany) Phase 1 "Non-resected Trial" | Recurrent HGG **No Resection** (n=31; 25 rGBM+6 AA) | 240 - 900 |
| Multi-Center (U.S./Germany) Phase 2 "Resected Trial" | Recurrent GBM **+ Resection** (n=32) | 90 - 300 |
| Multi-Center (U.S./Poland) Phase 2b | Recurrent *de novo* GBM **No Resection** (n=46) | 18 - 240 |

Phase 2b study was the most recently completed study

### Consolidated Safety Profile

- No systemic toxicity at any dose
- No clinically significant laboratory abnormalities
- Most adverse events were due to local effects and similar to those typically seen in this patient population
- Manageable inflammation and edema associated with tumor necrosis
- 2 grade 5 events unrelated to study drug
- MTD established at > 240 µg

# Phase 2b Results Published as the Cover Story in Neuro-Oncology

## Published in the June 2023 Issue and Received Editor's Choice with a Corresponding Editorial

**Editorial**

1098 Neuro-Oncology

25(6), 1098–1099, 2023 | https://doi.org/10.1093/neuonc/noad043 | Advance Access date 15 February 2023

**Phase II trials in the era of glioblastoma immunotherapy: New mechanisms of action, familiar challenges in trial design and tumor response assessment**

**Stephen J. Bagley**

All author affiliations are listed at the end of the article

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**Cover of June Issue**


Duke University School of Medicine · Cancer Therapy & Research Center UT Health Science Center San Antonio · UCSF University of California San Francisco · Cleveland Clinic · Penn Medicine · Oregon Health & Science University · Dana-Farber Cancer Institute · Boca Raton Regional Hospital · UCLA David Geffen School of Medicine · University of Oxford · St. Michael's Unity Health Toronto

# Phase 2b Study Completed Meeting Primary Endpoint

## Open-Label Single Arm Study of Bizaxofusp in rGBM Patients (N=47) (NCT02858895)

### ELIGIBILITY

- Adults ≥ 18 yrs
- ***de novo* GBM**
- **1st or 2nd relapse**
- **No resection**
- **KPS ≥ 70**
- **IDH wild-type only**
- Failed 1L surgery, radiation, and/or chemotherapy (Stupp Protocol)
- Retrospective IL-4R analysis from initial Dx

### TREATMENT

- Image-guided catheter placement
- Monitor real-time drug distribution with co-infusion of Magnevist ®
- Single infusion (median 26.5 hrs.)
- Total Dose range: 18-240µg
- Transient low-dose bevacizumab allowed for symptom control and/or steroid sparing

