

# ALX ONCOLOGY

August 8, 2022

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# ADVANCING A HIGHLY DIFFERENTIATED IMMUNO-ONCOLOGY PIPELINE

**ALX Oncology (Nasdaq: ALXO) is advancing a pipeline of candidates based on expertise in protein engineering and oncology led by the CD47 blocker, evorpaccept, currently in phase 2 clinical trials**



## **Evorpaccept (myeloid checkpoint inhibitor) as a cornerstone therapy**

Randomized phase 2 trials enrolling in 3 solid tumor indications: gastric/gastroesophageal cancer and 2 head and neck squamous cell carcinoma trials

Early clinical trials in 2 hematologic malignancies: myelodysplastic syndromes and acute myeloid leukemia

Continuing to broaden potential uses in new combinations and tumor types.



## **Building early stage pipeline**

Ongoing IND-enabling development of ALTA-002 through 50/50 joint collaboration.

Early preclinical development of tumor-activated antibody platform.



## **Strong financial position**

Cash, cash equivalents and investments of \$324.2M as of June 30, 2022.

Expected cash runway through the fourth quarter of 2024.

## **Collaboration partners**




Merck, Eli Lilly, Zymeworks





# EVORPACEPT'S BROAD CLINICAL DATA SUPPORTS ITS DIFFERENTIATED POTENTIAL

Evorpacept was designed to:



**Work in combinations**

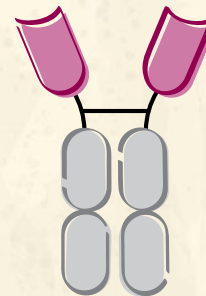
- +  Antibodies
- +  Checkpoint inhibitors
- +  Chemotherapy

**Target broad tumor indications**

-  Solid tumors
-  Hematology

**Be convenient and tolerable for patients**

-  Flexible dosing schedule
-  Targets cancer cells



**Evorpacept:**

A phase 2 CD47 blocker designed to be a cornerstone of cancer treatments

Evorpacept's clinical data shows promising initial activity in:

## Solid tumor combinations:



**GC**  
Gastric/Gastroesophageal junction cancer



Herceptin



Herceptin + Cyramza + Paclitaxel



**HNSCC**  
Head and neck squamous cell carcinoma



Keytruda



Keytruda + 5FU + Platinum

## Hematology combinations:



**MDS**  
Myelodysplastic syndromes



Azacitidine



**NHL**  
Non-Hodgkin's lymphoma



Rituximab

## Flexibility and tolerability:



### Dosing schedule

15 mg/kg QW, 30 mg/kg Q2W,  
45 mg/kg Q3W, 60 mg/kg Q4W.



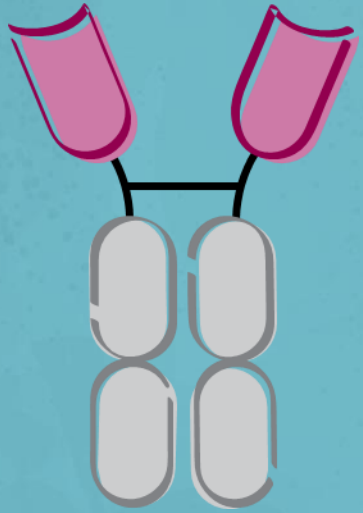
### Tolerability profile

No dose-dependent cytopenias

# ALX PIPELINE

Indication		Combination Agent	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Fast Track	Collaboration Partner
Evorpcept Combination Studies	SOLID TUMORS	<b>HNSCC</b> Head And Neck Squamous Cell Carcinoma	Keytruda (ASPEN-03)						<b>MERCK</b>
			Keytruda + 5FU + Platinum (ASPEN-04)						<b>MERCK</b>
		<b>GC</b> Gastric/Gastroesophageal Junction Cancer	Herceptin (ASPEN-01)						
			Herceptin + Cyramza + Paclitaxel (ASPEN-06)						<i>Lilly</i>
		<b>Urothelial Cancer</b>	Padcev (ASPEN-07)						
	HEMATOLOGY	<b>Breast Cancer</b>	Zanidatamab						<b>zymeworks</b>
		<b>MDS</b> Myelodysplastic Syndromes	Azacitidine (ASPEN-02)						
		<b>AML</b> Acute Myeloid Leukemia	Azacitidine + Venclexta (ASPEN-05)						
		<b>NHL</b> Non-Hodgkin's Lymphoma	Rituximab (ASPEN-01)						
	<b>ALTA 002*</b>	<b>Advanced Cancer</b>							<b>TALLAC</b> THERAPEUTICS

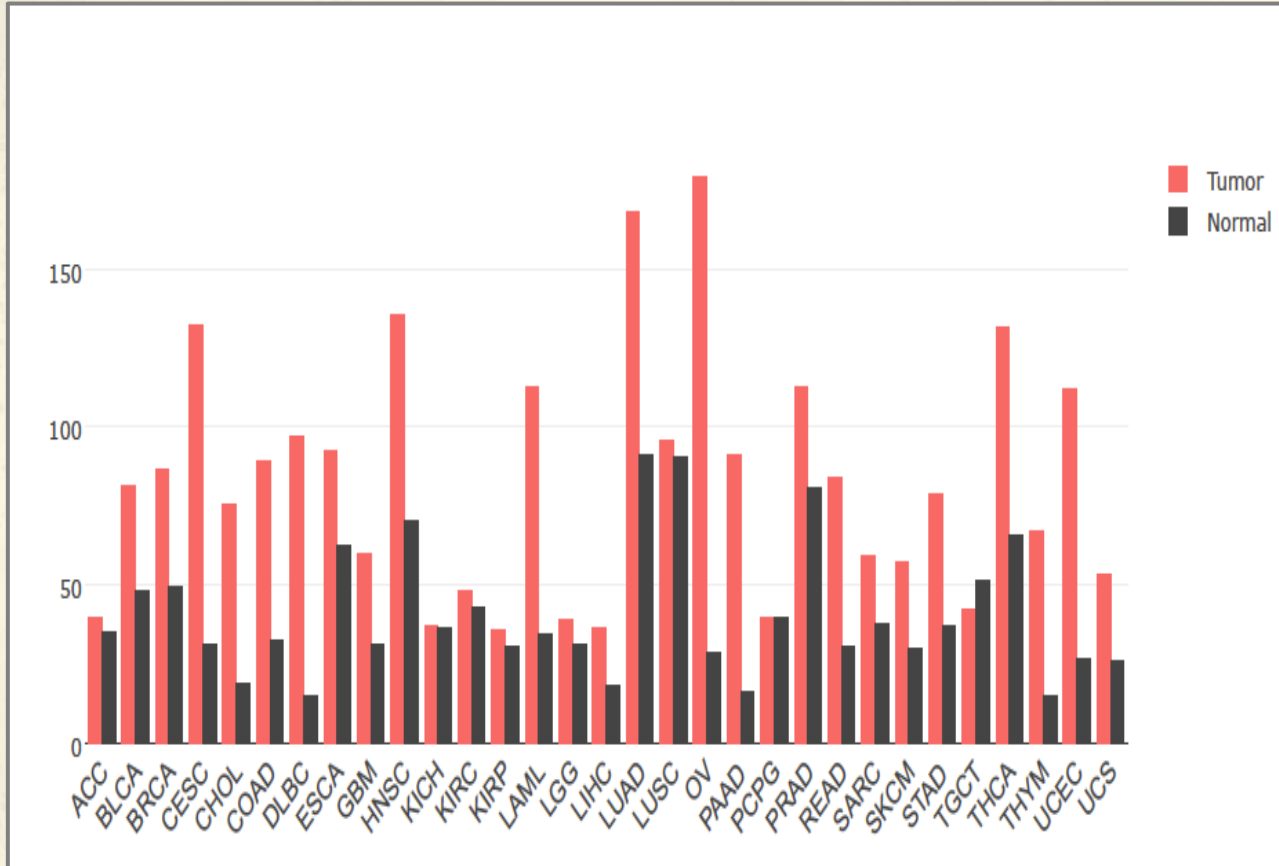
\*SIRPα Toll-like receptor agonist antibody conjugate (TRAAC)



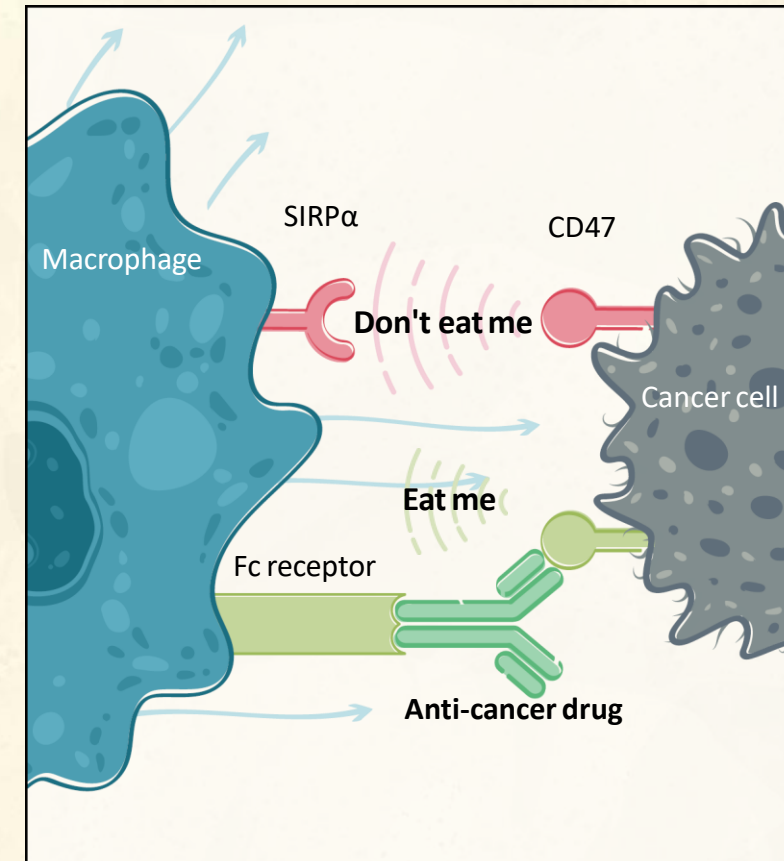
**EVORPACEPT  
(ALX148)**

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

TAA-Expression levels on cancer and normal cells



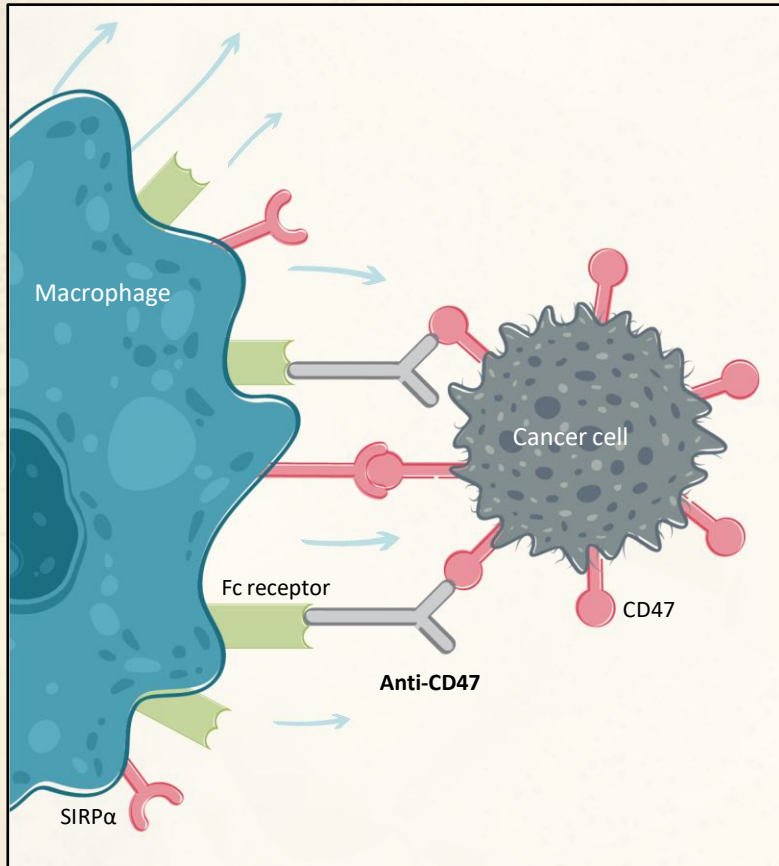
Checkpoint Mechanism: “do not eat me”



