

# ALX ΦNCOLOGY

October 5, 2021

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# TEAM



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venBio



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# OVERVIEW

ALX Oncology (Nasdaq: ALXO) is a clinical-stage immuno-oncology company focused on helping patients fight cancer by developing therapies that block the CD47 checkpoint pathway and bridge the innate and adaptive immune system

## **Lead product candidate evorpacept (also known as ALX148) initiating multiple Phase 2 trials**

CD47 blocker

- Designed for use in combination
- Tolerability profile enables higher dosing
- Higher dosing may enable greater efficacy

Clinical proof-of-principle in both hematologic and solid tumors

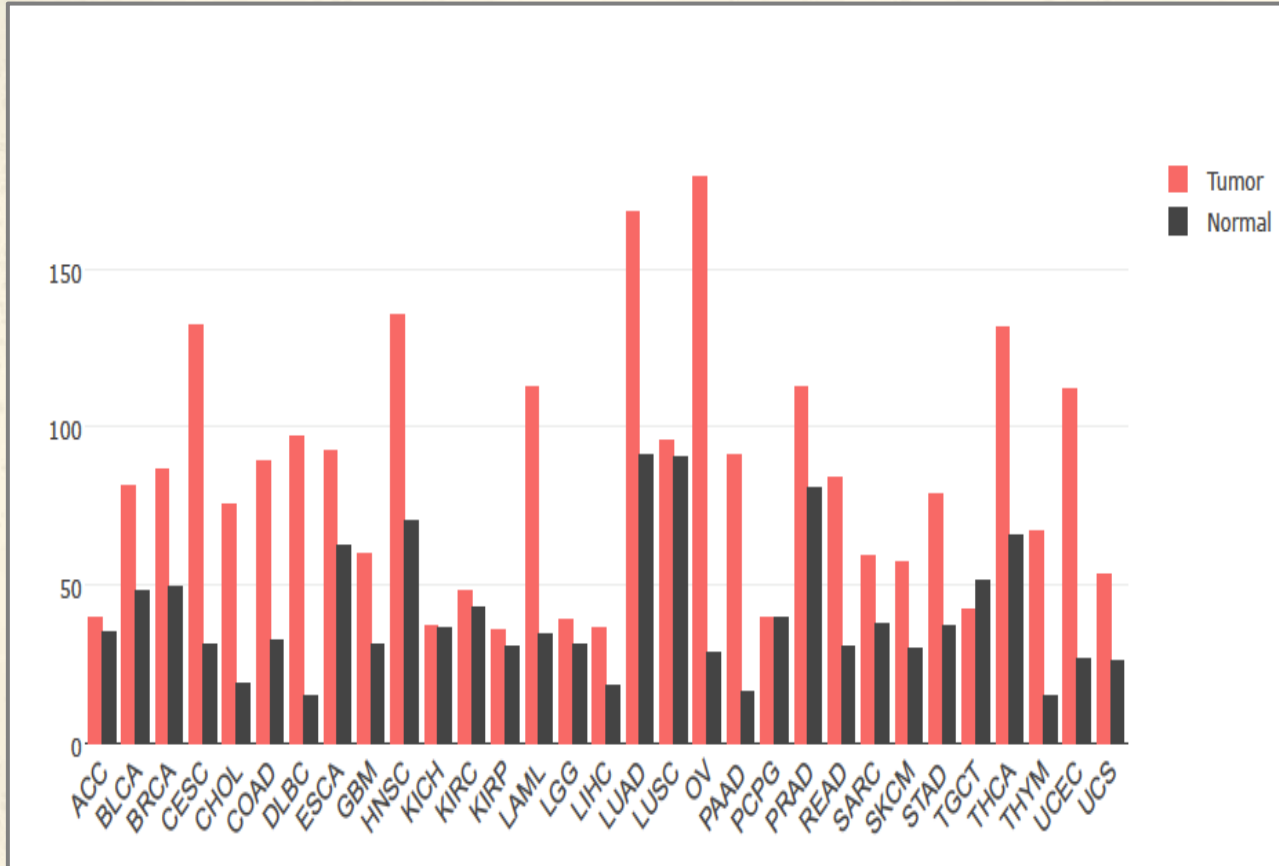
Initial focus on solid tumors, MDS, and AML

## **Early-stage antibody candidate ALTA-002\* for systemic CpG delivery**

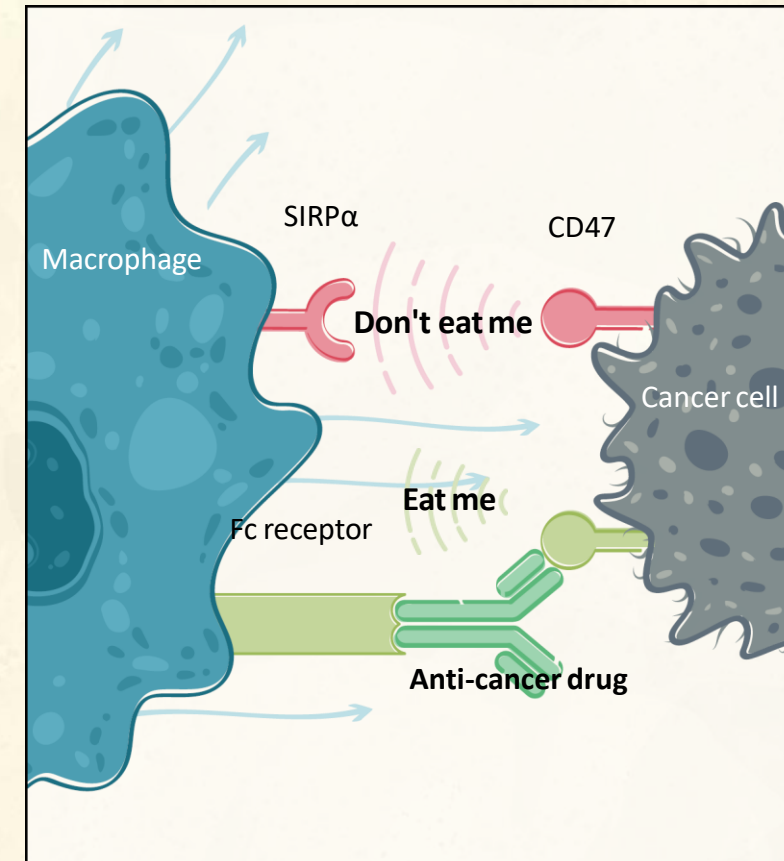
- IND by end of 2022

# CD47: TUMOR ASSOCIATED ANTIGEN (TAA)- MYELOID CHECKPOINT DUALITY

TAA-Expression levels on cancer and normal cells

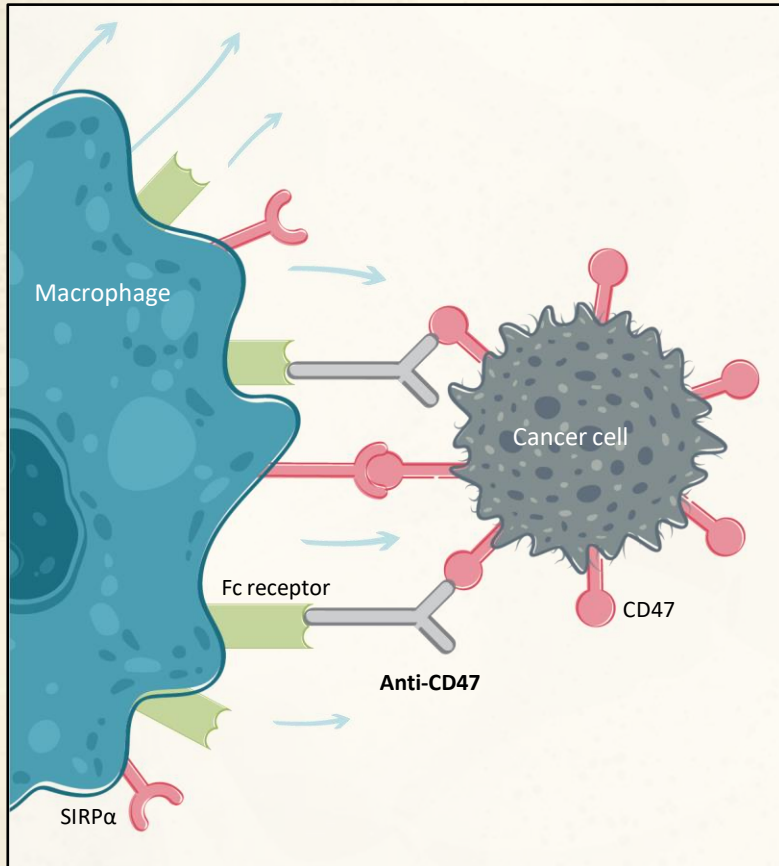


Checkpoint Mechanism: “do not eat me”

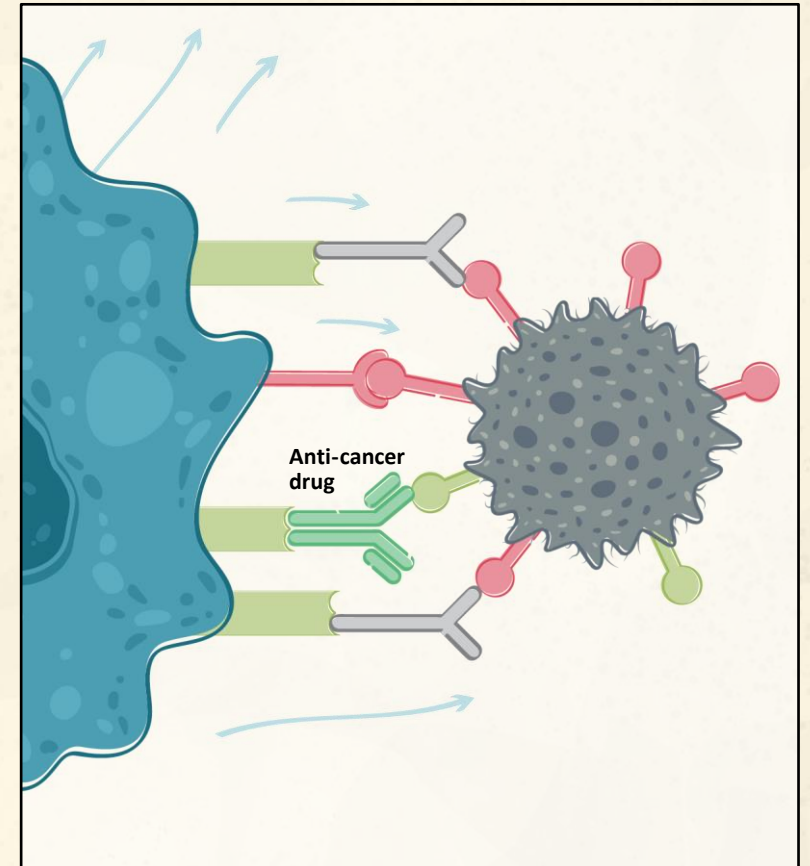
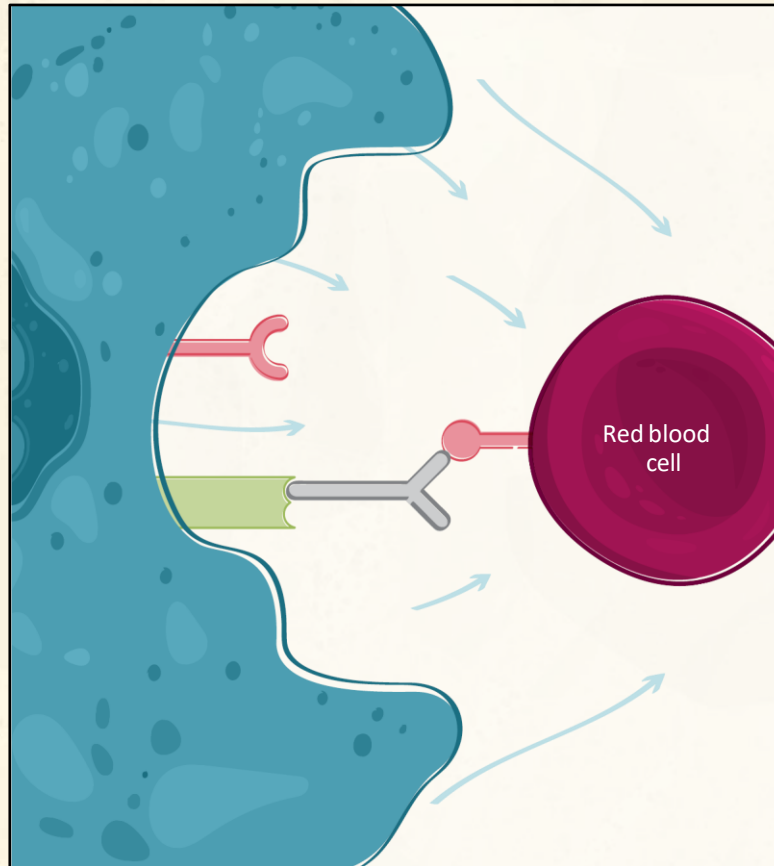


# TARGETING CD47 AS TUMOR ASSOCIATED ANTIGEN

But also targets normal cells



Anti CD47 with active Fc  
directly targets cancer cells

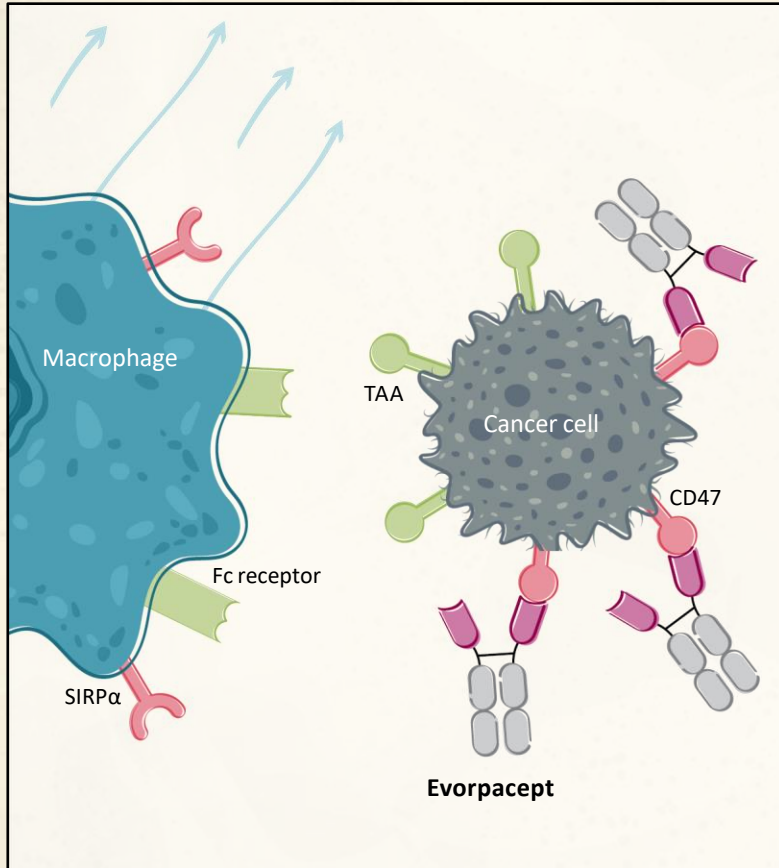


Dose limitations prevent full  
blockade of CD47 and active  
Fc competes with combo  
drug

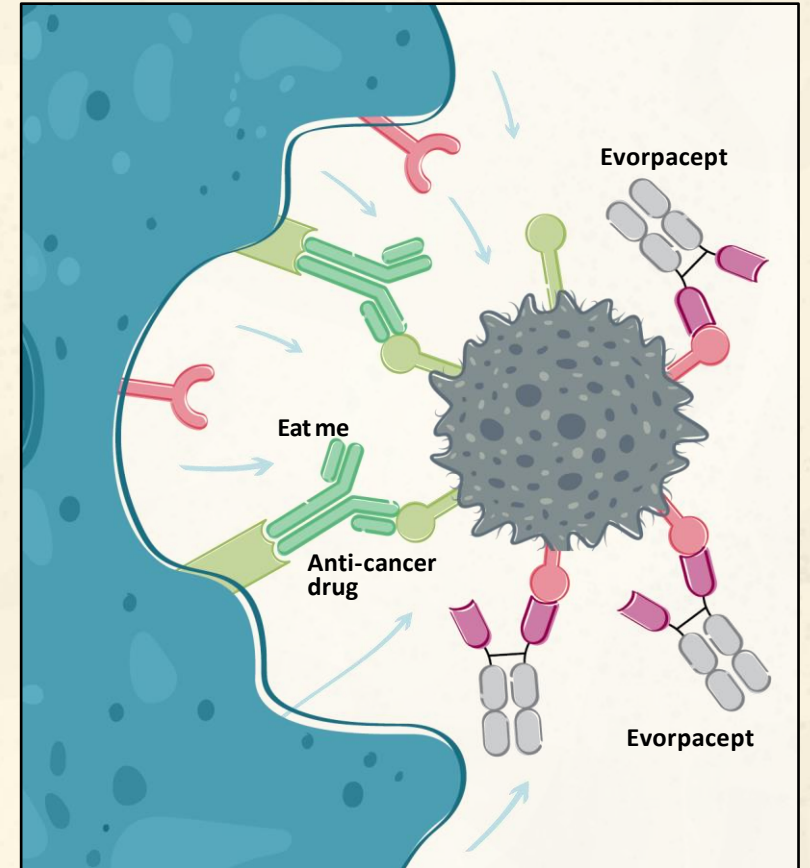
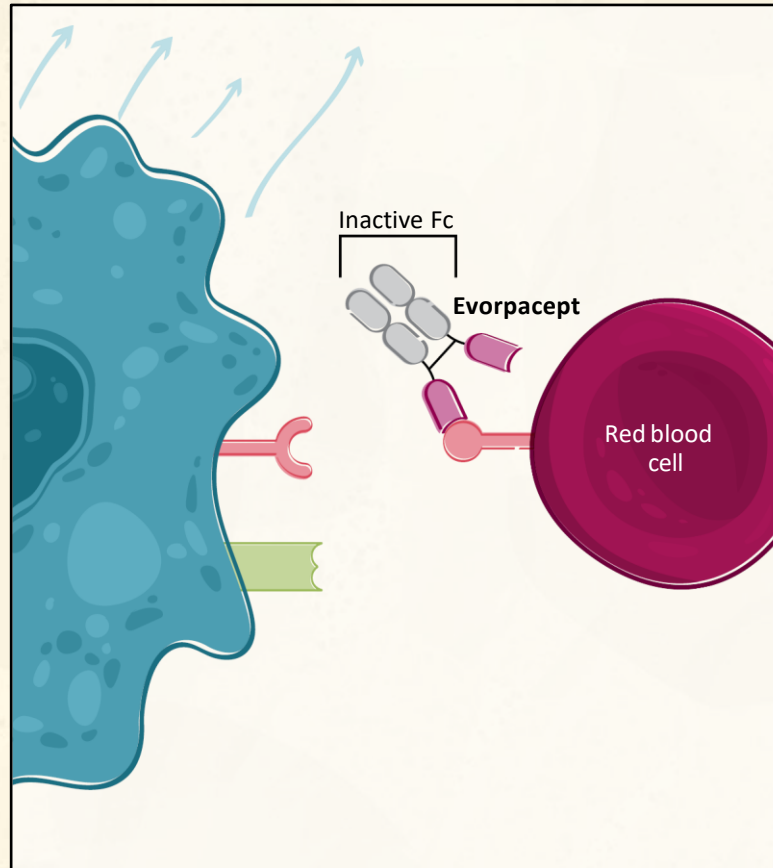


# TARGETING CD47 AS CHECKPOINT: ALX ONCOLOGY'S APPROACH

It spares normal cells



Anti CD47 with inactive Fc binds and block CD47-SIRPα interaction



High dose allows full blockade of CD47 and maximizes activity of combo drug

# EVORPACEPT: METICULOUSLY DESIGNED CD47 BLOCKER

High affinity CD47 binding domain of SIRP $\alpha$



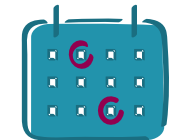
Potently blocks CD47 signal on cancer cells

Inactive Fc domain eliminates binding activity



No dose dependent cytopenia

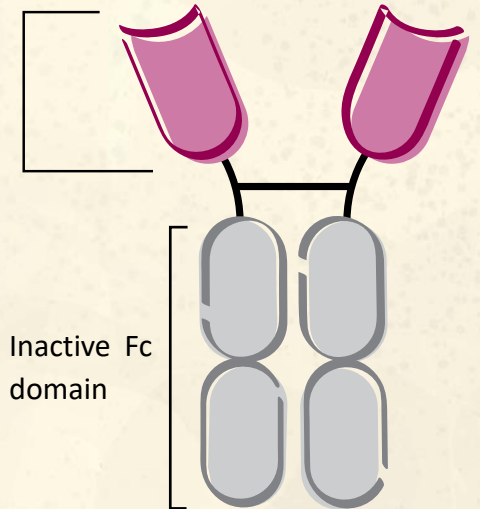
Presence of Fc domain ensures slow clearance and long half-life



Less frequent dosing

## Designed for safety and efficacy

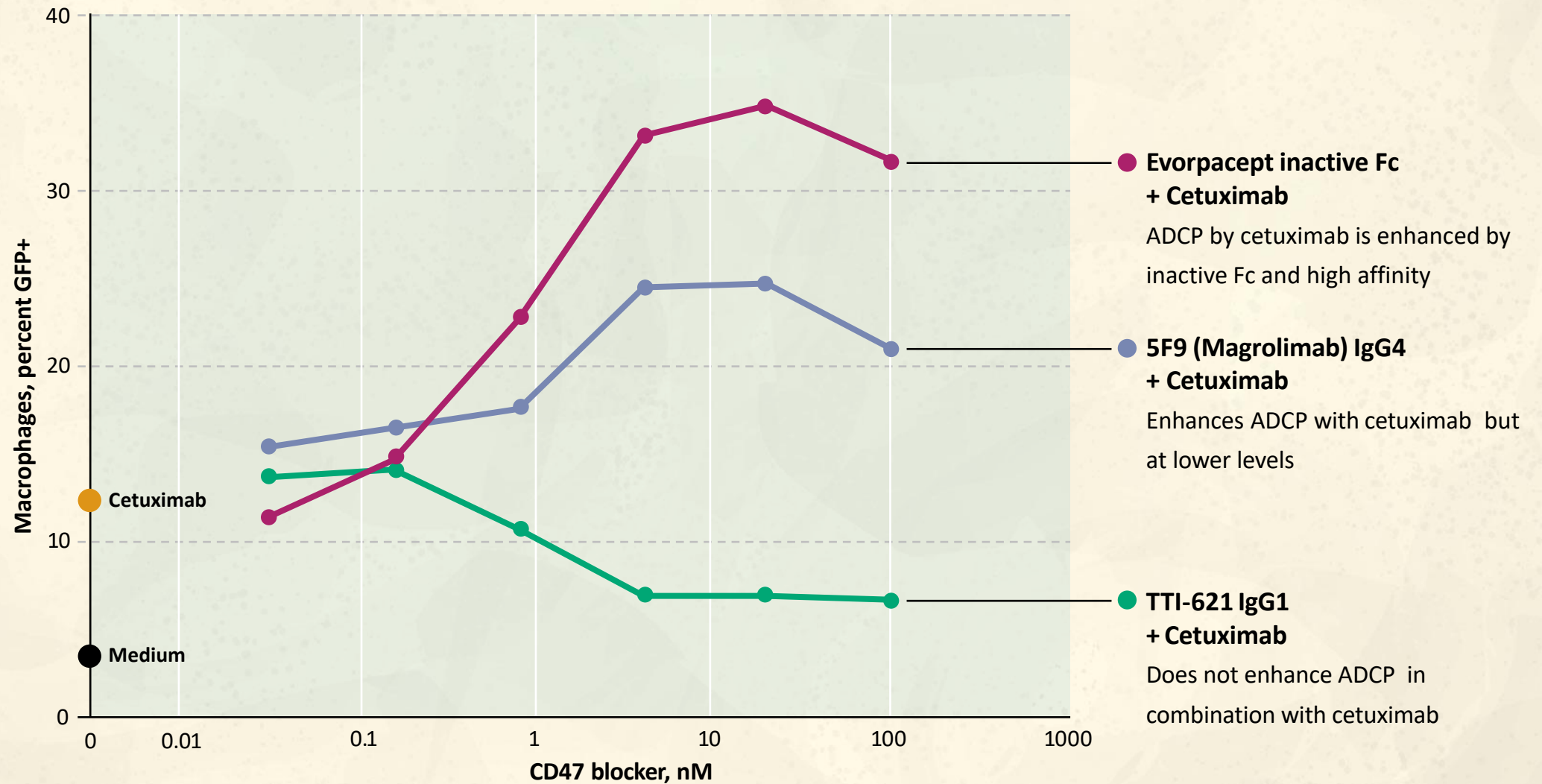
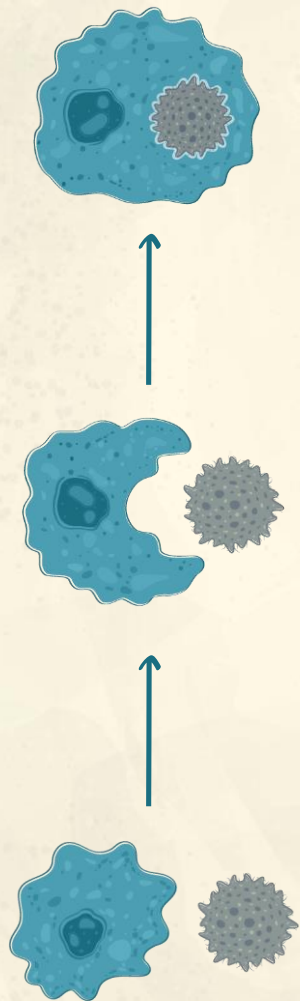
High affinity CD47 binding domains of SIRP $\alpha$