### ENDPOINTS

**1º Endpoint**

- OS

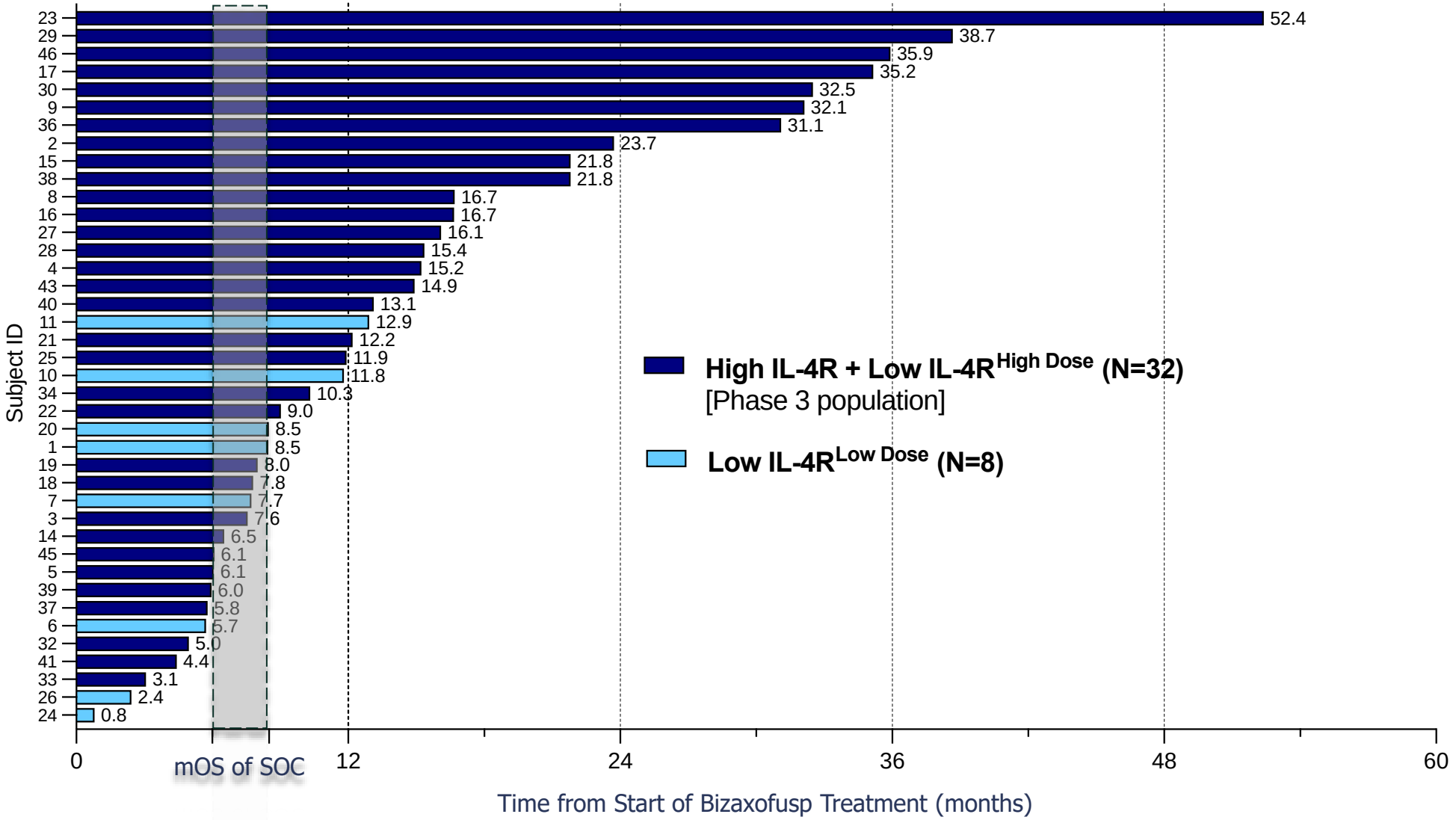
**2º Endpoint**

- ORR
- PFS
- OS vs. IL4R expression
- Safety

Phase 2b purposefully only included patients with characteristics associated with worse clinical outcomes

**Increases Confidence in Phase 2b Data and Reduces Phase 3 Risk**

# Bizaxofusp$^{\text{High Dose}}$ Improves Overall Survival Regardless of IL-4R Expression



# Bizaxofusp (MDNA55)

Retrospective Study with an Eligibility Matched ECA: Comparison of Survival in the Phase 2b Trial

