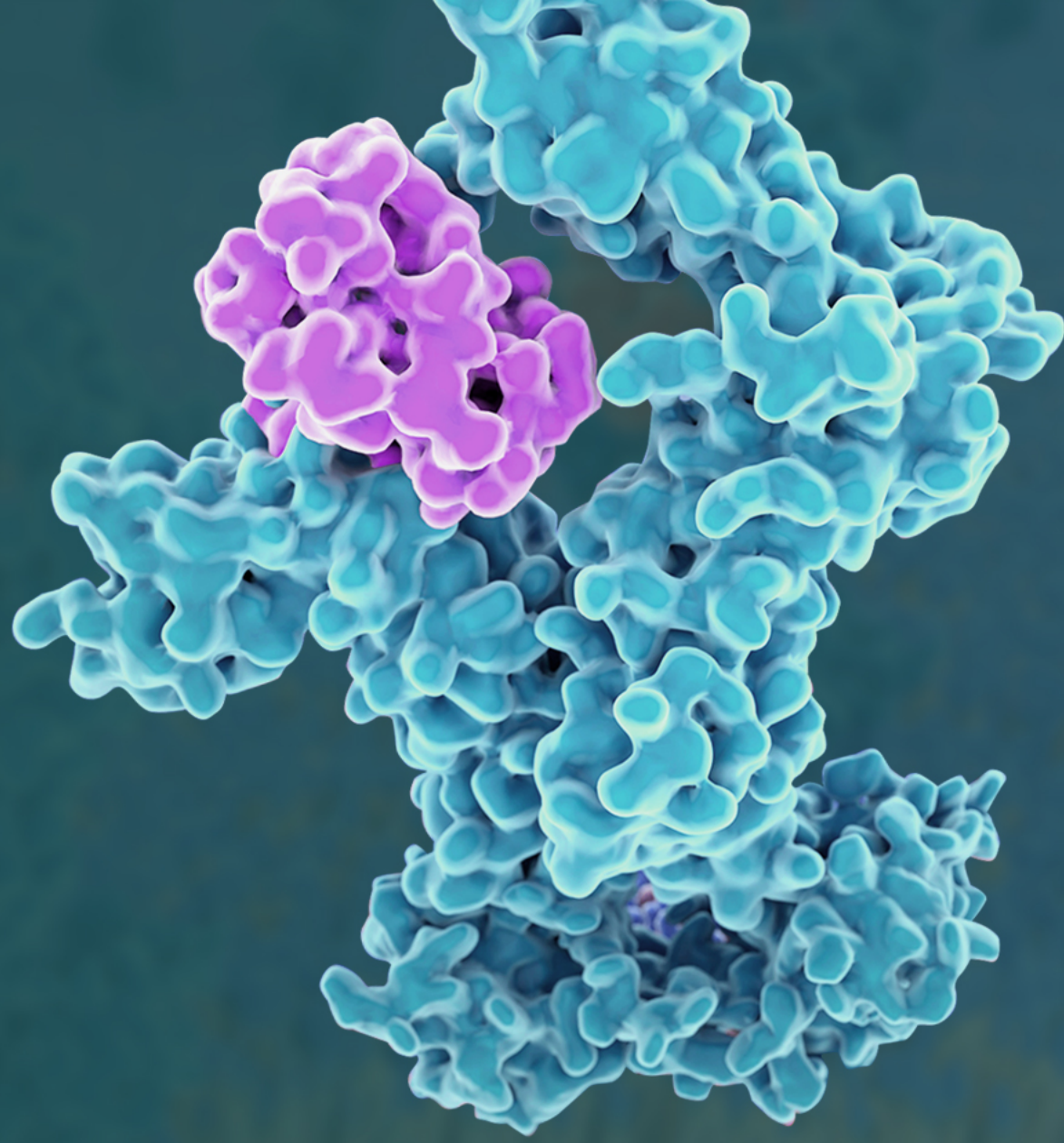
Q4, 2020

Evolutionary Cytokines Revolutionary Medicines

Fahar Merchant, Ph.D



MEDICENNA

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Certain statements in this presentation are “forward-looking statements. 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”.

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Company Overview

Evolutionary Cytokines, Revolutionary Medicines

Medicenna is a clinical stage immunotherapy company that uses directed evolution to generate engineered interleukins called Superkines that can modulate, fine-tune or amplify the immune system in order to combat the most challenging diseases and inspire hope in patients with unmet needs

Nasdaq	**MDNA**
TSX	**MDNA**
Headquarters	**Toronto, CA**
Cash	**CDN $34.2 million (9/30/20)**
Debt	**$0**
Preferred Shares	**0**
Cash Runway	**Funded through 2022**
Issued and Outstanding	**48,998,821**
Fully Diluted	**60,223,781**

Expanding Pipeline Anchored by MDNA55 and MDNA11

Candidate	Indication	Discovery	Preclinical	Phase 1	Phase 2	Pivotal
MDNA55 IL-4 Toxin Fusion	Recurrent Glioblastoma (GBM)					
MDNA11 IL-2 Super Agonist	Cancer Immunotherapies					
MDNA413 IL-4/13 Super Antagonist	Solid Tumors					
MDNA132 IL13Rα2 selective IL-13	Solid Tumors					

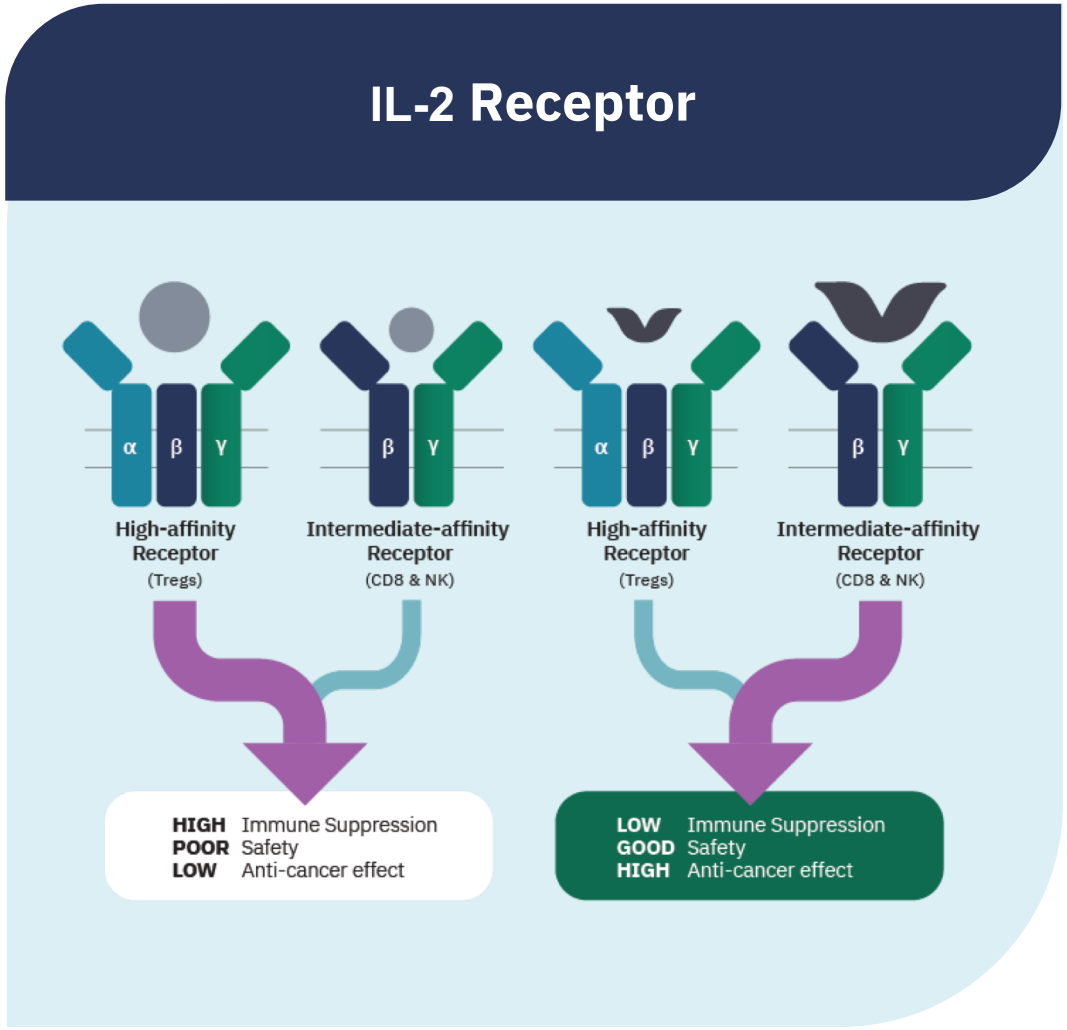
Multiple Near-Term Value Inflection Milestones

	H2 2020	H1 2021
MDNA11 MDNA11 to be Phase 1 Ready	**Pre-CTA Meeting** ✓	**Submit application to initiate Phase 1/2 monotherapy study**
MDNA55 End of Phase 2 Meeting with FDA	**End of Phase 2 meeting with FDA** ✓	**Pursue Partnership Opportunities**
Corporate	**Nasdaq Listing** ✓	**Strengthen Management and Advisory Team**

MDNA11

IL-2 Super Agonist for Cancer Immunotherapy

Targeting IL-2 Receptor Subunits in Cancer Therapy



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

- CD25 (IL-2Rα)
- CD122 (IL-2Rβ)
- CD132 (IL-2Rγ)