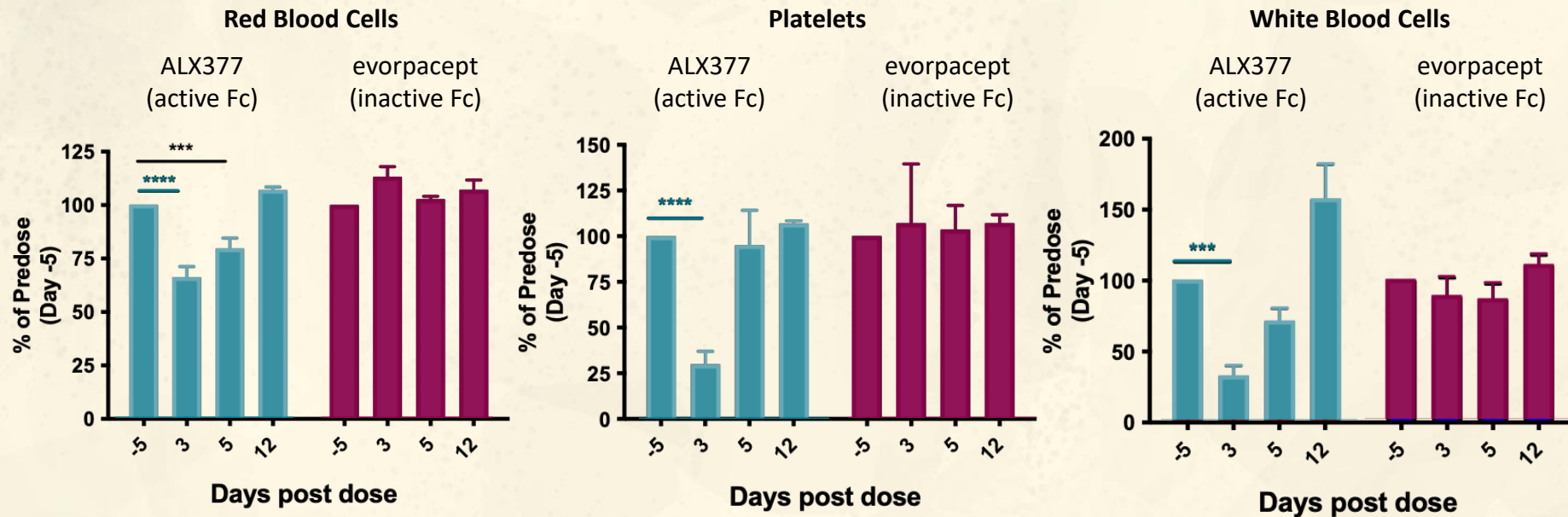
- ~Half the molecular weight of an antibody
- Increases solid tumor penetration
- Cross-reactive to human, monkey, mouse
- Standard antibody manufacturing process



# EVORPACEPT DEMONSTRATES SUPERIOR PHAGOCYTOSIS



# INACTIVE FC SHOWS REDUCED CYTOPENIA IN MICE IN VITRO



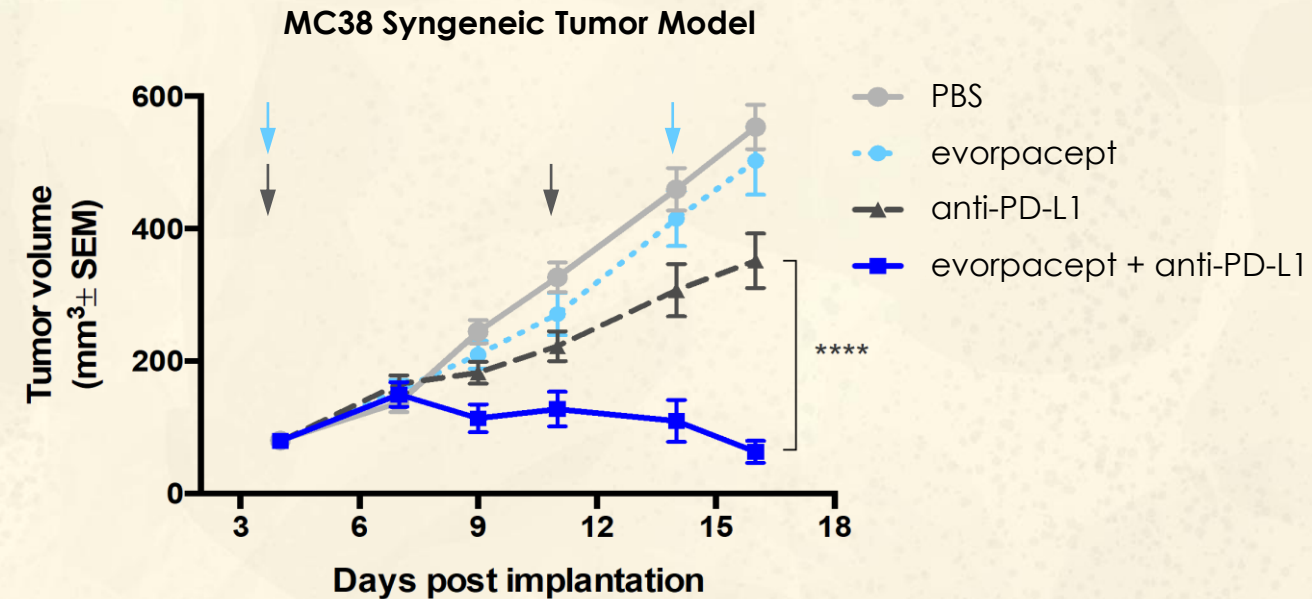
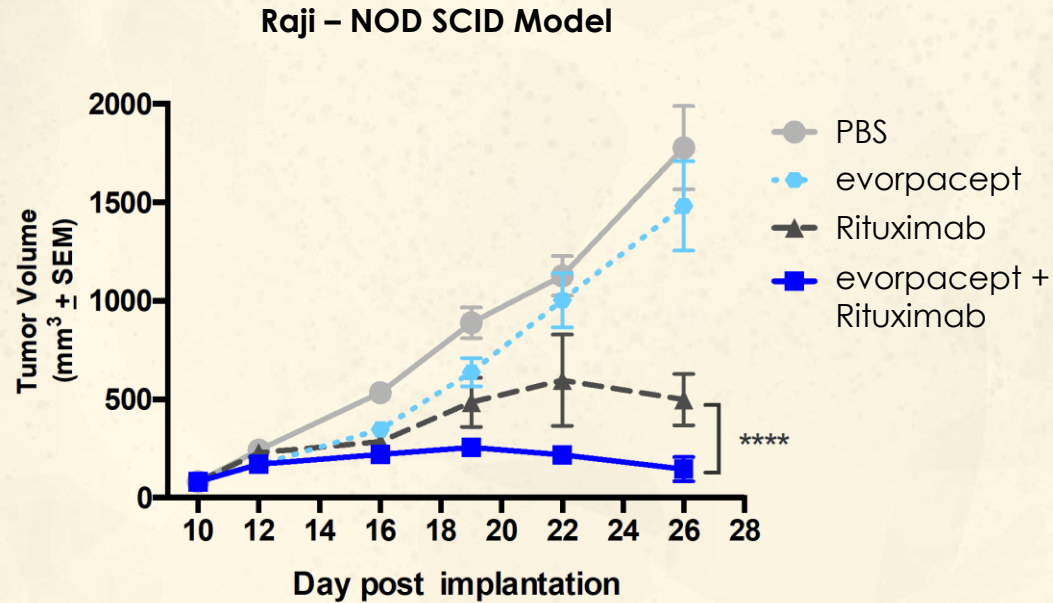
CD-1 mice received 30 mg/kg IV single dose

\*\*\*\*p<0.0001, \*\*\*p<0.001

Inactive Fc is the core determinant of safety profile

Mouse cross-reactivity allows for safety and efficacy testing in mouse models

# COMBINATION EFFICACY WITH TAA (RITUXIMAB) ANTIBODIES AND CHECKPOINT INHIBITOR (ATEZOLIZUMAB)

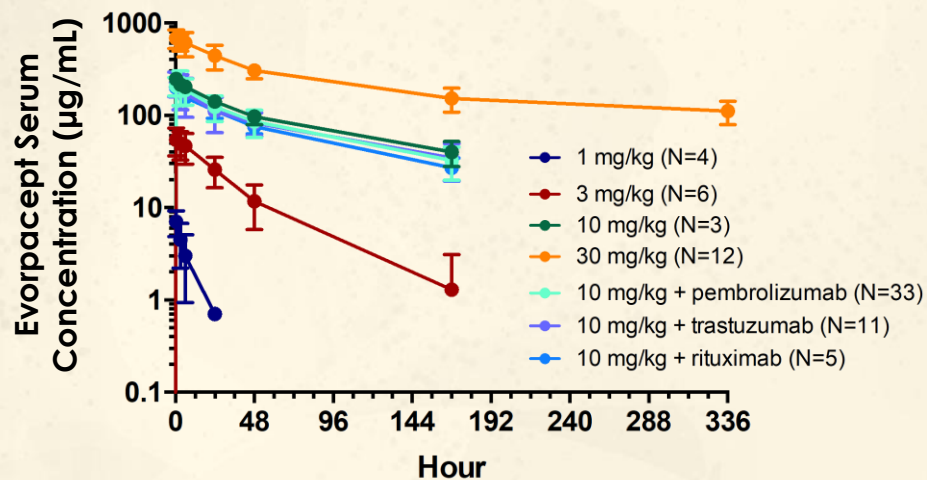


Mouse cross-reactivity allows for better clinical translation of preclinical models: presence of CD47 sink and mouse models with intact immune system



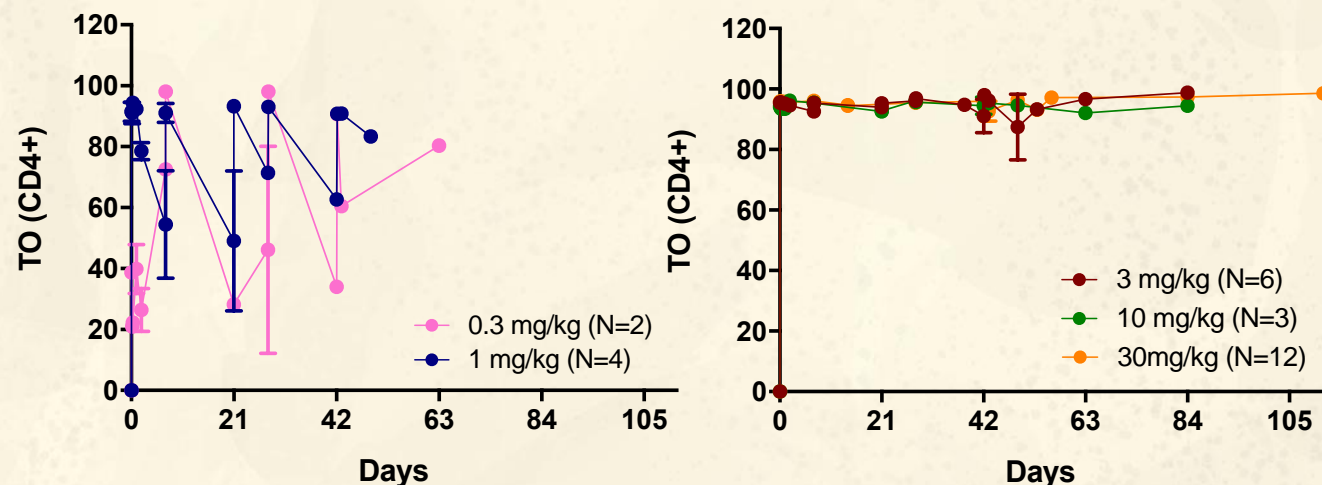
# EVORPACEPT CLINICAL PHARMACOKINETICS AND CD47 TARGET OCCUPANCY

Evorpacept Serum Levels for Cycle 1 Day 1





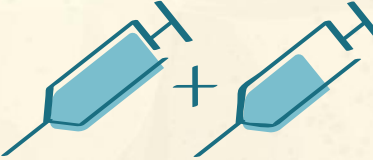
- Steady-state half-life of evorpacept at 10 mg/kg QW is predicted to be ~30 days.
- Evorpacept PK profile is not impacted by combination drugs.

CD47 Target Occupancy by Evorpacept



- Near complete CD47 target occupancy (TO) by evorpacept is maintained at  $\geq 3$  mg/kg QW across dosing interval
- 0.3 and 1 mg/kg QW show near complete target occupancy at peak, but not at trough

# EVORPACEPT DEMONSTRATES FAVORABLE TOLERABILITY PROFILE








	 Preclinical	 Single agent	 Combinations
Highest administered dose	<b>100 mg/kg<sup>1</sup></b> with no observable adverse events	<b>30 mg/kg Q2W<sup>2</sup></b> No evidence of dose-dependent cytopenias	<b>15 mg/kg QW</b> currently dosed <b>60 mg/kg Q4W</b> planned

<sup>1</sup>100 mg/kg of evorpacept  $\cong$  200 mg/kg of a typical antibody

<sup>2</sup>Single agent safety, ALX presentation, ASCO 2018 poster

Evorpacept  
has not yet reached a  
maximum tolerated  
dose

# ALX PIPELINE

Indication		Combination Agent	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Fast Track	Collaboration Partner
Evorpacept Combination Studies	SOLID TUMORS	HNSCC Head And Neck Squamous Cell Carcinoma	Keytruda	ASPEN-03					 MERCK
			Keytruda + 5FU + Platinum	ASPEN-04					 MERCK
		GC Gastric/Gastroesophageal Junction Cancer	Herceptin						
			Herceptin + Cytomab + Paclitaxel	ASPEN-06					
		Breast Cancer	Zanidatamab						
	HEMATOLOGY	MDS Myelodysplastic Syndromes	Azacitidine	ASPEN-02					
		AML Acute Myeloid Leukemia	Azacitidine + Venclexta	ASPEN-05					
		NHL Non-Hodgkin's Lymphoma	Rituximab						
ALTA-002*		Advanced Cancer							

\*SIRPα Toll-like receptor agonist antibody conjugate (TRAAC)



# EVORPACEPT DEMONSTRATES CONSISTENT TOLERABILITY PROFILE

Treatment related adverse events*	evorpacept + Herceptin + Cyramza + chemo (N=18)		evorpacept + Herceptin (N=30)		evorpacept + Keytruda + chemo (N=5)		evorpacept + Keytruda (N=52)		evorpacept + Rituximab (N=33)	
	Total n (%)	≥Grade 3	Total n (%)	≥Grade 3	Total n (%)	≥Grade 3	Total n (%)	≥Grade 3	Total n (%)	≥Grade 3
Fatigue	2 (11.1%)	-	9 (30.0%)	-	-	-	6 (11.5%)	-	4 (12.1%)	-
Rash	3 (16.7%)	-	-	-	-	-	5 (9.6%)	-	8 (24.2%)	-
AST increased	-	-	-	-	-	-	9 (17.3%)	-	-	-
Platelets decreased	-	-	5 (16.7%)	2 (6.7%)	-	-	4 (7.7%)	2 (3.8%)	-	-
ALT increased	-	-	-	-	-	-	7 (13.5%)	1 (1.9%)	-	-
Pruritus	2 (11.1%)	-	3 (10.0%)	-	-	-	5 (9.6%)	-	2 (6.1%)	-
Pyrexia	-	-	3 (10.0%)	-	-	-	3 (5.8%)	-	-	-
Decreased appetite	-	-	3 (10.0%)	-	-	-	2 (3.8%)	-	-	-
Anemia	-	-	2 (6.7%)	-	-	-	5 (9.6%)	1 (1.9%)	2 (6.1%)	1 (3.0%)
Infusion reaction	-	-	-	-	-	-	4 (7.7%)	-	-	-
Neutropenia / Neutrophil count decr	-	-	2 (6.7%)	2 (6.7%)	-	-	2 (3.8%)	1 (1.9%)	2 (6.1%)	2 (6.1%)
Nausea	-	-	2 (6.7%)	-	-	-	2 (3.8%)	-	2 (6.1%)	-
Alkaline phosphatase incr	-	-	-	-	-	-	3 (5.8%)	-	-	-
Arthralgia	-	-	-	-	-	-	3 (5.8%)	-	-	-
WBC decreased	-	-	-	-	-	-	3 (5.8%)	-	-	-
Myalgia	-	-	-	-	-	-	2 (3.8%)	-	2 (6.1%)	-
Diarrhea	3 (16.7%)	-	-	-	-	-	-	-	-	-
Urticaria	3 (16.7%)	-	-	-	-	-	-	-	-	-

Treatment related adverse events occurring in ≥2 subjects in all histologies at 10 & 15 mg/kg QW.

\*Data cut off: April 1, 2020 for combination cohorts of evorpacept plus Keytruda and Herceptin; October 1, 2020 for combination cohorts of evorpacept plus Rituxan, Keytruda and chemotherapy (5FU, platinum); May 03, 2021 for combination cohort of evorpacept plus Herceptin and chemotherapy (Cyramza, paclitaxel).

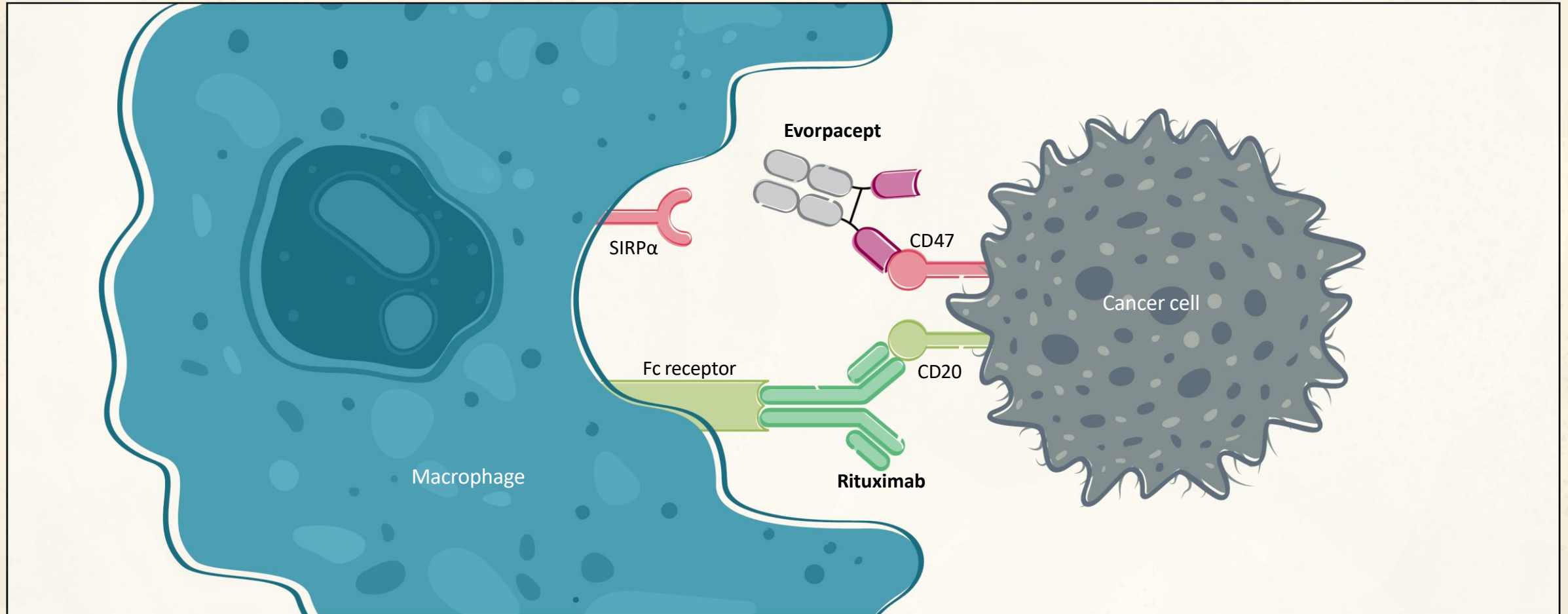
# EVORPACEPT HAS INITIAL CLINICAL ACTIVITY ACROSS TUMOR TYPES IN MULTIPLE TRIALS

Population	≥2L HER2+ GC		≥2L HER2+ GC	1L HNSCC		≥2L HNSCC (CPI-Naïve)		≥2L NHL (15mg/kg)
Combination	evorpacept + Herceptin + Cyramza + paclitaxel		evorpacept + Herceptin	evorpacept + Keytruda + 5FU + platinum		evorpacept + Keytruda		evorpacept + Rituximab
N-evaluable	18		19	4		10		10
ORR	evorpacept <b>72%</b>	benchmark 28%	<b>21%</b>	evorpacept <b>75%</b>	benchmark 36%	evorpacept <b>40%</b>	benchmark 15%	<b>70%</b>
mPFS (months)	<b>9.1</b>	4.4	<b>2.2</b>	<b>NC</b>	4.9	<b>4.6</b>	2.1	<b>NC</b>
mOS (months)	<b>NC</b>	9.6	<b>8.1</b>	<b>NC</b>	13.0	<b>22.1</b>	8.4	<b>NC</b>
Benchmark regimen	Cyramza + paclitaxel			Keytruda + 5FU + platinum		single agent Keytruda		

Evorpacept plus Herceptin and Cyramza and paclitaxel data as of May 03, 2021. All other data as of October 1, 2020. NC = unable to be calculated, ORR = Objective Response Rate, mPFS = median progression free survival, mOS = median overall survival. CPI = checkpoint inhibitor.

2L GC benchmark, Wilke, Lancet Oncology, 2014; 2L HNSCC benchmark, Cohen, Lancet, 2018; 1L HNSCC benchmark, Burtneess, Lancet, 2019.