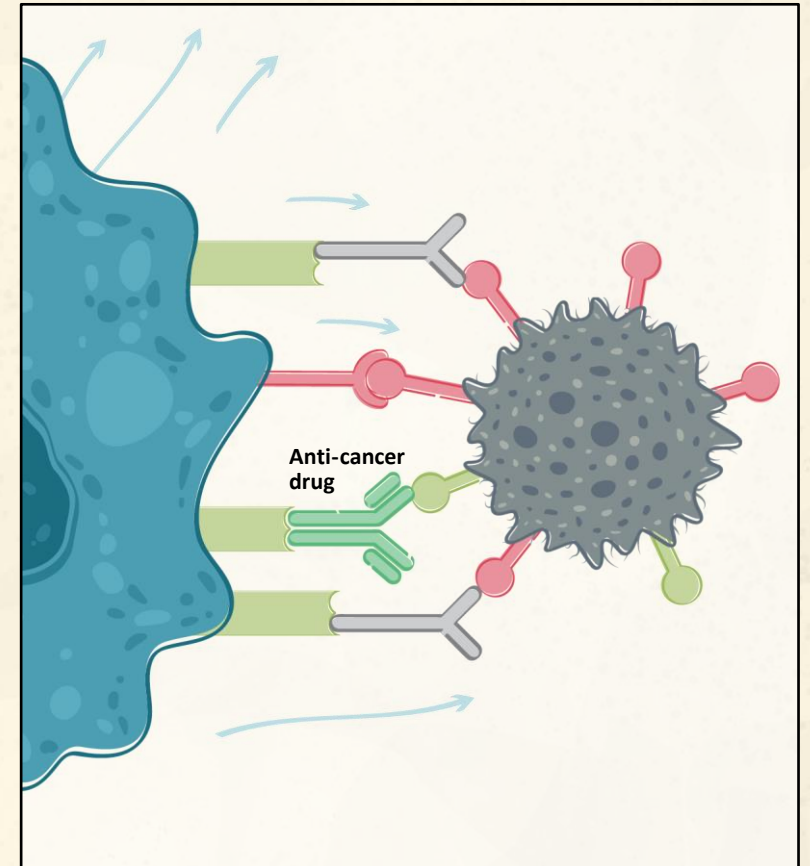
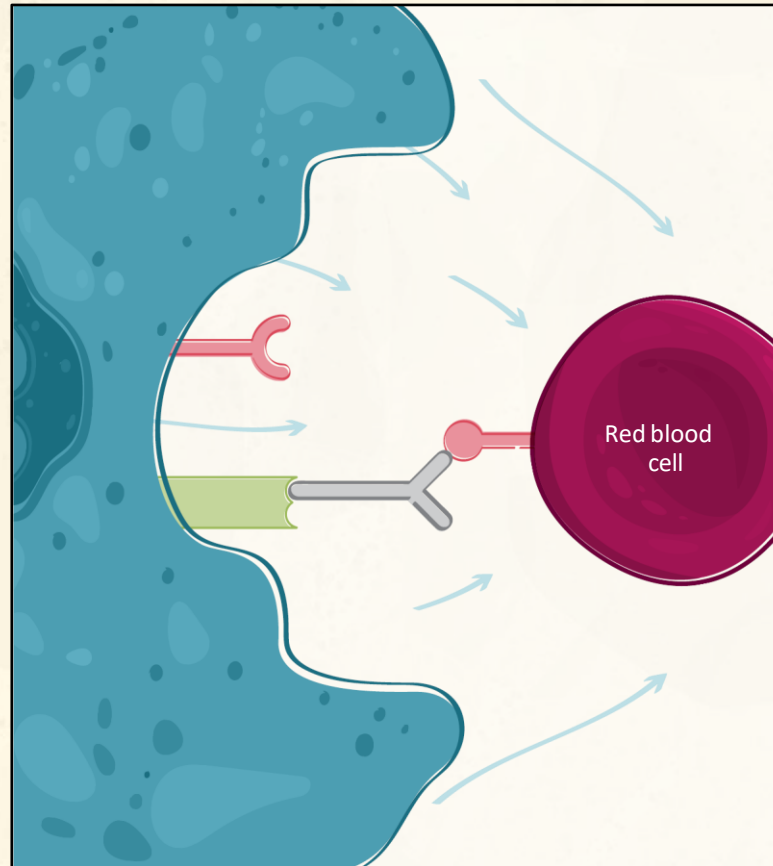


# TARGETING CD47 AS TUMOR ASSOCIATED ANTIGEN

But also targets normal cells



Anti CD47 with active Fc  
directly targets cancer cells

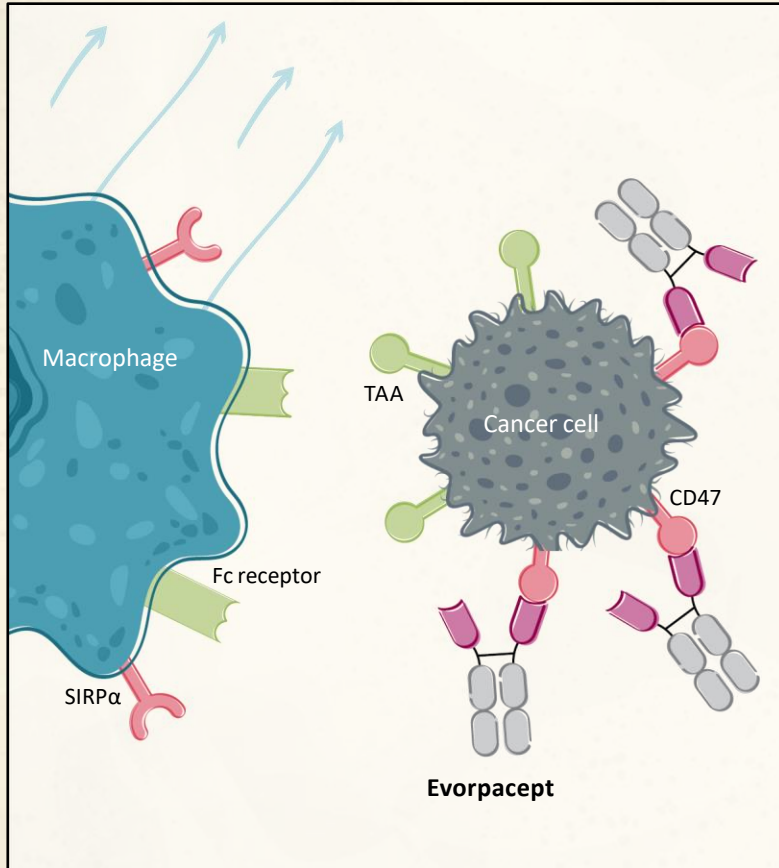


Dose limitations prevent full  
blockade of CD47 and active  
Fc competes with combo  
drug

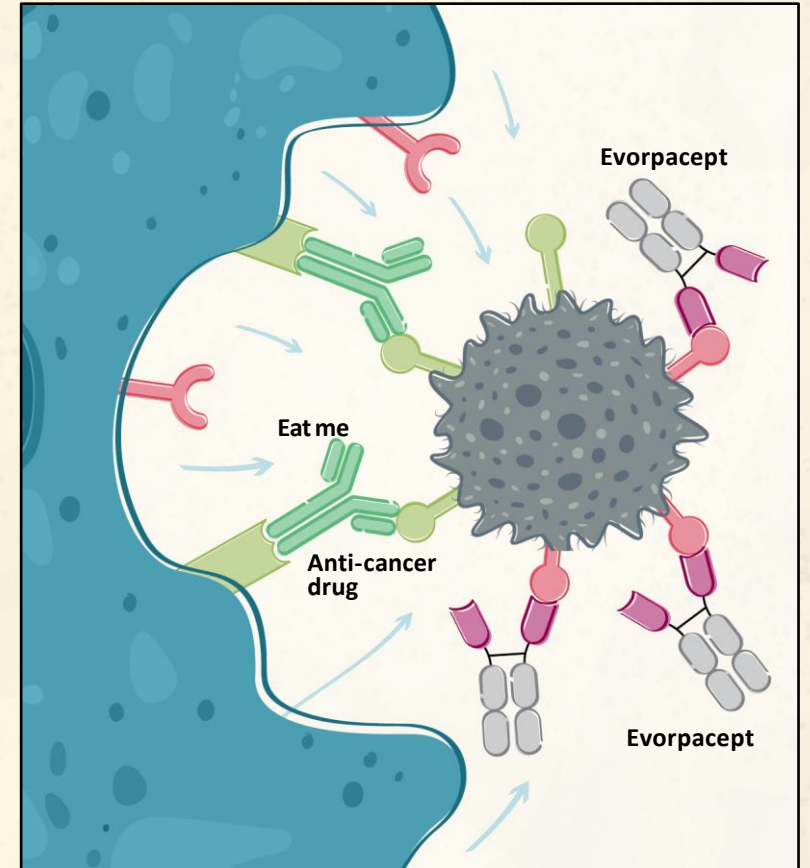
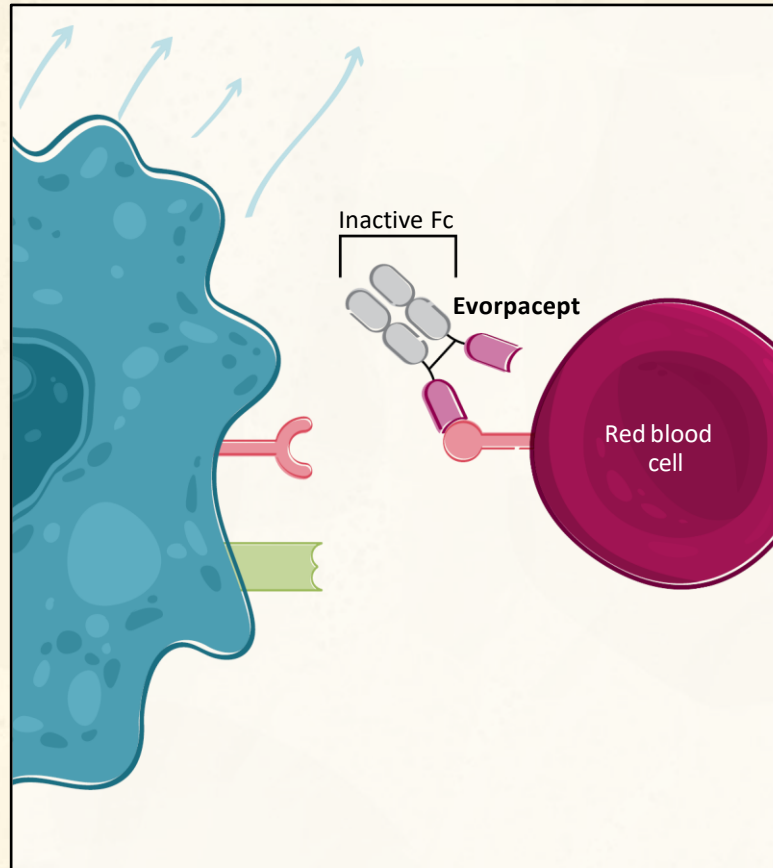


# TARGETING CD47 AS CHECKPOINT: ALX ONCOLOGY'S APPROACH

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 $\alpha$



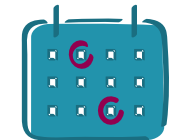
Potently blocks CD47 signal on cancer cells

Inactive Fc domain eliminates binding activity



No dose dependent cytopenia

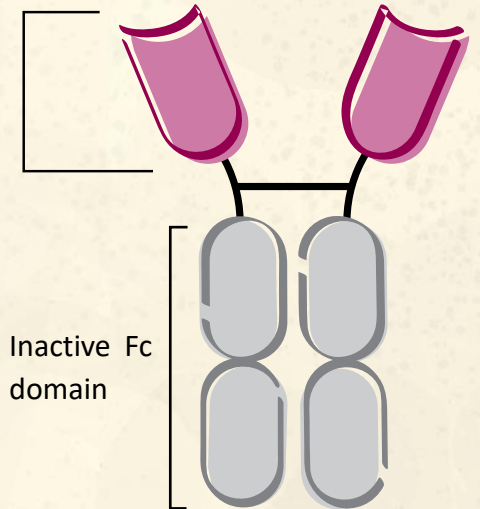
Presence of Fc domain ensures slow clearance and long half-life



Less frequent dosing and more flexibility

## 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 CONSISTENT TOLERABILITY PROFILE

Treatment related adverse events	evorpacept + Herceptin + Cyramza + chemo (N=18)		evorpacept + Keytruda + chemo (N=13)		evorpacept + Keytruda (N=52)		evorpacept + azacitidine (N=22)	
	Total n (%)	≥Grade 3	Total n (%)	≥Grade 3	Total n (%)	≥Grade 3	Total n (%)	≥Grade 3
Fatigue	2 (11.1%)	-	1 (7.7%)	-	6 (11.5%)	-	-	-
Rash / dermatitis acneiform	4 (22.2%)	-	-	-	5 (9.6%)	-	-	-
AST increased	-	-	-	-	9 (17.3%)	-	-	-
Platelets decreased	-	-	-	-	4 (7.7%)	2 (3.8%)	-	-
ALT increased	-	-	-	-	7 (13.5%)	1 (1.9%)	-	-
Pruritus	2 (11.1%)	-	-	-	5 (9.6%)	-	-	-
Pyrexia	-	-	-	-	3 (5.8%)	-	-	-
Decreased appetite	-	-	-	-	2 (3.8%)	-	-	-
Anemia	1 (5.6%)	-	1 (7.7%)	1 (7.7%)	5 (9.6%)	1 (1.9%)	-	-
Infusion reaction	-	-	-	-	4 (7.7%)	-	4 (18.2%)	-
Neutropenia / neutrophil count decrease	-	-	1 (7.7%)	-	2 (3.8%)	1 (1.9%)	3 (13.6%)	2 (9.1%)
Nausea	-	-	-	-	2 (3.8%)	-	2 (9.1%)	-
Alkaline phosphatase incr	-	-	-	-	3 (5.8%)	-	-	-
Arthralgia	-	-	-	-	3 (5.8%)	-	-	-
WBC decreased	-	-	-	-	3 (5.8%)	-	-	-
Myalgia	-	-	-	-	2 (3.8%)	-	-	-
Diarrhea	3 (16.7%)	-	-	-	-	-	-	-
Urticaria	3 (16.7%)	-	-	-	-	-	-	-
Lymphocyte count decreased	1 (5.6%)	1 (5.6%)	-	-	-	-	-	-
Headache	1 (5.6%)	-	-	-	-	-	-	-
Stomatitis	1 (5.6%)	-	-	-	-	-	-	-
Back pain	1 (5.6%)	-	-	-	-	-	-	-
Vision blurred	1 (5.6%)	-	-	-	-	-	-	-
Abdominal pain / abdominal pain upper	1 (5.6%)	-	-	-	-	-	-	-
Hypersensitivity	-	-	1 (7.7%)	1 (7.7%)	-	-	-	-
Pneumonitis	-	-	1 (7.7%)	-	-	-	-	-
Constipation	-	-	-	-	-	-	3 (13.6%)	-
Vomiting	-	-	-	-	-	-	2 (9.1%)	-