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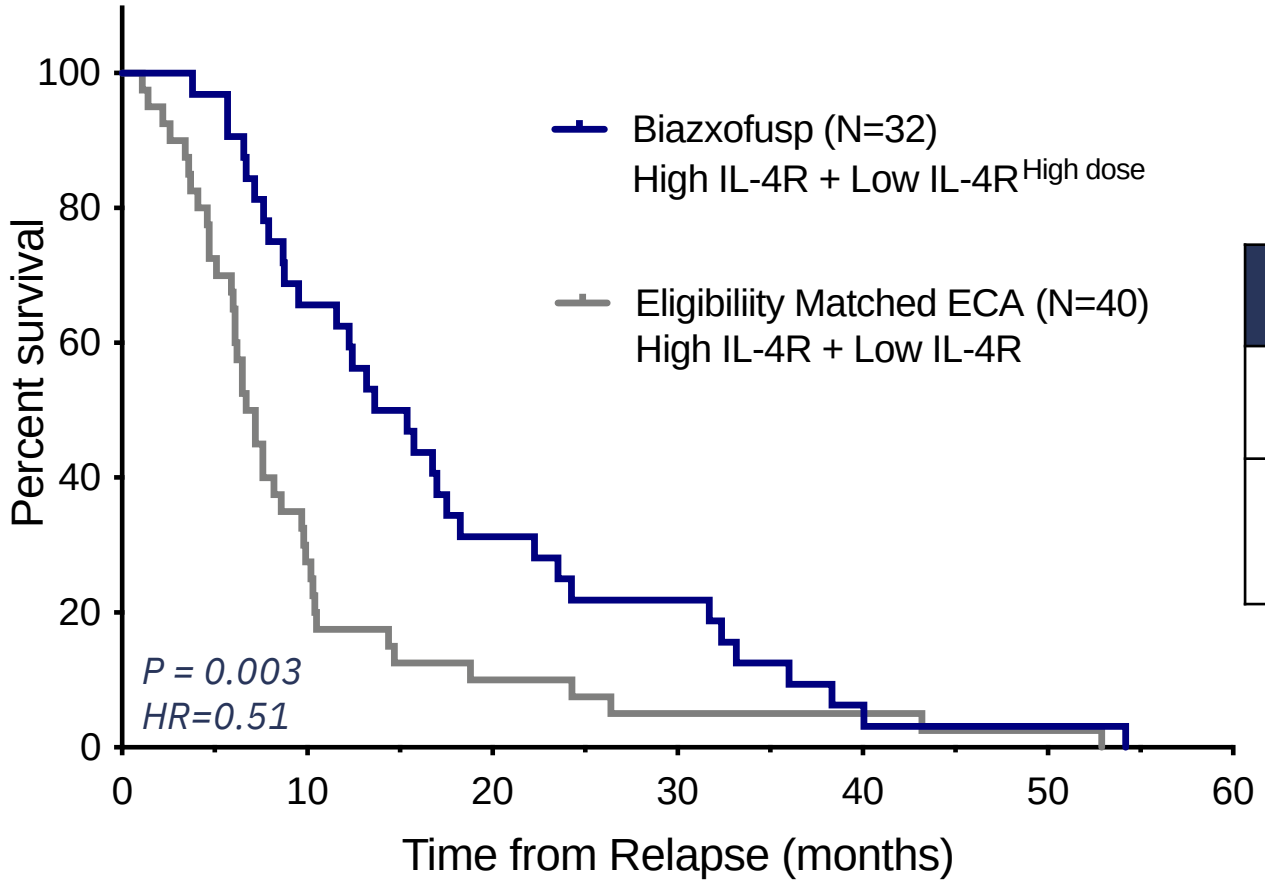
# Comparison of Survival Between Planned Phase 3 Population and ECA

| ELIGIBILITY | EXTERNAL CONTROL ARM | TREATMENT |
|---|---|---|
| • Adults ≥ 18 yrs<br>• ***de novo* GBM**<br>• **1st or 2nd relapse**<br>• **Not eligible for resection**<br>• **KPS ≥ 70**<br>• **IDH wild-type only**<br>• Archive tissue from initial Dx if available for IL-4R expression analysis | • Patient registries at:<br>- University of California, San Francisco (UCSF)<br>- St. Michael's Hospital (Toronto, Canada)<br>• Study conducted under IRB-approved protocols<br>• Investigators and Medicenna blinded to survival outcome<br>• IL-4R analysis used same IHC assay as Phase 2b study | Types of therapies received in the ECA (n=81):<br>• Avastin (26%)<br>• Lomustine (25%)<br>• Temozolomide (14%)<br>• Experimental Therapy (20%)<br>• Irinotecan (7%)<br>• Avastin + Lomustine (5%)<br>• Radiotherapy (2%)<br>• Avastin + Radiotherapy (1%) |

**Demonstrates proof-of-concept for the FDA-endorsed Phase 3 Trial Design**

# Bizaxofusp Significantly Increased mOS in Planned Phase 3 Population




| | mOS (months) | OS-12 | OS-24 |
|---|---|---|---|
| Bizaxofusp (N=32) High IL-4R + Low IL-4R High dose | 14.5 | 63% | 24% |
| Eligibility Matched ECA (N=40) High IL-4R + Low IL-4R | 7.0 | 18% | 10% |

Median OS from time of bizaxofusp treatment is 14.0 months; OS-12 = 56%; OS-24 = 22%

# Bizaxofusp (MDNA55)

Propensity Matched Study with an ECA: Comparison of Survival in the Phase 2b Trial Using FDA Guidance Documents for ECA with Propensity Scoring

MEDICENNA

# Propensity Matched Scoring Using FDA Guidance Documents

## ELIGIBILITY

- Adults ≥ 18 yrs
- ***de novo* GBM**
- **1st or 2nd relapse**
- **No resection**
- **KPS ≥ 70**
- **IDH wild-type only**
- IL4R analysis from initial Dx

## CRITERIA

- Age
- Sex
- KPS
- MGMT methylation status
- IL-4R expression level
- Time from initial diagnosis to relapse
- Number of prior relapses
- Extent of resection at initial diagnosis
- Tumor size/location at relapse
- Steroid use prior to treatment