# NHL TRIAL: EVORPACEPT + RITUXIMAB MECHANISM OF ACTION



**Evorpacept increases antibody dependent cellular phagocytosis in combination with Rituximab**



# NHL PROOF-OF-PRINCIPLE TRIAL

## Phase 1b NHL cohorts



relapsed/Refractory NHL,  
prior regimen with Rituximab



Treatment:

**evorpaccept** 10 or 15 mg/kg  
once a week (QW)  
+  
**Rituximab** 375 mg/m<sup>2</sup> once a week for  
4 weeks, once monthly  
for 8 months

		evorpaccept 10 mg/kg QW + Rituximab (n=22)	evorpaccept 15 mg/kg QW + Rituximab (n=11)
Primary Disease, n	Follicular	5	3
	Marginal Zone (MZL)	2	1
	Mantle Cell (MCL)	4	1
	DLBCL	11	6
Median Age, Years (range)		66 (32-80)	64 (53-78)
Sex, n	M	17	6
	F	5	5
Race, n	Asian	18	9
	White	4	2
ECOG, PS, n	0	7	2
	1	15	9
Median Prior Therapy, n (range)		3 (1-7)	3 (1 -5)

Data Cutoff October 1, 2020

# NHL PROOF-OF-PRINCIPLE TRIAL

evorpacept  
in  
**NHL**

Population	10 mg/kg QW		15 mg/kg QW	
	N	ORR	N	ORR
All	22	40.9%	10	70.0%
Aggressive	15	33.3%	6	50.0%
Indolent	7	57.1%	4	100.0%

Data Cutoff: October 1, 2020; ASH 2020 Abstract 3016

**N** = Response Evaluable Patients

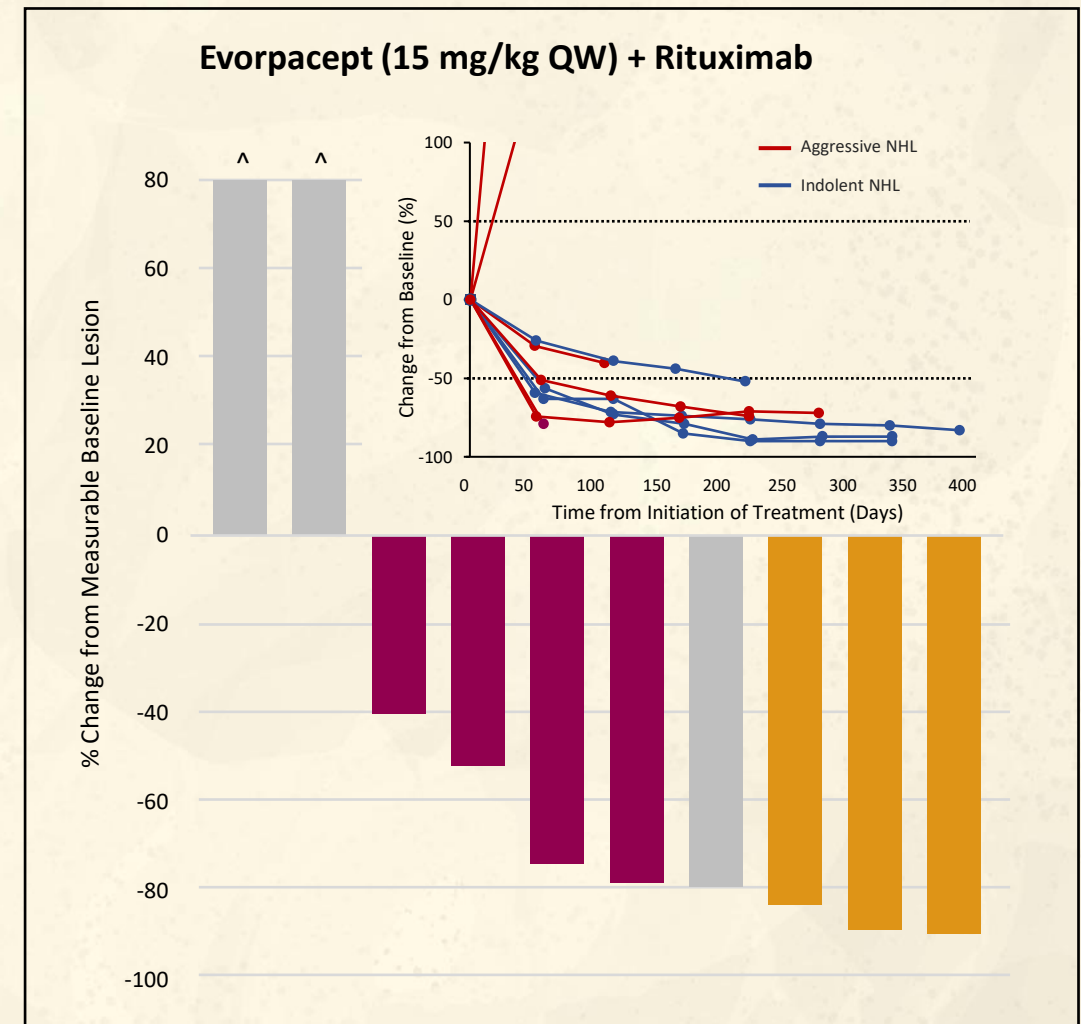
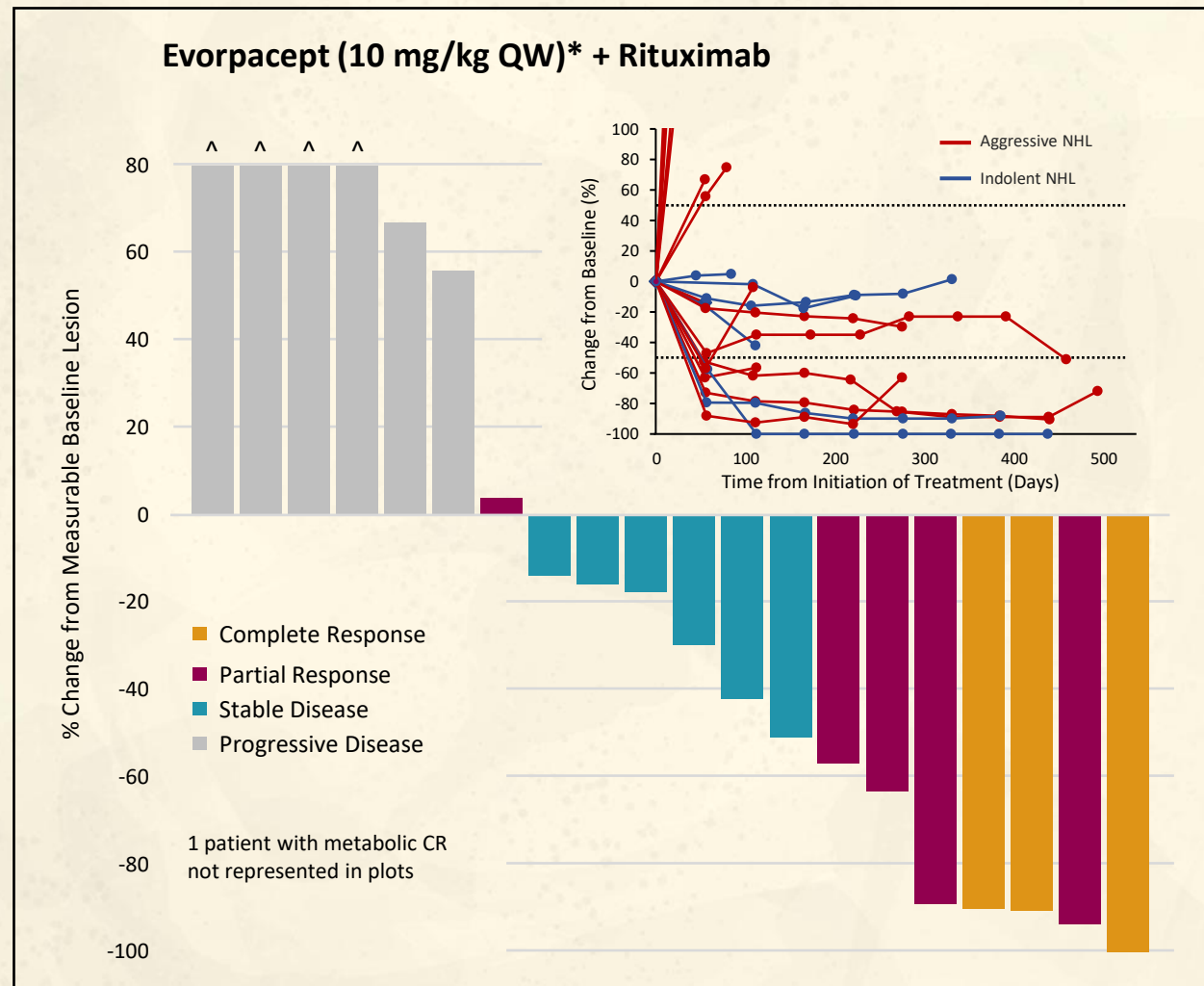
**Indolent** = Follicular Lymphoma and Marginal Zone Lymphoma.

**Aggressive** = Diffuse Large B-cell Lymphoma and Mantle Cell Lymphoma.

**ORR** = Objective Response Rate.

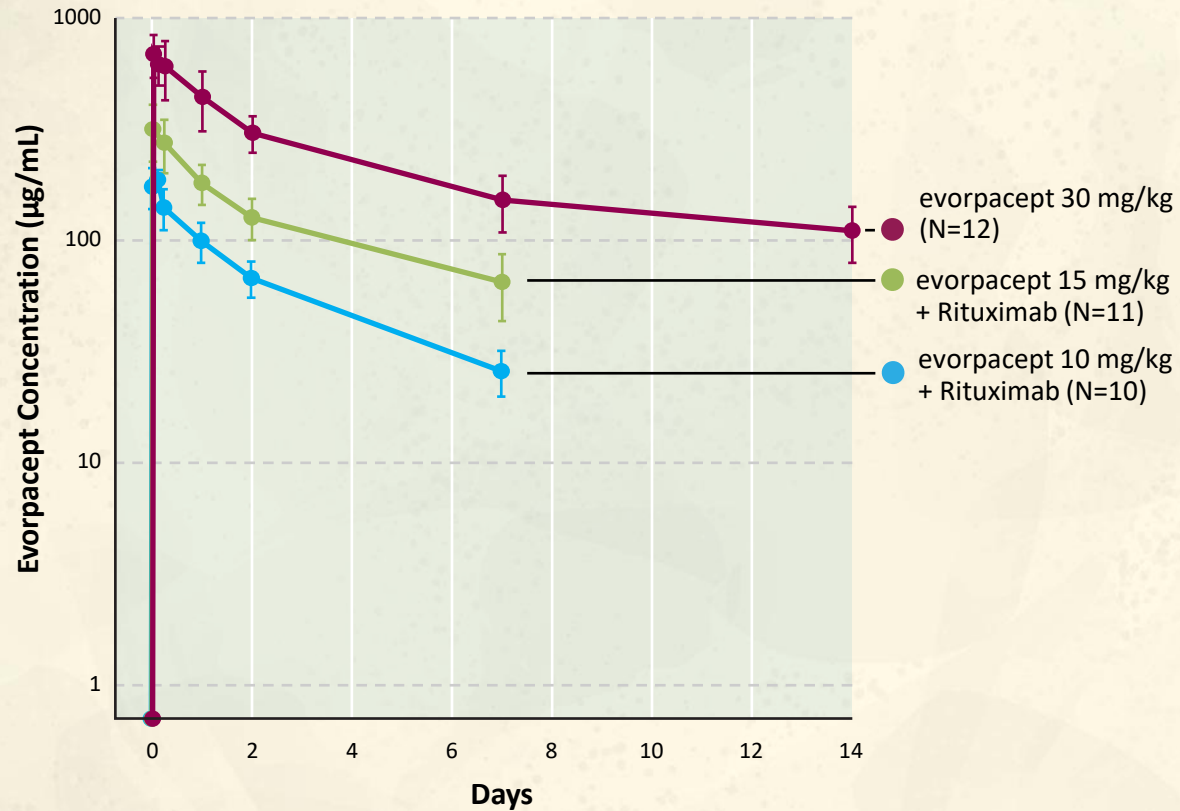
**Evorpacept**  
demonstrated higher  
response rate  
at higher dosing

# NHL: CLINICAL ACTIVITY OF EVORPACEPT + RITUXIMAB BY PATIENT

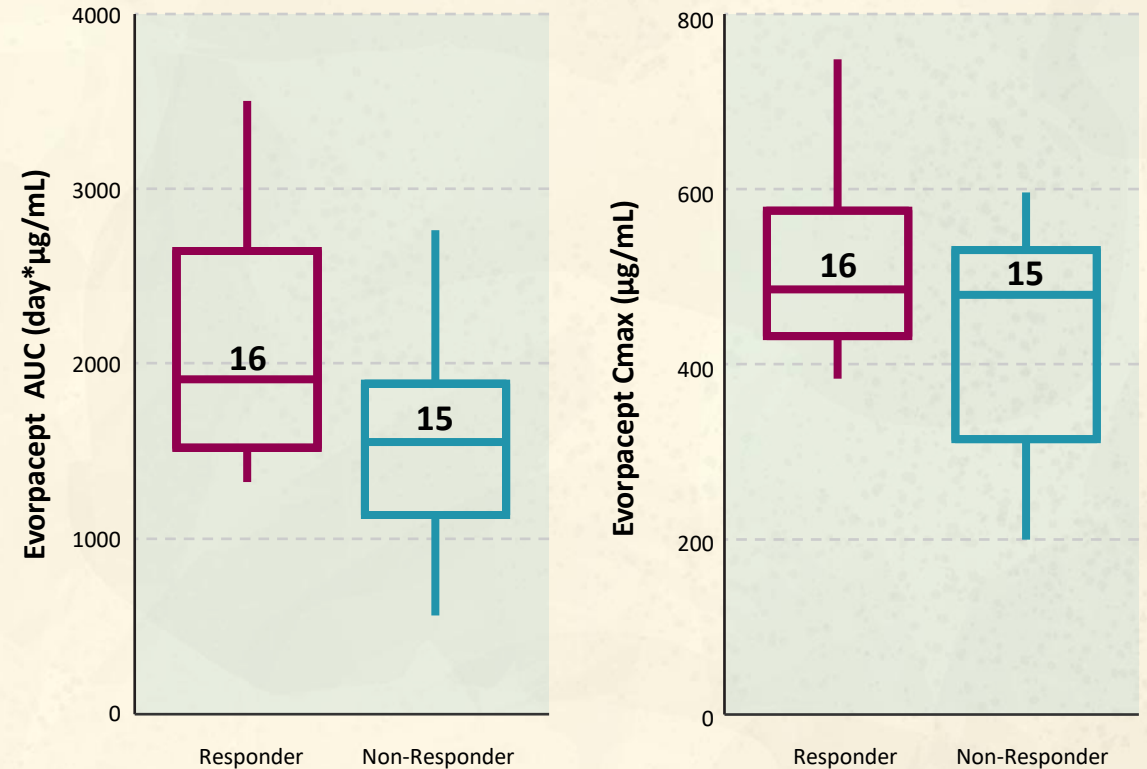




# NHL: EVORPACEPT CLINICAL PHARMACOKINETICS AND EXPOSURE-RESPONSE ANALYSIS



Evorpacept concentration-time profiles following first IV infusion at Cycle 1 Day 1 as single agent or in combination with Rituximab.



\*A significant improvement in patients with clinical response (PR,CR) with increased evorpacept exposure (AUC;  $p = 0.023$ ) was observed across the exposure range evaluated (10 mg/kg QW - 15 mg/kg QW).

# NON-HODGKIN LYMPHOMA PROOF-OF-PRINCIPLE SUMMARY

evorpacept  
in  
**NHL**



**Other agents in CD47 class  
reduced dosing leading to reduced  
responses**



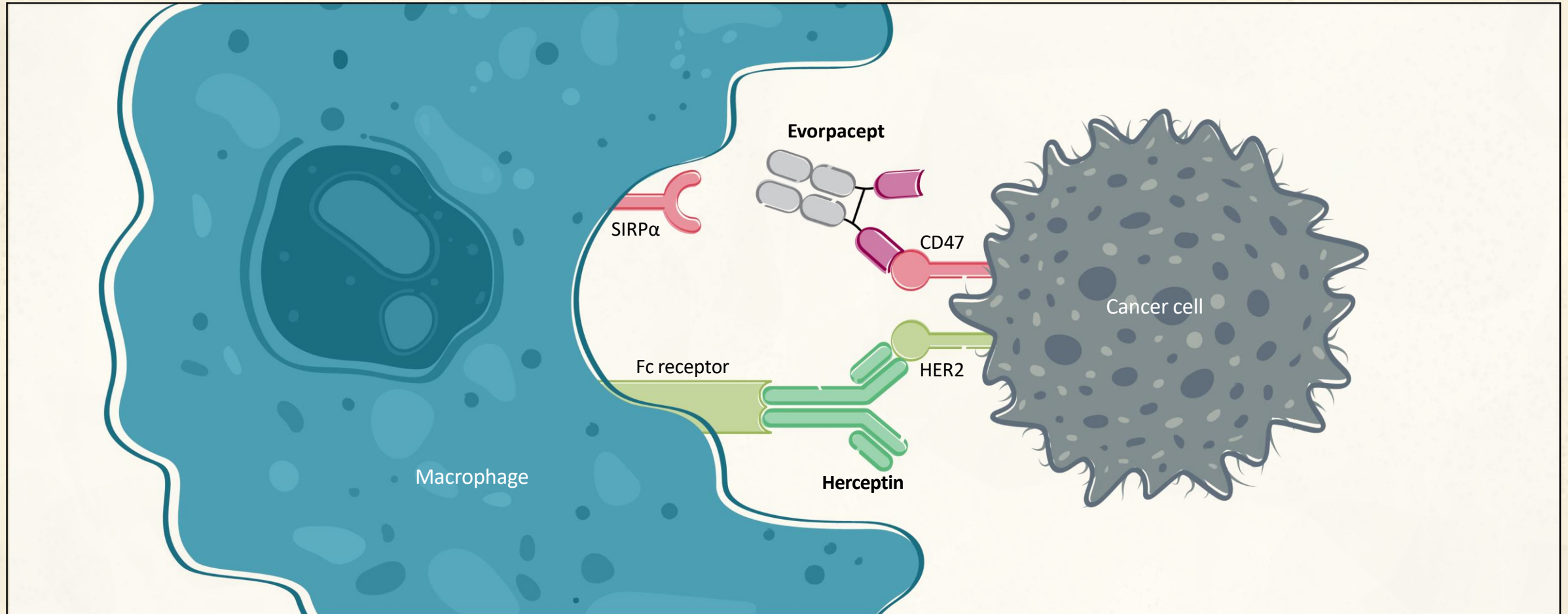
**Higher dosing enabled by  
evorpacept tolerability profile**



**Higher dosing of evorpacept  
led to higher responses**

# GC TRIAL: EVORPACEPT + HERCEPTIN MECHANISM OF ACTION

evorpaccept  
in  
GASTRIC



Evorpaccept increases antibody dependent cellular phagocytosis in combination with Herceptin

# PHASE 1B GC TRIALS: PATIENT BASELINE CHARACTERISTICS

		evorpaccept + Herceptin ≥2L GC (N=20)	evorpaccept + Herceptin + Cyramza/chemo ≥2L GC (N=18)
Median age, years (range)		<b>58 (45-79)</b>	<b>63 (36-83)</b>
Sex, n	M	<b>15</b>	<b>13</b>
	F	<b>5</b>	<b>5</b>
Race, n	Asian	<b>13</b>	<b>15</b>
	White	<b>6</b>	<b>3</b>
	Other	<b>1</b>	<b>-</b>
ECOG PS, n	0	<b>7</b>	<b>8</b>
	1	<b>13</b>	<b>10</b>
Progressed upon prior anti-HER2 therapy, n ( %)		<b>19 (95)</b>	<b>17 (94)</b>
Progressed upon ≥2 prior anti-HER2 therapy n ( %)		<b>9 (45)</b>	<b>1 (6)</b>
Progressed upon prior CPI therapy, n ( %)		<b>9 (45)</b>	<b>2 (11)</b>
Visceral distant metastasis, n ( %)		<b>17 (85)</b>	<b>17 (94)</b>



# PHASE 1B ≥2 LINE GC TRIAL: EVORPACEPT + HERCEPTIN

## Phase 1b GC trial:

 Response  
evaluable patients

**N=19** HER2 positive GC  
progressed on prior fluoropyrimidine,  
Herceptin or platinum.

 Treatment:

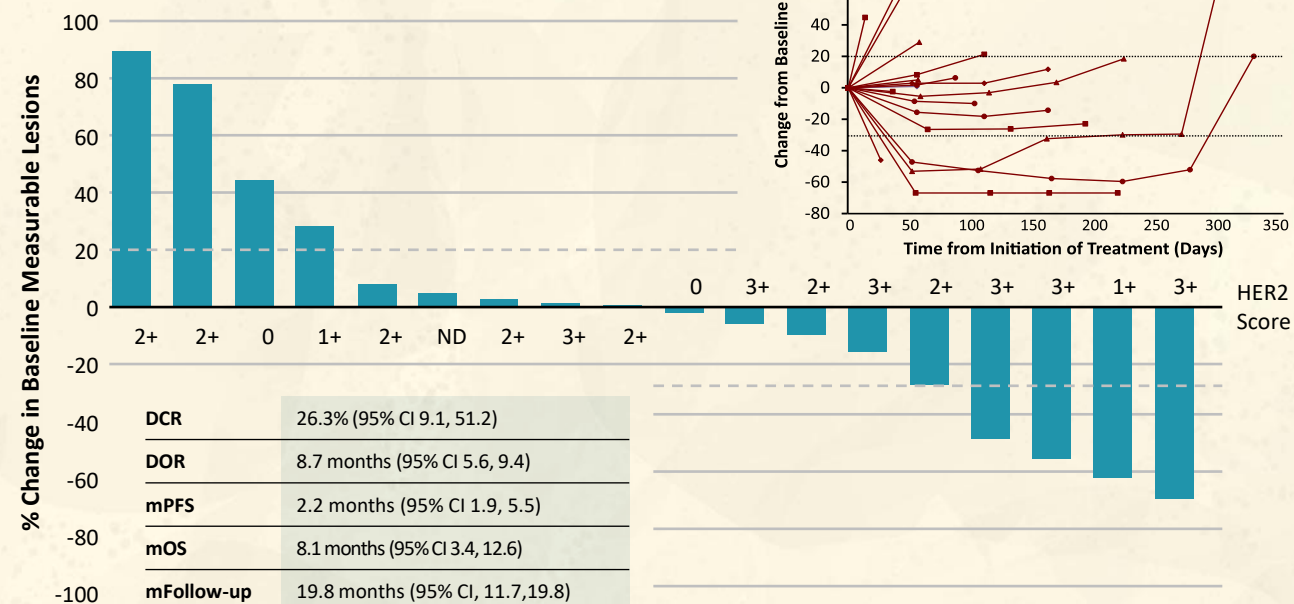
**evorpacept** 10 mg/kg  
once a week (QW)  
+ **Herceptin**  
8 mg/kg once, then  
6 mg/kg every three weeks (Q3W)

 Endpoints:

- maximum tolerated dose
- anti-cancer activity

Result:

**ORR 21.1% (4/19)**




**Notes:** Data Cutoff October 1, 2020. Patients who received at least one dose of evorpacept in the expansion phase, had a baseline assessment, and at least one post-baseline disease assessment; One patient with clinical progression not included in plots.  
**ORR** = Overall Response Rate. **ND** = Not Done. **HER2** Score retrospectively assessed using archival tissue by a central IHC lab.


**FDA granted evorpacept fast track designation for second-line treatment of HER2 positive GC**

# PHASE 1B ≥2 LINE GC TRIAL: EVORPACEPT + HERCEPTIN + CYRAMZA + PACLITAXEL


## Phase 1b higher dose + chemo trial:

**Patients:**

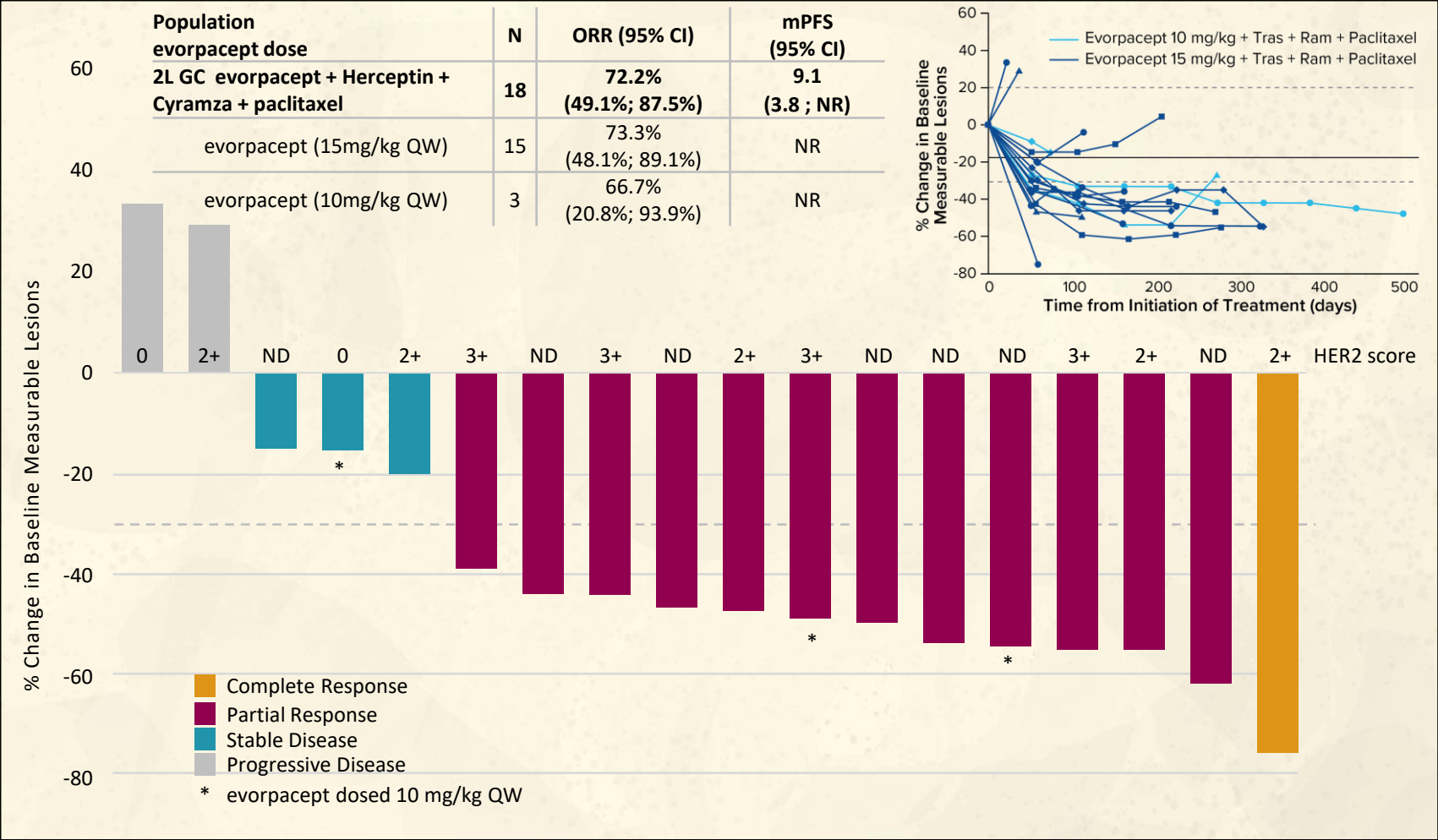
R/R HER2 positive GC, 2L or greater; Progressed on prior Herceptin and fluoropyrimidine or platinum.