## EVORPACEPT'S INITIAL CLINICAL ACTIVITY IS MAGNIFIED IN SURVIVAL-BASED ENDPOINTS ACROSS SOLID TUMOR TYPES IN MULTIPLE TRIALS (ASPEN-01 COHORTS)

Population	≥2L HER2+ GC		1L HNSCC		≥2L HNSCC (CPI-Naïve)	
Combination (N-evaluable)	evorpacept + Herceptin + Cyramza + paclitaxel (N=18)		evorpacept + Keytruda + 5FU + platinum (N=13)		evorpacept + Keytruda (N=10)	
ORR	evorpacept 72%	benchmark <sup>1</sup> 28%	evorpacept 39%	benchmark <sup>2</sup> 36%	evorpacept 40%	benchmark <sup>3</sup> 15%
mPFS (months)	17.1	4.4	5.6	4.9	4.6	2.1
mOS (months)	17.1	9.6	NR	13.0	24.5	8.4
OS rate at 12 months	79%	40%	88%	53%	80%	37%
Benchmark regimen	Cyramza + paclitaxel		Keytruda + 5FU + platinum		single agent Keytruda	



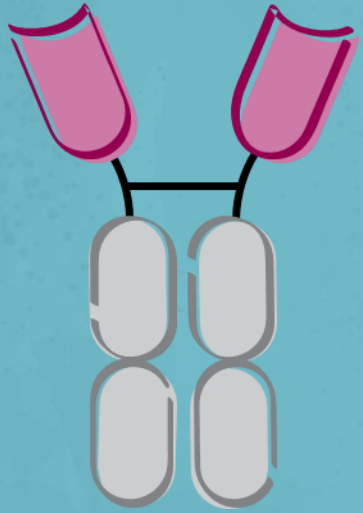
# EARLY DATA SHOWS EVORPACEPT COMBINATIONS HAVE ACHIEVED COMPLETE RESPONSES IN AGGRESSIVE HEMATOLOGIC MALIGNANCIES

## ASPEN-02

Population	Previously untreated higher risk myelodysplastic syndromes (MDS) with TP53 mutation		Relapsed / refractory MDS
Combination	Evorpacept + azacitidine	Magrolimab + azacitidine <sup>1</sup>	Evorpacept + azacitidine
N-evaluable	5	25	9
CR	2	10	-
mCR	1 with HI	5	5*
SD	1		2

## ASPEN-01

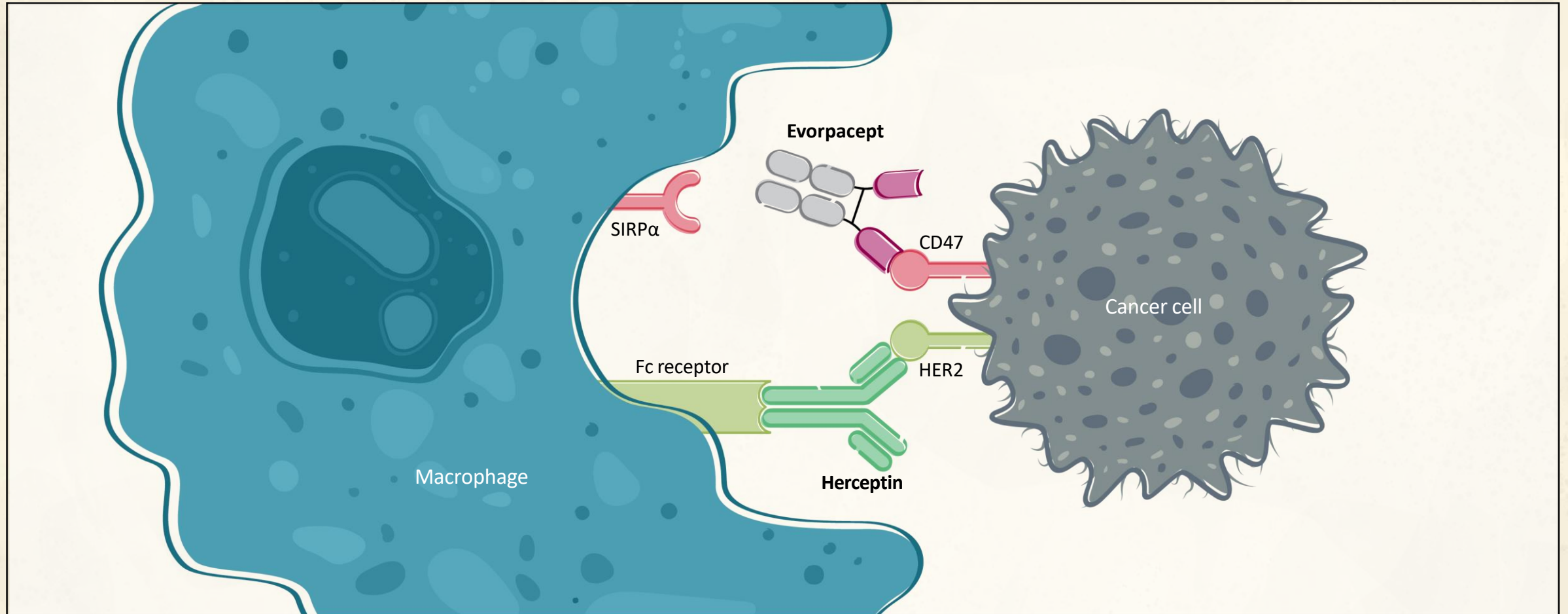
Population	≥2L aggressive non-Hodgkin's lymphoma	
Combination	Evorpacept + Rituximab <sup>2</sup>	Magrolimab + Rituximab <sup>3</sup>
N-evaluable	21	38
ORR (%)	8 (38%)	11 (29%)
CR (%)	1 (5%)	2 (5%)
PR (%)	7 (33%)	9 (24%)



**ASPEN-06:  
EVORPACEPT (ALX148)  
IN HER2+ GASTRIC/GEJ CANCER**

# GC TRIAL: EVORPACEPT + HERCEPTIN MECHANISM OF ACTION

evorpaccept  
in  
GASTRIC



Evorpaccept increases antibody dependent cellular phagocytosis in combination with Herceptin

# CLINICAL ACTIVITY OF HISTORICAL BENCHMARKS IN PATIENTS WITH HER2 POSITIVE GASTRIC CANCER

Population	N	ORR	DOR (m) [95% CI]	PFS (m) [95% CI]	OS (m) [95% CI]	OS rate at 12 m
≥2L Gastric ramucirumab/paclitaxel RAINBOW <sup>1</sup>	330	28%	4.4 [IQR 2.8–7.5]	4.4 [4.2-5.3]	9.6 [8.5-10.8]	40%
≥2L Gastric trastuzumab/ram/paclitaxel <sup>2</sup>	50	52%	5.1 [3.3-6.9]	7.4 [6.5-8.3]	13.6 [9.6-17.5]	-
2L Gastric trastuzumab-deruxtecan DESTINY 02 <sup>3</sup>	79	38%	8.1 [4.1-NE]	5.5 [4.2-7.3]	-	-
≥3L Gastric trastuzumab-deruxtecan DESTINY 01 <sup>4</sup>	126	41%	11.3 [5.6-NE]	5.6 [4.3-6.9]	12.5 [9.6-14.3]	52%



# ASPEN-01 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>67.5 (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>2 (11)</b>
Progressed upon prior CPI therapy, n ( %)		<b>9 (45)</b>	<b>2 (11)</b>
Visceral distant metastasis, n ( %)		<b>17 (85)</b>	<b>15 (83)</b>

# ASPEN-01 PHASE 1B $\geq 2$ 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.



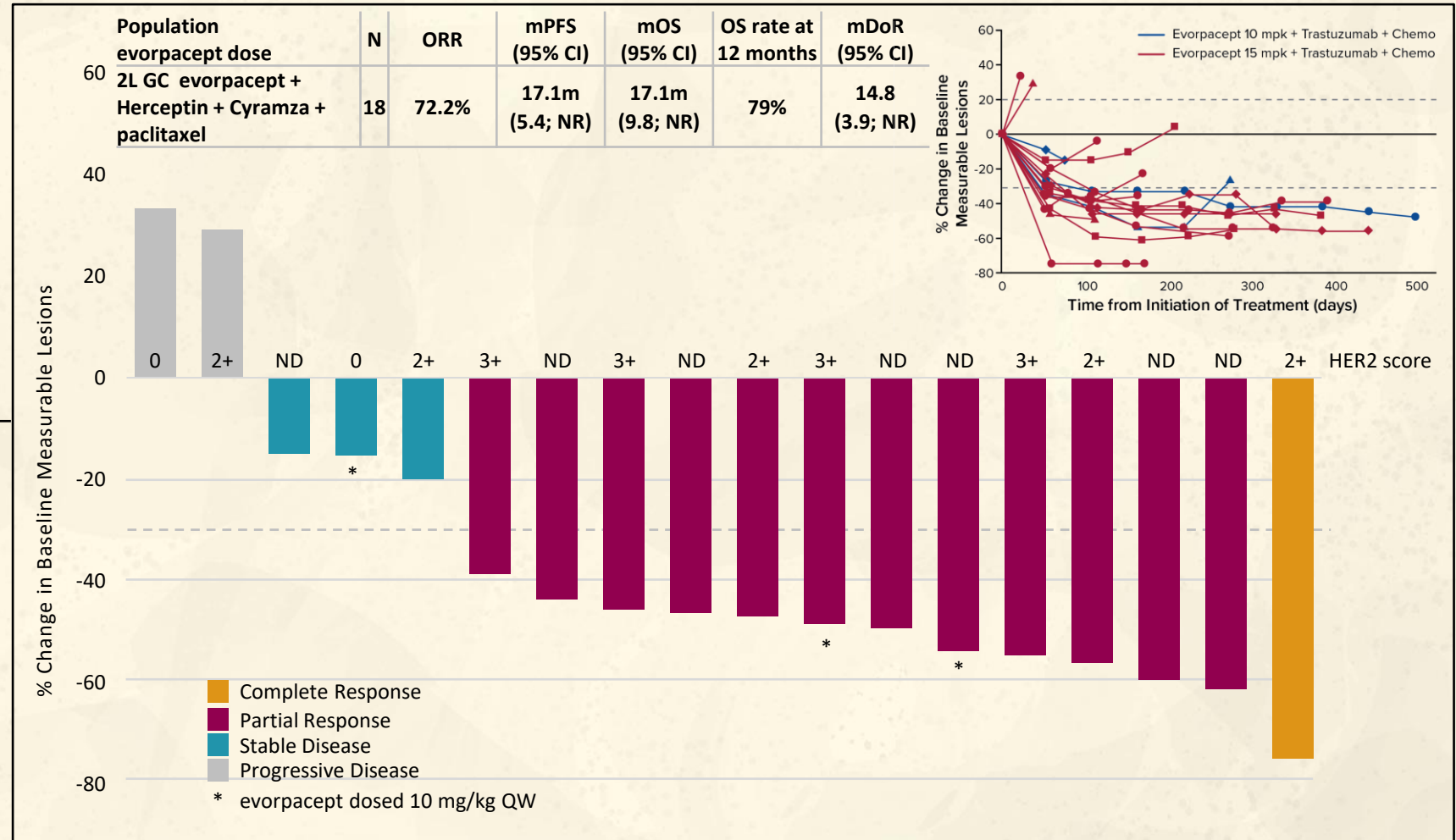
### Treatment:

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



### Endpoint:

- safety of combination
- anti-cancer activity



Data Cutoff September 1, 2021. ND = Not Done. NR = Not Reached.

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

## Randomized Phase 2: Open for Accrual



**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

# ASPEN-01 PHASE 1B $\geq 2$ 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:

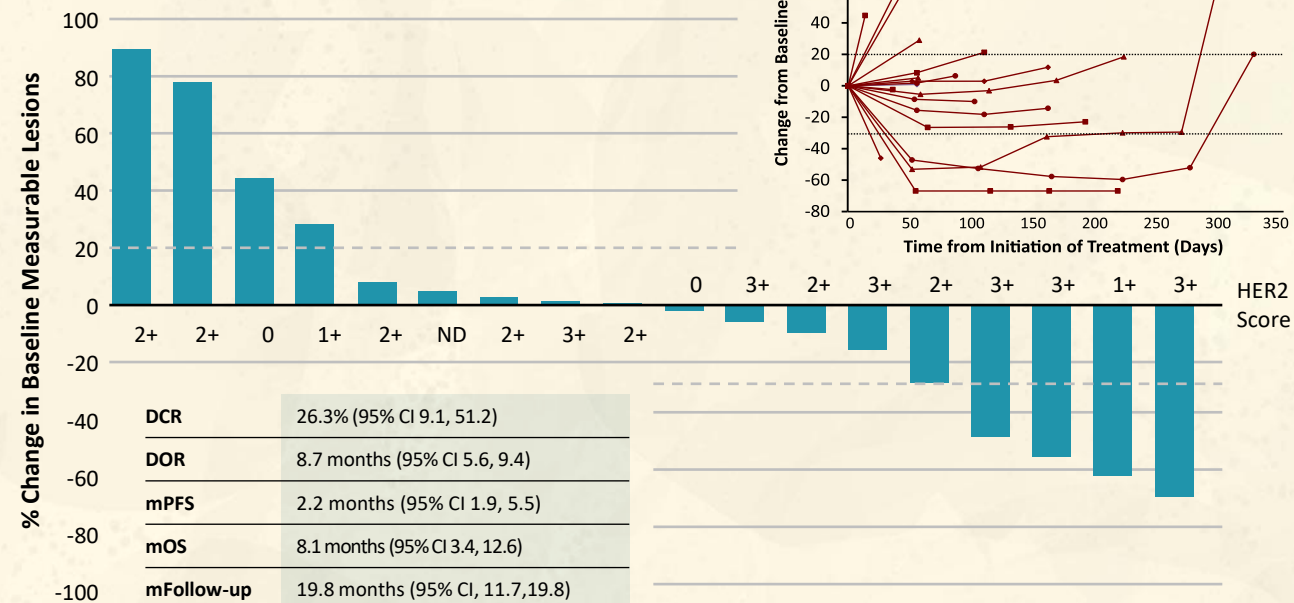
**evorpacept** 10 mg/kg  
once a week (QW)  
+ **Herceptin**  
8 mg/kg once, then  
6 mg/kg every three weeks (Q3W)

 Endpoints:

- maximum tolerated dose
- anti-cancer activity

Result:

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

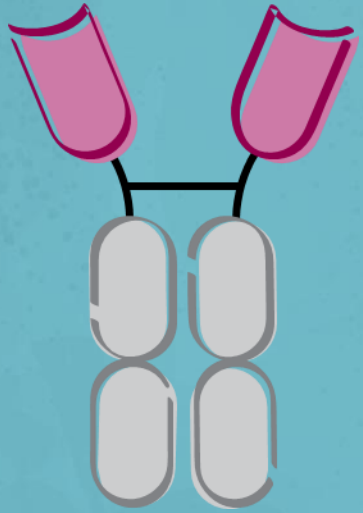


**Notes:** Data Cutoff October 1, 2020. Patients who received at least one dose of evorpacept in the expansion phase, had a baseline assessment, and at least one post-baseline disease assessment; One patient with clinical progression not included in plots.