Stimulation of CD122

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

Stimulation of CD25

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

Proleukin (recombinant human [rh] IL-2), which selectively stimulates CD25, is approved for the treatment of metastatic melanoma and renal cell carcinoma

Improved IL-2 Variants are Needed

Medicenna has developed MDNA11 to overcome the shortcomings of Proleukin and competing IL-2 variants

Proleukin

Poor safety profile due to selective stimulation of CD25

- Patients are often unable to receive a full course of therapy
- Patients must be treated in the intensive care unit

Poor pharmacokinetic profile

- Half-life on the order of minutes
- Requires dosing every 8 hours for 9 days

Competing IL-2 variants

Have low CD122 affinity

- Limited efficacy

Rely on pegylation for half-life extension

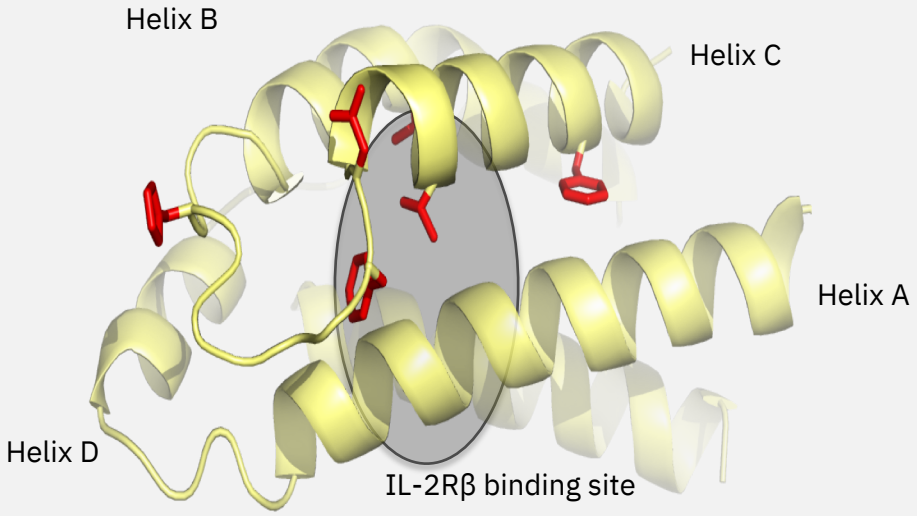
- Complex manufacturing increases cost of goods

Superkines: First-Generation IL-2 Variants

LETTER

nature

Exploiting a natural conformational switch to engineer an interleukin–2 'superkine'

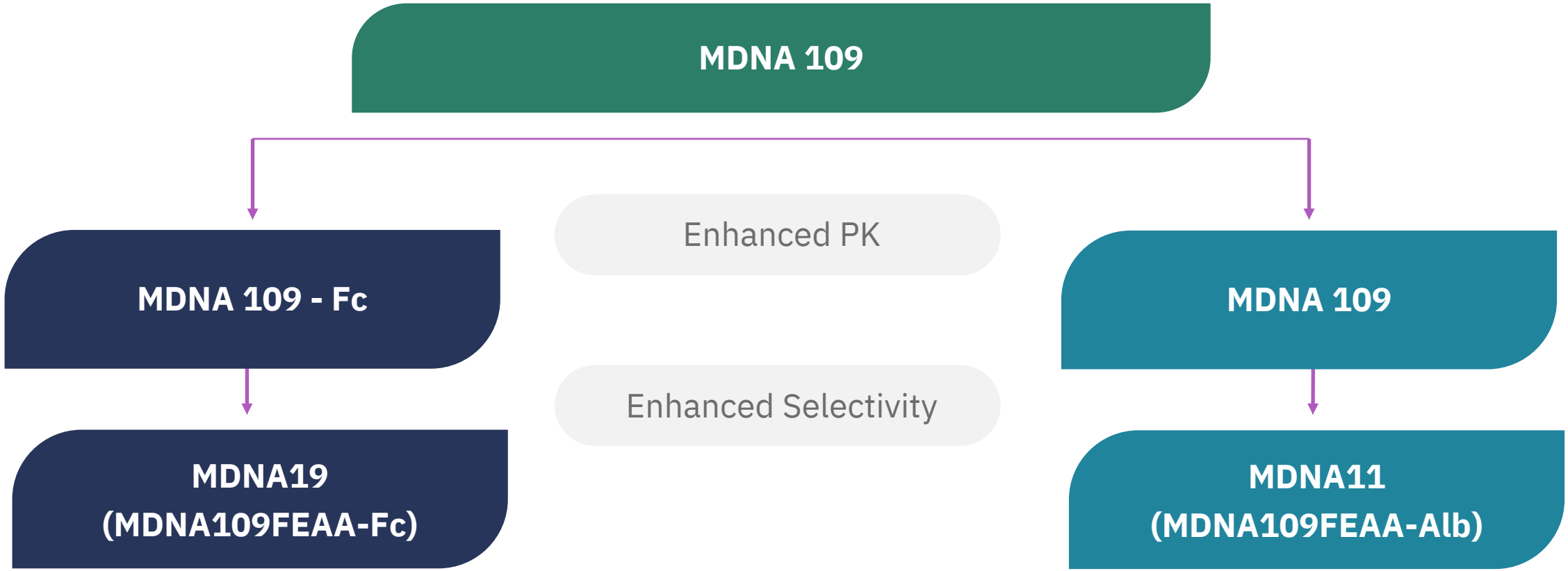


Levin, Bates, and Ring et. al, Nature, 2012

Medicenna's MDNA109 platform produced first generation IL-2 variants with 200-fold higher affinity for CD122 (IL-2Rβ), which is key for the activation of immune cells responsible for cancer killing (CD8+ T cells, naïve T cells, NK cells), yet similar affinity to CD25

	Similar affinity to CD25	**200X increased affinity to CD122**
SPR data (nM)	CD25	CD122
IL-2	6.6	280
MDNA109	**6.6**	**1.4**

MDNA11: Next-Generation IL-2 Superkine

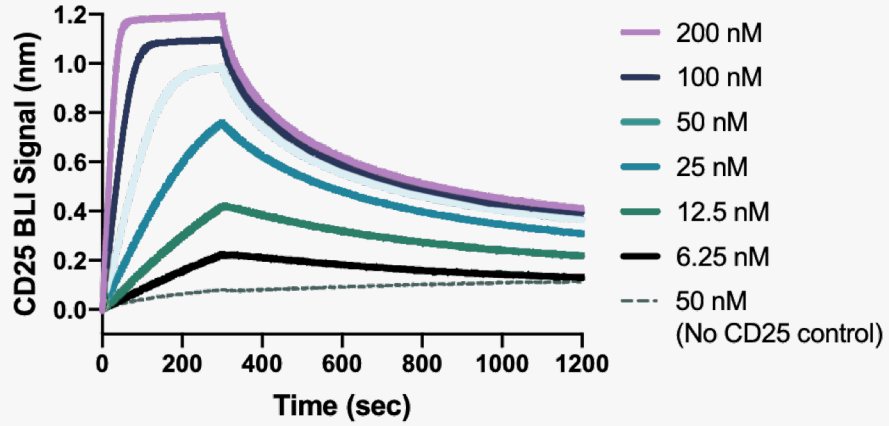


MDNA11 is a ***potentially best-in-class next-generation IL-2 superkine*** with superior CD122 binding without CD25 affinity, thereby preferentially stimulating cancer killing effector T cells and NK cells when compared to competing IL-2 programs.

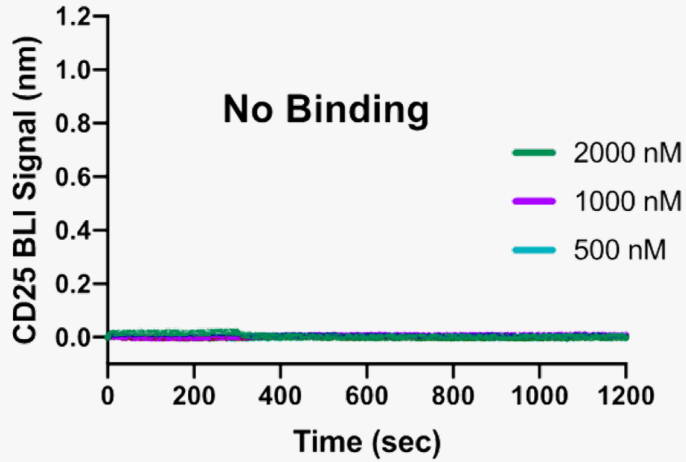
MDNA11

No CD25 Binding and Enhanced Affinity and Selectivity for CD122 Compared to rhIL-2