**Treatment:**

**evorpacept** 10 and 15 mg/kg (QW)  
+ **Herceptin**  
+ **Cyramza**  
+ **paclitaxel**

**Endpoint:**

- safety of combination
- anti-cancer activity



Data Cutoff May 03, 2021. ND = Not Done

# SECOND LINE GC: PLANNED RANDOMIZED PHASE 2 CLINICAL TRIAL, ASPEN-06

## Randomized Phase 2:



Patients:  
N=100

2L or greater HER2 positive GC  
with prior HER2 targeted therapy



Treatment

evorpacept 30 mg/kg (Q2W)

+ Herceptin

+ Cyramza

+ paclitaxel

vs.

+ Herceptin

+ Cyramza

+ paclitaxel



Endpoint: • Anticancer activity: including ORR, DOR, PFS, OS

## Randomized Planned Phase 3:



Patients:

2L or greater HER2 positive GC  
with prior HER2 targeted therapy



Treatment

evorpacept 30 mg/kg (Q2W)

+ Herceptin

+ Cyramza

+ paclitaxel

vs.

+ Cyramza

+ paclitaxel

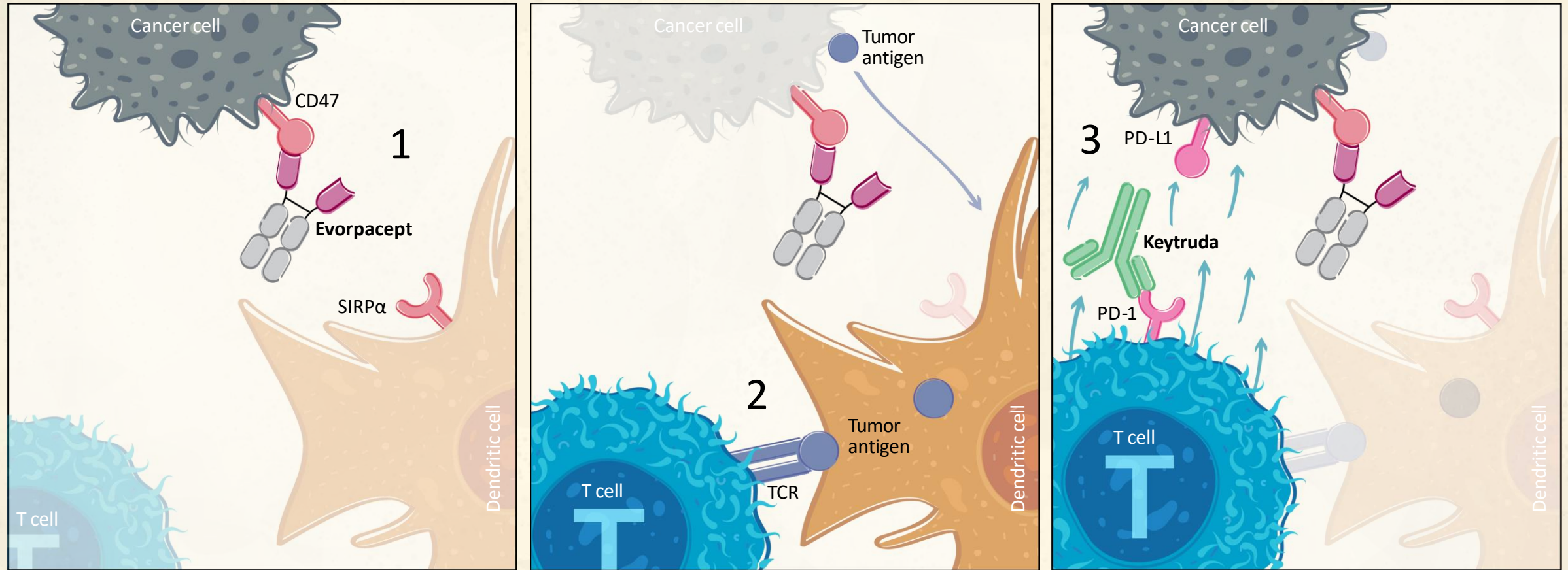


Endpoint: • Anticancer activity: including OS, PFS, ORR, DOR



# HNSCC TRIAL: EVORPACEPT + KEYTRUDA MECHANISM OF ACTION

evorpacept  
in  
HNSCC



Evorpacept activates dendritic cells and enhances cross-priming of T cells



# HNSCC STANDARD OF CARE & OPPORTUNITY

	ORR	mPFS (months)	mOS (months)	≥Gr3 TRAEs
<b>Keytruda + chemo<sup>1</sup></b> (KEYNOTE 048)	<b>36%</b>	<b>4.9</b>	<b>13.0</b>	<b>72%<sup>2</sup></b>
<b>Keytruda monotherapy</b> (KEYNOTE 048)	<b>17%</b>	<b>2.3</b>	<b>11.5</b>	<b>17%</b>
<b>Keytruda monotherapy</b> (KEYNOTE 040)	<b>15%</b>	<b>2.1</b>	<b>8.4</b>	<b>13%</b>

- Keytruda monotherapy ORR of 15% in ≥2L CPI naïve HNSCC
- Significant unmet need
- Increasing use of Keytruda monotherapy<sup>3</sup>
- Keytruda 2020 WW Sales \$14.4B<sup>4</sup>

<sup>1</sup>5FU + cisplatin or carboplatin.

<sup>2</sup>83% occurrence in chemo control arm.

<sup>3</sup>Wiley 2019, Real-world treatment patterns for patients with metastatic head and neck squamous cell carcinoma treated with immuno-oncology therapy.

<sup>4</sup>Merck 10-K February 25, 2021

# HNSCC TRIALS: PATIENT BASELINE CHARACTERISTICS

		evorpaccept + Keytruda ≥2L HNSCC (N=20)	evorpaccept + Keytruda + 5FU/platinum 1L HNSCC (N=5)
Median age, years (range)		62.5 (35-81)	61 (45-63)
Sex, n	M	15	4
	F	5	1
Race, n	Asian	6	4
	White	12	1
	Other	2	-
ECOG PS, n	0	7	4
	1	13	1
Progressed upon prior CPI therapy, n (%)		10 (50)	0 (0)
Visceral distant metastasis, n (%)		12 (60)	1 (20)

# PHASE 1B ≥2 LINE HNSCC TRIAL: EVORPACEPT + KEYTRUDA

## Phase 1b ≥2L HNSCC trial:



Response evaluable patients

**N=20:** recurrent/metastatic HNSCC, at least one prior systemic therapy



Treatment:

**evorpaccept** 10 mg/kg  
once a week (QW)  
+

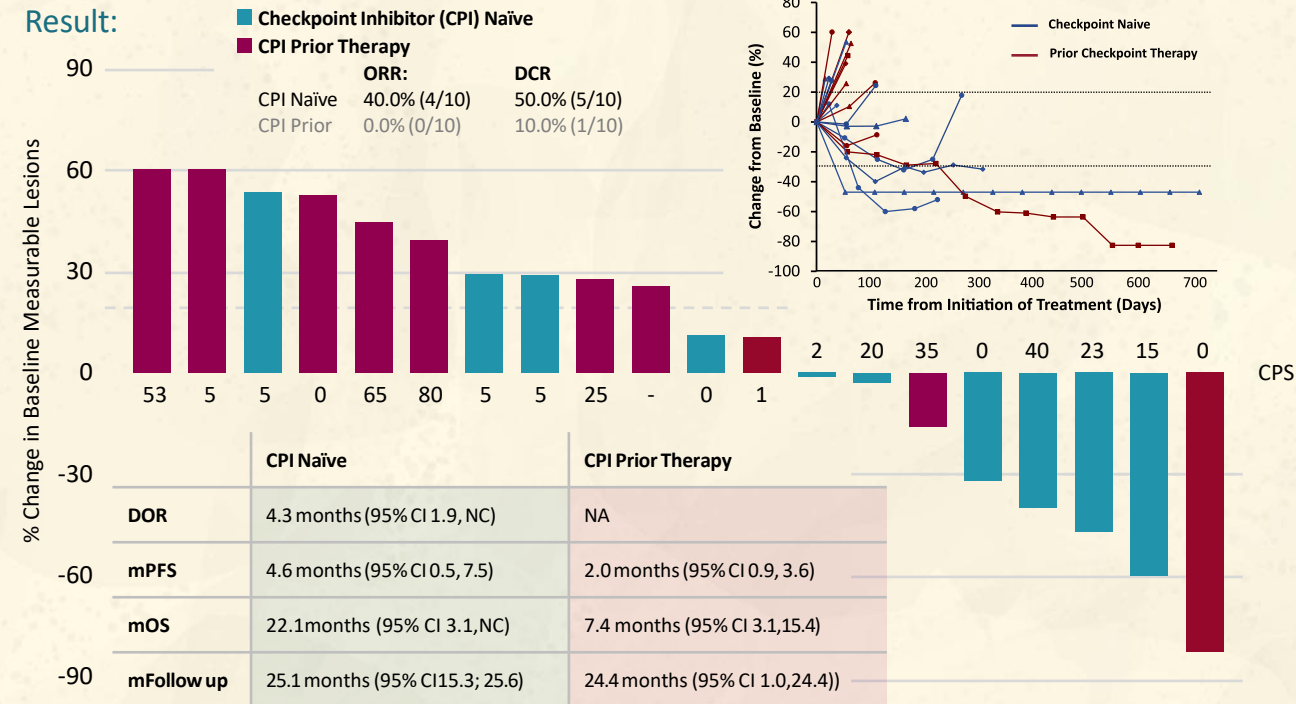
**Keytruda**  
200 mg every three weeks (Q3W)



Endpoints:

- maximum tolerated dose
- anti-cancer activity

## Result:




**Notes:** Data Cutoff October 1, 2020. Patients who received at least one dose of evorpaccept in the expansion phase, had a baseline assessment, and at least one post-baseline disease assessment.

**ORR** = Overall Response Rate. **DCR** = Disease Control Rate. **CPS** = Combined Positive Score.

**FDA granted evorpaccept Fast Track designation for first-line treatment of patients with HNSCC**

# PHASE 1B HNSCC: EVORPACEPT + KEYTRUDA + 5FU/PLATINUM FIRST LINE CHECKPOINT NAIVE

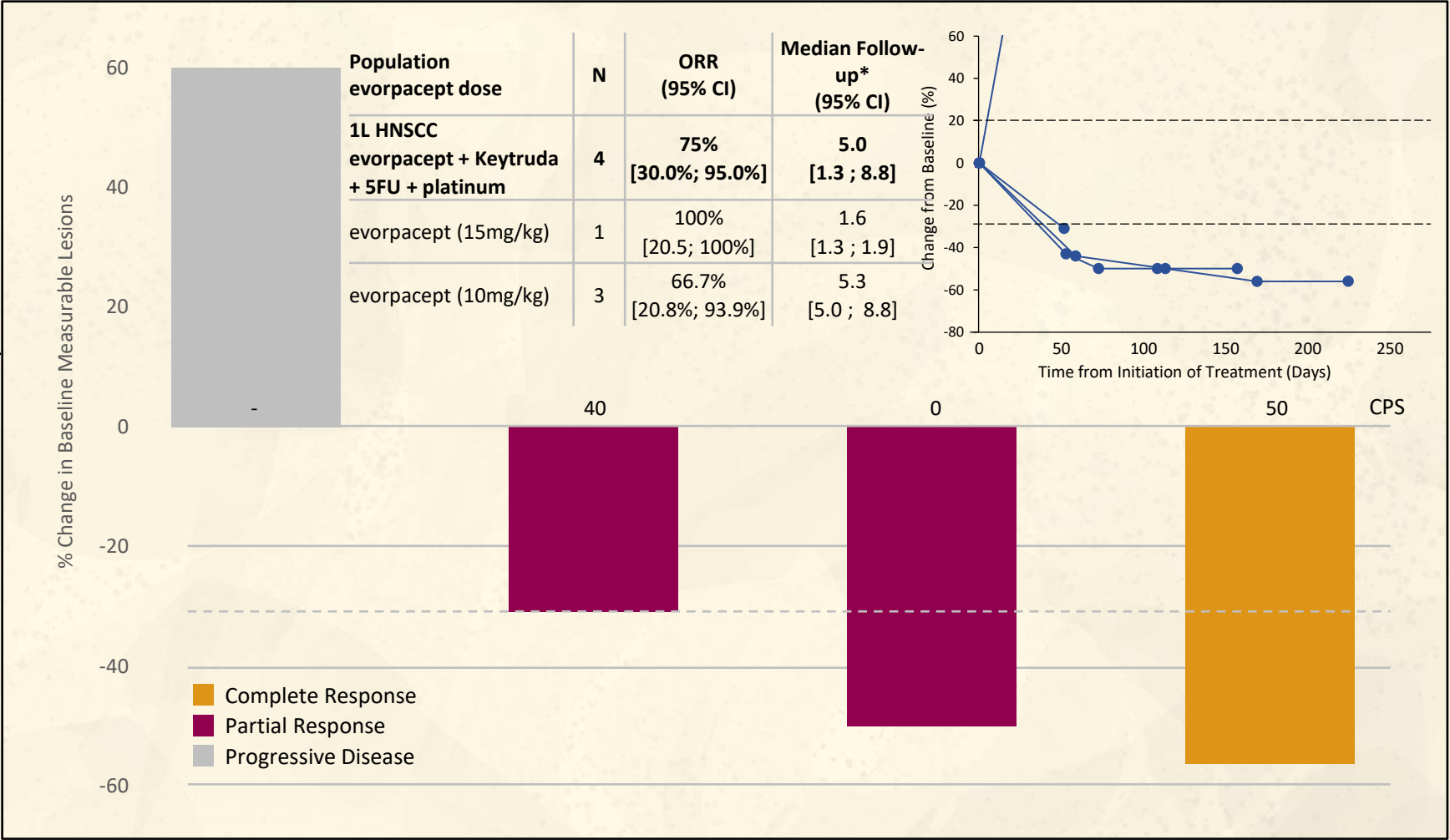
Phase 1b ≥1L HNSCC dose confirmation:



Treatment:

**evorpacept 10 & 15 mg/kg (QW)**  
**+ Keytruda**  
**+ 5FU**  
**+ Cisplatin or carboplatin**

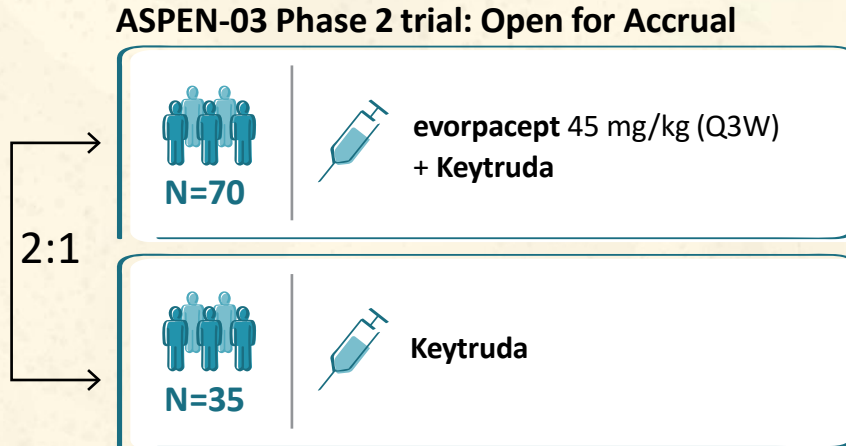
No prior treatment  
for advanced disease





# FIRST LINE HEAD & NECK CANCER: PHASE 2 DEVELOPMENT PLAN, ASPEN-03 AND ASPEN-04

evorpaccept  
+  
Keytruda



- First patient enrolled May 2021

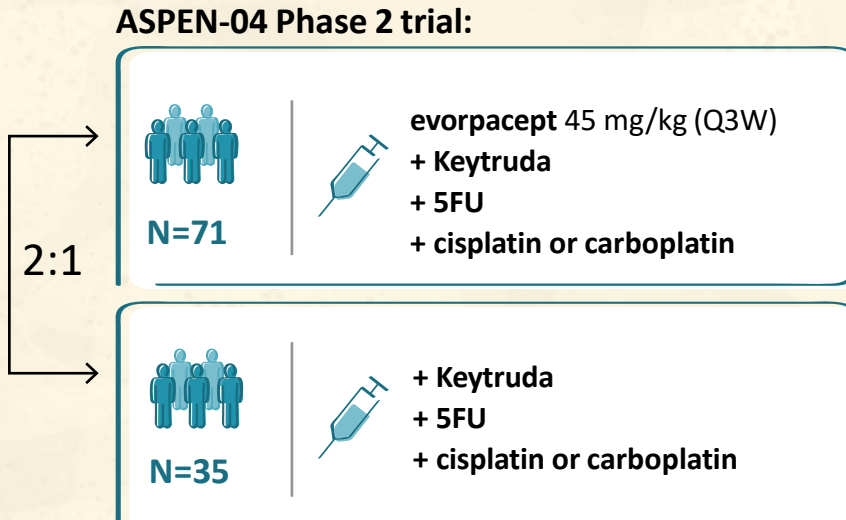


Endpoint:

- ORR (from benchmark of 17% to goal of 33%)

(Safety lead-in prior to randomization)

evorpaccept  
+  
Keytruda  
+  
chemo



- First patient enrolled July 2021



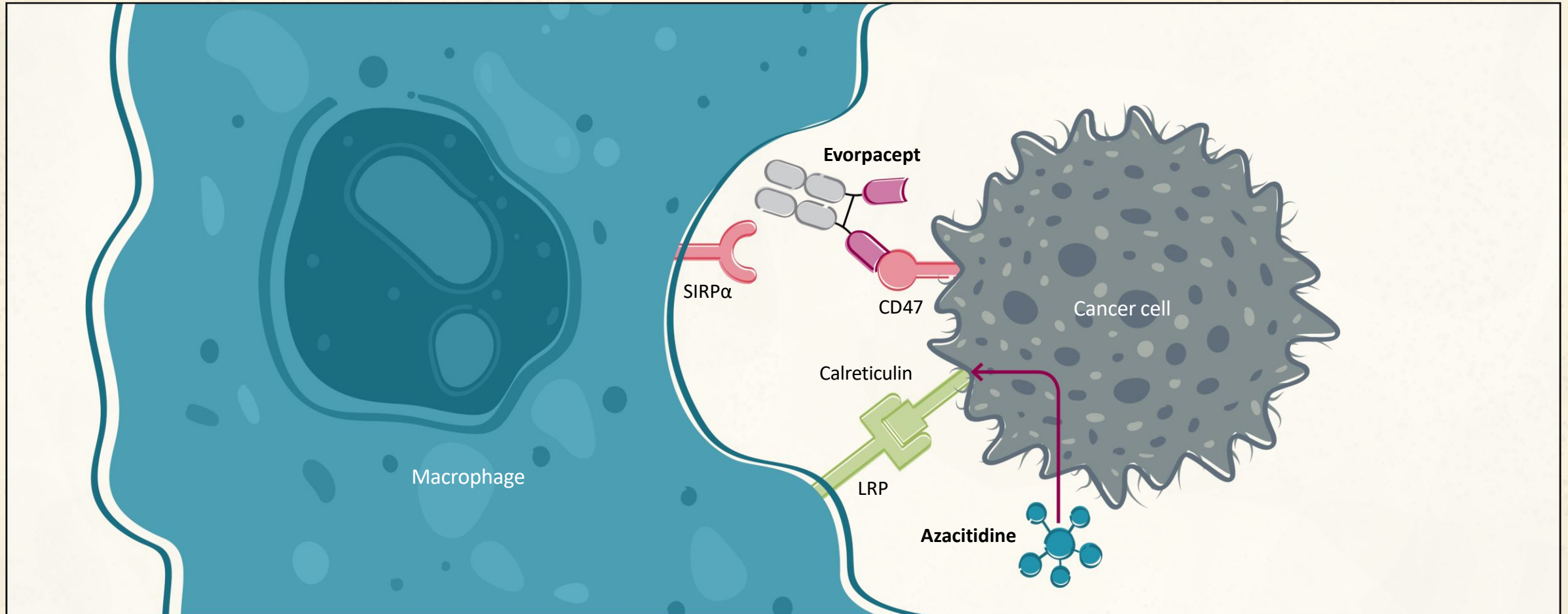
Endpoint:

- ORR (from benchmark of 36% to goal of 54%)

(Safety lead-in prior to randomization)

# MDS TRIAL: EVORPACEPT + AZACITIDINE MECHANISM OF ACTION

evorpacept  
in  
MDS



**Evorpacept increases pro-phagocytic signal provided by azacitidine**

# CD47 BLOCKADE IS CLINICALLY VALIDATED WITH SIGNIFICANT OPPORTUNITY TO IMPROVE ON MAGROLIMAB

Best Overall Response	1L MDS N=33
ORR	30 (91%)
CR	➡ 14 (42%)
CRi	NA
PR	1 (3%)
MLFS/marrow CR	8 (24%) 4 with marrow CR + HI
Hematologic improvement (HI)	7 (21%)
SD	3 (9%)
PD	0

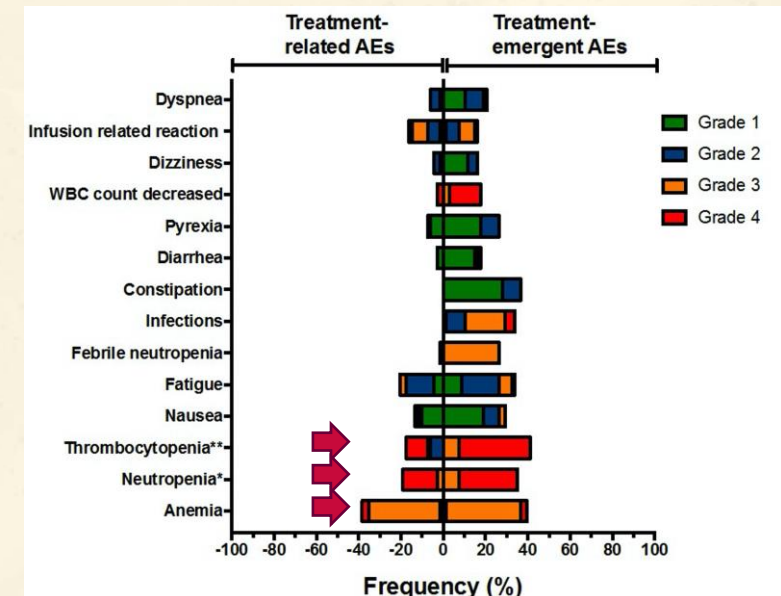
## Magrolimab with azacitidine

Sallman, ASCO 2020

Best Overall Response	R/R AML/MDS 5F9 mono N=10
ORR	1 (10%)
CR	➡ 0
CRi	0
PR	0
MLFS/ marrow CR	1 (10%)
HI	-
SD	7(70%)
PD	2 (20%)

## Magrolimab monotherapy

Sallman, ASCO 2019



All grade TRAEs: 38% Anemia  
19% Neutropenia  
18% Thrombocytopenia

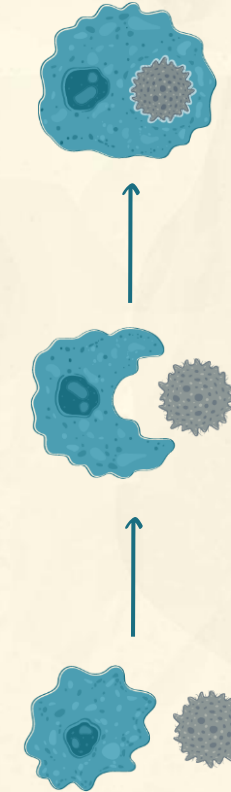
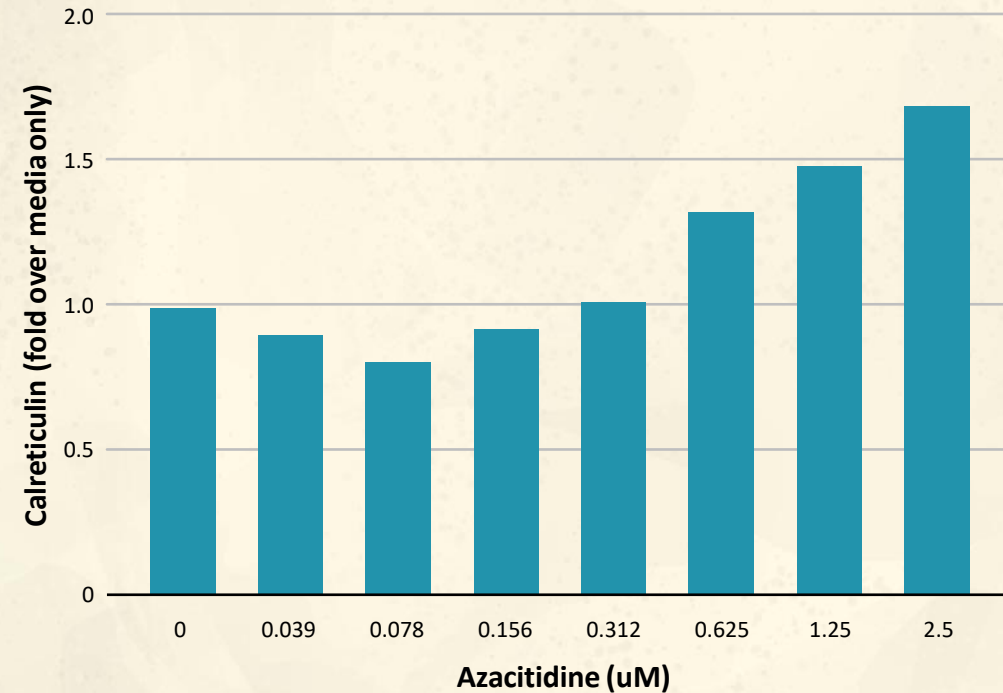
Sallman, ASCO 2020