**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**

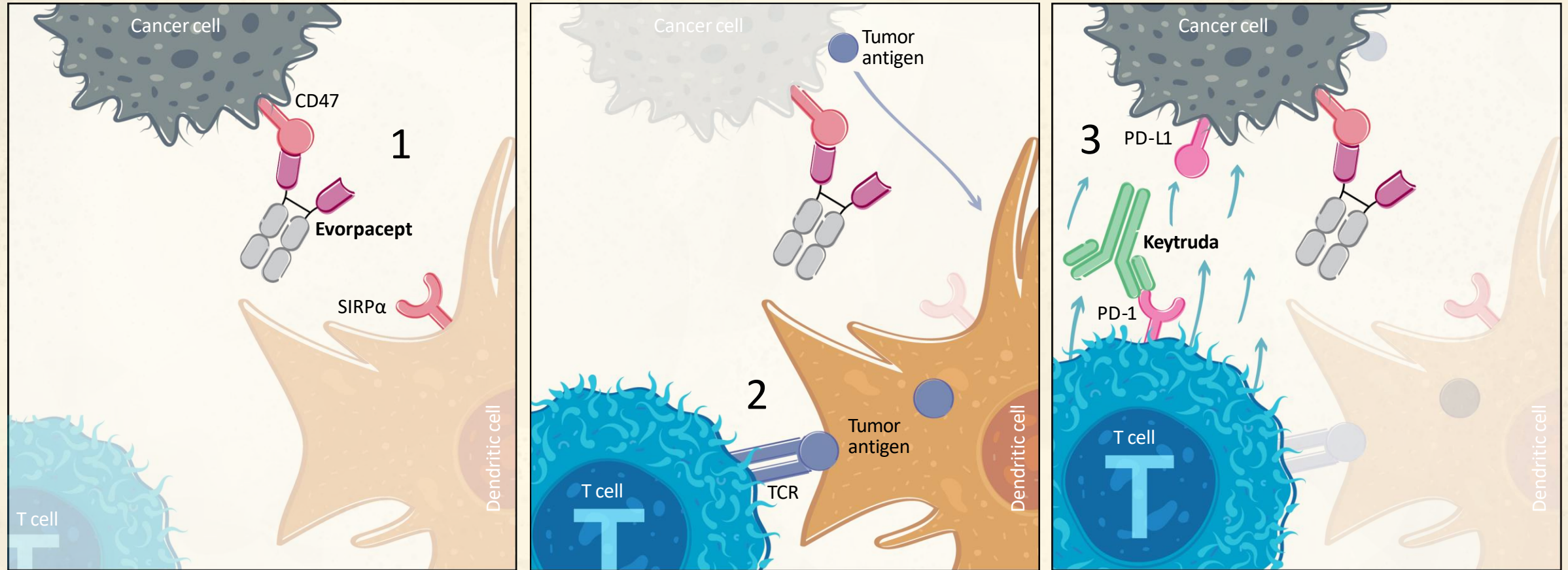




**ASPEN-03 AND ASPEN-04:  
EVORPACEPT (ALX148)  
IN 1L HNSCC**

# HNSCC TRIAL: EVORPACEPT + KEYTRUDA MECHANISM OF ACTION

evorpacept  
in  
HNSCC



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

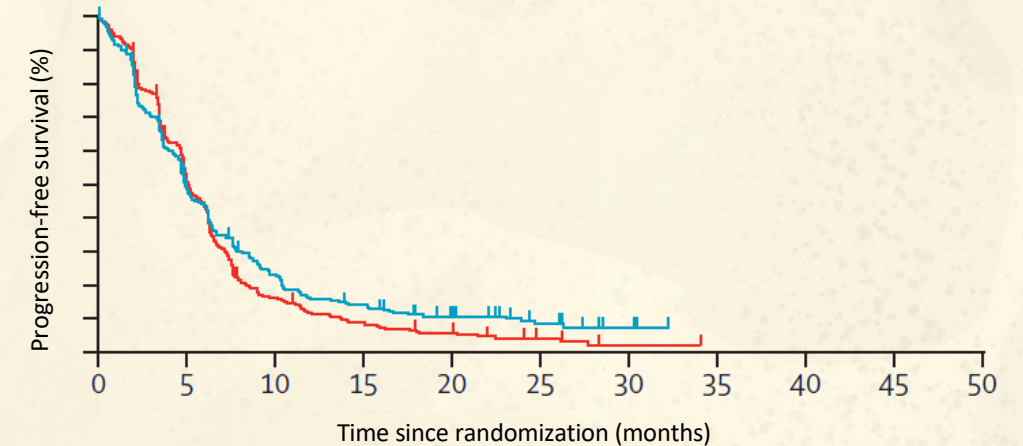
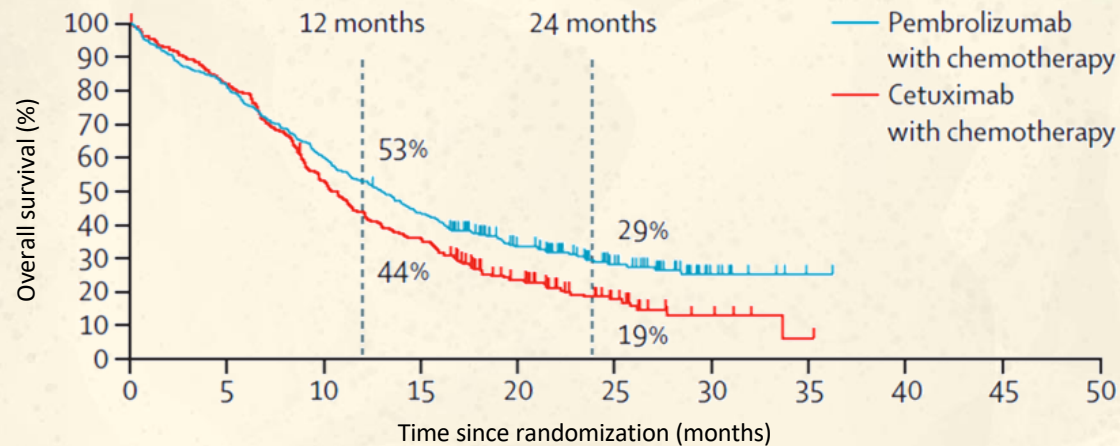
# OS RATE AT 12 MONTHS PREDICTIVE OF OVERALL SURVIVAL

Population	N	ORR (%)	PFS (m) [95% CI]	OS Rate at 12 m	OS (m) [95% CI]	Follow Up (m) [95% CI]
<b>KEYNOTE-048: 1L HNSCC</b> pembrolizumab + 5FU/platinum	281	36%	4.9 [4.7–6.0]	53%	13.0 [10.9–14.7]	13 [6.4–26.6]
<b>KEYNOTE-048: 1L HNSCC</b> cetuximab + 5FU/platinum	300	36%	5.1 [4.9–6.0]	44%	10.7 [9.3–11.7]	10.7 [6.6–19.7]
<b>KEYNOTE-040: 2L HNSCC (CPI naïve)</b> pembrolizumab	247	14.6%	2.1 [2.1–2.3]	37%	8.4 [6.4–9.4]	8.4 [3.3–14.5]
<b>KEYNOTE-040: 2L HNSCC (CPI naïve)</b> Phys Choice: methotrexate, docetaxel, or cetuximab	248	10.1%	2.3 [2.1–2.8]	26.5%	6.9 [5.9–8.0]	7.1 [3.7–12.4]

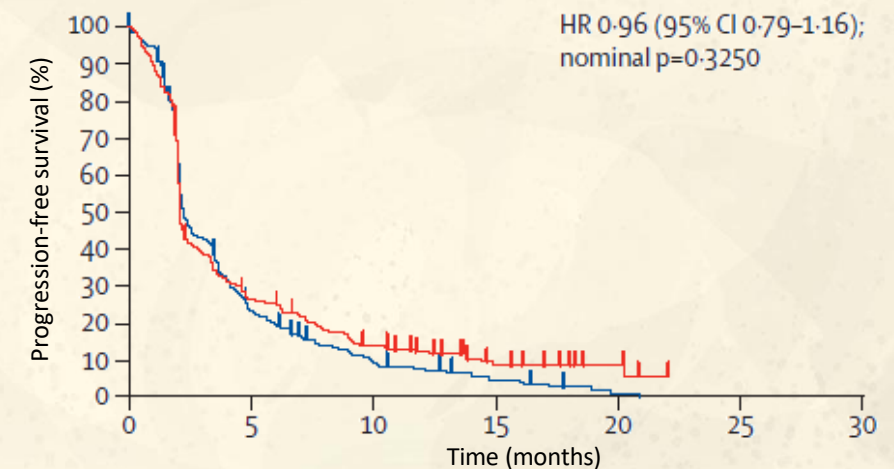
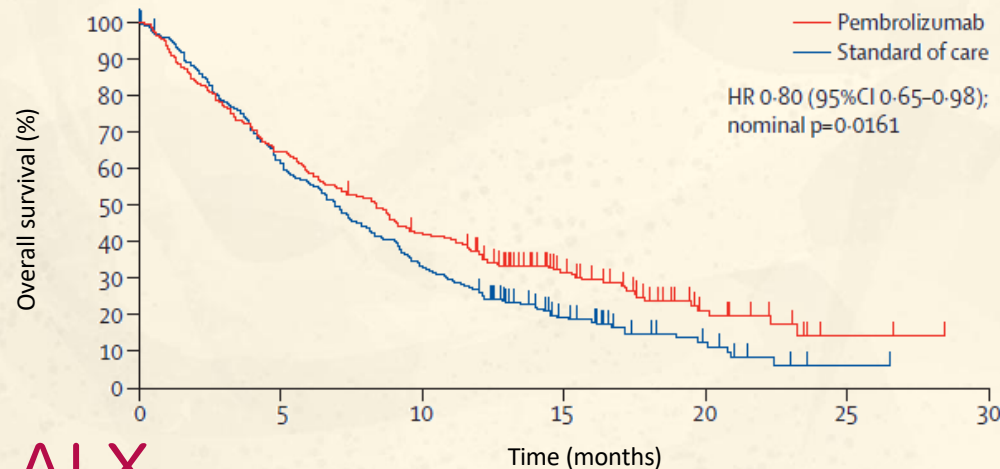