## PROCESS

**STEP 1**
Data preparation: feasibility and quality, mapping, standardization, covariates

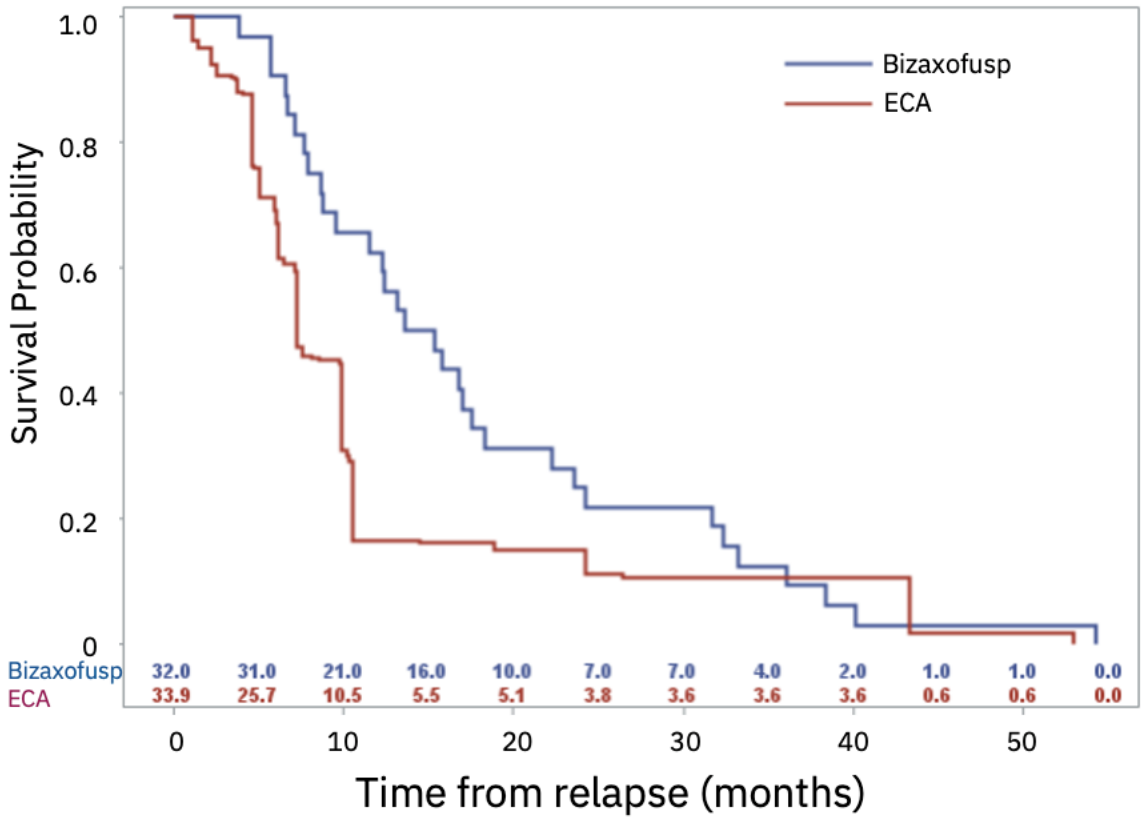
**STEP 2**
Estimate propensity scores: statistical models