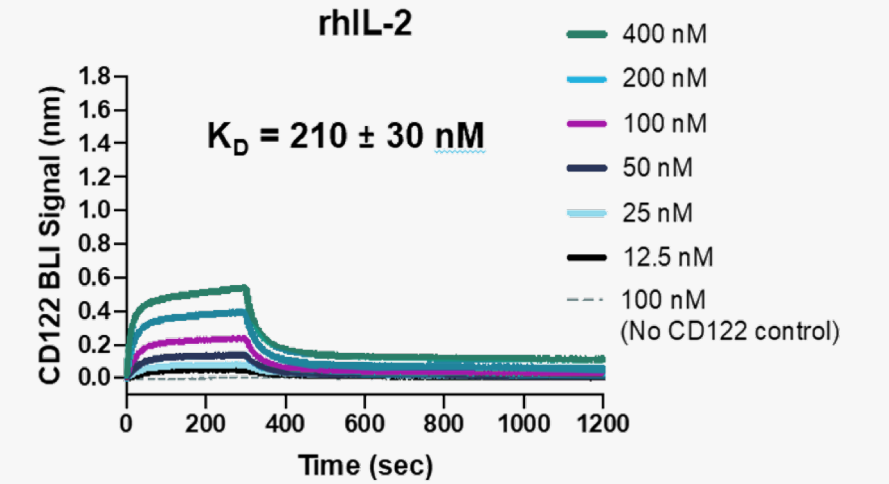
rhIL-2 – CD25 Binding



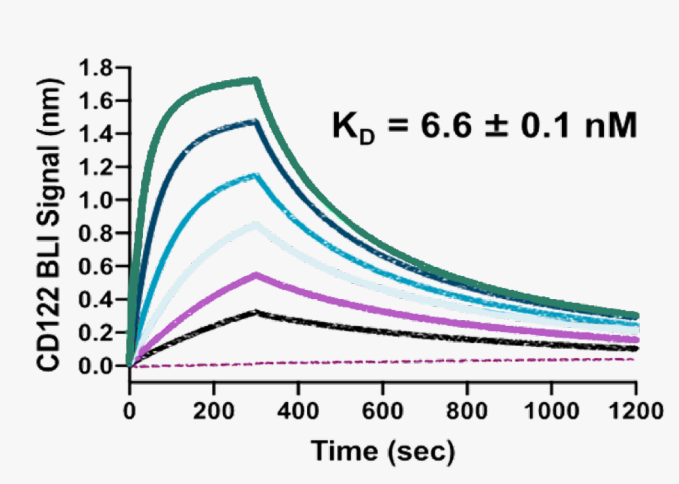
MDNA11 – CD25 Binding



rhIL-2 – CD122 Binding



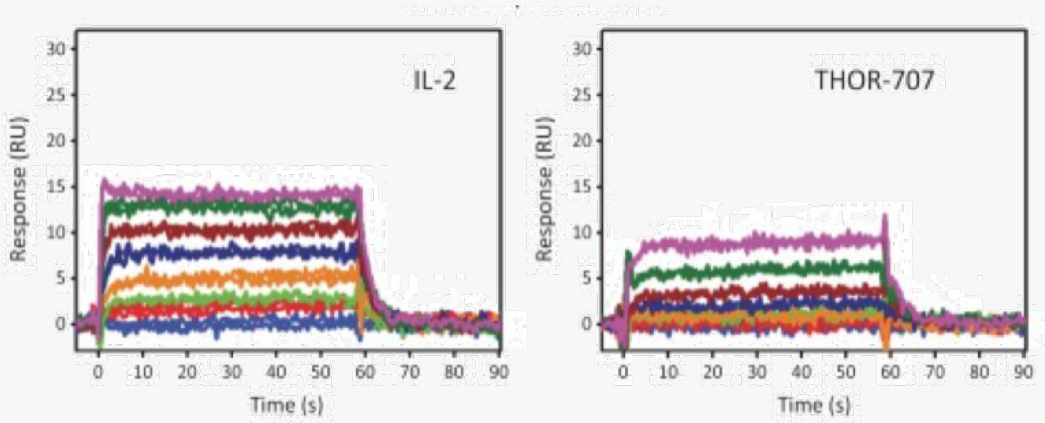
MDNA11 – CD122 Binding



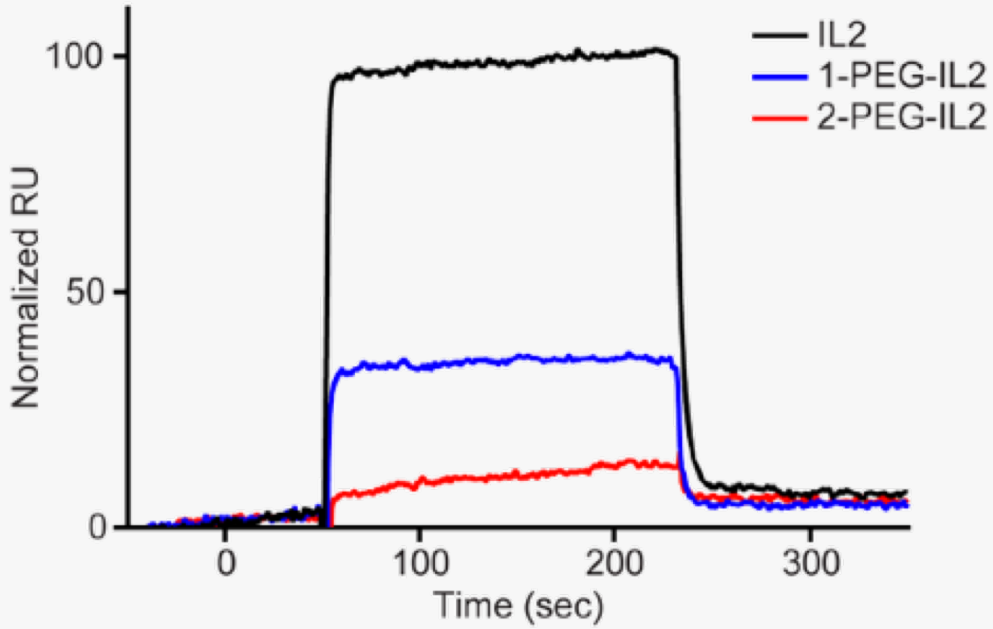
Competing IL-2 Variants are Weak CD122 Binders

THOR-707: Reduced Binding to IL2Rβ (CD122)

IL2Rβ (CD122)



1-PEG-IL2 (Most Active Form of NKTR-214) is a Weak IL2Rβ (CD122) Binder



MDNA11: Enhanced Selectivity & Potency to Immune Cells

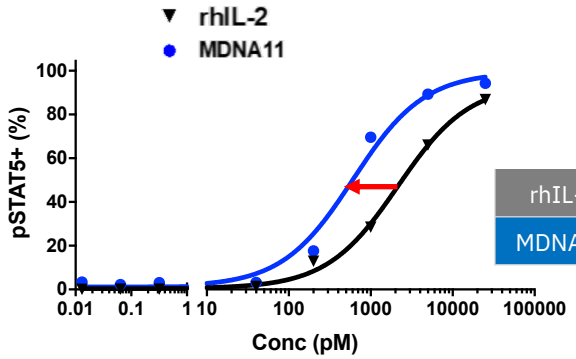
Compared to WT IL-2 (proleukin) MDNA11 exhibits both:

Enhanced potency toward anti-tumor CD8+ T-cells

Reduced potency toward pro-tumor Treg cells

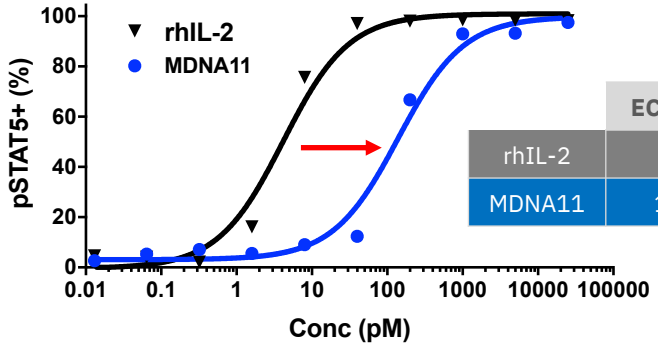
MDNA11

Naïve CD8+T-cells



	EC_{50} pM
rhIL-2	3390
MDNA11	460

Tregs



	EC_{50} pM
rhIL-2	5.6
MDNA11	160

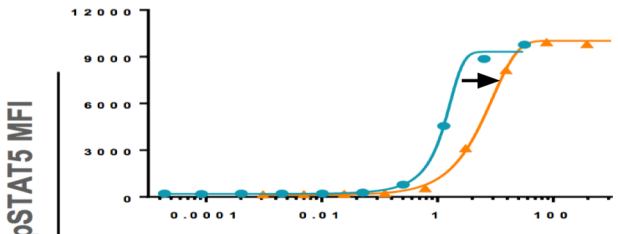
Compared to WT IL-2 (proleukin) THOR-707 has:

Reduced potency toward anti-tumor CD8+ T-cells

Reduced potency toward pro-tumor Treg cells

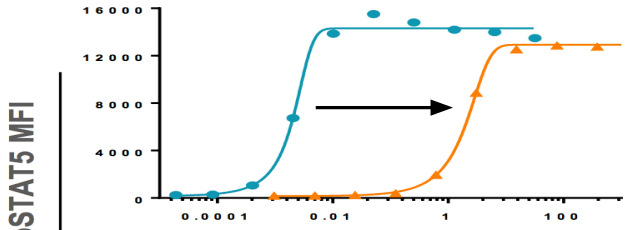
THOR-707

Naïve CD8+T-cells



Protein	EC_{50} nM
IL-2	1.47
THOR-707	5.71

Tregs

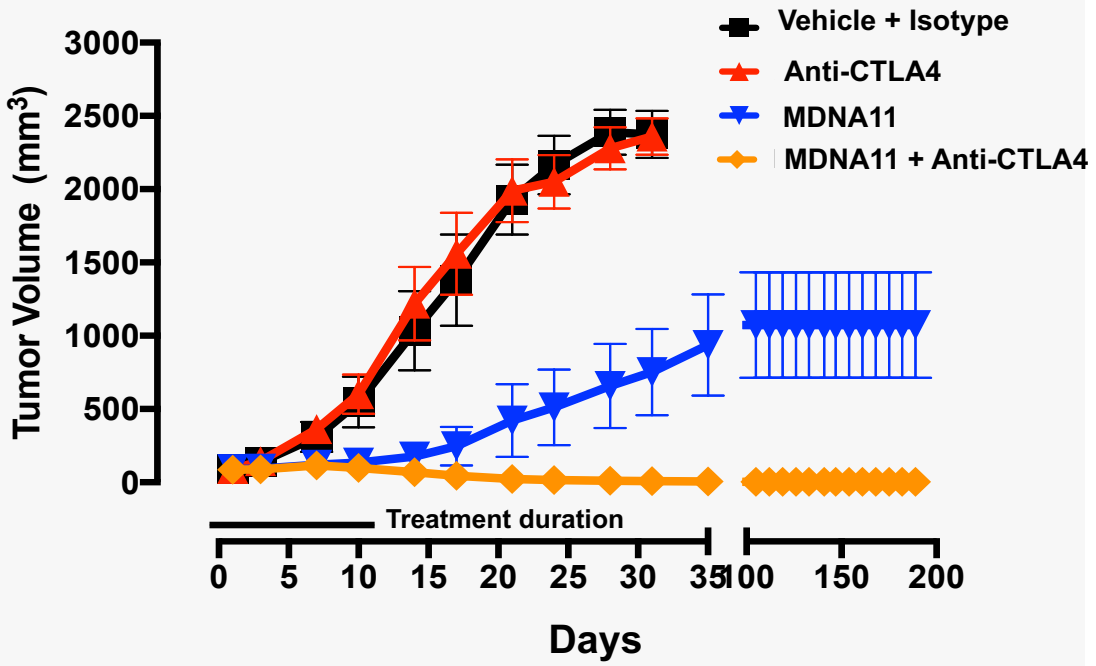


Protein	EC_{50} nM
IL-2	0.0022
THOR-707	1.95

Superior Effect in Combo with Checkpoint Inhibitor

Demonstrated in CT26 Tumor Model

MDNA11 + Anti-CTLA4 (n=10/group)

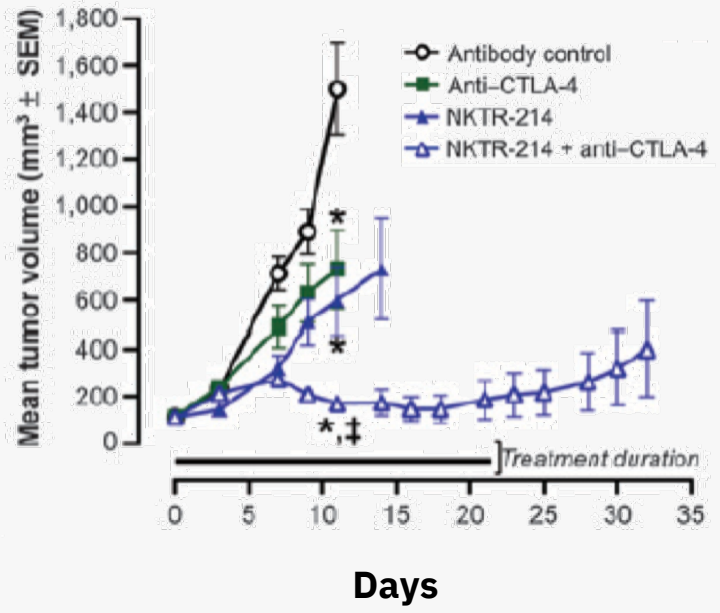


MDNA11 (5 mg/kg, IP, 1x/wk for 2 wks)

Anti-CTLA4 (4F10, 100 µg, 2x/wk for 2 wks)

Average tumor size at initiation of dosing ~ 90 mm^3

NKTR-214



NKTR-214 (0.8 mg/kg, IP, 1x/9 days for 3 doses)

Anti-CTLA4 (4F10, 100 µg, 2x/wk through day 18)

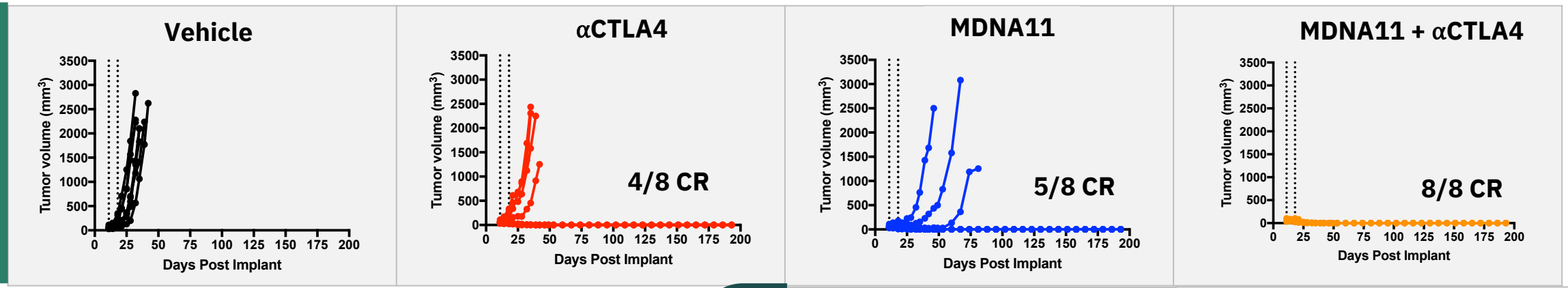
Average tumor size at initiation of dosing ~ 100 mm3

Charych, D. et al, Clin Cancer Res, 2016

MDNA11 + αCTLA4

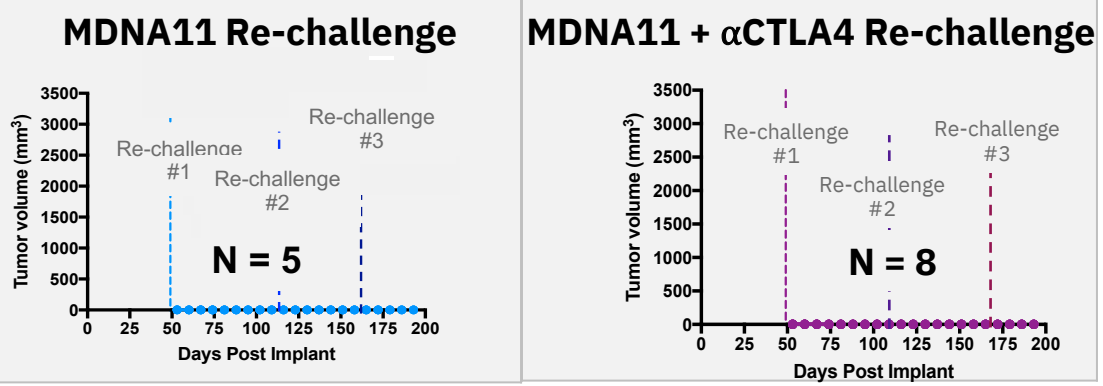
Inhibits Tumor Growth and Induces Memory Response

Primary Tumor



MDNA11 in combination with αCTLA4 exhibited synergistic effect generating 100% complete response in CT26 tumor mice models. Additionally when re-challenged, all mice in **MDNA11 + αCTLA4** group exhibited strong memory response with no tumor growth.

Re-challenge



→ CT26 tumor (~60 mm3) bearing Balb/c mice were treated with MDNA11 (5 mg/kg 1x/week, 2 weeks) or Anti-CTLA4 (200 µg 2x/week, 2 weeks) by IP injection. Re-challenge experiment performed by implanting 2 x 106 CT26 cells in opposite flank (Day 49, Day 116 and Day 165), without further treatment.

Pilot Non-human Primate (Cynomolgus Monkey) Study

Study Design to Evaluate Safety, PK and PD Profile

Adult cynomolgus monkeys (age: 8-12 years) received 2 doses of MDNA11 by slow IV bolus 14-days apart and monitored for total of 28 days.