CD47 blocker 5F9 (magrolimab) shows complete responses only when paired with azacitidine, and causes frequent incidence of treatment-related, high-grade cytopenia

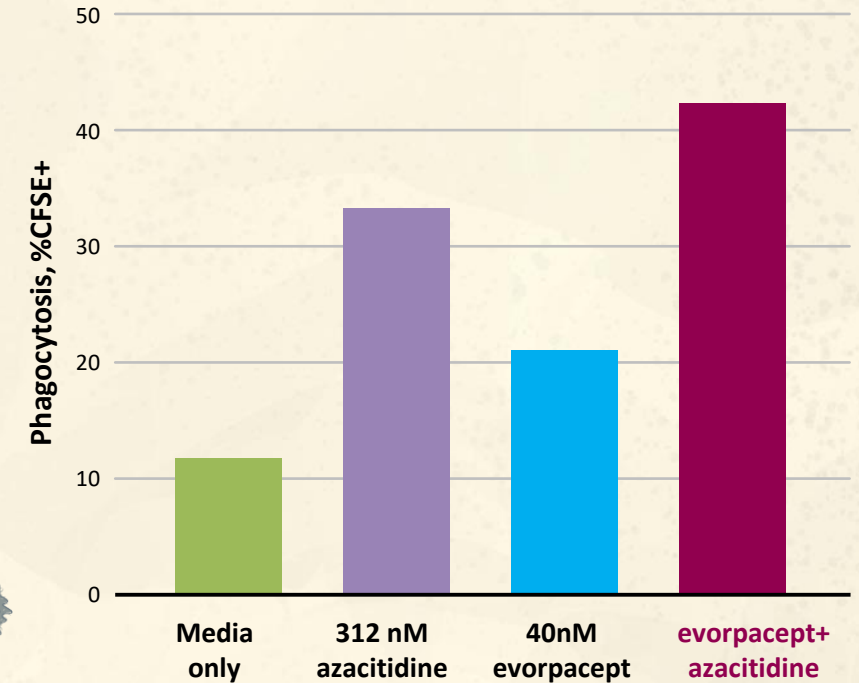


# PRECLINICAL: EVORPACEPT INCREASES PHAGOCYTOSIS OF BACKBONE MDS DRUG, AZACITIDINE

Calreticulin levels on HL60 Cells



Phagocytosis of HL60 Cells



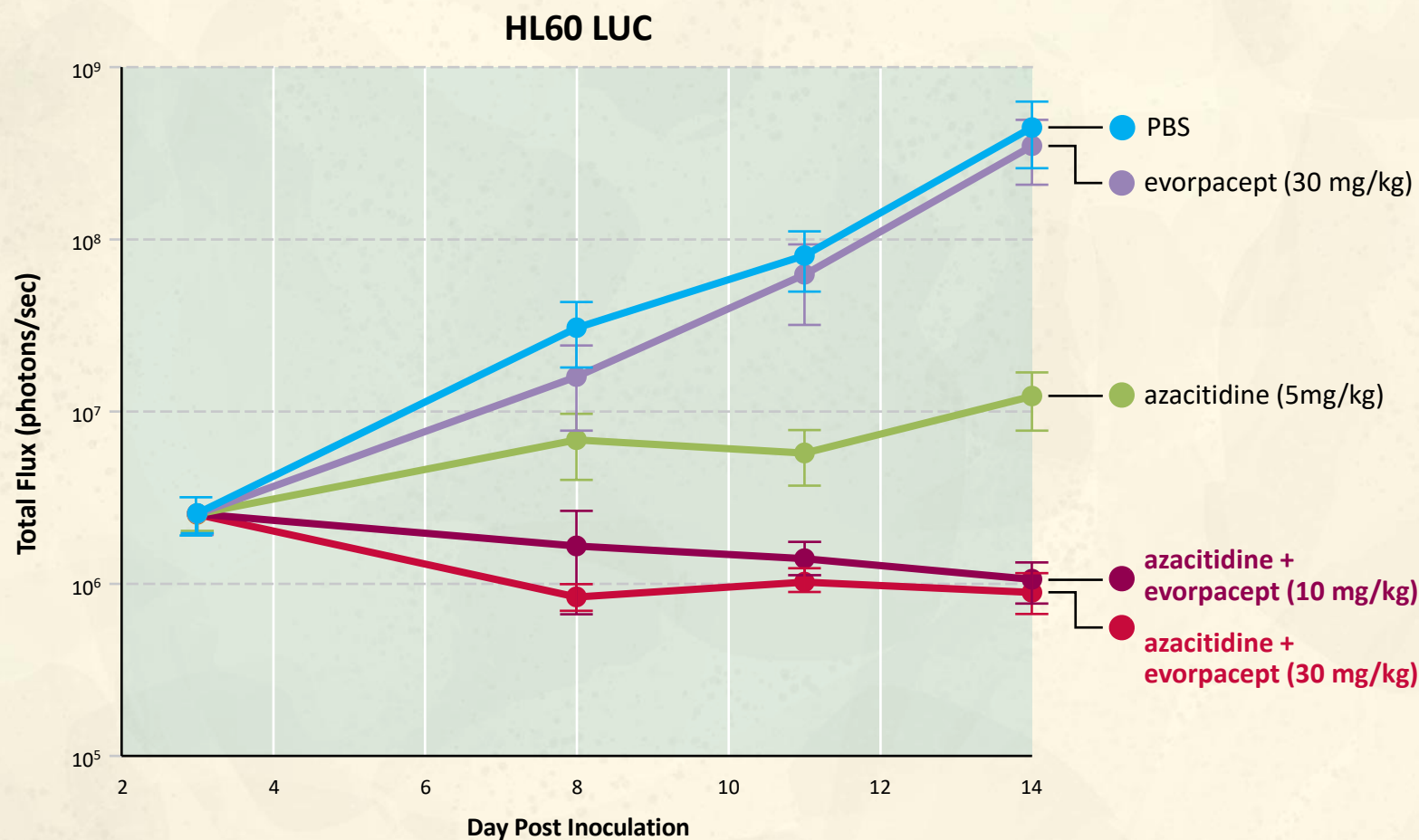
Azacitidine induces calreticulin display.

Evorpacept increases phagocytosis in combination with azacitidine.



# EVORPACEPT INCREASES TUMOR INHIBITION OF AZACITIDINE

evorpacept  
in  
MDS

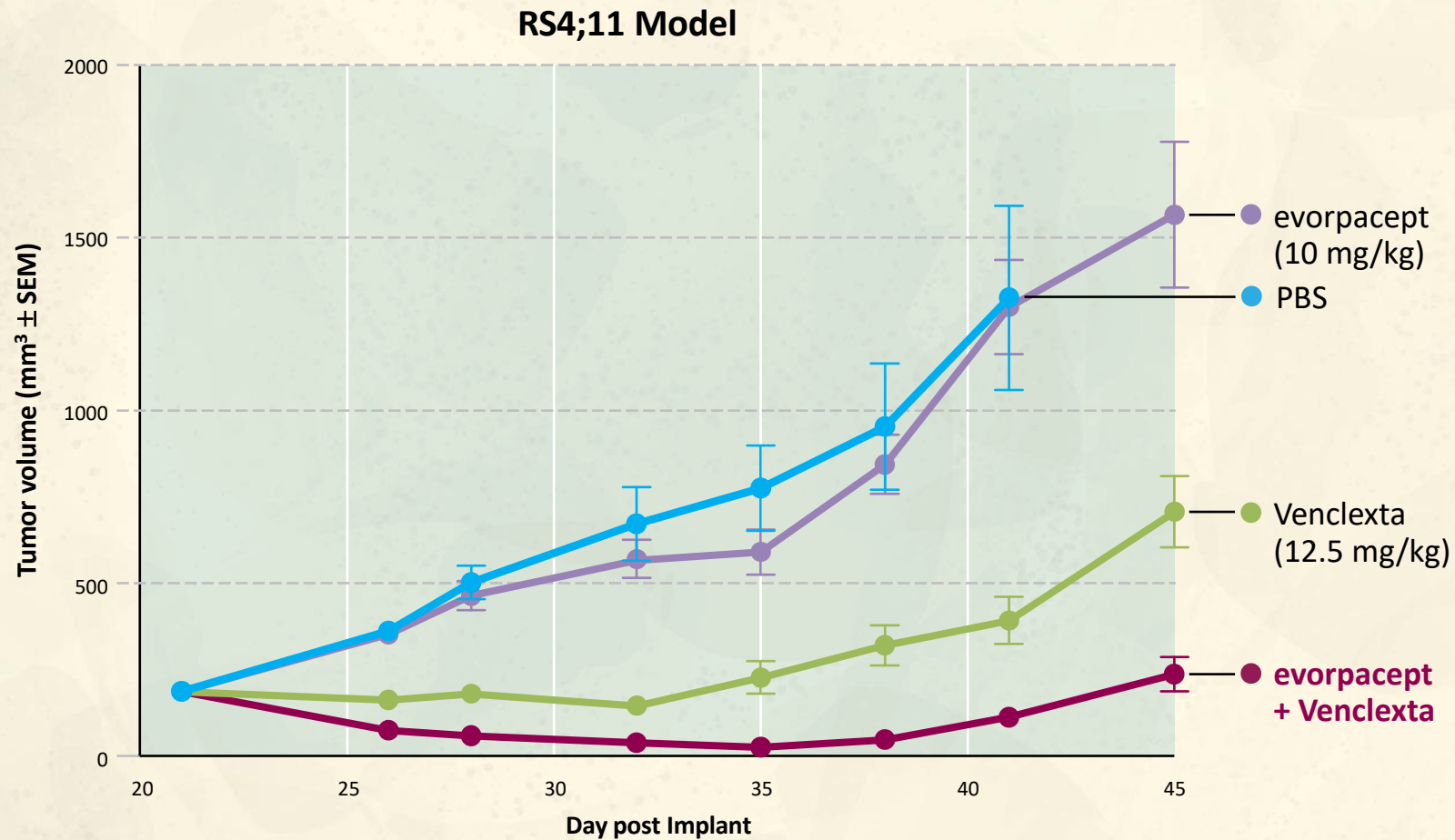


Disseminated AML mouse model

Combination  
opportunity in MDS  
and AML

# EVORPACEPT INCREASES TUMOR INHIBITION OF VENCLEXTA

evorpacept  
in  
AML



Combination  
opportunity  
in AML

# MDS TRIAL PLANS, ASPEN-02

## Phase 1 trial: Open for Accrual



Patients:

**N=~24**

R/R and treatment naïve  
IPSS-R intermediate,  
high, very high risk MDS



Treatment:

**evorpaccept**

20 mg/kg (Q2W)  
30 mg/kg (Q2W)  
or 60 mg/kg (Q4W)

+

**azacitidine**

75 mg/m<sup>2</sup> daily for 7 days  
of 28 day cycle



Endpoint:

- safety of combination

## Phase 2 Randomized Trial



Patients:

treatment naïve  
IPSS-R intermediate, high, very  
high risk MDS



Treatment:

**evorpaccept**

recommended phase 2 dose  
+  
**azacitidine**

vs.

**azacitidine**

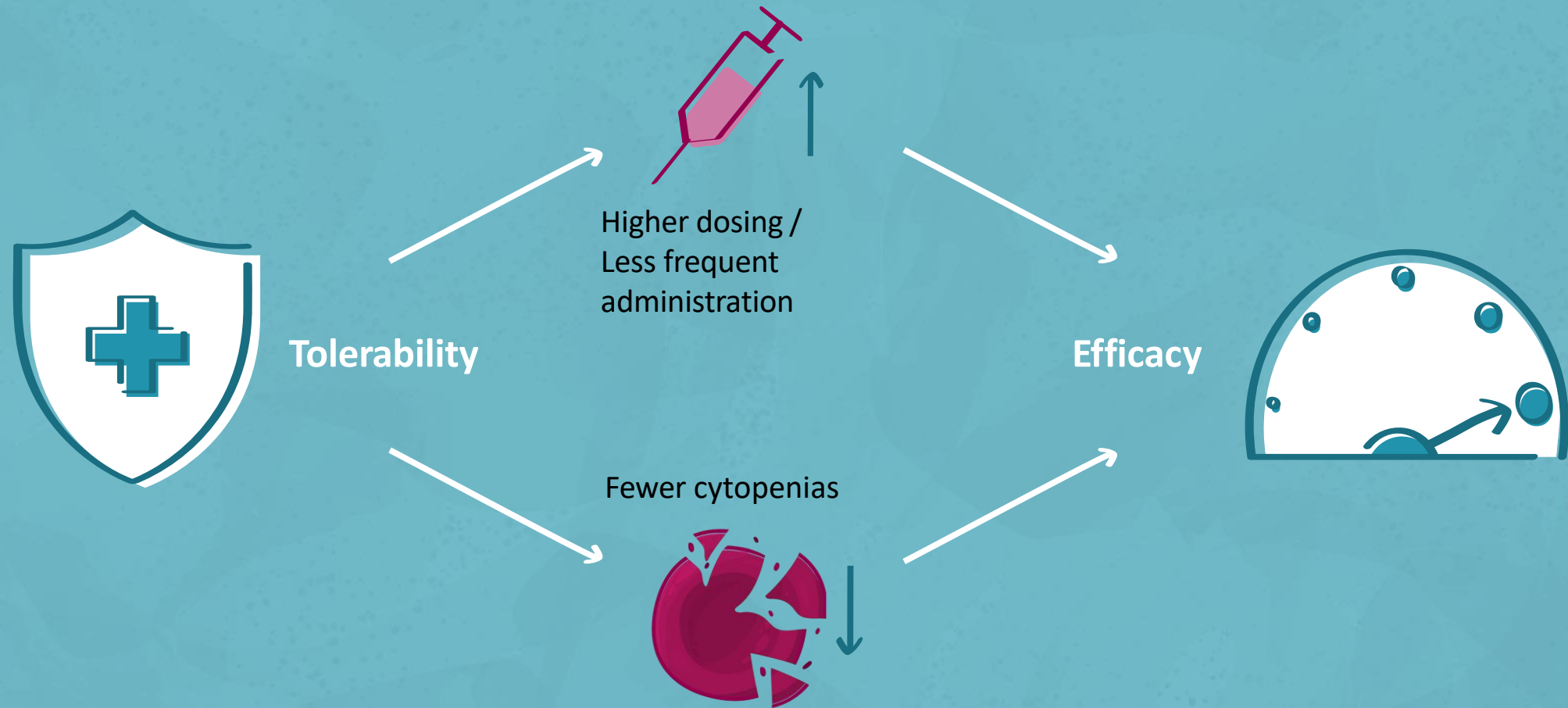


Endpoint:

- complete response rate (CRR)  
(from benchmark of 17% to goal of 35%)

# EVORPACEPT DIFFERENTIATION POTENTIAL ENABLED BY TOLERABILITY

evorpacept  
in  
MDS





# EVORPACEPT SUMMARY



**Evorpacept tolerability profile  
enables combination with range  
of agents**



**Evorpacept higher dosing and  
smaller molecular weight  
facilitate tumor penetration for  
greater efficacy**

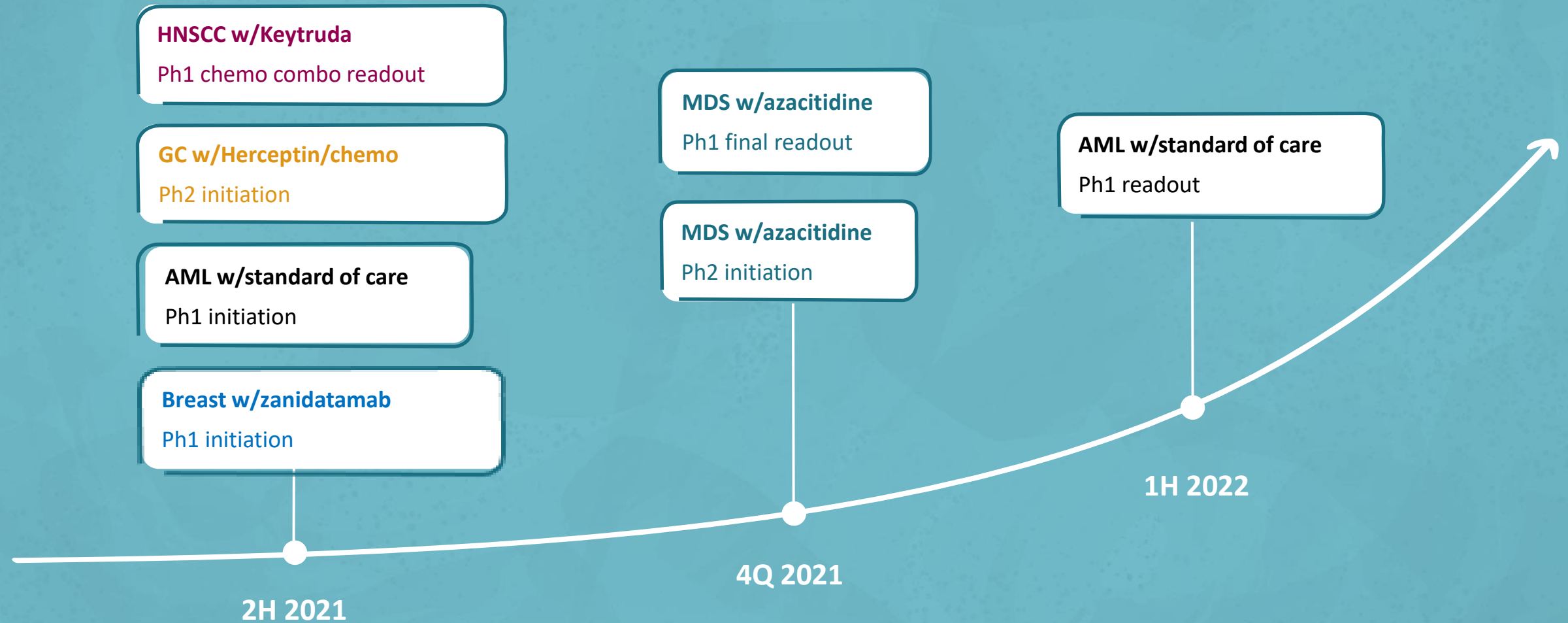


**Clinical proof-of-principle in  
hematologic  
and solid tumors**



**Evorpacept is the  
only CD47 blocker to show  
encouraging response data in solid  
tumor indications**

# EVORPACEPT DEVELOPMENT PROGRESS AND FUTURE PLANS



## EARLY STAGE PIPELINE: SIRP $\alpha$ -TRAAC COLLABORATION

# ALX ONCOLOGY AND TALLAC THERAPEUTICS 50/50 JOINT COLLABORATION ON NOVEL SIRP $\alpha$ ANTIBODY – TLR9 AGONIST CONJUGATE (SIRP $\alpha$ TRAAC)



Provides  
SIRP $\alpha$  antibody

- CD47-SIRP $\alpha$  is a dominant myeloid checkpoint mechanism where SIRP $\alpha$  is expressed on myeloid and dendritic cells as well as on a range of tumor cells.
- SIRP $\alpha$  expression on tumor cells enables tumor microenvironment localization of SIRP $\alpha$  TRAAC.



Provides  
TRAAC platform  
and TLR9 agonist

- Toll-like receptor 9 (TLR9) is a key receptor in the innate immune response.
- Synthetic CpG oligonucleotides (CpG ODNs) are potent TLR9 agonists that stimulate antitumoral cytokine production and immune activation.
- Novel Toll-like receptor agonist antibody conjugation platform (TRAAC) enables systemic delivery of targeted TLR9 activation.

**SIRP $\alpha$  TRAAC induces targeted immune activation, bridging innate and adaptive immune responses.**

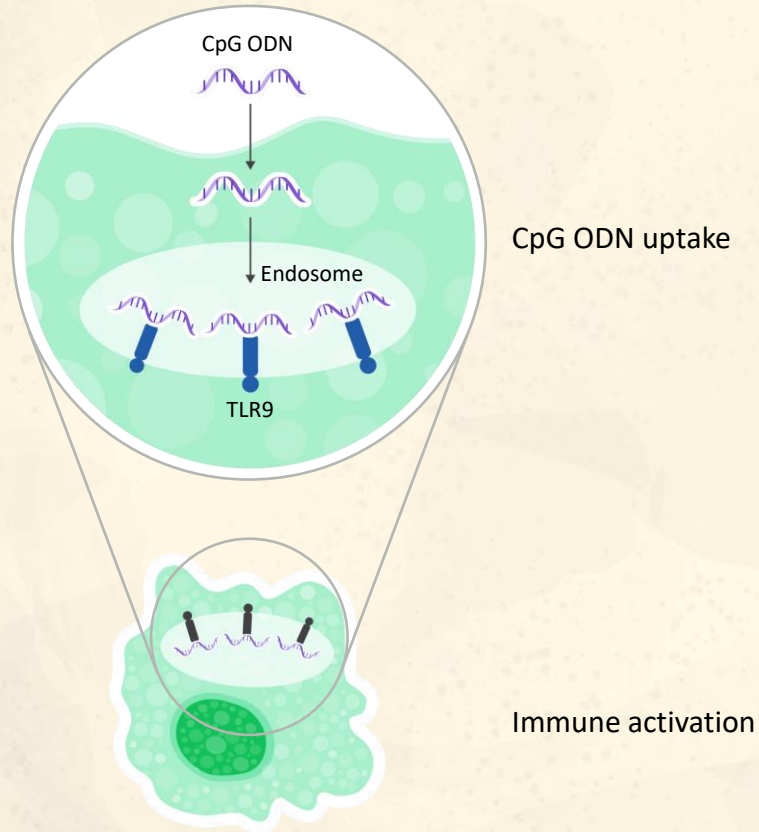
**SIRP $\alpha$  TRAAC simultaneously overrides “don’t eat me” signals by blocking CD47-SIRP $\alpha$  myeloid checkpoint pathway and induces TLR9-based immune activation in antigen presenting cells (APCs).**



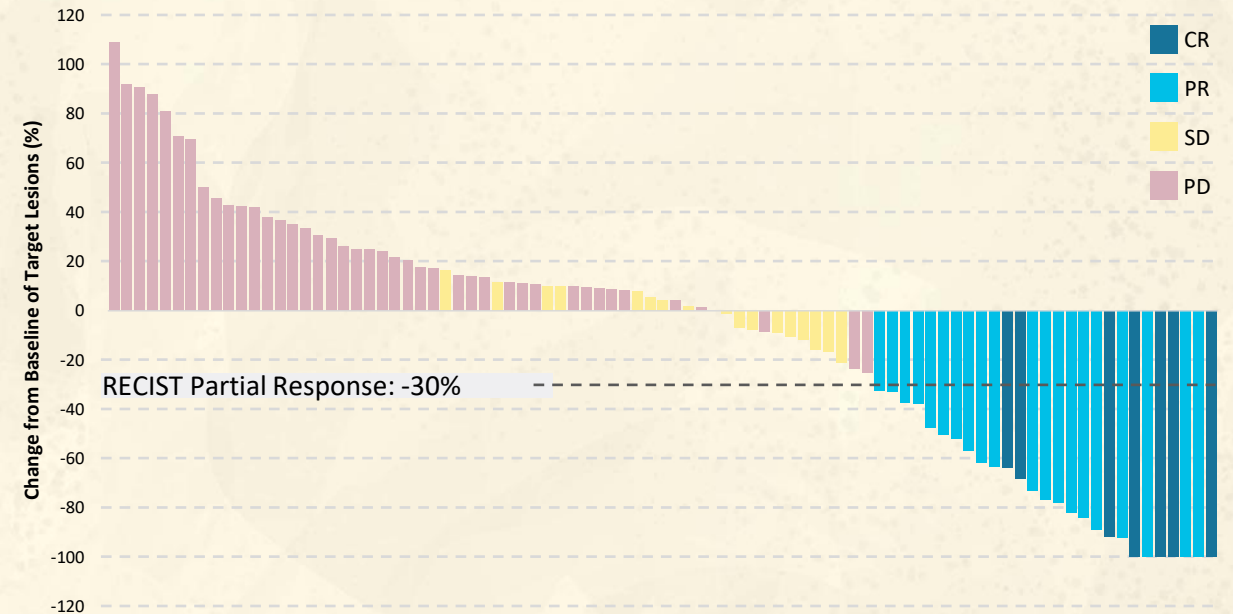
# TOLL-LIKE RECEPTOR 9 (TLR9): A KEY INNATE PATHWAY

## PROOF-OF-CONCEPT DATA IN MELANOMA PATIENTS WITH INTRATUMORAL TLR9 AGONISTS

TLR9 stimulation by CpG ODN leads to immune cell activation



Intratumoral programs have demonstrated clinical activity



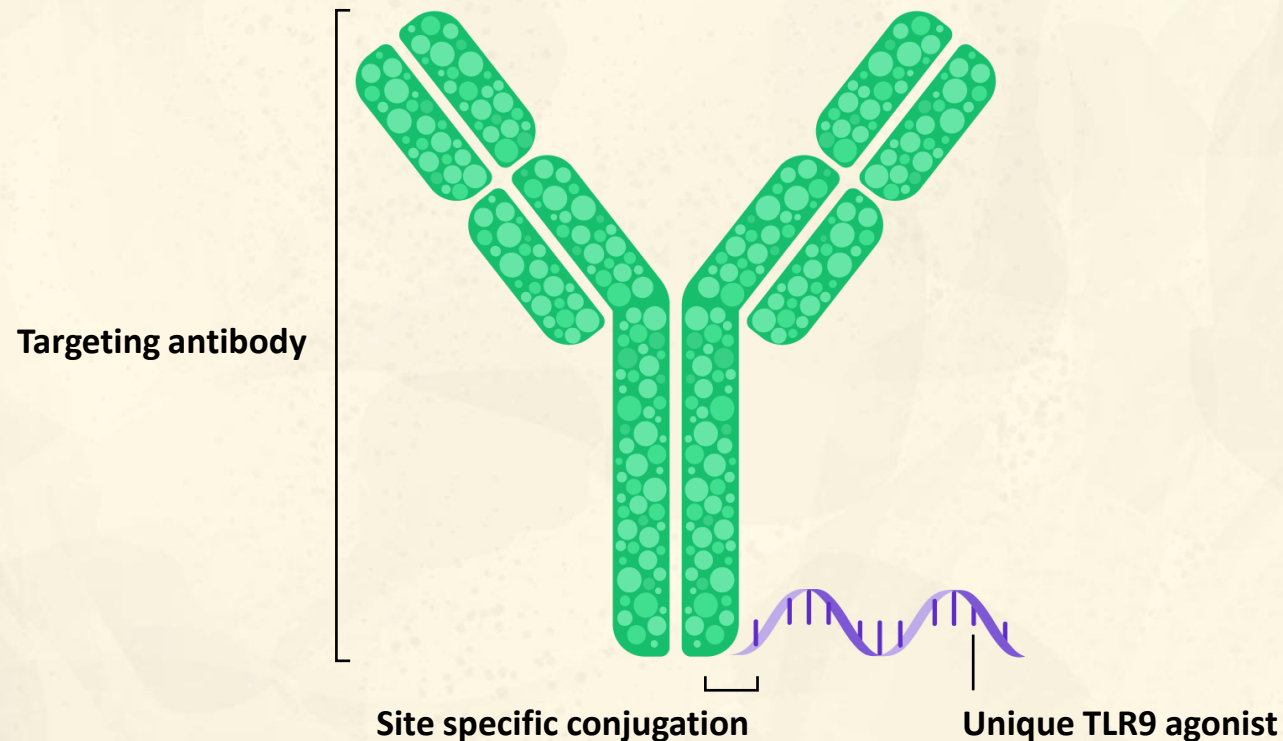
CMP-001 (Checkmate) + Pembrolizumab in Anti-PD-1 Refractory Melanoma, <sup>1-4</sup>Checkmate, S1 2020.