**STEP 3**
Propensity score balancing algorithm - weighting

**STEP 4**
Evaluation of balance in baseline characteristics

# Bizaxofusp Doubles Overall Survival in Phase 3 Population vs ECA

## OS Increased by 370% at 1 Year | OS at 2 Years Improved by >50%



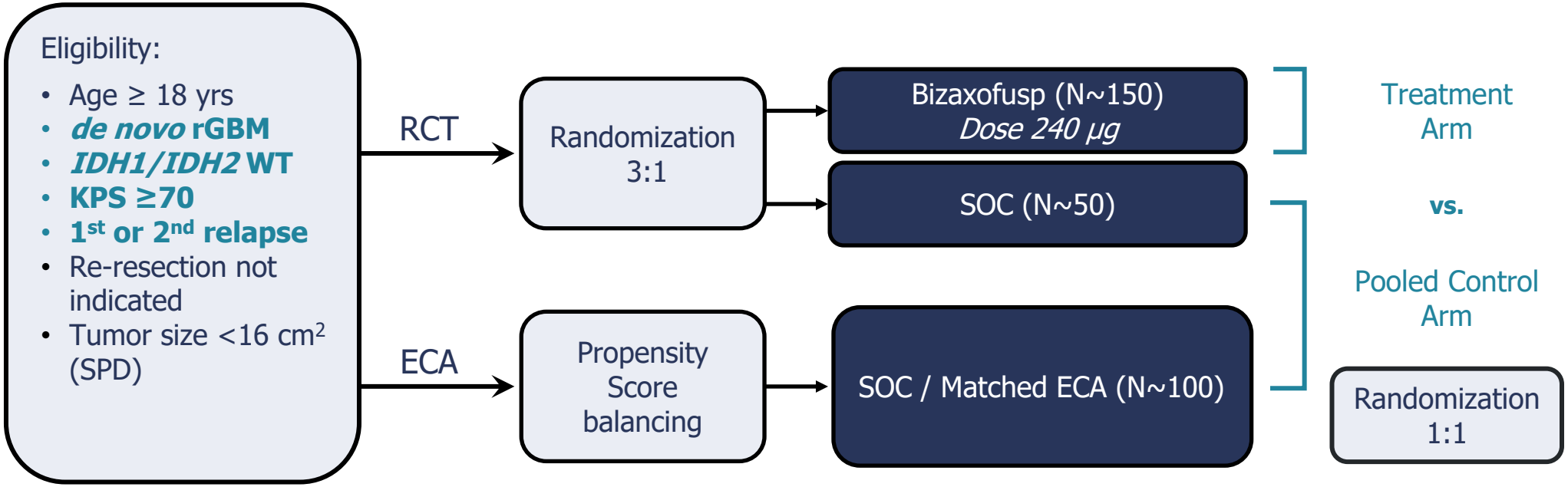

| Group | mOS (months) | OS-12 | OS-24 |
|---|---|---|---|
| Bizaxofusp (n=32) | 14.5 | 62.5% | 25% |
| ECA (n=34) | 7.2 | 16.7% | 16.1% |

| Comparison | HR | 95% Confidence Limits | |
|---|---|---|---|
| Bizaxofusp vs ECA | 0.629 | 0.382 | 1.038 |

**Compelling survival benefit justifies registration trial endorsed by FDA**

# FDA Guided Phase 3 Trial Design

## Hybrid with ECA: The First Time FDA has Endorsed Inclusion of an ECA in a Phase 3 Trial for Brain Cancer



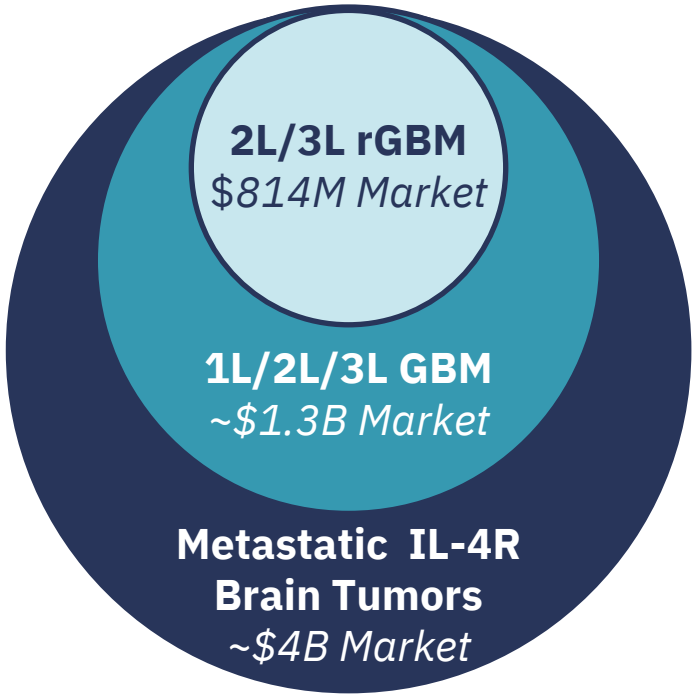

**SOC therapies allowed:**
- Bevacizumab (Avastin®)
- Lomustine (CCNU, CeeNU®, Gleostine™)
- Temozolomide (Temodar®)
- Tumor Treating Fields (Optune®)
- Radiation Therapy

**Primary Endpoint:**
- **OS**

**Assumptions:**
- **Effect size = 4.6 months in mOS**
- 90% power
- HR of Bizaxofusp vs. pooled control = 0.65
- 2-sided alpha = 0.05