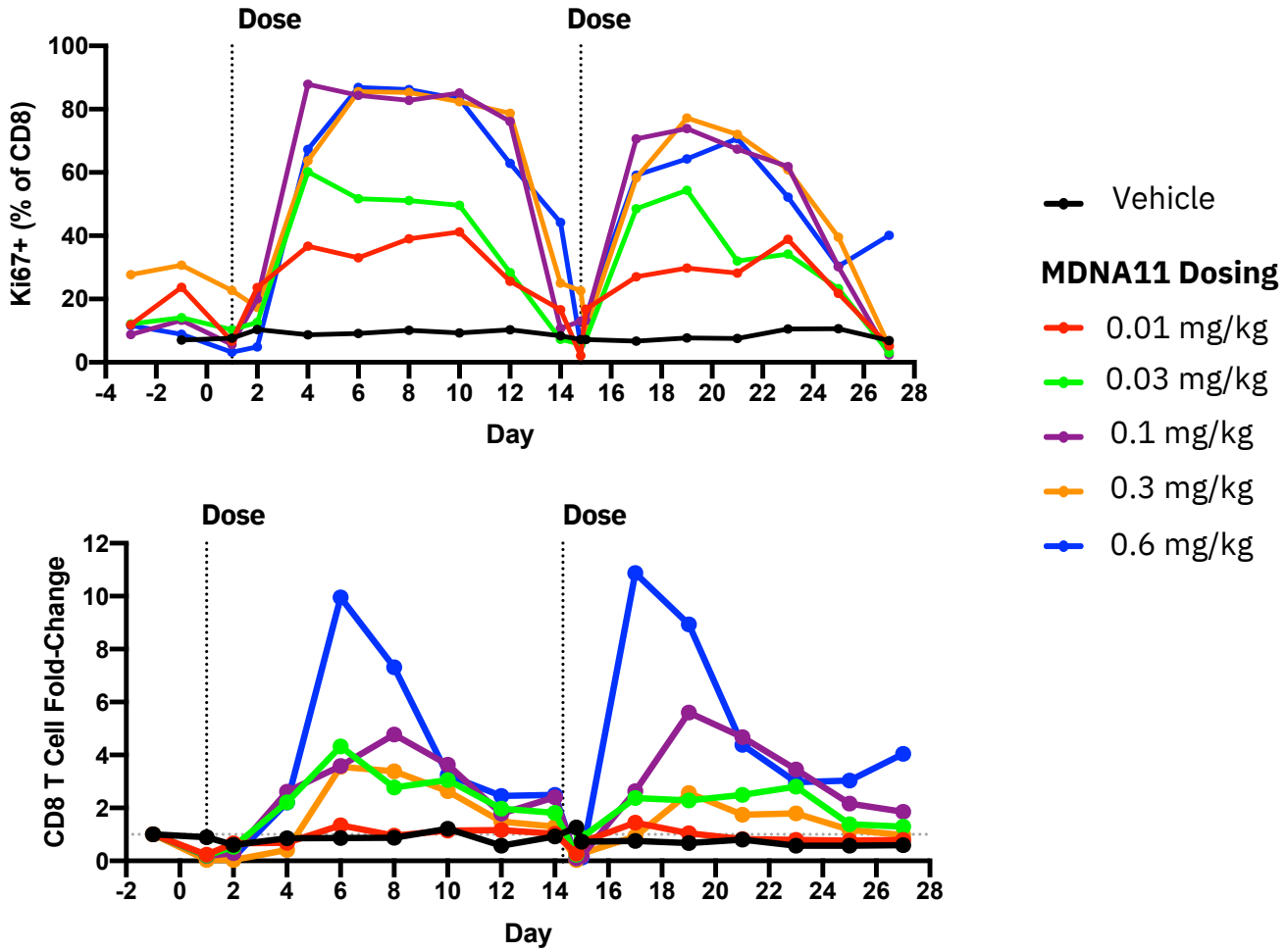
- Dose: 10, 30, 100, 300, and 600 mcg/kg
- One male monkey per group
- One monkey also received single dose of 300 mcg/kg MDNA11 and total of 21 days monitoring

Study measurements included

1. Clinical observations
2. Clinical chemistry
3. Hematology
4. Immune-profiling with Ki67 analysis of peripheral blood
5. Organ weights and macroscopic pathology

→ Sample collection also for (1) PK , (2) ADA and (3) cytokines/chemokines.

Durable, Dose-Dependent Ki67 Expression and CD8+ T-Cell Expansion



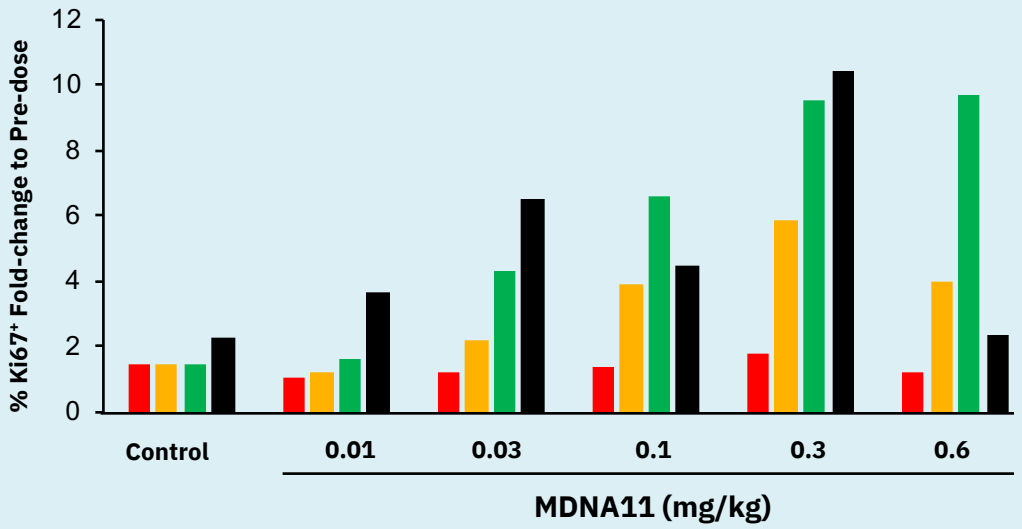
Ki67 is a key marker of anti-tumor CD8+ T-cell proliferation

Target Ki67 expression of >50% clearly demonstrated with MDNA11 treatment

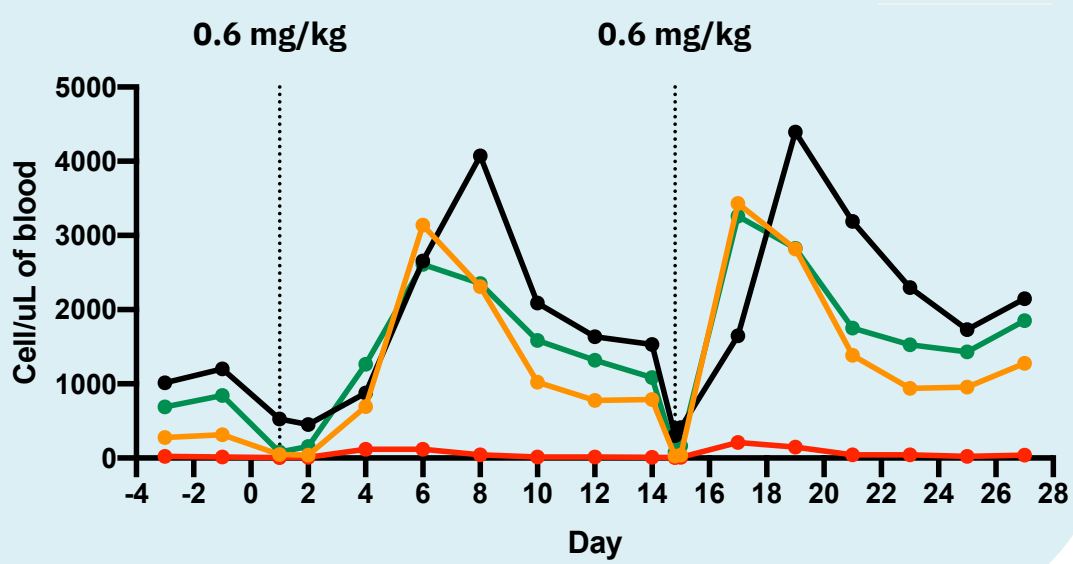
Proliferation & Expansion of Immune Cells but Not Tregs

MDNA11 induced up to 10-fold expansion in cancer-fighting immune cells (CD4+ T, CD8+ T, and NK Cells) in non-human primate study without: (a) Treg expansion, (b) generating anti-drug antibodies, (c) causing hypotension associated with vascular leak syndrome, (d) cytokine storms, or (e) other undesirable immune mediated side effects.