# IMMUNO-ONCOLOGY AGENTS IN CPI NAÏVE HNSCC POPULATIONS: PFS AND OS AS ENDPOINTS IN KEYNOTE-040 AND 048

## KEYNOTE-048: OS and PFS at the Second Interim Analysis in the 1L HNSCC CPI Naïve Population



## KEYNOTE-040: OS and PFS at the Final Analysis in the 2L HNSCC CPI Naïve Population

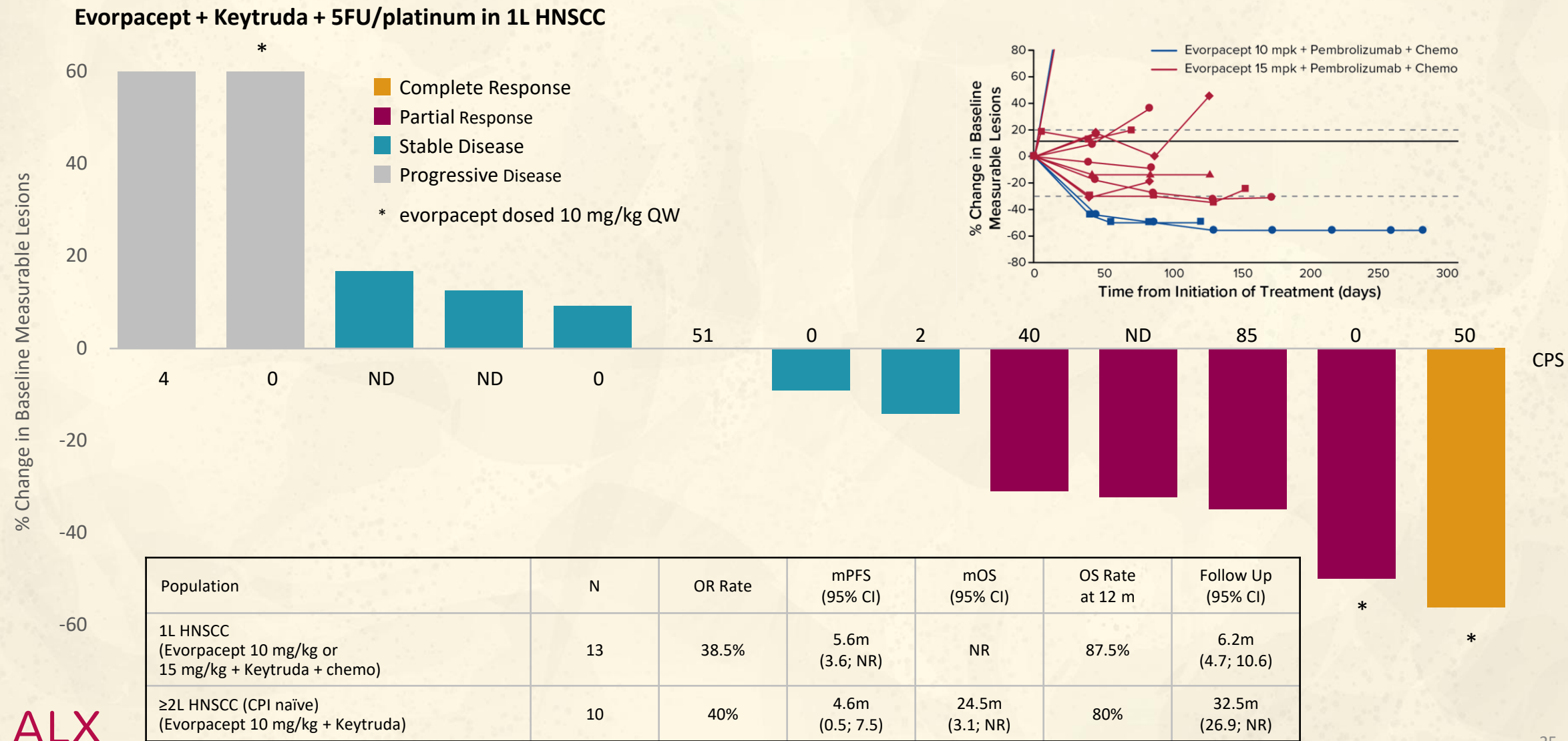




# ASPEN-01 HNSCC TRIALS: PATIENT BASELINE CHARACTERISTICS

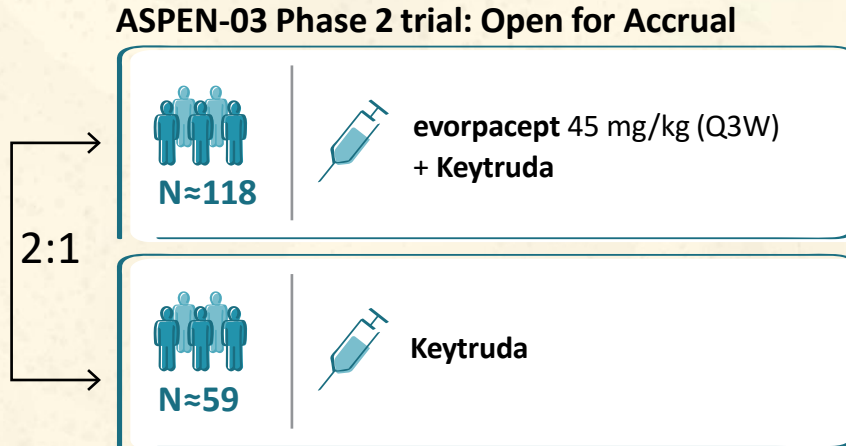
		evorpaccept + Keytruda ≥2L HSCC (N=10)	evorpaccept + Keytruda + 5FU/platinum 1L HNSCC (N=13)
Median age, years (range)		63 (35-81)	61 (45-70)
Sex, n	M	7	12
	F	3	1
Race, n	Asian	5	10
	White	4	3
	Black	1	-
ECOG PS, n	0	3	8
	1	7	5
Progressed upon prior CPI therapy, n (%)		0 (0)	0 (0)
Visceral distant metastasis, n (%)		6 (60)	7 (54)

# ASPEN-01 PHASE 1B HNSCC: EVORPACEPT + KEYTRUDA + 5FU/PLATINUM FIRST LINE CHECKPOINT NAIVE



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

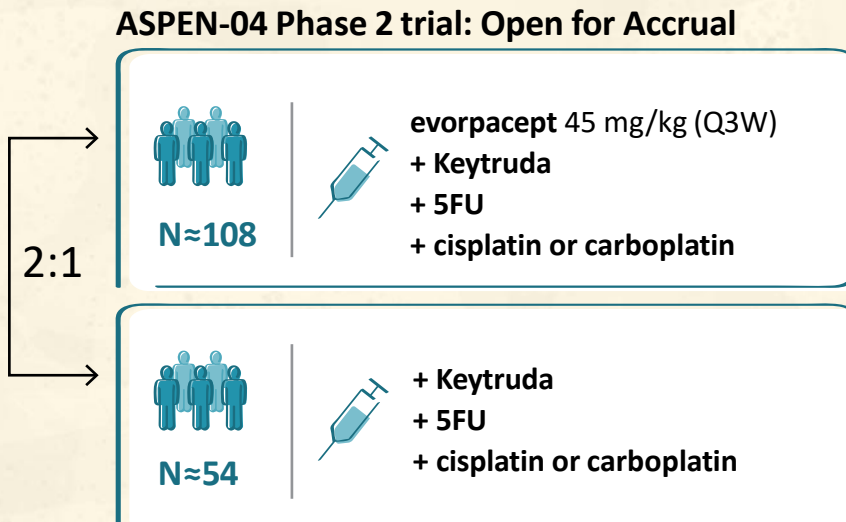
evorpacept  
+  
Keytruda



- Co-Primary Endpoints:
- 12-month OS rate
  - ORR

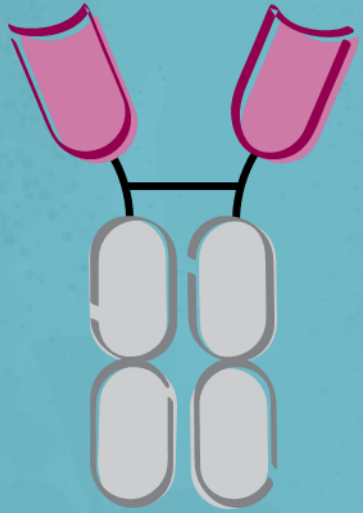
(Safety lead-in prior to randomization)

evorpacept  
+  
Keytruda  
+  
chemo



- Co-Primary Endpoints:
- 12-month OS rate
  - ORR

(Safety lead-in prior to randomization)

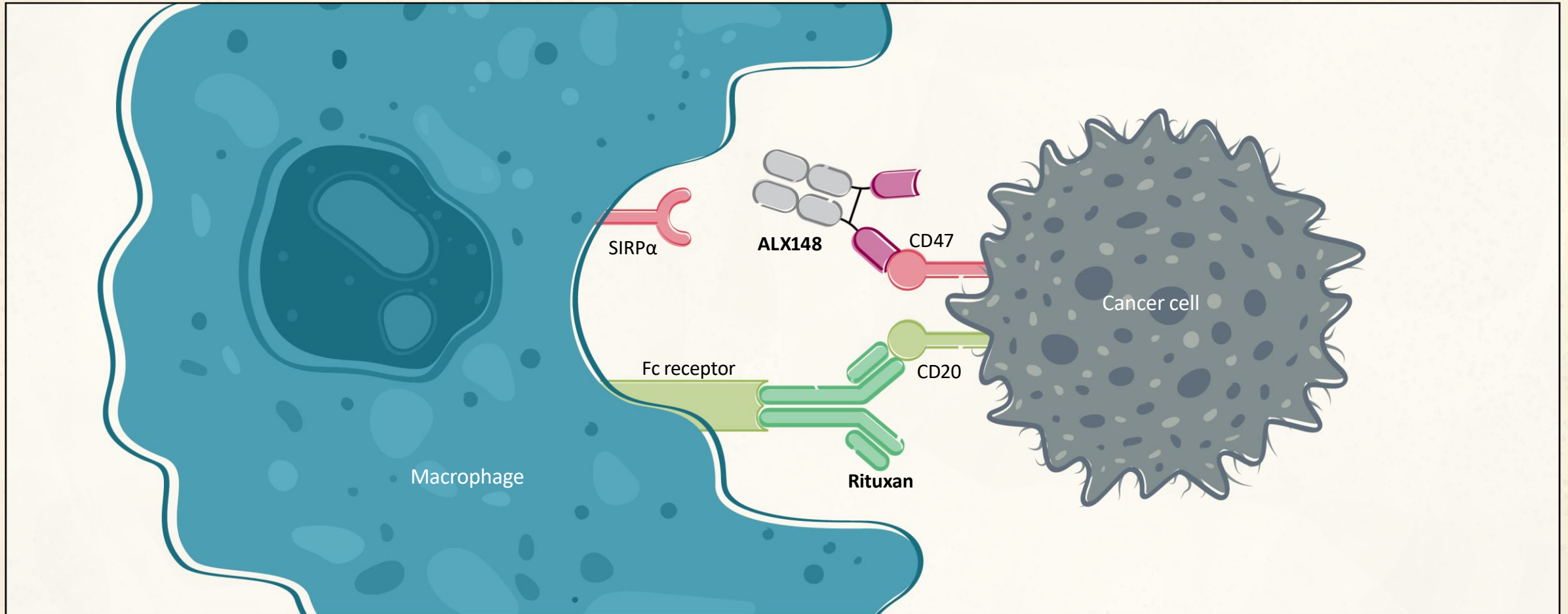


## **EVORPACEPT (ALX148) IN HEMATOLOGIC MALIGNANCIES**



# NHL TRIAL: ALX148 + RITUXAN MECHANISM OF ACTION

ALX148  
in  
NHL



**ALX148 increases antibody dependent cellular phagocytosis in combination with Rituxan**

# EVORPACEPT SHOWS CLINICAL ACTIVITY IN HEMATOLOGIC MALIGNANCY: ASPEN-01 NHL

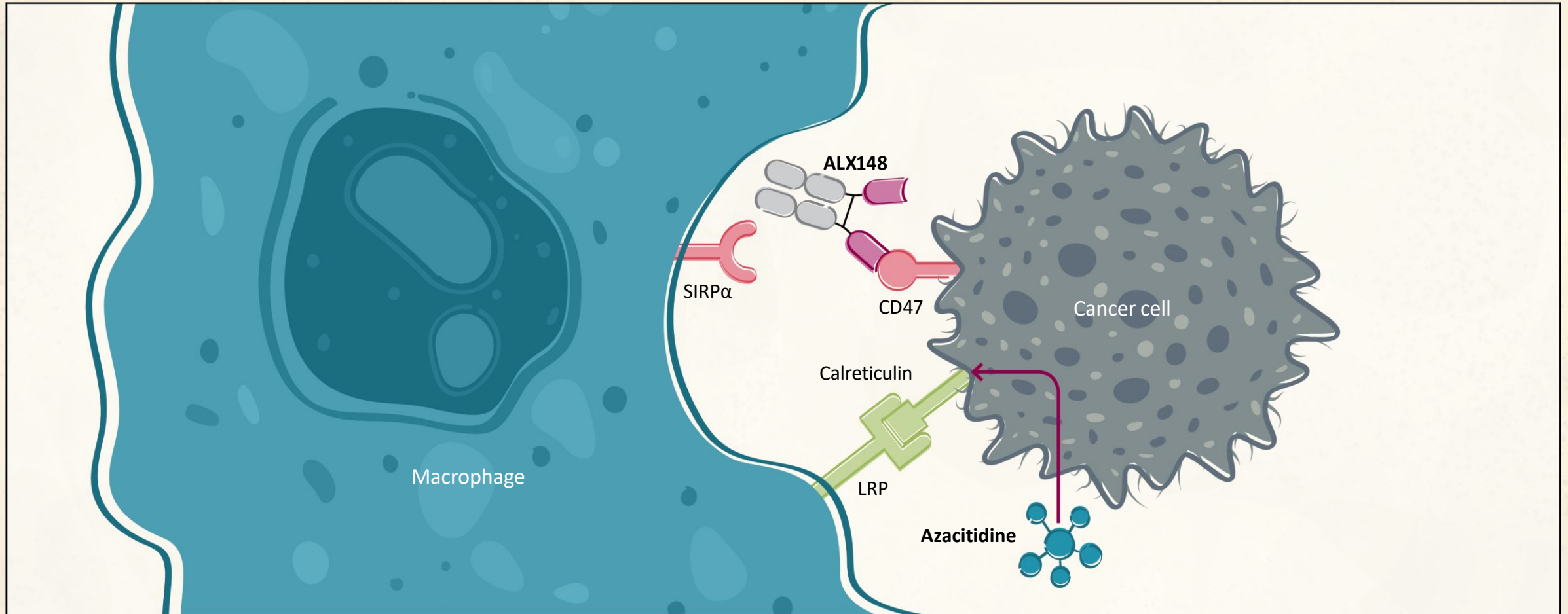
evorpacept  
in  
**NHL**

Population	Evorpacept (10 mg/kg QW) + Rituximab		Evorpacept (15 mg/kg QW) + Rituximab	
	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%