Additional clinical data from SD-101 (Dynavax), IMO-2125 (Idera) and AST-008 (Exicure) further validate TLR9 agonism in cancer.

# TALLAC TRAAC PLATFORM: SYSTEMIC, TARGETED IMMUNE ACTIVATION

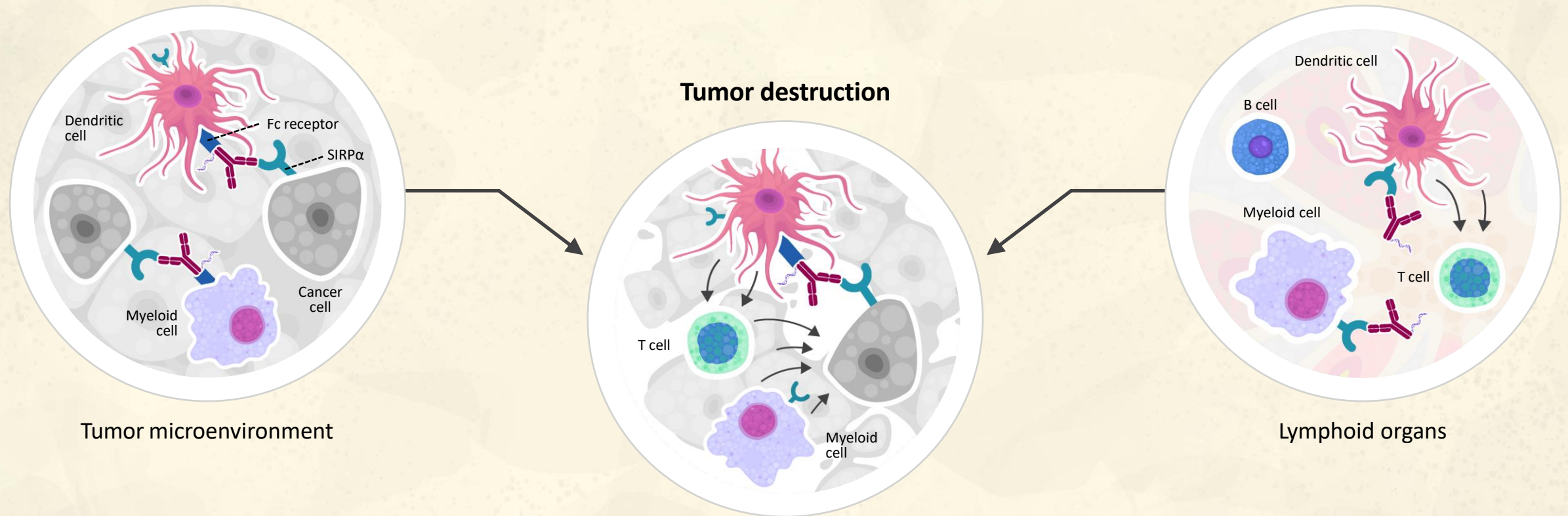
## ANTIBODY DIRECTS TLR9 AGONIST (T-CPG) TO SPECIFIC IMMUNE CELLS

**TLR9 Agonist Antibody Conjugate (TRAAC):**  
Systemic dosing with cell specific TLR9 activation



Targeted-CpG (T-CpG) designed specifically for compatibility with antibody conjugation, superior PK, receptor-mediated uptake and TLR9 stimulation

# SIRP $\alpha$ IS EXPRESSED ON MYELOID AND DENDRITIC CELLS AS WELL AS SELECTED TUMOR TYPES



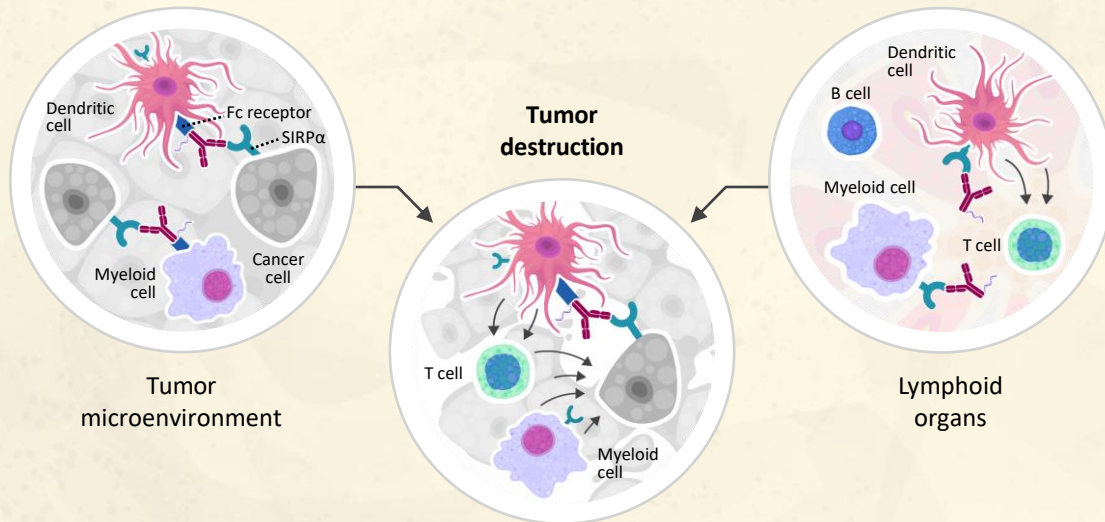
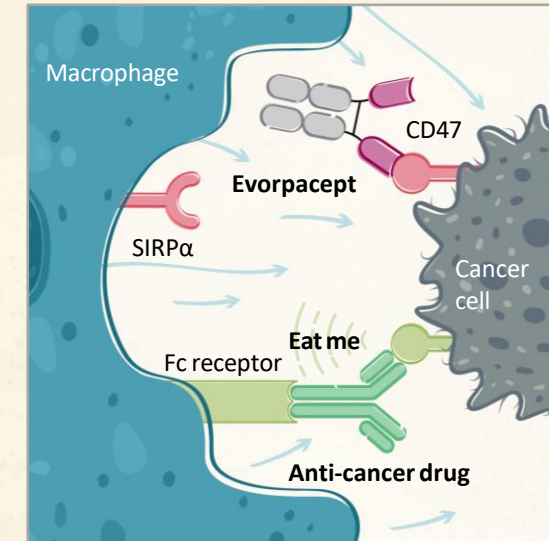
- SIRP $\alpha$  TRAAC binding to myeloid cells targets TLR9 activation in myeloid cells that matter (e.g. dendritic cells).
- SIRP $\alpha$  expression on tumor cells enables tumor microenvironment localization of SIRP $\alpha$  TRAAC.
- SIRP $\alpha$  TRAAC blocks CD47-SIRP $\alpha$  myeloid checkpoint pathway.



# SIRP $\alpha$ TRAAC PROGRAM IS COMPLEMENTARY TO EVORPACEPT

Evorpaccept is an antagonistic molecule designed to maximize the activity of a wide array of anti-cancer agents by blockade of the CD47 myeloid checkpoint.

Removal of the CD47 inhibitory signal requires constant, full blockade of the pathway.

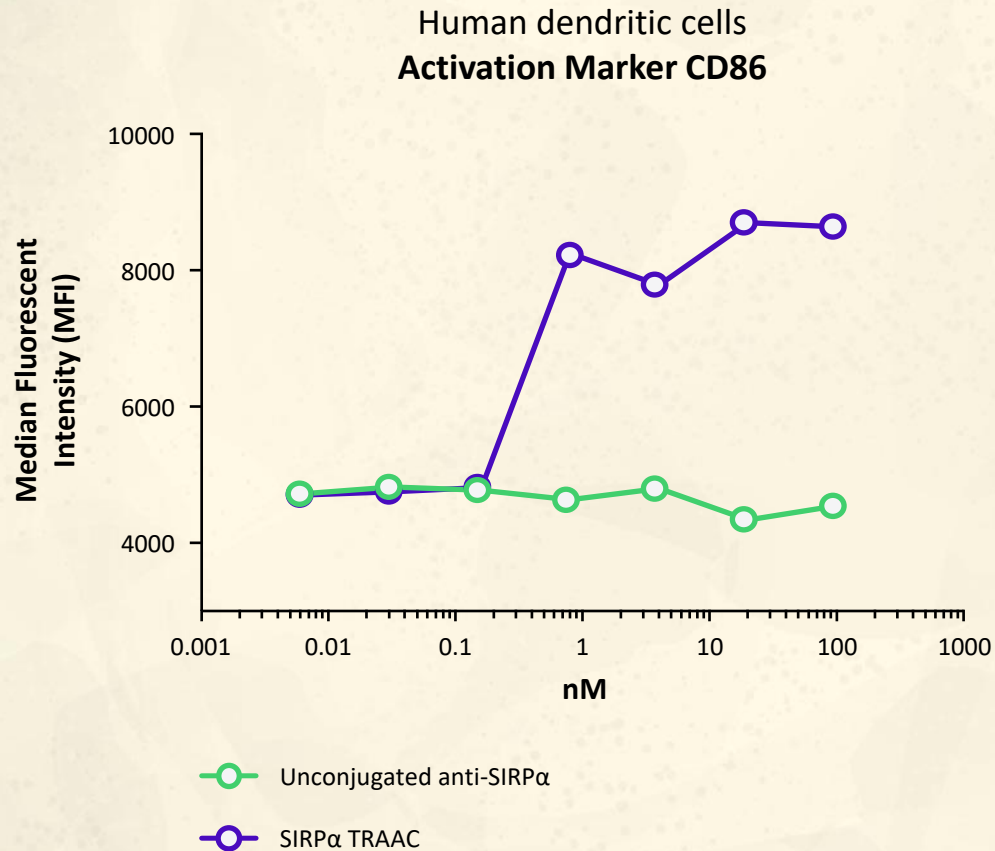


SIRP $\alpha$  TRAAC is an agonistic molecule that directly activates dendritic cells and initiates a coordinated innate and adaptive immune response against cancer.

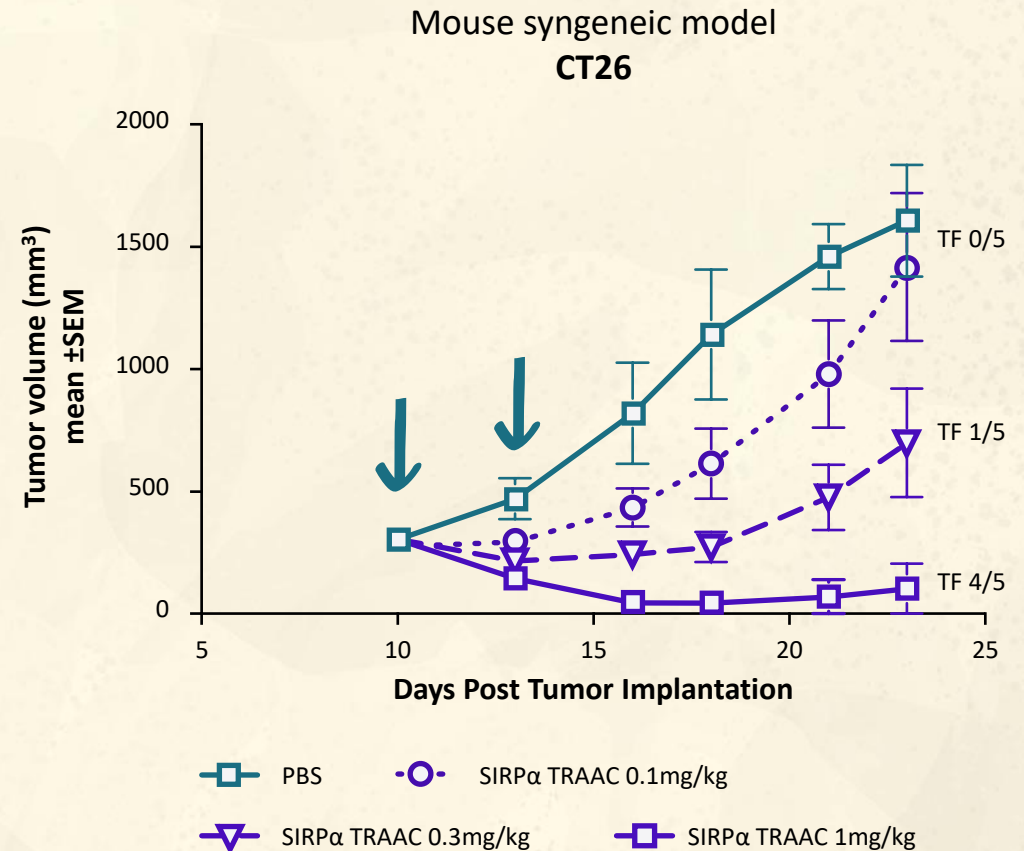
In the case of agonistic molecules (TLR9 agonist), constant blockade is not required.



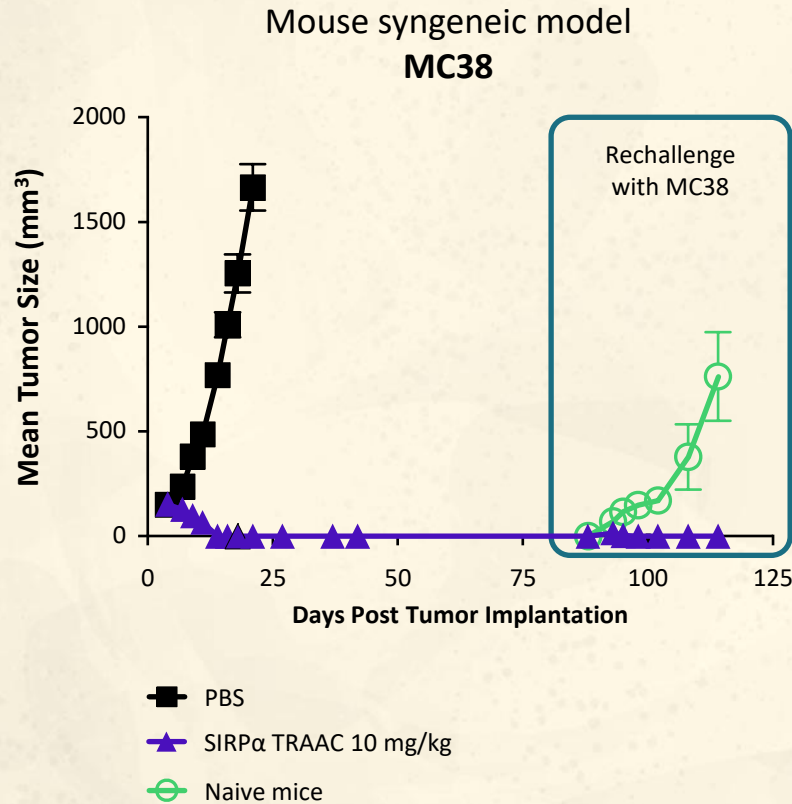
# SIRP $\alpha$ TRAAC INDUCES POTENT AND SELECTIVE IMMUNE ACTIVATION AND LEADS TO POTENT SINGLE AGENT ACTIVITY IN TUMOR MODELS



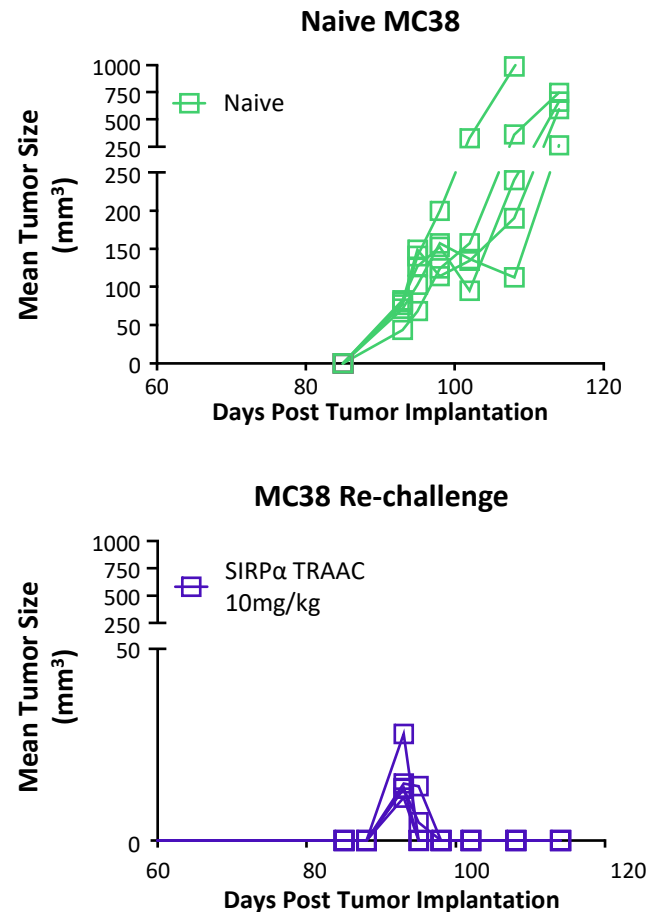
Harrabi et al., SITC, 2020



# SYSTEMIC ADMINISTRATION OF SIRP $\alpha$ TRAAC GENERATES DURABLE ANTI-TUMOR RESPONSE AND IMMUNOLOGICAL MEMORY

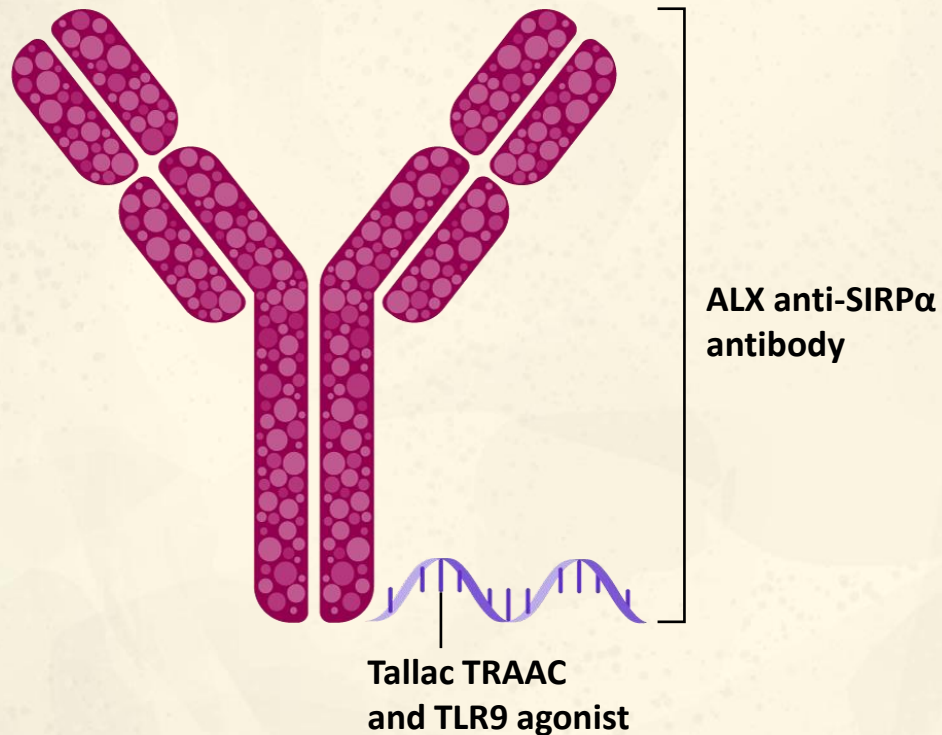


Harrabi et al., SITC, 2020



- Established MC38 tumors were eradicated following 10 mg/kg 2q3d systemic treatment with SIRP $\alpha$  TRAAC.
- These tumor free mice were then re-challenged 60-70 days post tumor clearance.
- SIRP $\alpha$  TRAAC treatment group demonstrated immune protection from the tumor re-challenge.
- Naïve age-matched mice were used as control for tumor growth.

## ALTA-002: TARGETING IMMUNE ACTIVATION TO WHERE IT MATTERS

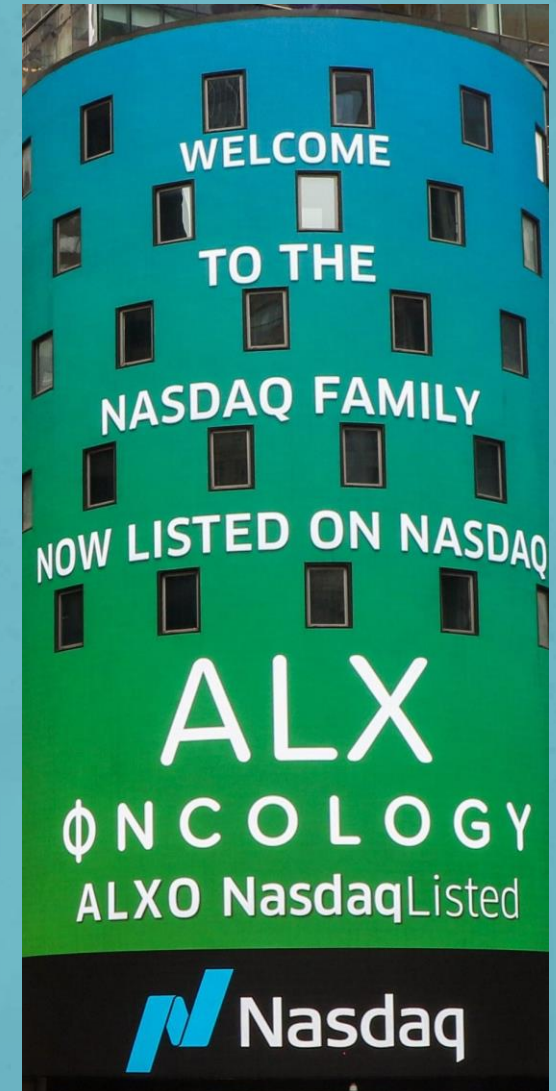


- SIRPα TRAAC binding to myeloid cells targets TLR9 activation in key myeloid cells (e.g. dendritic cells).
- SIRPα expression on tumor cells enables localization of SIRPα TRAAC to tumor microenvironment.
- SIRPα TRAAC blocks CD47-SIRPα myeloid checkpoint pathway.
- Antibody-like PK profile allows for convenient dosing.
- Antibody conjugate produced through established manufacturing processes.