# Primary Research Confirms $800M Market for rGBM in US and EU

**Potential $4 Billion** market for follow-on IL-4R adult metastatic brain tumors indications




**Near-term**

**2L/3L rGBM**

**KOL backing**
Strong market adoption

**Catalysts**
Phase 3 results

**Medium-term**

**Non-resectable GBM**

**Total market**
~18,000 annually (US/EU)

**Catalysts**
Robust uptake from 2L/3L rGBM market

**Longer-term**

**Metastatic IL-4R Brain Tumors**

Renal | Breast | Colon | Leptomeningeal

**Total market**:
~76,000 annually (US/EU)

**Catalysts**
Follow-on studies in other tumors

Several Precedent Market Transactions have Demonstrated the Potential for Medicenna's Pre-Clinical Assets

# Pre-clinical assets

MDNA113 | Anti PD-1-IL-2 Masked BiSKIT

MDNA209 | IL-2/15 Super Antagonist

MDNA413 | IL-4/13 Super Antagonist

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# MDNA113: An Anti PD-1-IL-2 Masked BiSKIT*

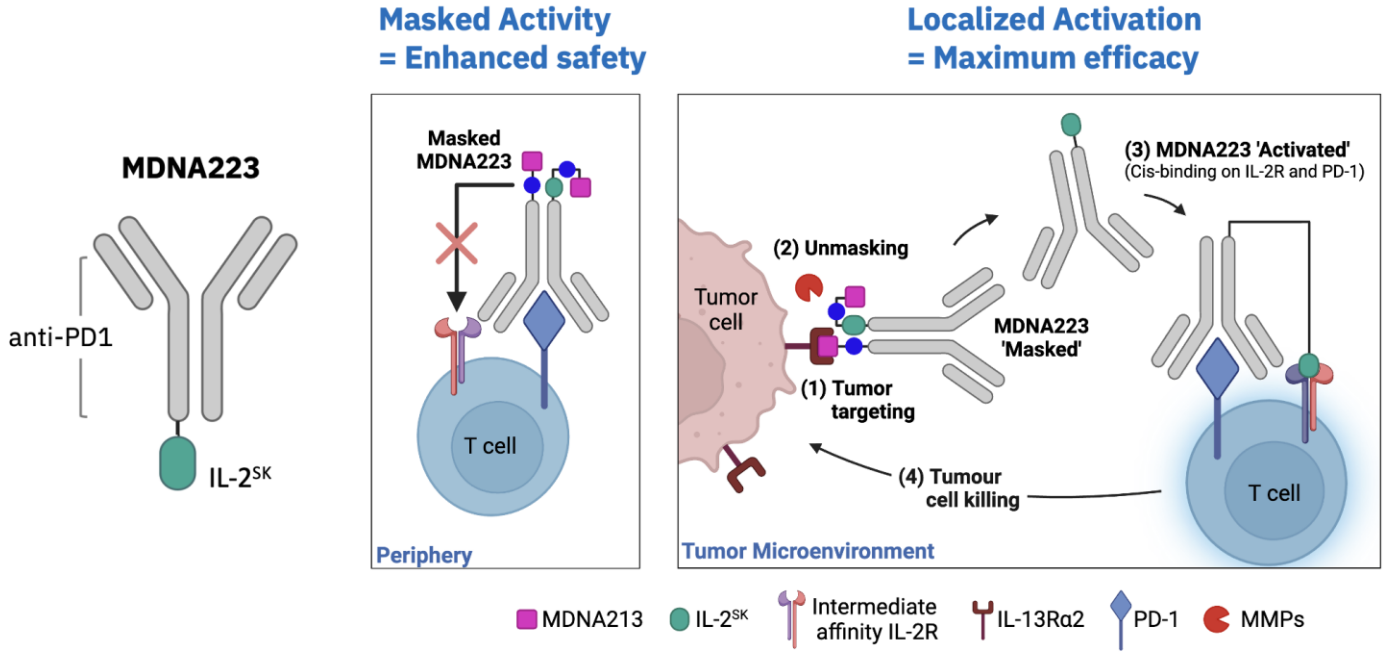
## Masked Superkines Have the Potential to Increase Safety Even Further, whilst Maintaining the Same Anti-Tumor Efficacy as the Original Superkine