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

# MDS TRIAL: ALX148 + AZACITIDINE MECHANISM OF ACTION

ALX148  
in  
MDS



ALX148 increases pro-phagocytic signal provided by azacitidine

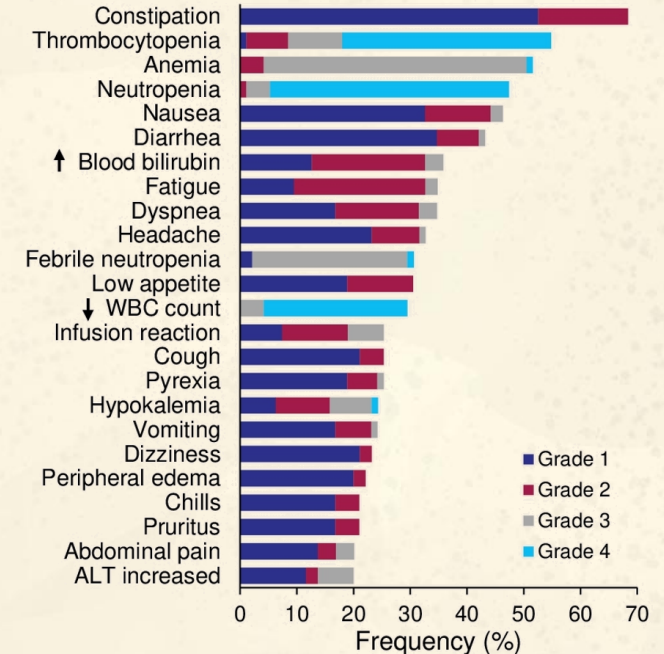


# CD47 BLOCKADE IS CLINICALLY VALIDATED WITH SIGNIFICANT OPPORTUNITY TO IMPROVE ON MAGROLIMAB

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%)

Outcome	All (N = 95)*
ORR, % <sup>†</sup>	74.7
CR, % (95% CI)	32.6 (23.4, 43.0)
Marrow CR, %	31.6
Any HI, %	58.9
Marrow CR with HI, %	16.8
SD with HI, %	10.5
DCR, median (95% CI), mo	11.1 (7.6, 13.4)
Time to CR, median (range), mo	3.7 (1.7, 7.2)
DOR, median (95% CI), mo	9.8 (8.8, 12.9)
Time to OR, median (range), mo	1.9 (0.7, 10.9)
Conversion to RBC transfusion independence, n/N (%) <sup>‡</sup>	13/37 (35.1)
PFS, median (95% CI), mo	11.6 (9.0, 14.0)
OS, median (95% CI), mo	NR (16.3, NR)

Figure 3. TEAEs by Grade (N = 95)\*



## Magrolimab monotherapy<sup>(1)</sup>

## Magrolimab with azacitidine in 1L higher risk MDS<sup>(2)</sup>

38% received 30 mg/kg QW and 59% 30 mg/kg Q2W  
magrolimab maintenance dose

- Gr3/4 TEAE (all causality): 47% anemia; 46% neutropenia; 46% thrombocytopenia
- 60% of ≥Gr3 TEAE related to magrolimab
- Gr5 TEAE (all causality): intracranial hemorrhage, myocardial ischemia, leukemia, pulmonary embolus, sepsis, pneumonia, COVID19

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



# CLINICAL ACTIVITY OF HISTORICAL BENCHMARKS IN PATIENTS WITH MDS

Population	N	ORR	CRR	mOS (m)
<b>Phase 3 AZA-002: 1L HR-MDS<sup>1</sup></b> Azacitidine	179	29%*	17%	24.5
<b>Retrospective analysis: 1L HR-MDS with TP53 mutation and complex cytogenetics<sup>2</sup></b> Azacitidine	261	~63%	~22%	10.7
<b>Phase 2: 2L MDS<sup>4</sup></b> Guadecitabine	56	14%	4%	7.1
<b>Phase 1b: ≥2L MDS<sup>3</sup></b> Venetoclax + azacitidine	38	40%	8%	-

\*CR + PR per IWG 2000 criteria. HR = higher risk.

# ASPEN-02 MDS TRIAL: DESIGN AND PATIENT BASELINE CHARACTERISTICS

## Phase 1 Design

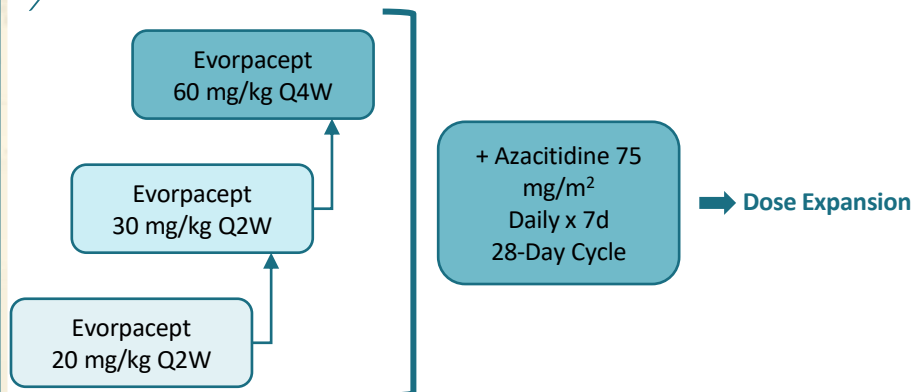


Patients:

Relapsed/refractory and treatment naïve higher risk MDS (IPSS-R >3.5)



Treatment:



Endpoint:

- safety of combination

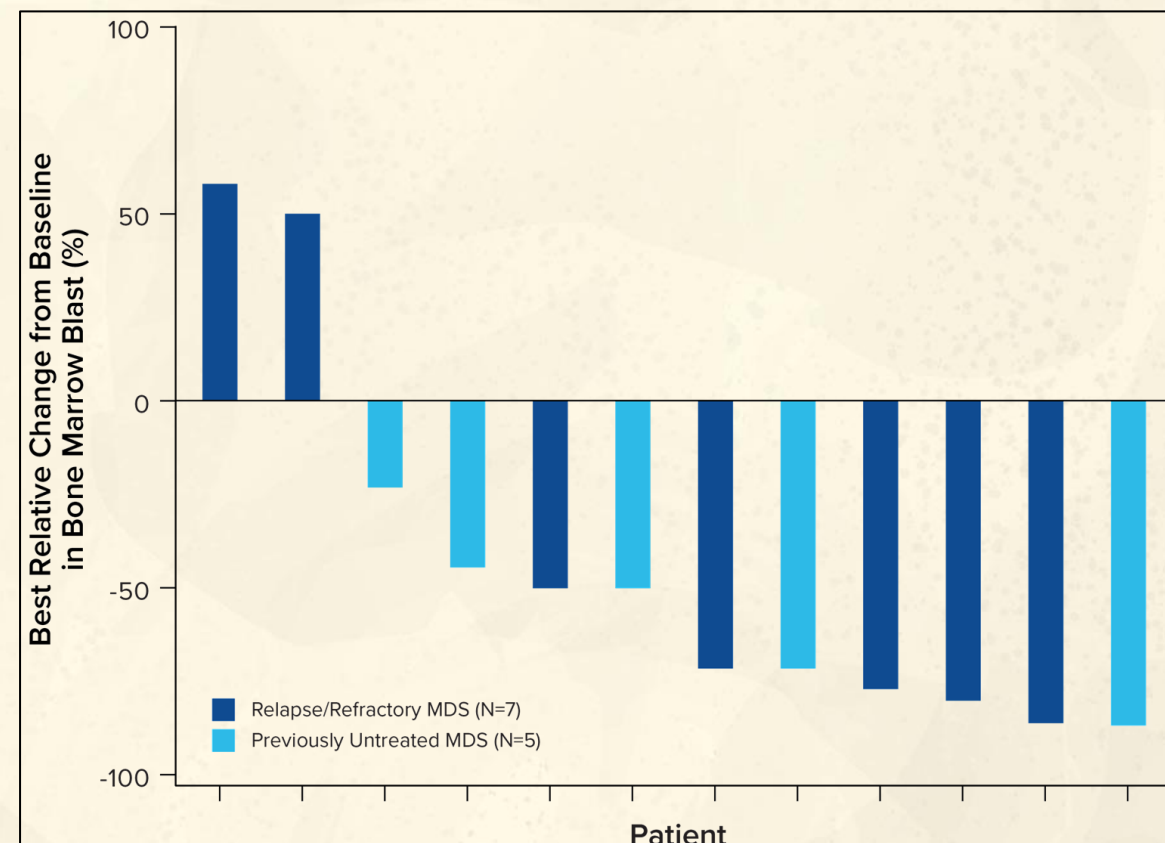
## Patient Baseline Characteristics

		evorpacept + azacitidine (N=22)
Median age, years (range)		70.5 (56 – 81)
Sex, n	F	8
	M	14
Race, n	White	17
	Black	4
	Unknown	1
ECOG PS, n	0	6
	1	16
	2	0
MDS Status, n	Previously untreated HR-MDS	9
	• Therapy related	6
	Relapsed/Refractory MDS	13
	• Prior HMA treatment	13
IPSS-R Score	Mean	6.0
	Median	5.8
	Min-Max	1.0-10.0
Mutation Status, n (%)	TP53	8 (36%)
	ASXL1	4 (18%)
	TET2	3 (14%)
	DNMT3A	2 (9%)
	SF3B1	1 (4.5%)
	SRSF2	1 (4.5%)
	RUNX1	1 (4.5%)
Cytogenetic Risk at Diagnosis, n (%)	Very Good	0
	Good	2 (9%)
	Intermediate	0
	Poor	2 (9%)
	Very Poor	8 (36%)
	Not Available	10 (45%)

# ASPEN-02 PHASE 1A MDS: EVORPACEPT + AZACITIDINE FOR PREVIOUSLY UNTREATED HIGHER RISK (HR) MDS AND RELAPSED/REFRACTORY MDS

Initial Patients' Data Presented at ASH 2021

	Previously Untreated HR-MDS (N=6)	Previously Untreated HR-MDS with TP53 mutation (N=5)	Relapsed/Refractory MDS (N=9) <sup>#</sup>
ORR	3	3	5 *
CR	2	2	0
PR	0	0	0
Marrow CR	1 with HI	1 with HI	5 *
HI	0	0	0
SD	2	1	2
PD	1	1	1



Data Cutoff 25Oct2021; Response evaluable population (n=15); \*includes 3 unconfirmed responses; <sup>#</sup>One subject with an unrelated G5 event prior to first disease assessment; On graphic, 2 subjects (1 Relapsed/Refractory and 1 Previously Untreated) with missing data and the previously described subject with an unrelated G5 event not represented.  
ORR – Objective response rate; CR – Complete response; PR – Partial response; HI – Hematologic improvement; SD – Stable disease; PD – Disease progression

# MDS TRIAL PLANS, ASPEN-02

## Phase 1 Dose Escalation: Accrual Complete



Patients:

N~18

Relapsed/refractory and treatment naïve  
higher risk MDS (IPSS-R >3.5)



Treatment:

**evorpacept**  
20 mg/kg (Q2W)  
30 mg/kg (Q2W)  
or 60 mg/kg (Q4W)  
+  
**azacitidine**



Endpoint:

- safety of combination

## Phase 1 Dose Expansion: Open for Accrual



Patients:

N~40

Treatment naïve higher risk MDS  
(IPSS-R >3.5)



Treatment:

**evorpacept**  
40 mg/kg (Q4W)  
or 60 mg/kg (Q4W)  
+  
**azacitidine**



Endpoint:

- safety of combination

## Phase 2 Randomized Trial



Patients:

Treatment naïve higher risk MDS  
(IPSS-R >3.5)



Treatment:

**evorpacept**  
recommended phase 2 dose  
+  
**azacitidine**  
  
**vs.**  
**azacitidine**



Endpoint:

- complete response rate (CRR)



# AML TRIAL PLANS, ASPEN-05

## Phase 1 Dose Escalation and Expansion: On pause after dose escalation



**Patients:**  
**N~20+**

Relapsed/refractory AML or previously untreated AML who are not considered suitable for intensive induction therapy



### Treatment

#### evorpacept

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

+ Venclexta  
+ azacitidine



**Endpoint:** • safety of combination, recommended phase 2 dose

## Phase 2:



**Patients:**  
**N~84**

Previously untreated AML who are not considered suitable for intensive induction therapy



### Treatment

#### evorpacept

recommended phase 2 dose

+ Venclexta  
+ azacitidine



**Endpoint:** • complete remission rate



## **ALX ONCOLOGY MILESTONES AND FINANCIAL INFORMATION**

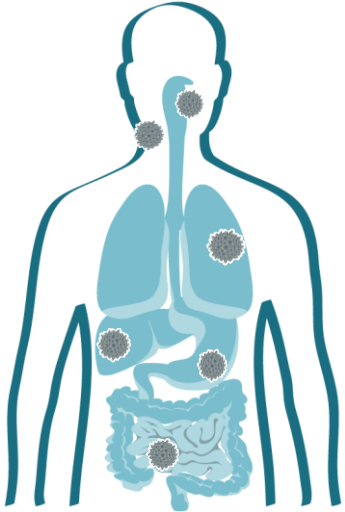
# EVORPACEPT IS DESIGNED TO BE A CORNERSTONE OF CANCER TREATMENTS

Evorpaccept's ongoing clinical development plan encompasses significant development opportunities...