IND expected end of 2022

## FINANCIAL INFORMATION

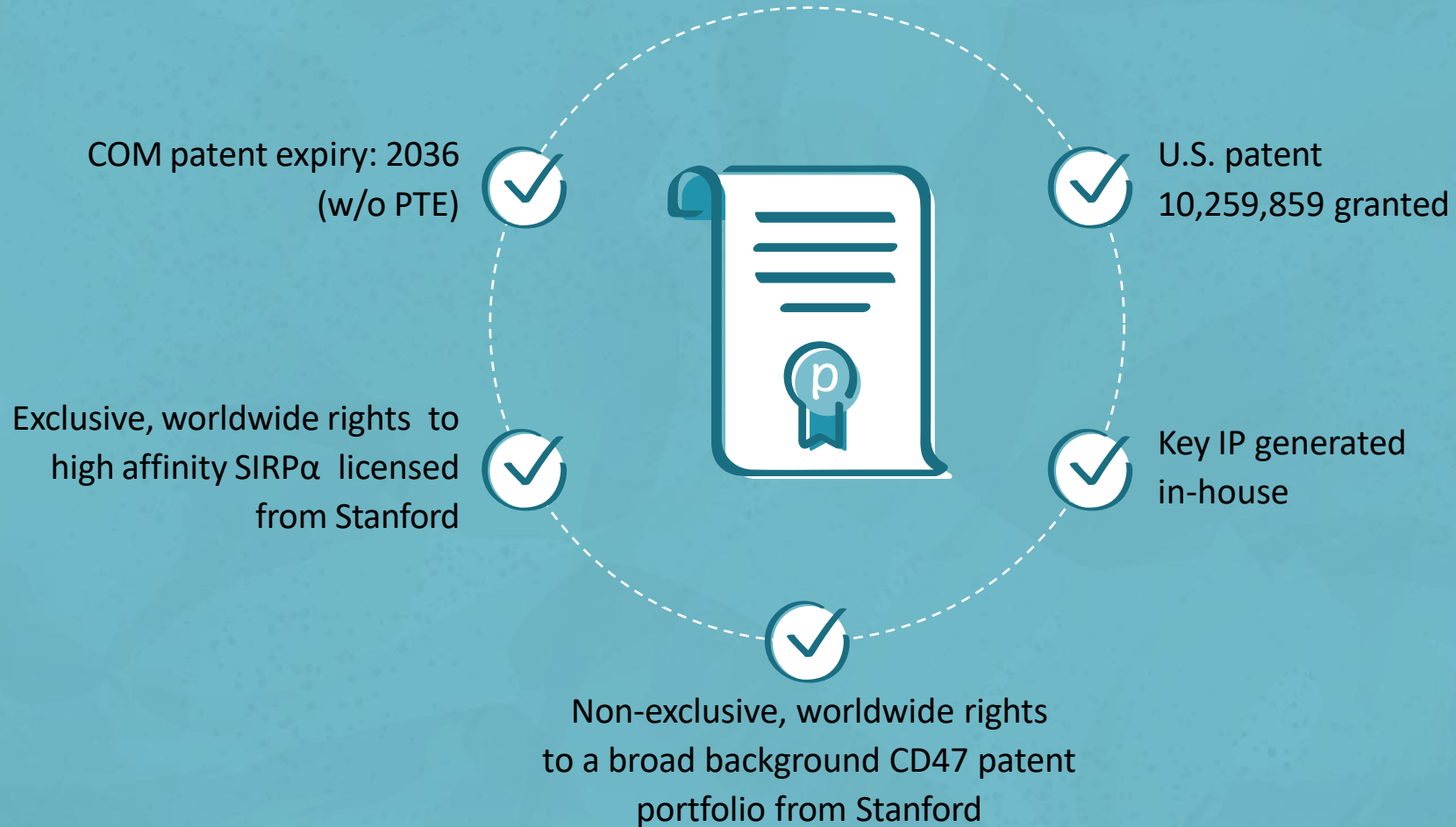
- Consummated IPO on July 21, 2020
- Closed follow-on offering on December 14, 2020
  - Gross proceeds of \$208.0 million
  - 2.737 million shares at \$76 per share
- Cash and cash equivalents as of June 30, 2021:
  - \$410.0 million
- Expected cash runway through 2024





# STRONG INTELLECTUAL PROPERTY

## Robust patent position



# WHY INVEST IN ALX ONCOLOGY: LEADER IN CD47 THERAPY



**CD47 is a novel immune checkpoint pathway with clinical proof-of-concept**



**Clinical proof-of-principle in hematologic and solid tumors**



**Evorpaccept is a CD47 blocker with potential for greater efficacy and tolerability due to unique mechanism of action**

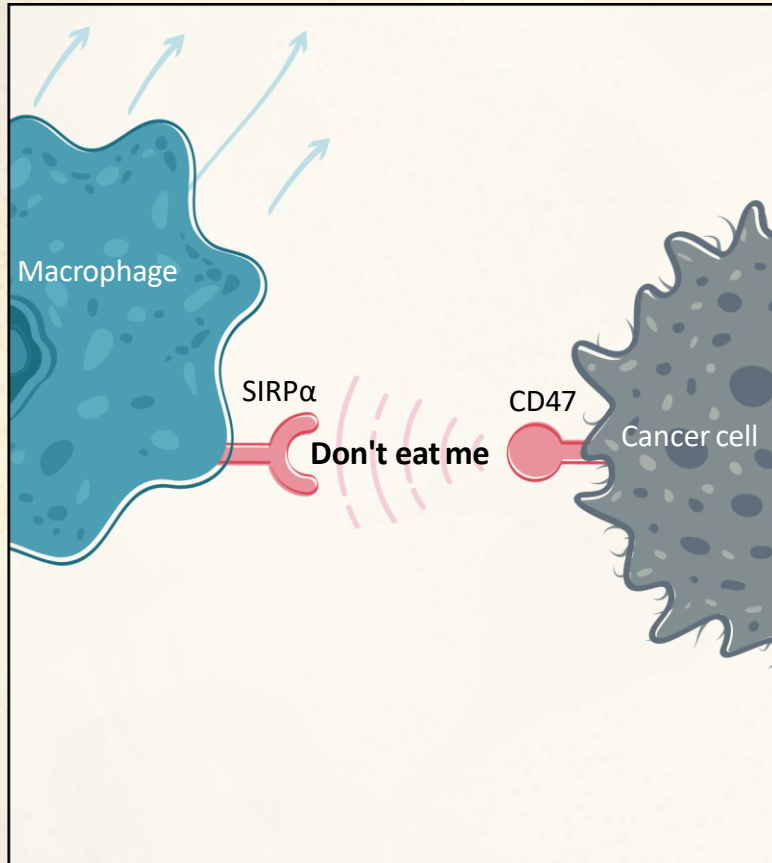


**Growing pipeline in myeloid biology**

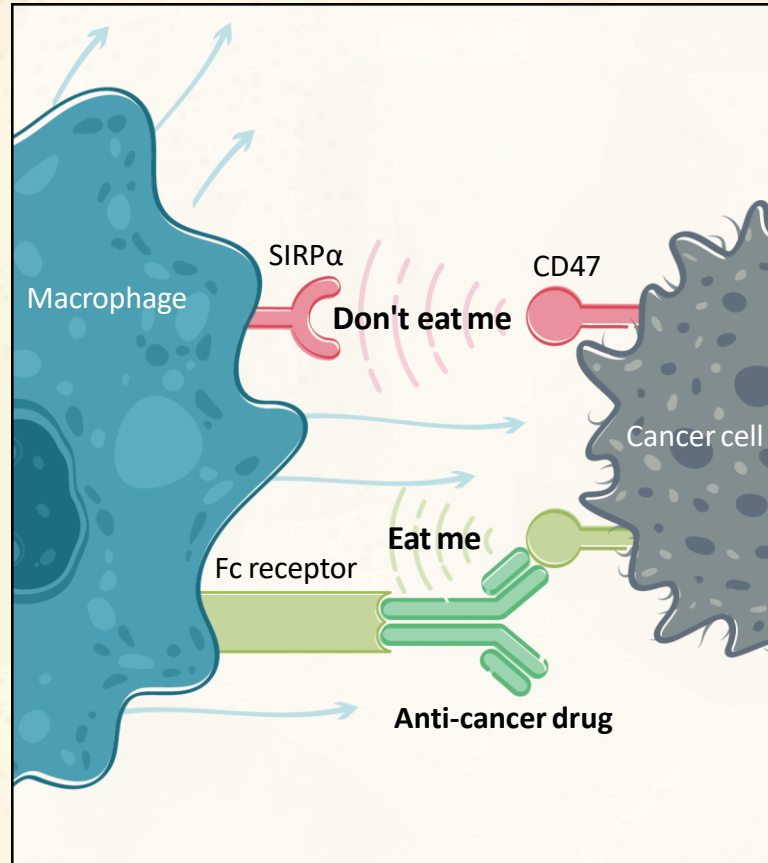
## BACKUP SLIDES

# CD47 MECHANISM OF ACTION AS MYELOID CHECKPOINT

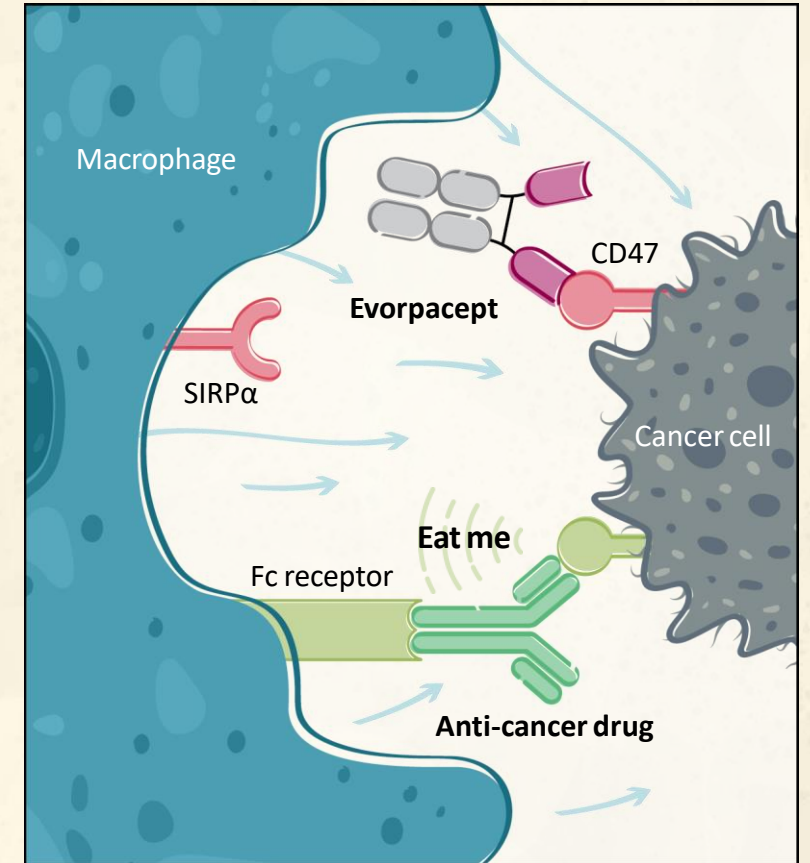
Basal state:



Anti-cancer drug alone:



Evorpaccept combined with anti-cancer drug:



**Evorpaccept: designed to work with partner anti-cancer drugs to maximize phagocytosis of cancer cells**



# NHL TOLERABILITY

Selected hematologic, treatment related adverse events	evorpaccept + Rituxan (N=33) <sup>1</sup>		CC-90002 + Rituxan (n=26) <sup>2</sup>		5F9 (magrolimab) + Rituxan (n=115) <sup>3</sup>	
	Total % (n)	≥Grade 3	Total % (n)	≥Grade 3	Total %	≥Grade 3
Neutropenia	6% (2)	6% (2)	50% (13)	39% (10)	~13%	~7%
Thrombocytopenia/ Decreased Platelets	-	-	35% (9)	23% (6)	~20%	~13%
Anemia	6% (2)	3% (1)	12% (3)	4% (1)	~30%	~15%

<sup>1</sup>ASH 2020 Abstract 3016

<sup>2</sup>ASH 2019 Abstract 4089

<sup>3</sup>EHA 2019 Abstract S867

**Evorpaccept:**  
Tolerability profile  
compares favorably to  
other CD47 blockers

# MAGROLIMAB NHL RESPONSE RATES AND DOSING



DLBCL w/ Rituxan	Ph1	Ph2
N	21	38
Dosing (mg/kg)	up to 30 <b>Weekly</b>	30 and 45 <b>Every Other Week</b>
ORR	48%	29%
CR	33%	5%
PR	14%	24%

Reduced dosing led to  
reduced overall  
response rate in NHL

ORR = overall response rate.  
CR = complete response rate.  
PR = partial response rate.

EHA 2019 Abstract S867

# NHL: PRELIMINARY CLINICAL TOLERABILITY

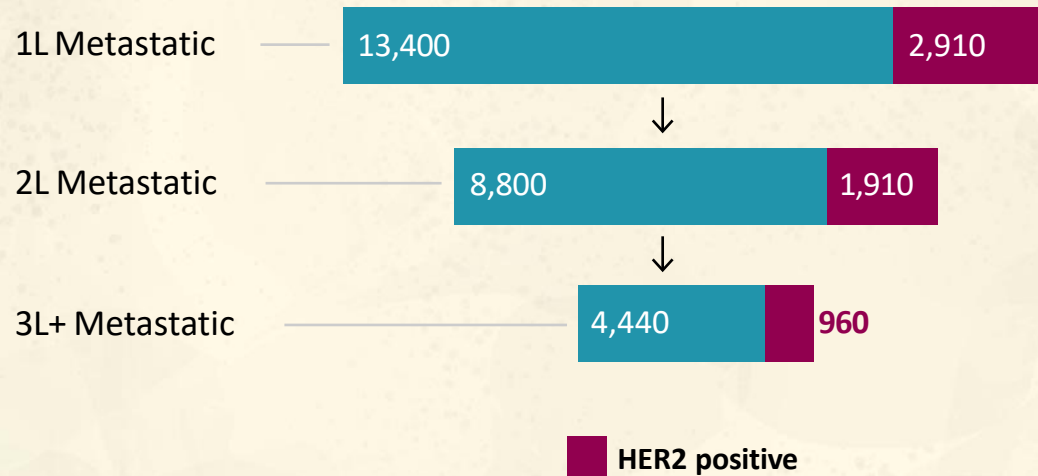
## evorpacept + Rituximab (N=33)

Treatment Related Adverse Event	Total n (%)	≥Grade 3 n (%)
Rash	8 (24.2)	—
Fatigue	4 (12.1)	—
Nausea	2 (6.1)	—
Neutrophil Count Decreased	2 (6.1)	2 (6.1)
Anemia	2 (6.1)	1 (3.0)
Myalgia	2 (6.1)	—
Pruritus	2 (6.1)	—

Data Cutoff: October 1, 2020

# HER2 POSITIVE GC UNMET NEED

2020 US patient population  
by line of systemic therapy<sup>1</sup>



- Herceptin is an anti-HER2 antibody that has multiple FDA approvals in patients with HER2 positive cancers
- Clinical trials show that re-treatment with Herceptin has no activity in 2L HER2 positive gastric cancer<sup>3</sup>

5-year OS in metastatic gastric cancer is only 6%<sup>2</sup>



# PHASE 1B ≥2 LINE GC TRIAL: EVORPACEPT + HERCEPTIN + CYRAMZA + PACLITAXEL TREATMENT RELATED ADVERSE EVENTS

## Treatment Related Adverse Events

evorpacept + trastuzumab + ramucirumab + paclitaxel  
(N=18)

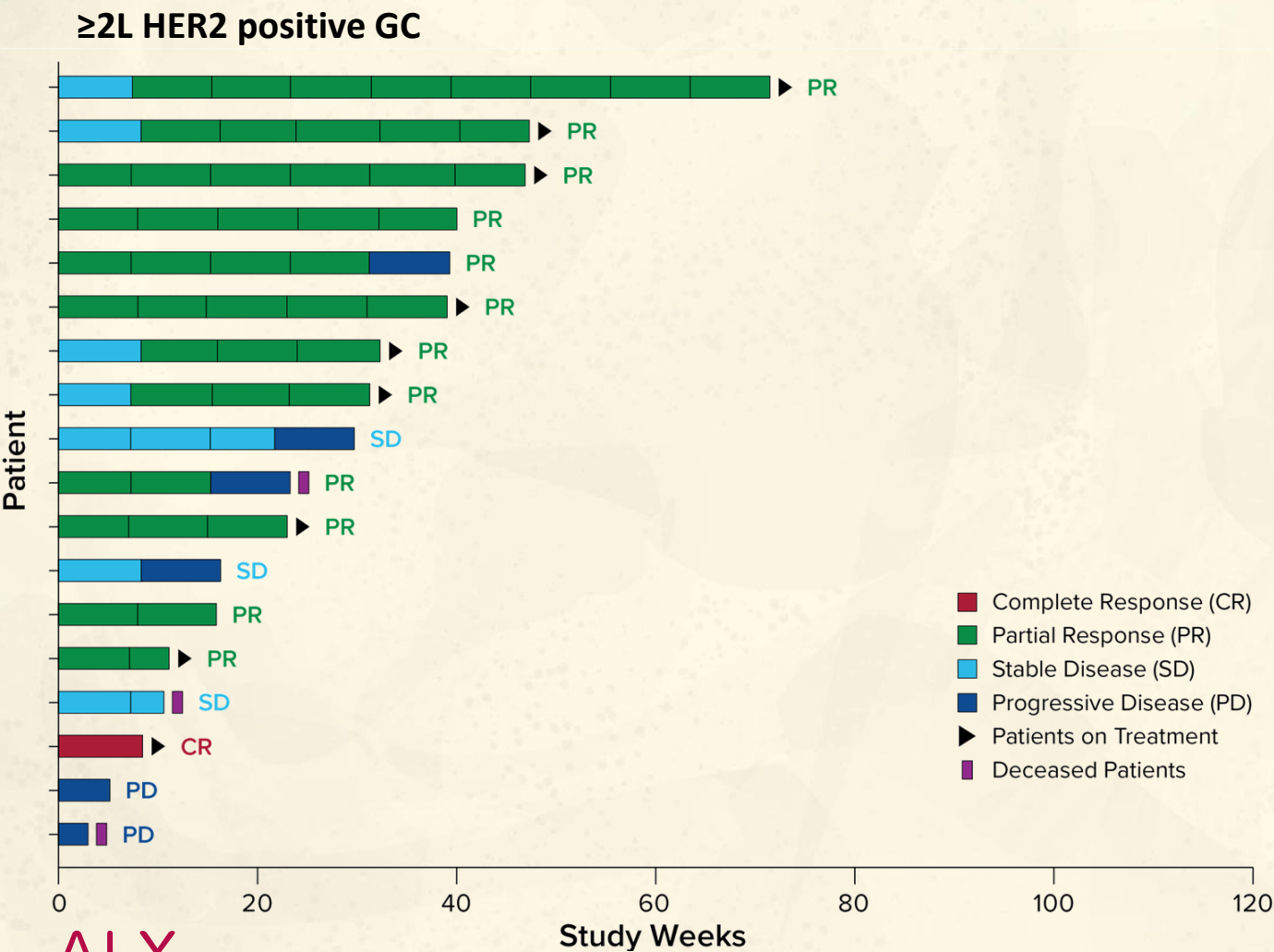
Adverse Event	Total n(%)	
	evorpacept 10 mg/kg QW	evorpacept 15 mg/kg QW
Diarrhea	-	3(16.7)
Rash	-	3(16.7)
Urticaria	-	3(16.7)
Pruritus	-	2(11.1)
Fatigue	1(5.6)	1(5.6)
Lymphocyte count decreased	-	1(5.6)
Abdominal pain	-	1(5.6)
Anemia	-	1(5.6)
Back pain	-	1(5.6)
Dermatitis acneiform	-	1(5.6)
Stomatitis	-	1(5.6)
Vision blurred	-	1(5.6)

## ≥ Grade 3 Adverse Events

evorpacept + trastuzumab + ramucirumab + paclitaxel  
(N=18)

Adverse Event	Total n(%) All Causality				Total n(%) Related				
	Grade	3		4		3		4	
		10 mg/kg	15 mg/kg	10 mg/kg	15 mg/kg	10 mg/kg	15 mg/kg	10 mg/kg	15 mg/kg
evorpacept dose QW									
Neutrophil count decreased	1(5.6)	4(22.2)	1(5.6)	1(5.6)	-	-	-	-	
Hypertension	2(11.1)	4(22.2)	-	-	-	-	-	-	
Anemia	-	3(16.7)	-	-	-	-	-	-	
Fatigue	-	2(11.1)	-	-	-	-	-	-	
Hypophosphatemia	-	1(5.6)	-	-	-	-	-	-	
Lymphocyte count decreased	-	1(5.6)	-	-	-	1(5.6)	-	-	
Platelet count decreased	-	1(5.6)	-	-	-	-	-	-	
Urinary tract infection	-	1(5.6)	-	-	-	-	-	-	
Aspartate aminotransferase increased	-	1(5.6)	-	-	-	-	-	-	
Asthenia	-	1(5.6)	-	-	-	-	-	-	
Diverticulitis	-	1(5.6)	-	-	-	-	-	-	
Dysphagia	-	1(5.6)	-	-	-	-	-	-	
Non-cardiac chest pain	-	1(5.6)	-	-	-	-	-	-	

PHASE 1B ≥2 LINE GC TRIAL:  
EVORPACEPT + HERCEPTIN + CYRAMZA + PACLITAXEL  
BEST OVERALL AND DURATION OF RESPONSE WHILE ON TREATMENT



# CLINICAL ACTIVITY OF EVORPACEPT COMBINATIONS IN RESPONSE EVALUABLE PATIENTS WITH ≥2L HER2 POSITIVE GC CANCER

Population	N (EVAL)	ORR (%) [95% CI]	DOR (m) [95% CI]	PFS (m) [95% CI]	PFS rate at 6 m	OS (m) [95% CI]	OS rate at 12 m	Follow up (m) [95% CI]
≥2L Gastric (evorpaccept -10 mg/kg or 15 mg/kg + tras/ram/pac)	18	72.2 [49.1% ; 87.5%]	NR	9.1 [3.8 ; NR]	74.5%	NR	75.8%	10.5 [4.8 ; 12.5]
Gastric (evorpaccept-10 mg/kg + TRP)	3	66.7 [20.8% ; 93.9%]	NR	NR	100%	NR	66.7%	14.3 [12.0;NR]
Gastric (evorpaccept-15 mg/kg + TRP)	15	73.3 [48.1% ; 89.1%]	NR	NR	68.3%	NR	80.8%	9.4 [4.2 ; 12.5]
≥2L Gastric tras/ram/paclitaxel Rha et al ASCO 2021 <sup>3</sup>	50	52	5.1	7.4	-	13.6	-	22.9
3L Gastric Enhertu DESTINY 01 <sup>1</sup>	126	41	11.3	5.6	43%	12.5	52%	-
≥2L Gastric ramucirumab/paclitaxel RAINBOW-ASIA Region <sup>2</sup>	109	34	-	5.5	-	12.1	-	7.9
≥2L Gastric (evorpaccept-10 mg/kg + tras)	19	21.1 [8.5% ; 43.3%]	8.7 [5.6; NR]	2.2 [1.9 ; 5.5]	16.7%	8.1 [3.4 ; 12.6]	38.2%	27.0 [NR]
≥3L Gastric Irinotecan or Paclitaxel DESTINY 01ControlArm <sup>1</sup>	62	11.3	3.9	3.5	21%	8.4	29%	-

PHASE 1B FIRST LINE HNSCC:

EVORPACEPT + KEYTRUDA + 5FU/PLATINUM

TREATMENT RELATED ADVERSE EVENTS

No TRAEs were reported  
in 1L HNSCC patients (n=5)