Percent Ki67⁺ Cell Fold Change



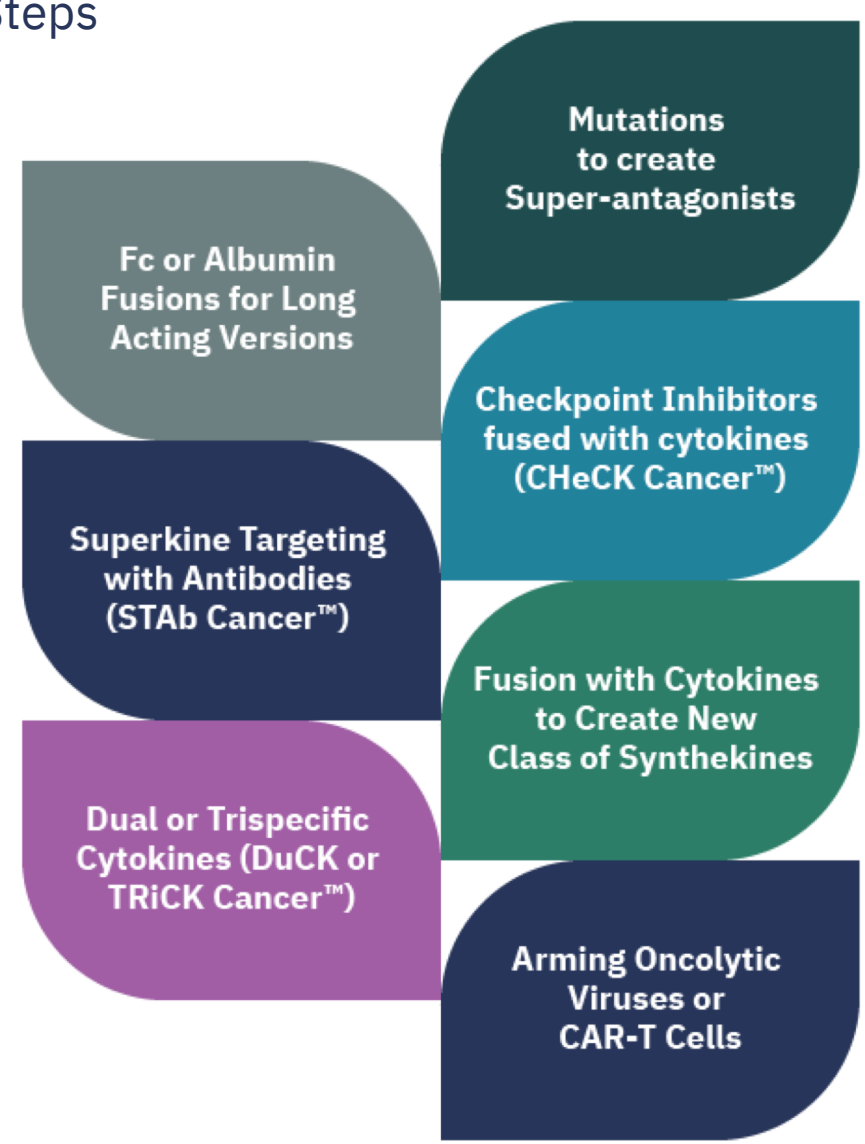
Immune Cell Counts



Tregs CD4⁺ T Cell CD8⁺ T Cell NK Cell

IL-2 Superkine Program

Next Steps



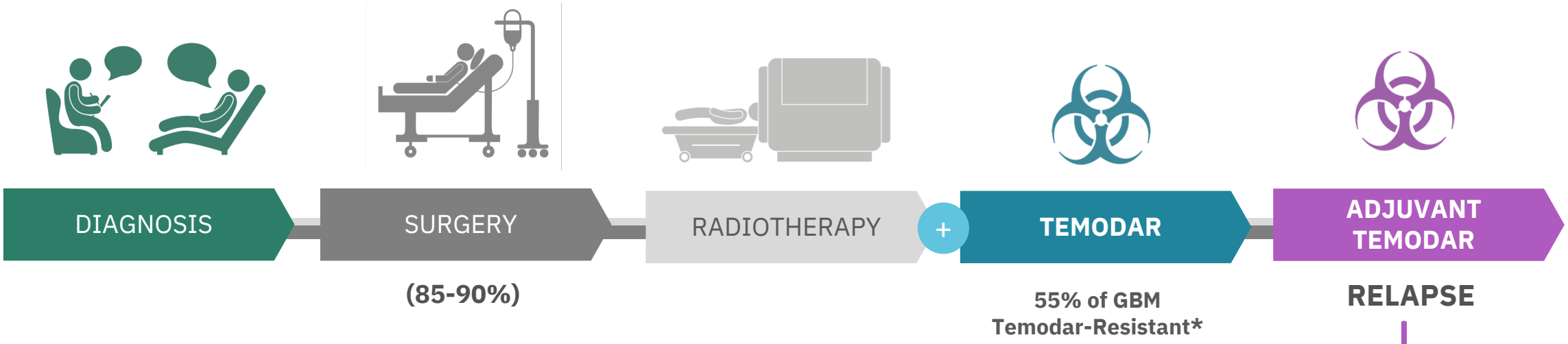
MDNA11 Next Steps

- Pre-CTA meeting **(H2 2020)**
- Initiate Phase 1 clinical trial **(Mid 2021)**
- Report Safety, PK/PD and Biomarker Results from Phase 1 monotherapy study **(End 2021)**

MDNA55

A Powerful Molecular Trojan Horse Targeting Glioblastoma

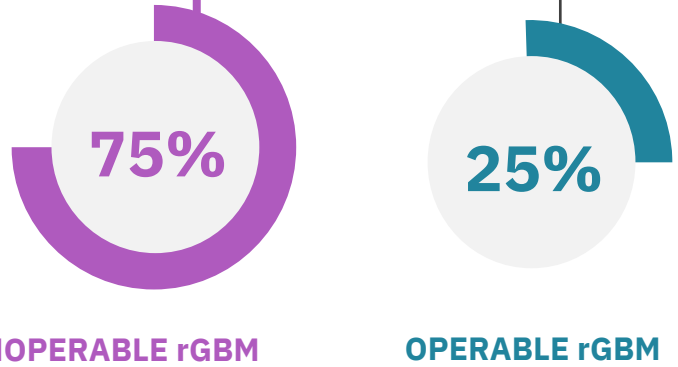
Current Treatment Strategies for GBM are Ineffective



Glioblastoma (GBM) & IL4 Receptor

- Uniformly fatal – virtually all tumors will recur
- New treatment strategies are needed
- IL4 receptor (IL4R) is overexpressed in GBM cells and the tumor microenvironment making it a promising target for GBM treatments

MDNA55 Treatment
Direct infusion into tumor
via convection enhanced delivery (CED)



* Expression of the DNA repair protein O6-methylguanine-DNA methyltransferase (MGMT) is responsible for resistance to Temodar used in GBM treatment.

MDNA55: A Targeted Immunotherapy for GBM

MDNA55

Targets the IL4R, which is expressed in brain tumors and in the tumor microenvironment (TME), but not the healthy brain

Highly Selective

Avoids off-target toxicity

Disrupts the TME

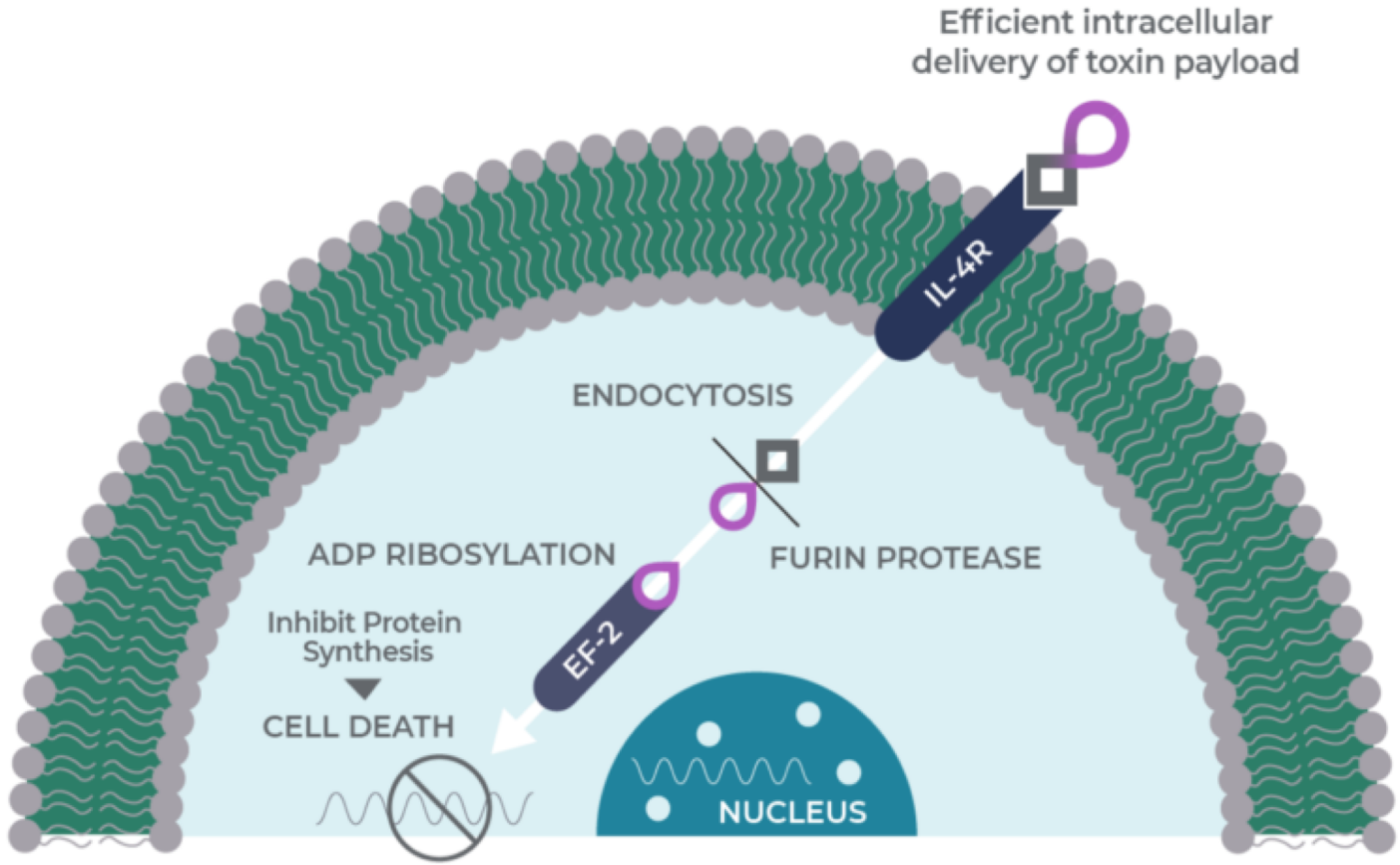
By targeting IL4R positive cells found throughout the TME, MDNA55 unblinds the tumor to the body's immune system