**MDNA113**

**Designed to facilitate cis-binding to IL-2R and PD1 on immune cells**

**Selectively targets IL-13Rα2 on solid tumors via MDNA213**

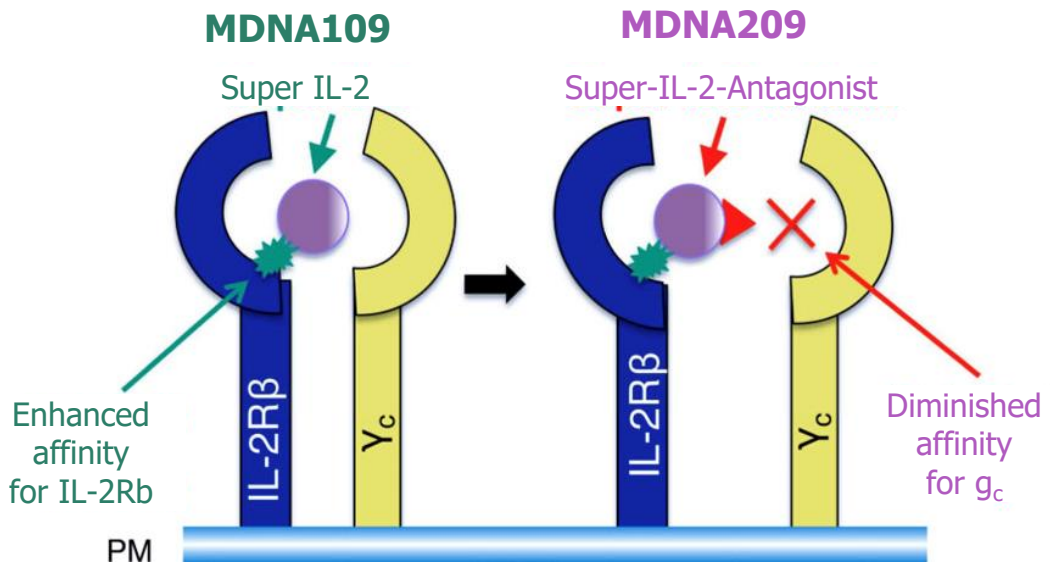
**IL-13Rα2 Positive Cancers: Annual World-Wide Incidence > 2M**

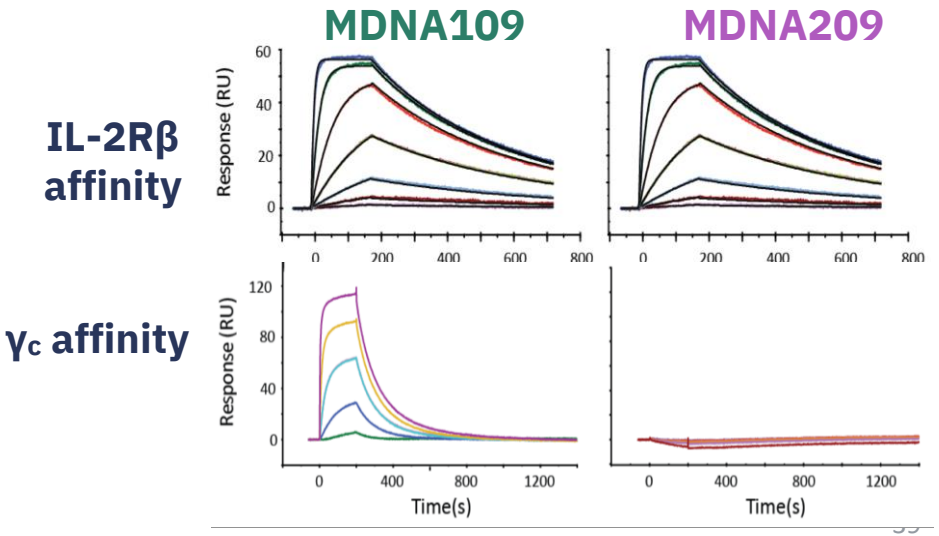



**A potential solution to the 2028 expiration of "Big Pharma"s anti-PD-1 IP**

# MDNA209: An IL-2/IL-15 Pathway Antagonist with a Unique MOA

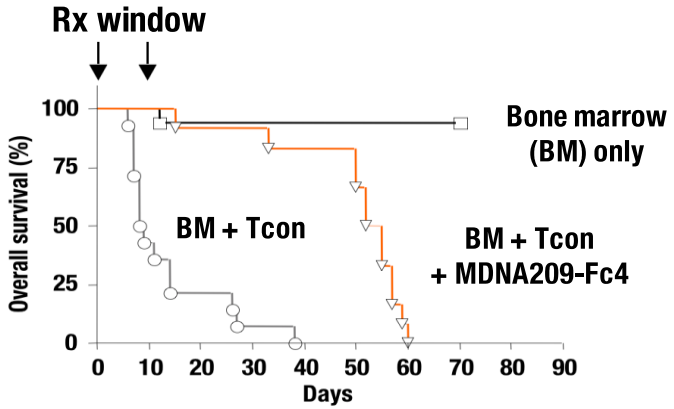
## Targeted Mutations Transformed IL-2 into a High-Affinity IL-2 Receptor Antagonist