≥ Grade 3 Adverse Events

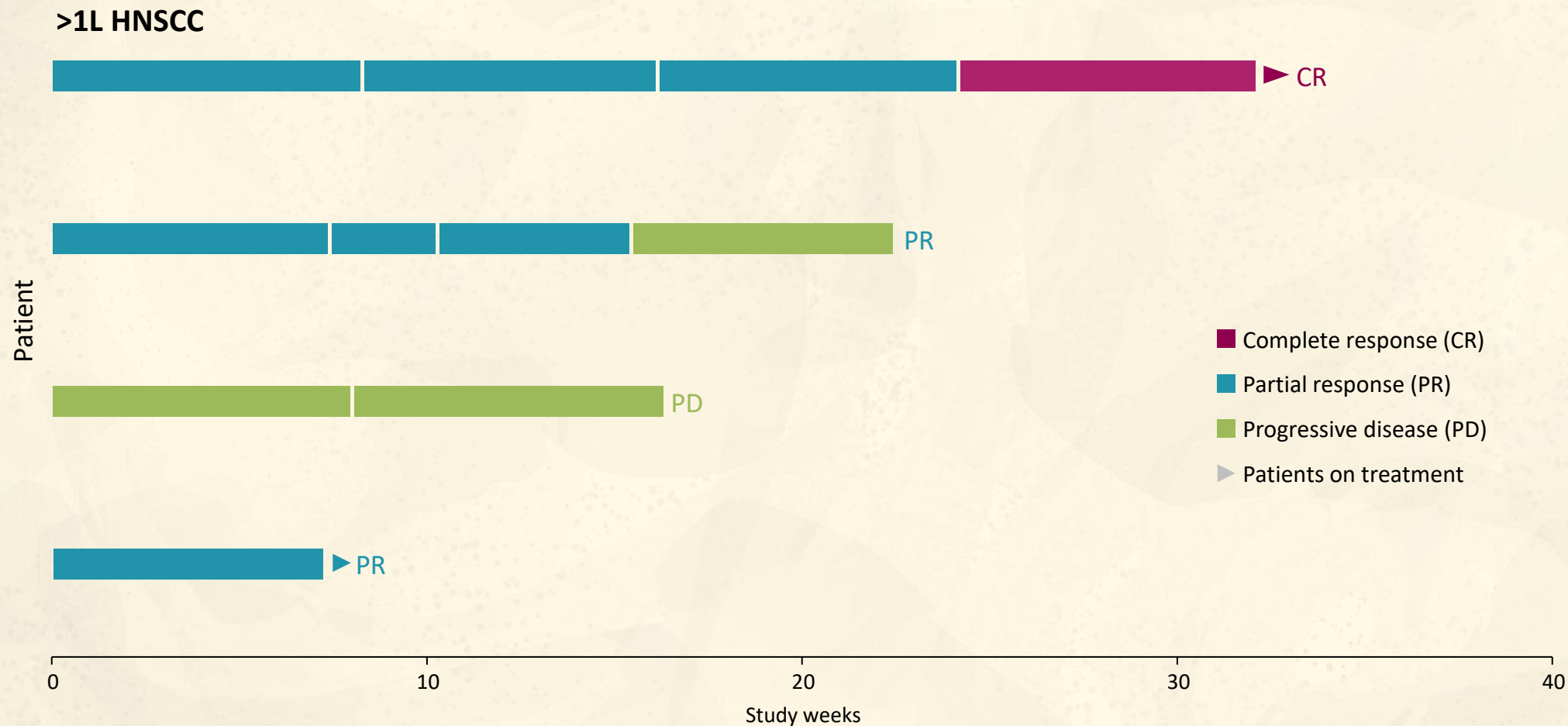
evorpaccept (10 and 15 mg/kg QW) + Keytruda + 5FU + platinum (N=5)

Adverse Event	Total n(%) All Causality		Total n(%) Related	
	Grade 3	Grade 4	Grade 3	Grade 4
Neutrophil count decreased	1 (20)	-	-	-
Anemia	1 (20)	-	-	-
Cardiac tamponade	-	1 (20)*	-	-
Dysphagia	1 (20)	-	-	-
Pericarditis constrictive	1 (20)*	-	-	-
Supraventricular tachycardia	1 (20)*	-	-	-

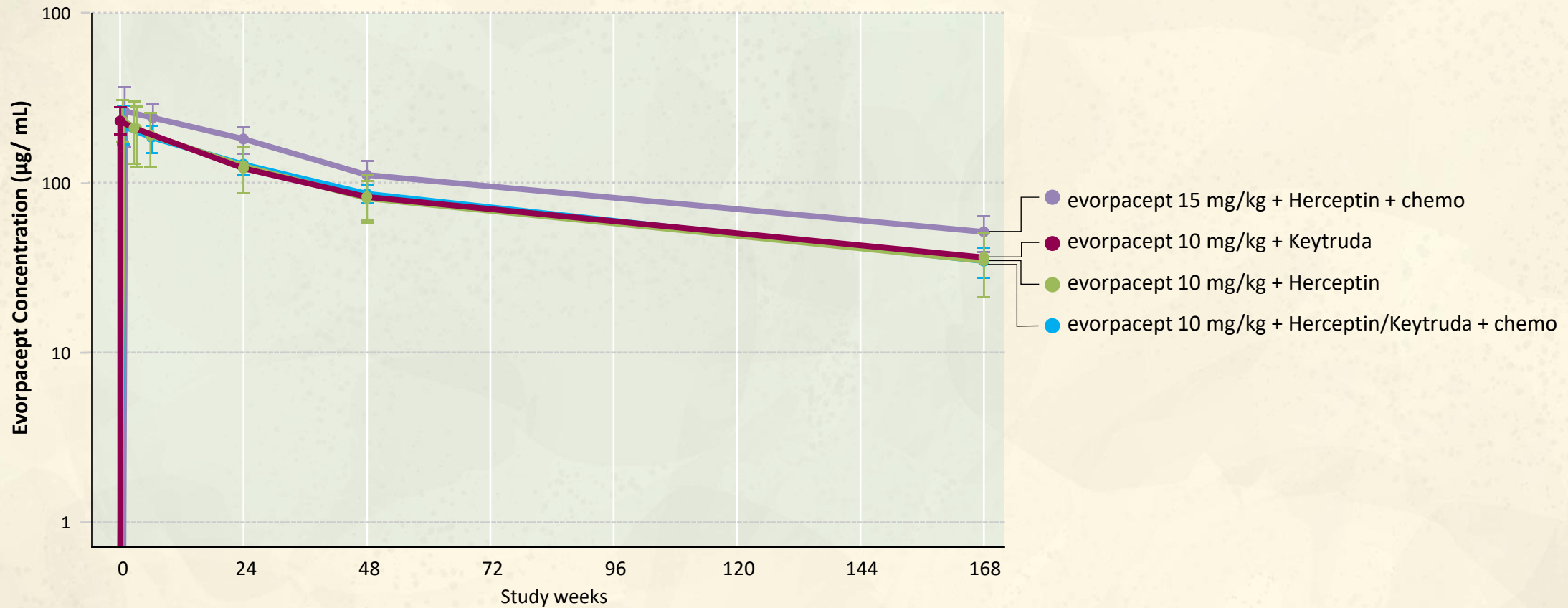
\*Events occurred in a single patient with malignant pericardial effusion



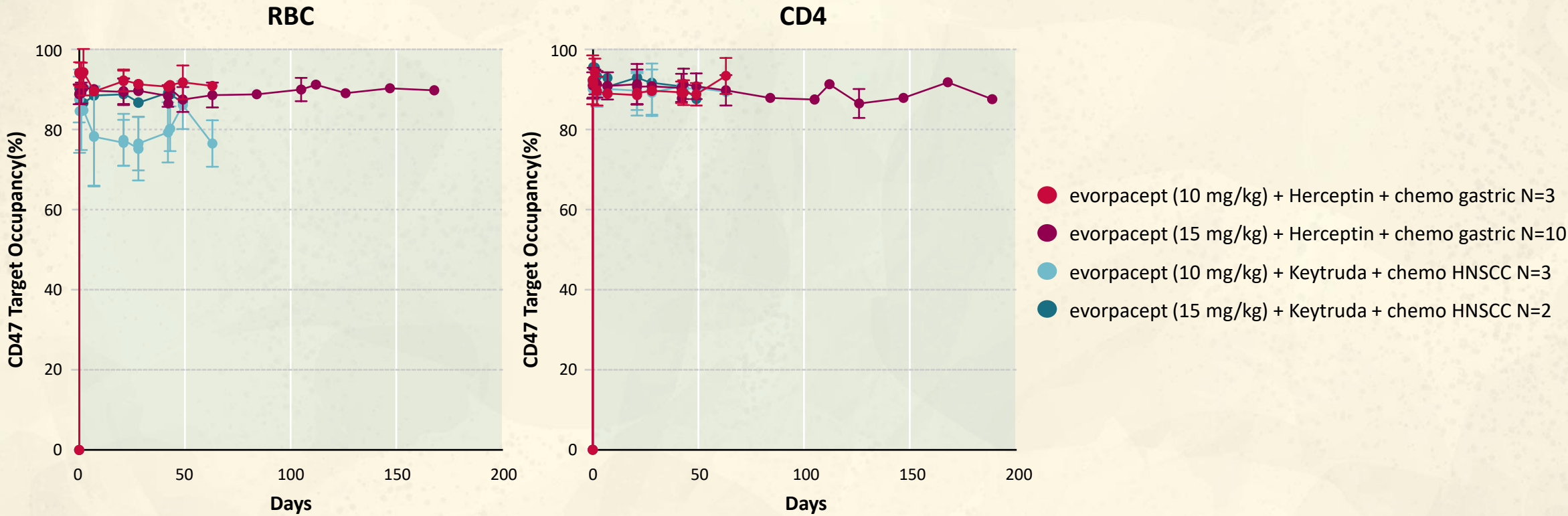
# PHASE 1B FIRST LINE HNSCC: EVORPACEPT + KEYTRUDA + 5FU/PLATINUM BEST OVERALL AND DURATION OF RESPONSE WHILE ON TREATMENT



# EVORPACEPT PK FOLLOWING COMBINATION THERAPIES IS COMPARABLE WITH AND WITHOUT CHEMOTHERAPY



# NEAR COMPLETE CD47 TARGET OCCUPANCY IS MAINTAINED THROUGHOUT EVORPACEPT DOSING INTERVAL WHEN COMBINED WITH CHEMOTHERAPY CONTAINING REGIMENS

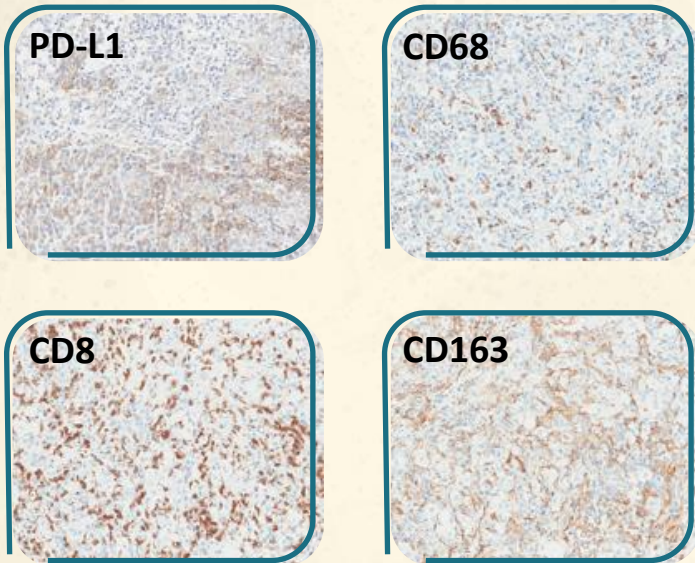




# PRE-TREATMENT IHC RESULTS IN HOT AND COLD TUMORS

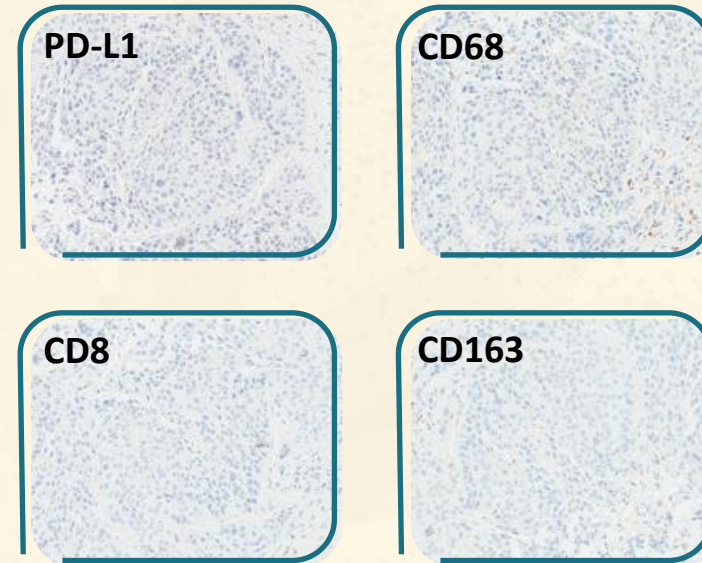
## HNSCC PATIENT 1 (PD-L1 POSITIVE) AND PATIENT 2 (PD-L1 NEGATIVE)

**Patient 1 Best Overall Response: CR**  
Immunologically “hot” tumor



**Patient 1:** HNSCC (CPS 50) characterized as immunologically “hot” with a high density of infiltrating T lymphocytes (CD8) and tumor associated macrophages and myeloid cells (CD68 and CD163).

**Patient 2 Best Overall Response: PR**  
Immunologically “cold” tumor

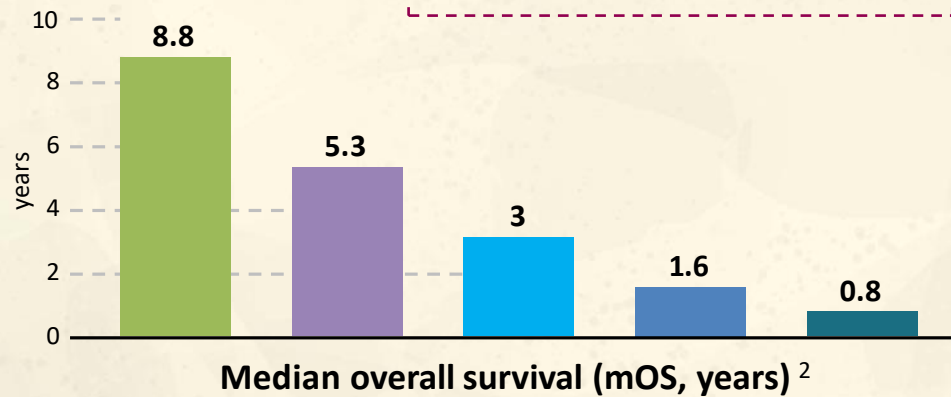
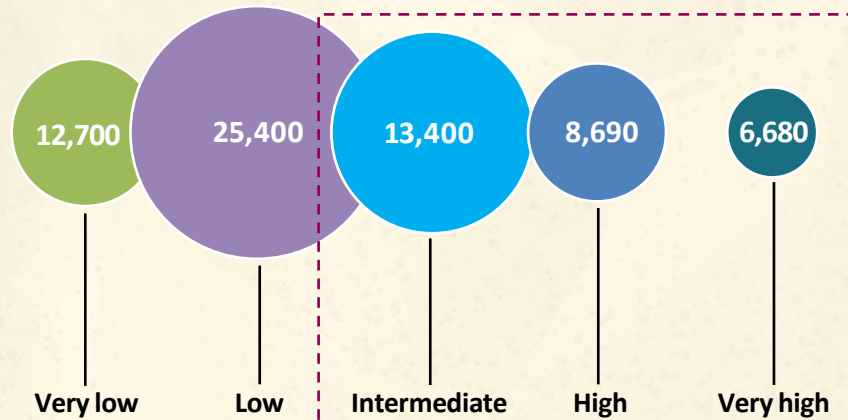


**Patient 2:** HNSCC (CPS 0) characterized as immunologically “cold” where immune cells are excluded from the tumor core while present at lower density in the peri-tumoral regions.



# MDS OPPORTUNITY

US Diagnosed Prevalent Cases <sup>1</sup>



## Higher Risk (HR) MDS



Bone marrow transplant

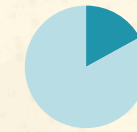


Azacitidine,  
Decitabine



**<10%**

Receive  
allogeneic transplant <sup>3</sup>



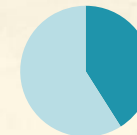
**17%**

Treated with azacitidine  
achieve a CR <sup>4</sup>

## Overall MDS



Nearly all pts  
transfused due  
to cytopenias

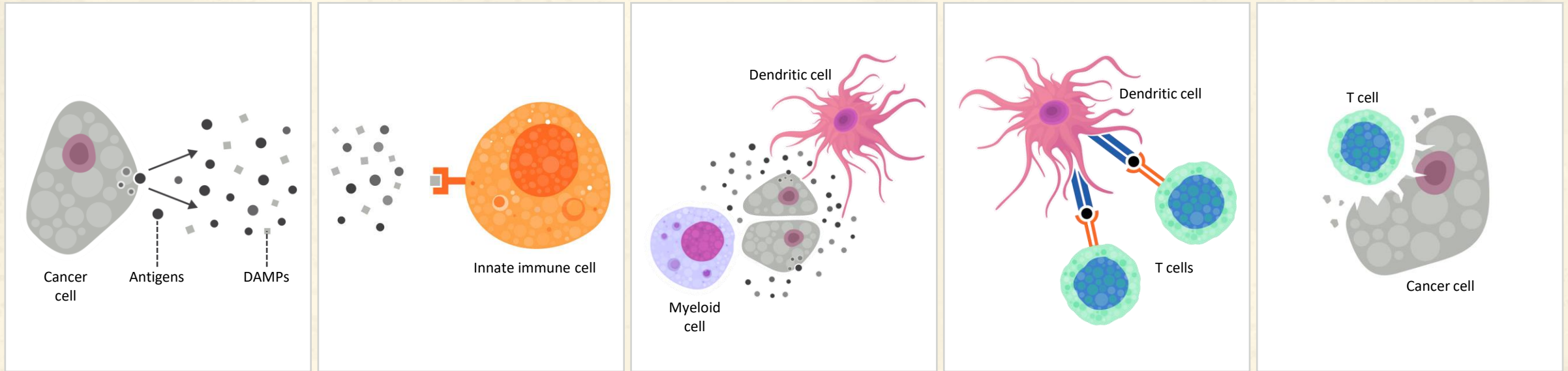


**41 of 100**

Will die from  
cytopenia-related causes <sup>5</sup>

Higher risk MDS patients are an area of high unmet need.

# HARNESSING THE POWER OF INNATE AND ADAPTIVE IMMUNE RESPONSES TO CANCER



**1. Release of PAMPs/DAMPs and tumor antigens**

**2. Detection by PRRs on innate immune cells**

**3. Amplification of innate immune cell activation**

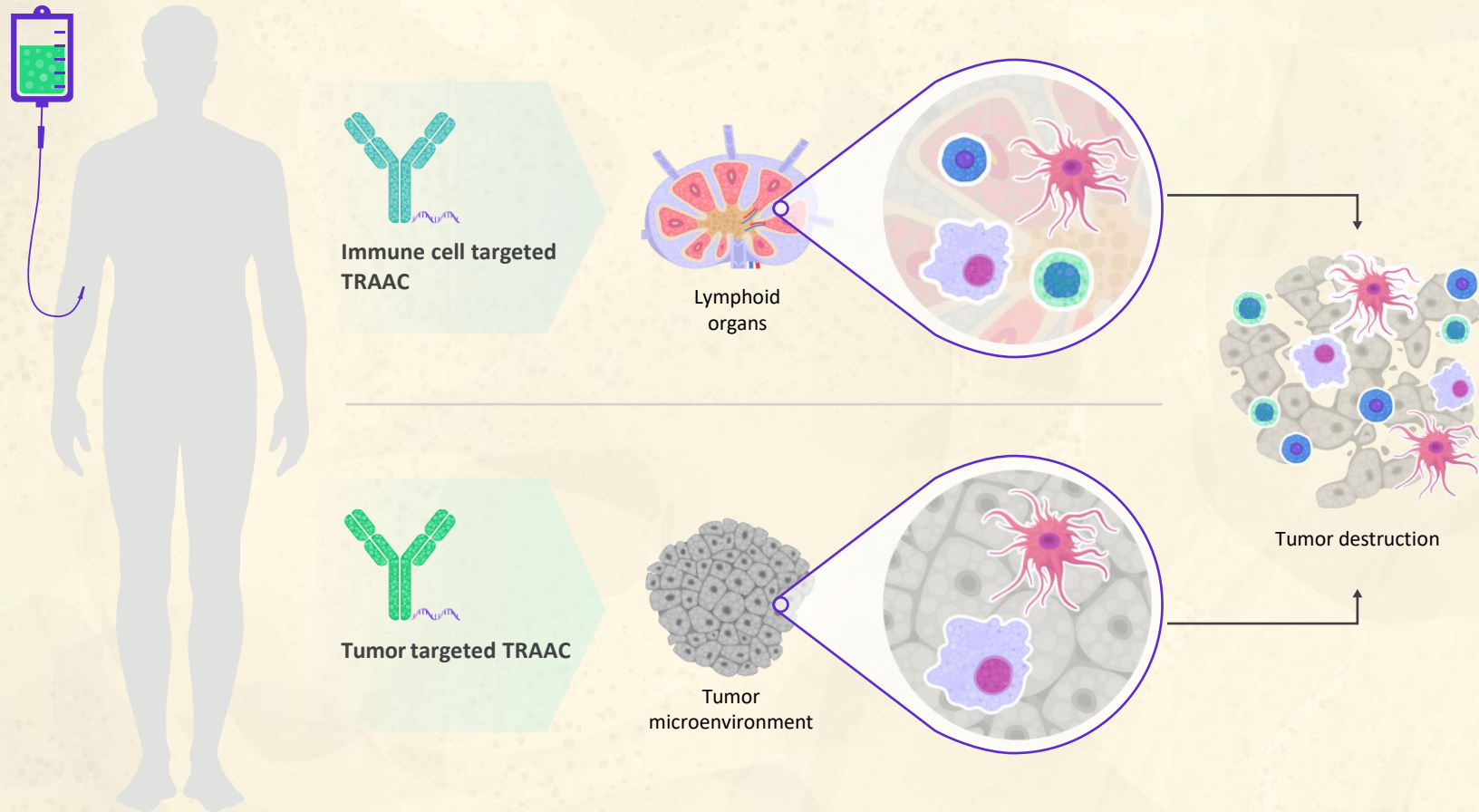
**4. Antigen presentation and activation of T cells**

**5. Recognition and elimination of tumor by T cells**

- Successful immune-mediated elimination of cancer requires coordination between the innate and adaptive arms of the immune system.
- Innate immune cells (macrophages, myeloid cells and dendritic cells) may utilize a variety of signaling pathways, including TLR9, TLR7 or 8, STING and CD40, to trigger proinflammatory programs and engage the adaptive immune system.

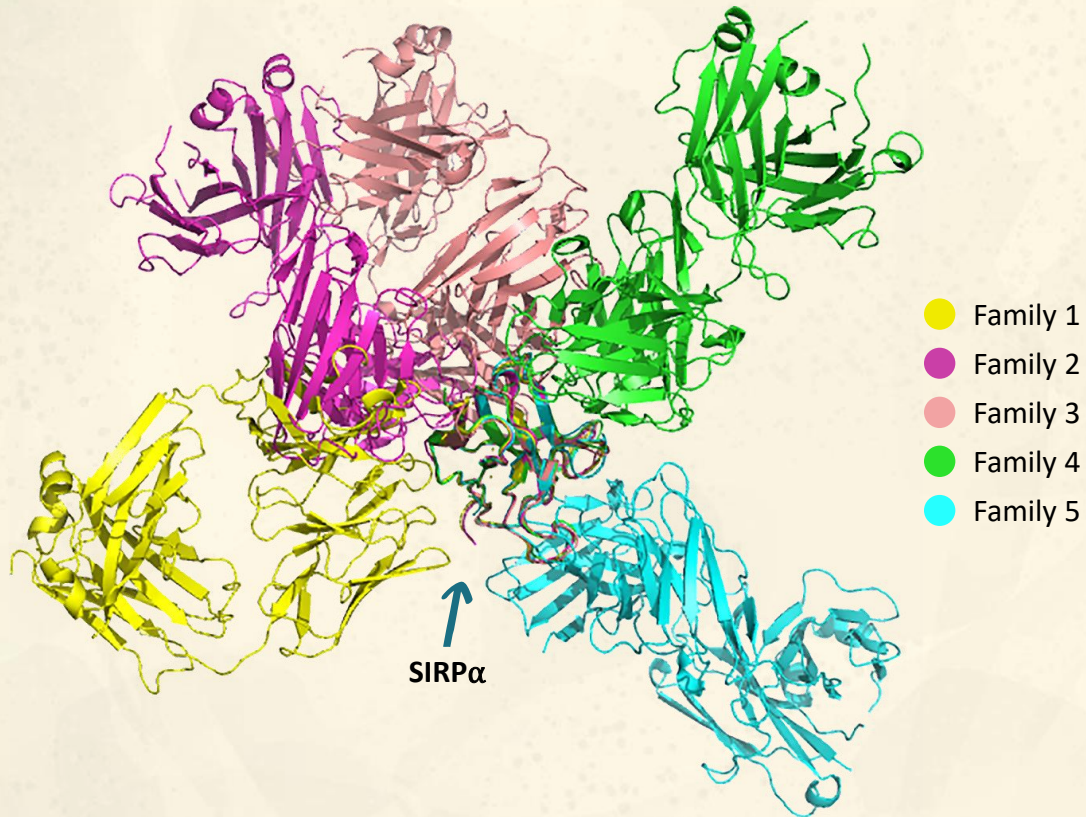
DAMPs: damage-associated molecular patterns  
PAMPs: pathogen-associated molecular patterns  
PRRs: pattern recognition receptors

# TLR9 AGONIST ANTIBODY CONJUGATE (TRAAC) ENABLES VERSATILE TARGETING OF IMMUNE CELLS THAT MATTER





# ALX ONCOLOGY'S SIRP $\alpha$ ANTIBODIES: HIGH AFFINITY AND DIVERSE EPITOPES



## ALX's diverse range of SIRP $\alpha$ antibodies

Diversity allows selection of best-in-class SIRP $\alpha$  antibodies:

- Binds human SIRP $\alpha$  variants V1 and V2
- Cross reacts with rodent, monkey and human SIRP $\alpha$
- Wide range of affinities
- Full coverage of SIRP $\alpha$  domain 1 surface allows selection for optimal epitope