		Indication	Combination Agent	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Fast Track	Collaboration Partner
Evorpaccept 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 (ASPEN-01)							
			Herceptin + Cyramza + Paclitaxel (ASPEN-06)						✓	Lilly
		Breast Cancer	Zanidatamab							zyme works
	HEMATOLOGY	Urothelial Cancer	Padcev (ASPEN-07)							
		MDS Myelodysplastic Syndromes	Azacitidine (ASPEN-02)							
		AML Acute Myeloid Leukemia	Azacitidine + Venclexta (ASPEN-05)							
		NHL Non-Hodgkin's Lymphoma	Rituximab (ASPEN-01)							
		ALTA 002*	Advanced Cancer							TALLAC THERAPEUTICS

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

And is designed to be active across more tumor types and anti-cancer combinations

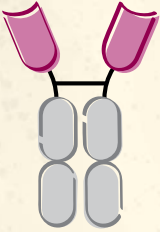


Continued expansion of immuno-oncology activity across tumor types



Combined with standard of care and emerging anti-cancer modalities

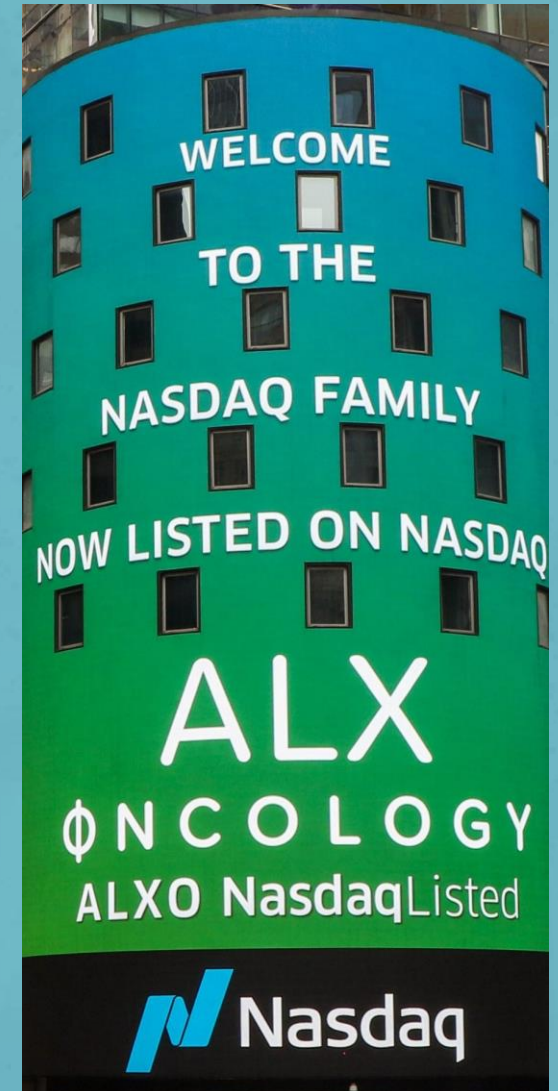
# 2022 FOCUSED ON DRIVING CLINICAL DEVELOPMENT

	Completed	2022	2023	2024
 <b>Evorpcept</b>	<b>ASPEN-01 (Phase 1b)</b> Updated gastric/GEJ and HNSCC trial data at SITC	<b>ASPEN-06 (Phase 2/3)</b> Randomized gastric/GEJ cancer trial first patient dosed March 2022	<b>ASPEN-06 (Phase 2)</b> Randomized gastric/GEJ cancer trial presentation	<b>ASPEN-03 (Phase 2)</b> Randomized HNSCC trial presentation with pembrolizumab
	<b>ASPEN-02 (Phase 1a)</b> Initial MDS trial presentation at ASH	<b>ASPEN-05 (Phase 1a)</b> AML dose escalation presentation	<b>ASPEN-02 (Phase 1b)</b> MDS dose optimization trial presentation	<b>ASPEN-04 (Phase 2)</b> Randomized HNSCC trial presentation with pembrolizumab and chemo
	<b>ASPEN-03 Initiation (Phase 2)</b> Randomized HNSCC trial with pembrolizumab	<b>ASPEN-07 (Phase 1) initiation</b> Urothelial carcinoma with enfortumab vedotin-ejfv		
	<b>ASPEN-04 Initiation (Phase 2)</b> Randomized HNSCC trial with pembrolizumab and chemo	Ongoing collaborations (Zymeworks) and Investigator Sponsored Trials (NHL, CRC)		
	<b>ASPEN-05 Initiation (Phase 1a)</b> AML trial			
<b>Preclinical pipeline</b>	Built pipeline through ScalmiBio acquisition and Tallac collaboration	Select clinical development candidates from preclinical pipeline	File IND for ALTA-002	



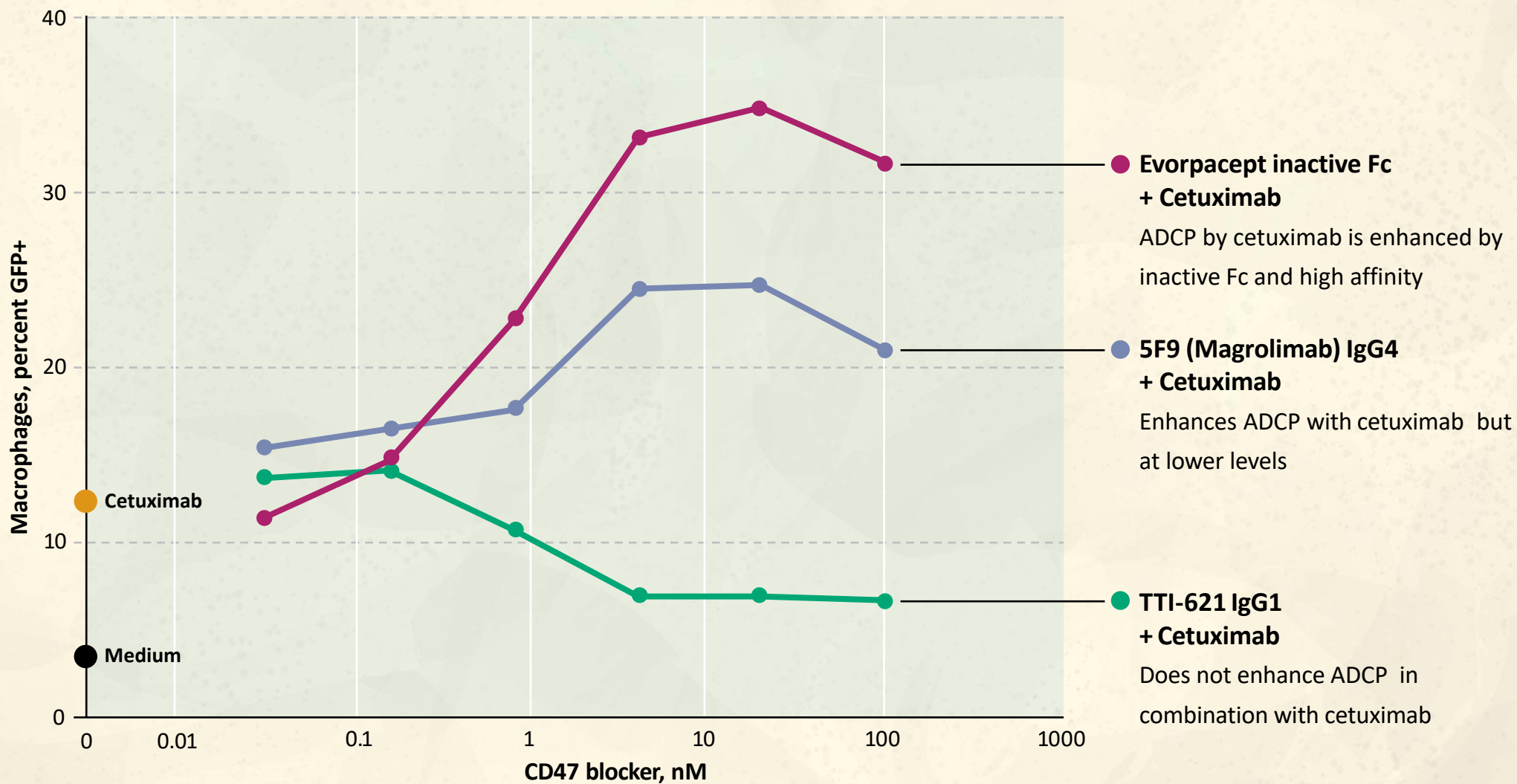
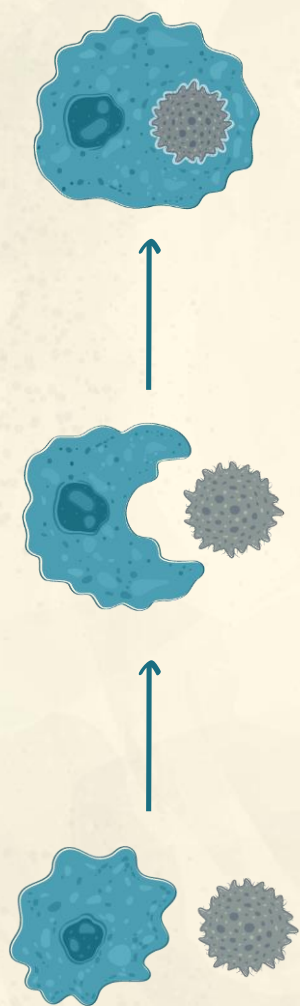
## FINANCIAL INFORMATION

- 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, cash equivalents and investments as of June 30, 2022:
  - \$324.2 million
- Expected cash runway through the fourth quarter of 2024

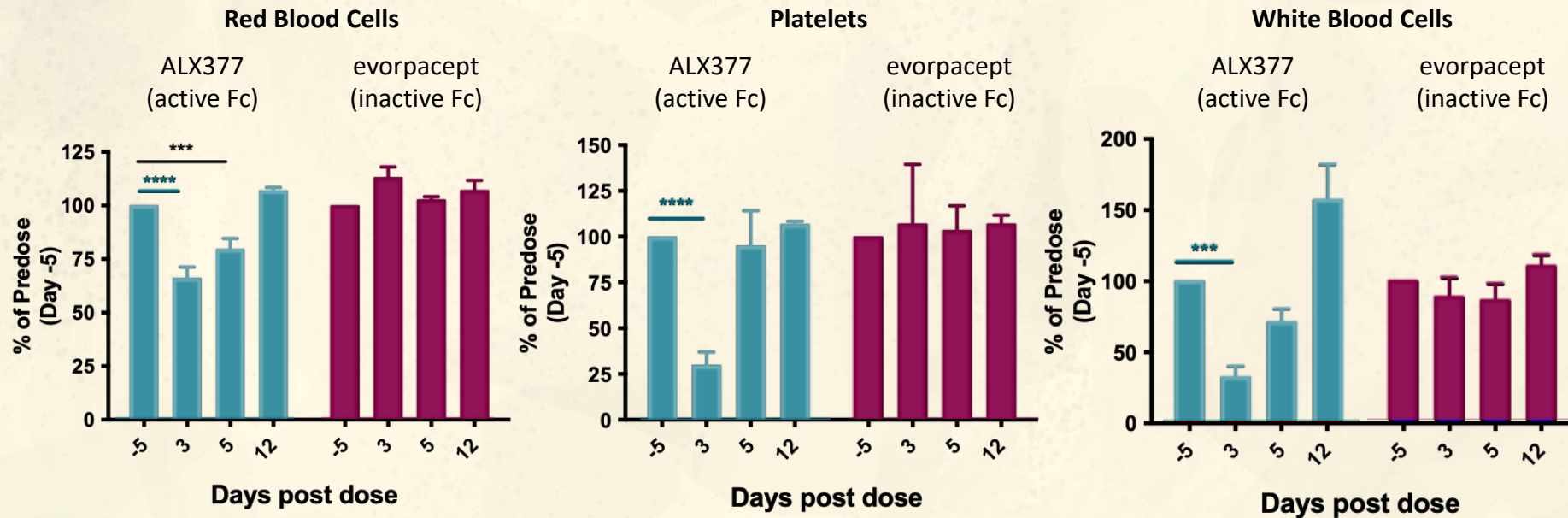


# APPENDIX

# EVORPACEPT DEMONSTRATES SUPERIOR PHAGOCYTOSIS



# INACTIVE FC SHOWS REDUCED CYTOPENIA IN MICE IN VITRO



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

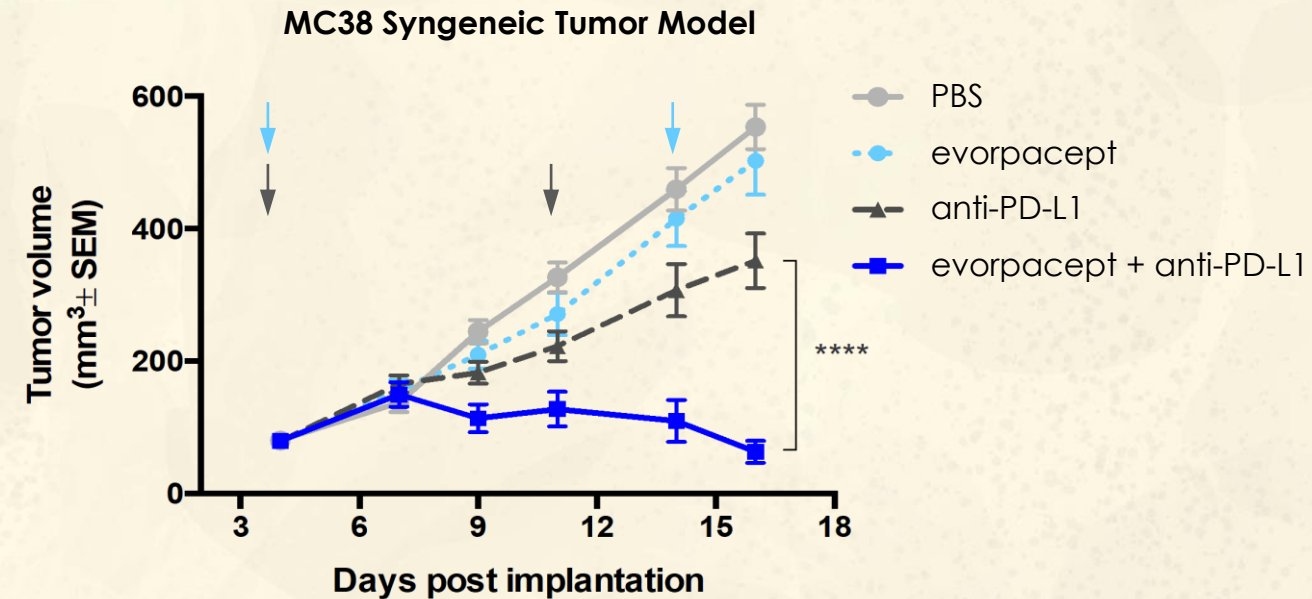
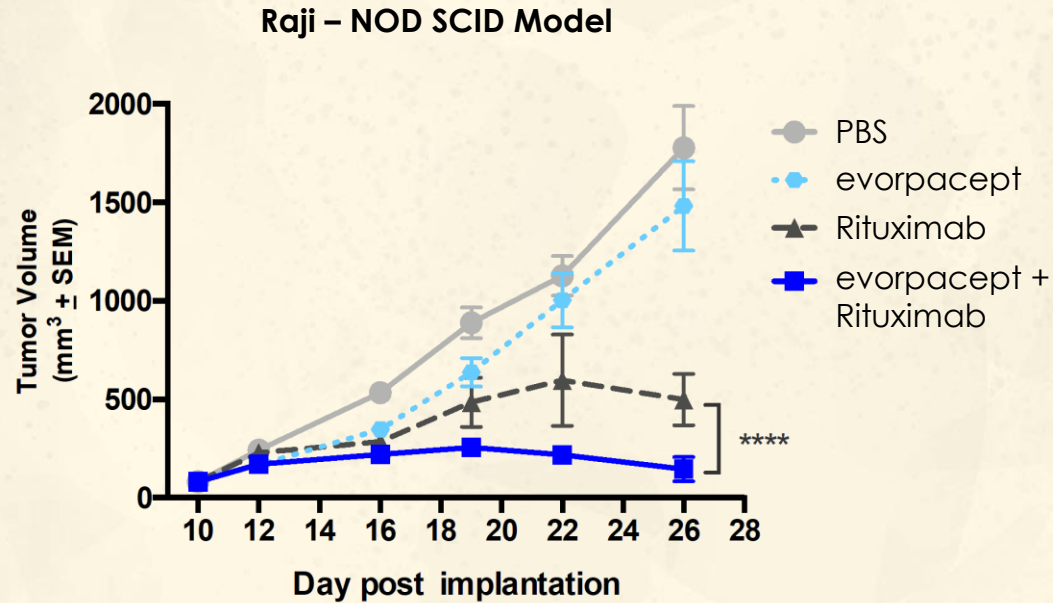
\*\*\*\*p<0.0001, \*\*\*p<0.001