Sustained Immune Memory Response

Anti-tumor immunity is initiated and remains active after MDNA55 is cleared

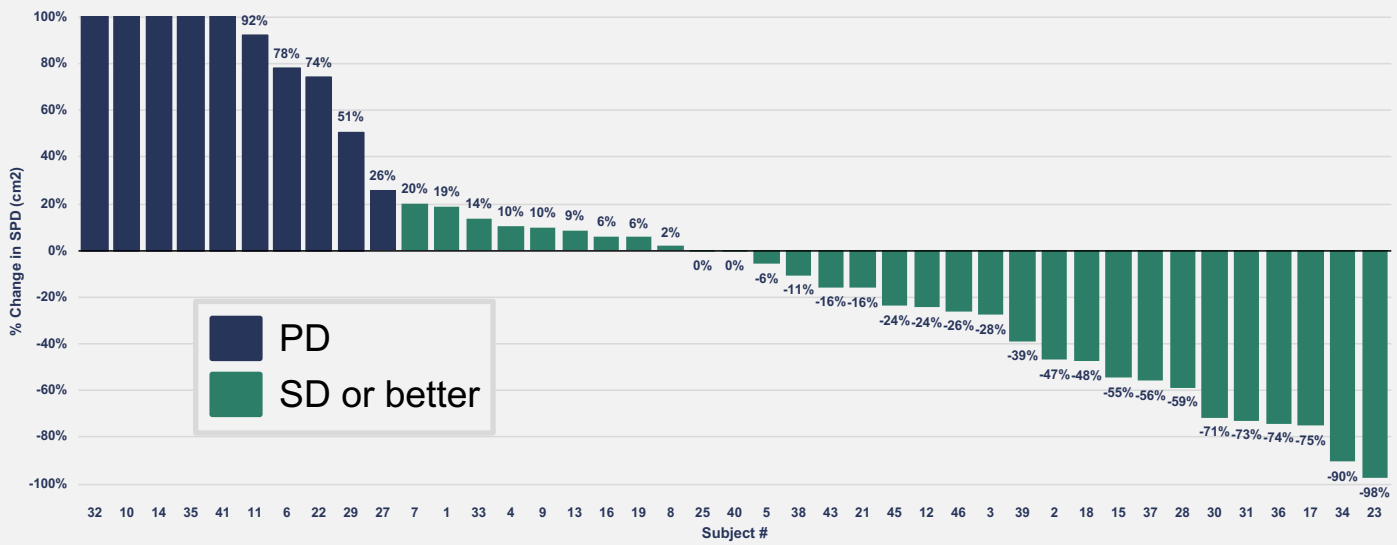
Targeting Domain
Circularly Permuted Interleukin-4 (cpIL-4)

Lethal Payload
Catalytic domain of *Pseudomonas* Exotoxin A (FDA approved Moxetumomab pasudotox)



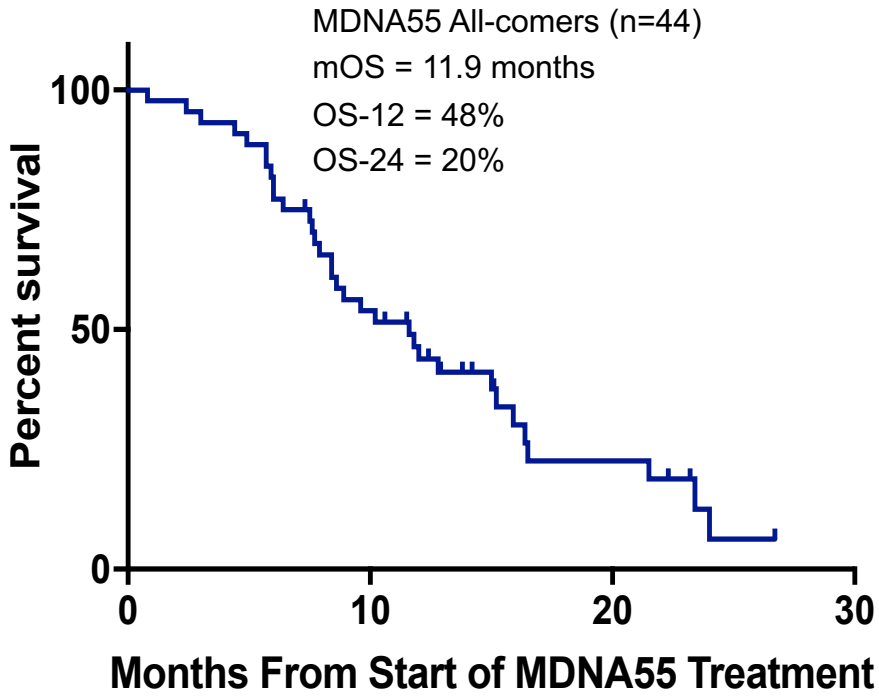
High Tumor Control Rate & Extended Survival

Best Response per Modified RANO (following initial PsP)



Shown is tumor response from nadir based on radiologic assessments only

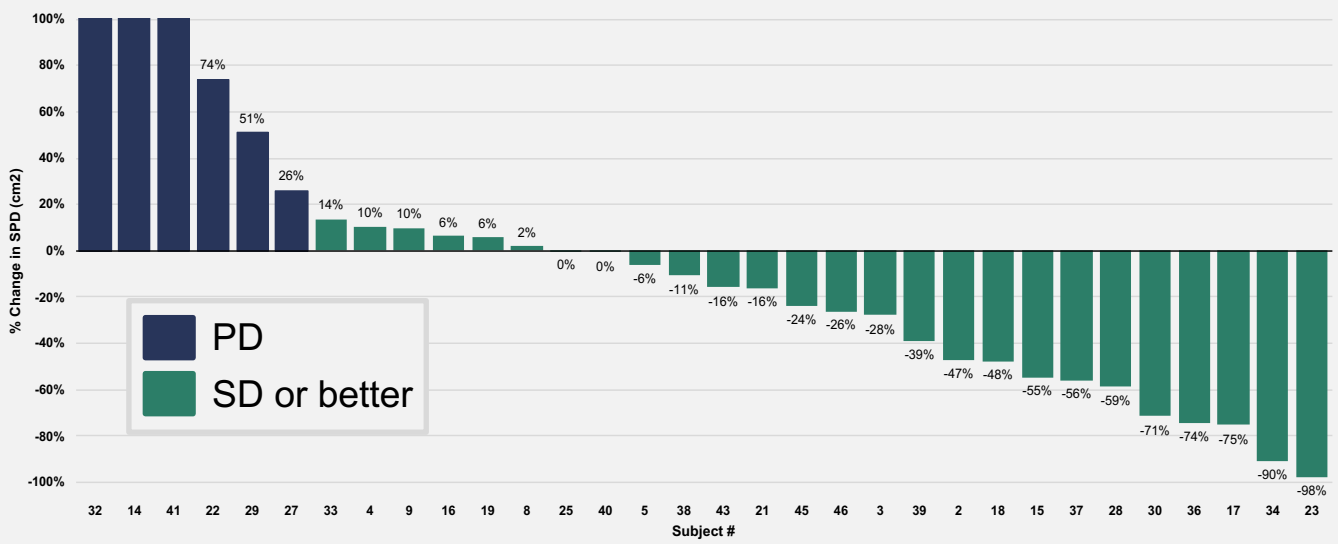
Tumor Control Rate = 76% (31/41)



Improved Tumor Control Rate & Survival in Proposed Population

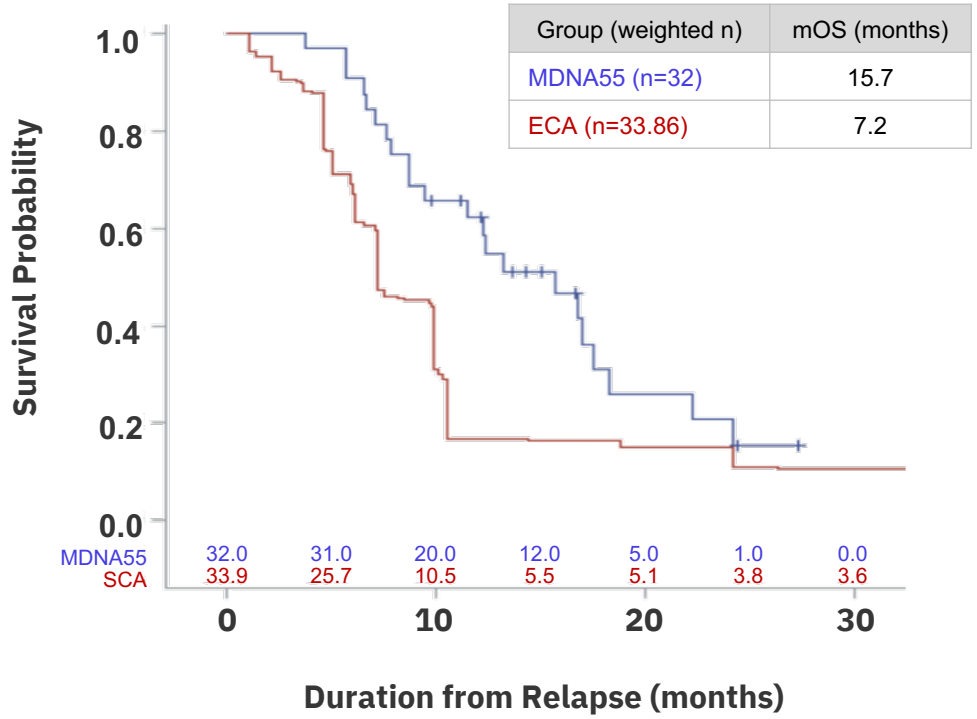
A Proposed Population comprised of all IL4R High (irrespective of dose) as well as IL4R Low patients receiving the high dose showed over 100% improvement in survival when compared to an External Control Arm (ECA)