| Cytokine | Engineering | Significance |
|---|---|---|
| **IL-2 WT** | Naturally Occurring | Not selective but preferential stimulation of Tregs at low-doses |
| **MDNA109** *(intermediate step)* | Mutations increase affinity for IL2Rβ chain | Increased function of effector CD4, CD8 and NK cells (and not Tregs) |
| **MDNA209** | Mutations ablate $\gamma_c$-binding | Dominant negative inhibition of effector CD4, CD8 and NK cells |

**Therapeutic in vivo Efficacy in GVHD**




- ✓ 10-day treatment with MDNA209-Fc4 provides >5-fold extension of median survival


GVHD, graft-versus-host disease; Mitra S, *et al.*, Immunity. 2015

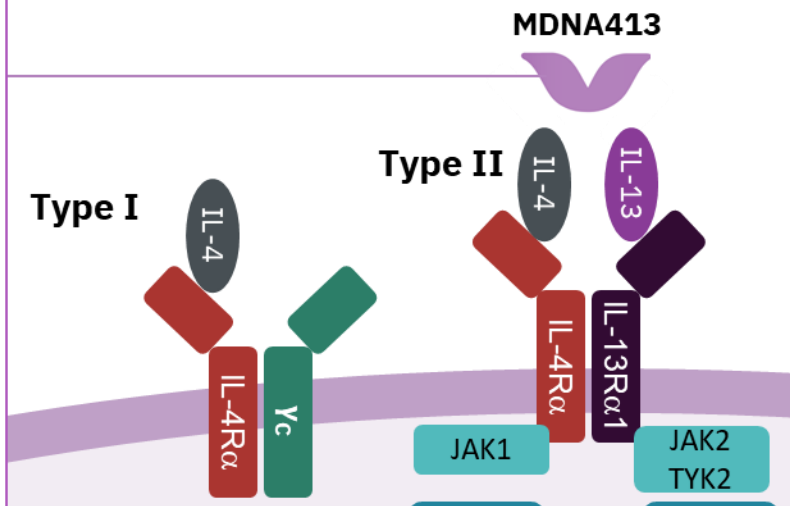
# MDNA413: An IL-4/IL-13 Pathway Super-Antagonist

## The Potential to Address the IL-4/IL-13 Pathway in Cancer and Th2-Mediated Diseases

**MDNA413**

**Type II IL-4R Antagonist**

- High affinity inhibitor of IL-13Rα1
- Preserves endogenous type I IL-4R signaling
- Potential to synergize with anti-IL-4Rα inhibitors
- Fc added to extend half-life




**Cancer**

- Skewing towards M2a TAMs
- Promotion of MDSCs
- Pro-tumor TME
- Promotes tumor growth and metastasis

**Th2-Mediated Diseases**

- Activation of myeloid cells and non-hematopoietic cells (i.e., nerve fibers)
- Promotes pathogenesis of airway inflammation, AD, EoE, itch, and other allergic indications

# Evolutionary Cytokines Revolutionary Medicines

## Superkine Platform

Medicenna's Drug Discovery Engine

### 2 First-in-Class Clinical Stage Assets

Bizaxofusp (MDNA55) | MDNA11

### Deep and Scalable Pipeline

BiSKITs | MDNA113 | MDNA209 | MDNA413

### Anticipated 2024 Milestones

MDNA11 Phase 1/2 Preliminary Data
Monotherapy | Combination with KEYTRUDA®

Bizaxofusp Partnering | BTD | EMA Alignment

## Financial Highlights

| | |
|---|---|
| **TSX \| OTCQB** | MDNA \| MDNAF |
| **Headquarters** | Toronto, CA |
| **Market Capitalization** | $66.9M CAD[1] |
| **Cash** | $21.8M CAD[2] |
| **Debt** | $0 |
| **Preferred Shares** | None |
| **Basic SO** | ~70 Million[2] |
| **Fully Diluted SO** | ~70 Million[2] |
| **Insider Ownership** | ~24%[2] |

[1] As of 02/16/2024
[2] As of 12/31/2023

# Thank you

Investor Relations | ir@medicenna.com