Best Response per Modified RANO (following initial PsP)



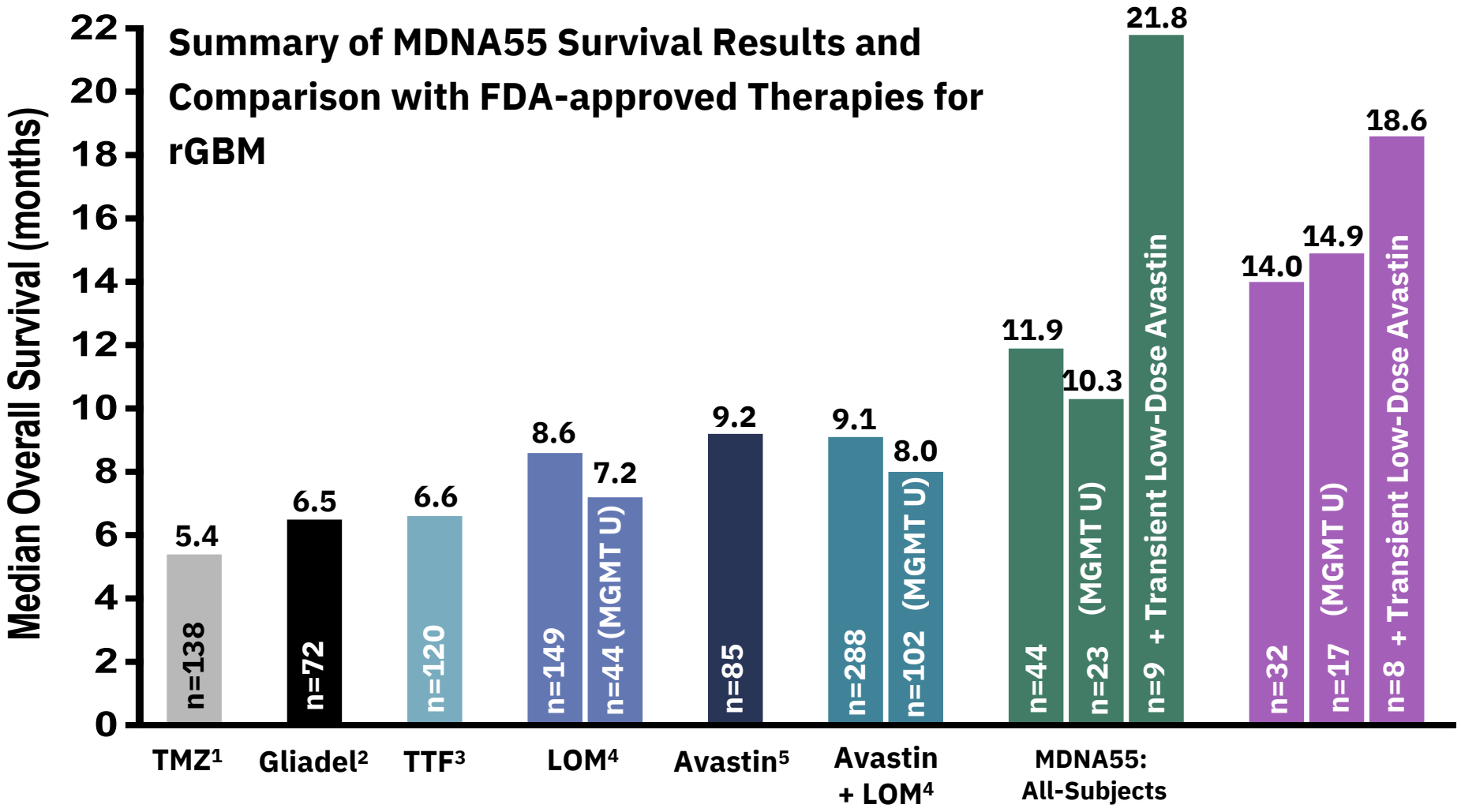
Shown is tumor response from nadir based on radiologic assessments only

Tumor Control Rate = 81% (26/32)



Group (weighted n)	mOS (months)
MDNA55 (n=32)	15.7
ECA (n=33.86)	7.2

Encouraging Survival Rates Compared to Approved Therapies



TTF = Tumor Treating Fields;

LOM = Lomustine;

MGMT U = MGMT unmethylated promoter

Refences:

1=Brada et al., 2001;

2=Gliadel FDA Label 2018;

3=Stupp et al., 2012;

4=Wick et al., 2017;

5=Friedman et al., 2009

Favorable Safety Profile and Well Tolerated

To date 118 patients have been treated with MDNA55:

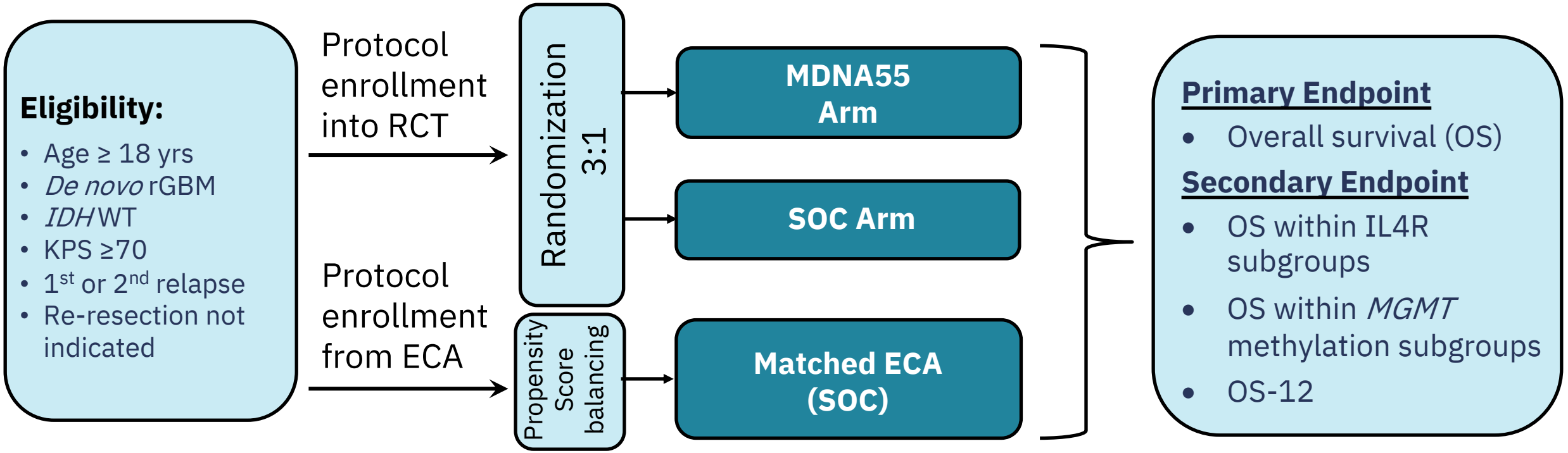
No systemic toxicity and no clinically significant laboratory abnormalities

Drug-related adverse events were primarily neurological/aggravation of pre-existing neurological deficits characteristic with GBM and have generally been manageable with standard measures

Maximum Tolerated Dose established at 240 µg for the current study. Notably, there is no evidence of a differential rate of neurological toxicities between doses of MDNA55 up to 240 µg and a range of up to 900 µg explored in previous studies.

Planned Phase 3 Trial

Pioneered a Hybrid Design Using External Control



Brain Cancer Represents a Significant Market Opportunity

Market Size Estimated at $2 Billion Annually

Tumor Type	Annual Incidence[1]	Projected Market[2]
Recurrent Glioblastoma (rGBM)	33,300	$650M
Metastatic Brain Cancer[3]	91,500	$1.30B
Pediatric Glioma	3,800	$50M
Total	**133,500**	**$2.0B**

1. GLOBOCAN 2012 http://globocan.iarc.fr/Default.aspx
2. U.S., Europe and Japan
3. Metastatic Brain Cancer numbers from colon, breast and kidney cancer only

Brain Cancer Next Steps

Pursue Partnership Strategy for Further Development

Visionary Medicines

MDNA11: IL-2 Superkine	MDNA55: Targets IL4R	Near Term Milestones	Corporate Snapshot
Best In Class IL-2 Super-agonist	**Compelling Clinical Efficacy** Positive Phase 2b clinical data in recurrent glioblastoma (rGBM)	**MDNA55 End Of Phase 2 Meeting Update** Held September 29, 2020	**Experienced Management Team** C-suite Has Combined 6+ Decades Of Experience In Biotech/Pharma
Exceptional CD122 Selectivity Boosts cancer killing immune cells without toxicity	**Orphan/Fast Track** Orphan Designation from EMA/FDA Fast Track Designation from FDA	**Submit IND to Commence Phase 1/2 MDNA11 Trial** (mid-2021)	**World Class Expertise** Clinical And Scientific Advisors, Collaborators And Inventors
Excellent PK/PD Profile Vast improvement over Proleukin	**$2 Billion** Potential market of MDNA55 for brain cancer ($US)[1,3]	**Safety Portion Of MDNA11 Phase 1 Monotherapy Study** Expected Completion In H2 2021	**17 Patent Families** Offer Strong Protection For Proprietary Technology Platforms

1. BioXcel Strategic Analysis Report, 2014.
2. Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide 2012.
3. Decision Resources, Inc Glioblastoma Report, Sept 2013.

Infinite Hope

Thank you

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