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

Inactive Fc is the core determinant of safety profile



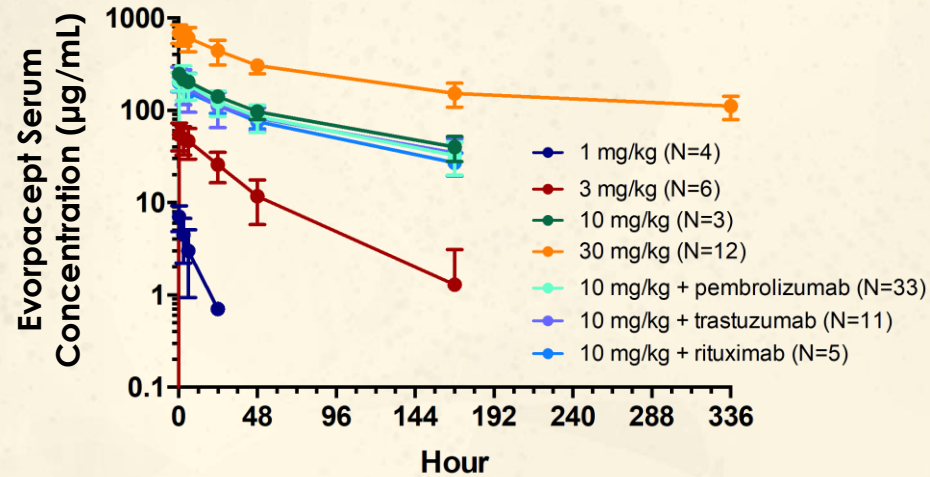
# COMBINATION EFFICACY WITH TAA (RITUXIMAB) ANTIBODIES AND CHECKPOINT INHIBITOR (ATEZOLIZUMAB)



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

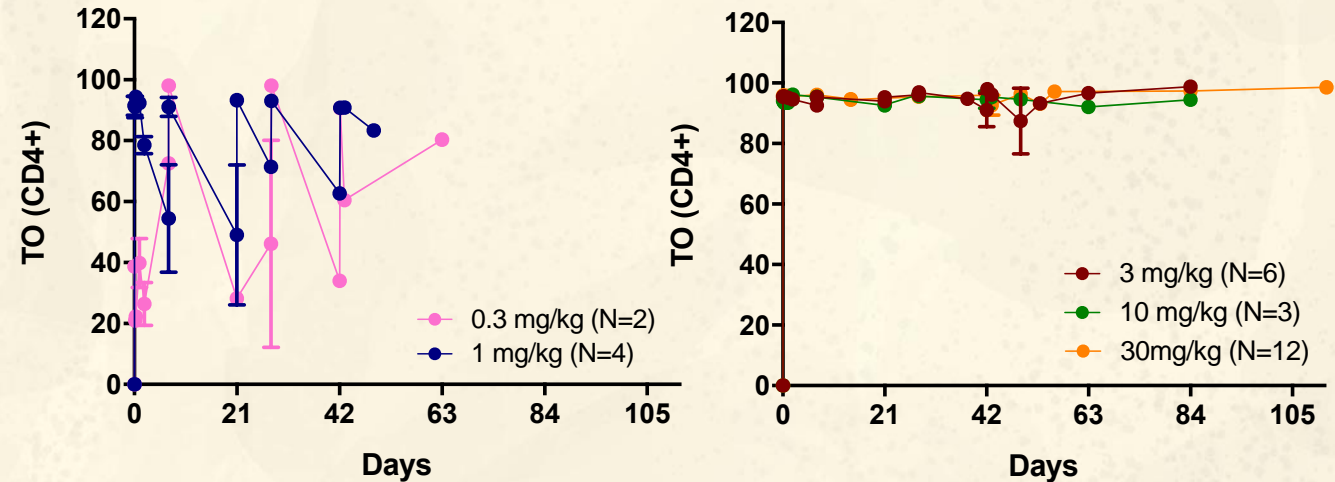
# EVORPACEPT CLINICAL PHARMACOKINETICS AND CD47 TARGET OCCUPANCY

Evorpaccept Serum Levels for Cycle 1 Day 1



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

CD47 Target Occupancy by Evorpaccept



- Near complete CD47 target occupancy (TO) by evorpaccept 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

# NHL TOLERABILITY

Selected hematologic, treatment related adverse events	evorpacept + Rituximab (N=33) <sup>1</sup>		CC-90002 + Rituximab (n=26) <sup>2</sup>		5F9 (magrolimab) + Rituximab (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%

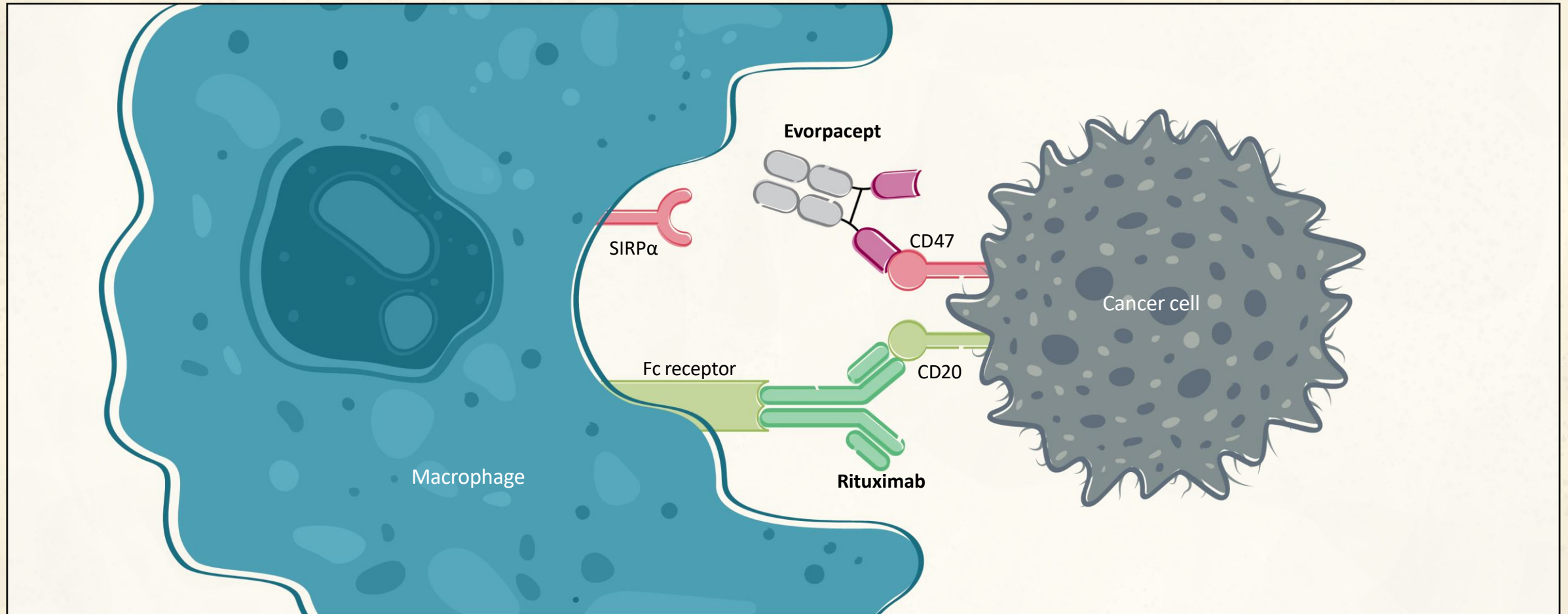
<sup>1</sup>ASH 2020 Abstract 3016

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

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

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

# NHL TRIAL: EVORPACEPT + RITUXIMAB MECHANISM OF ACTION



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



# ASPEN-01 NHL PROOF-OF-PRINCIPLE TRIAL

## Phase 1b NHL cohorts



relapsed/Refractory NHL,  
prior regimen with Rituximab



Treatment:

**evorpacept** 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

		evorpacept 10 mg/kg QW + Rituximab (n=22)	evorpacept 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

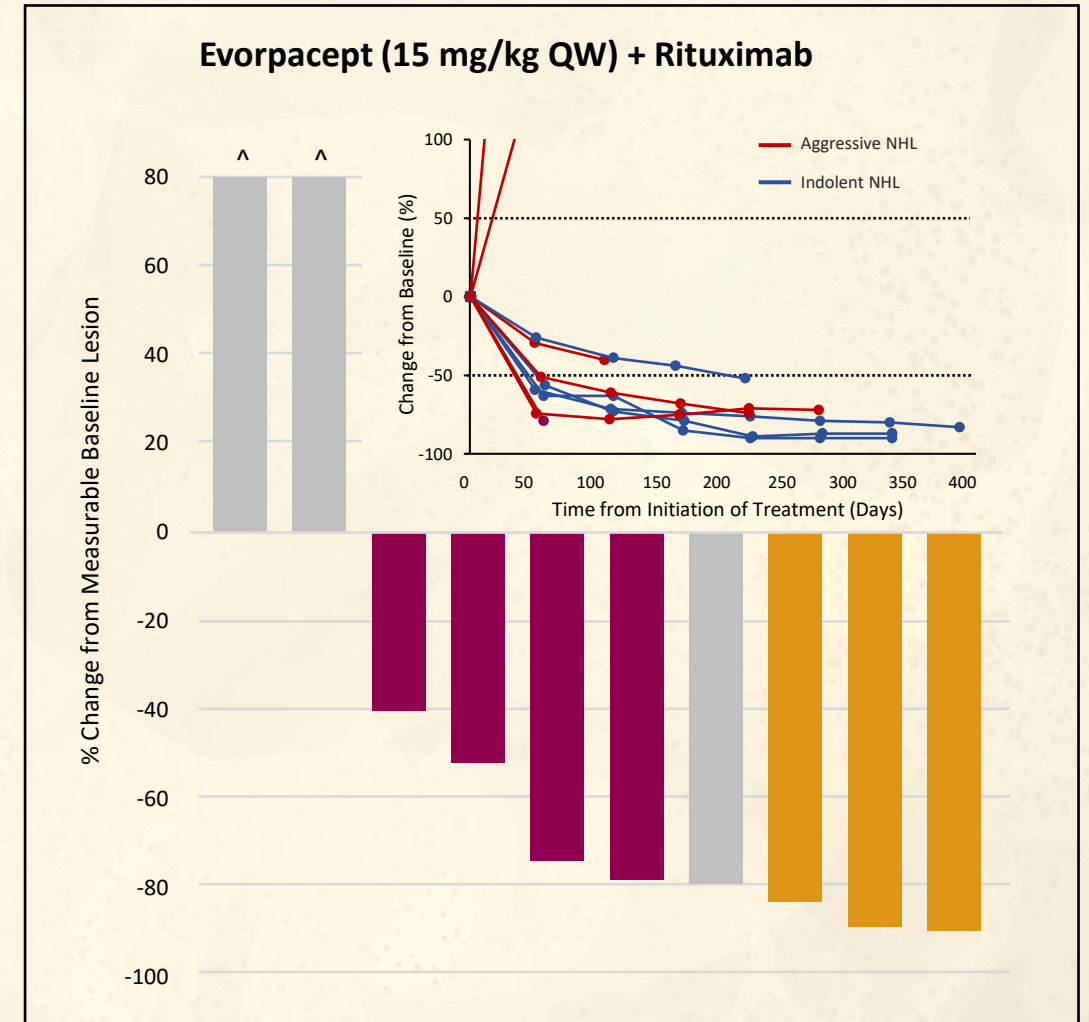
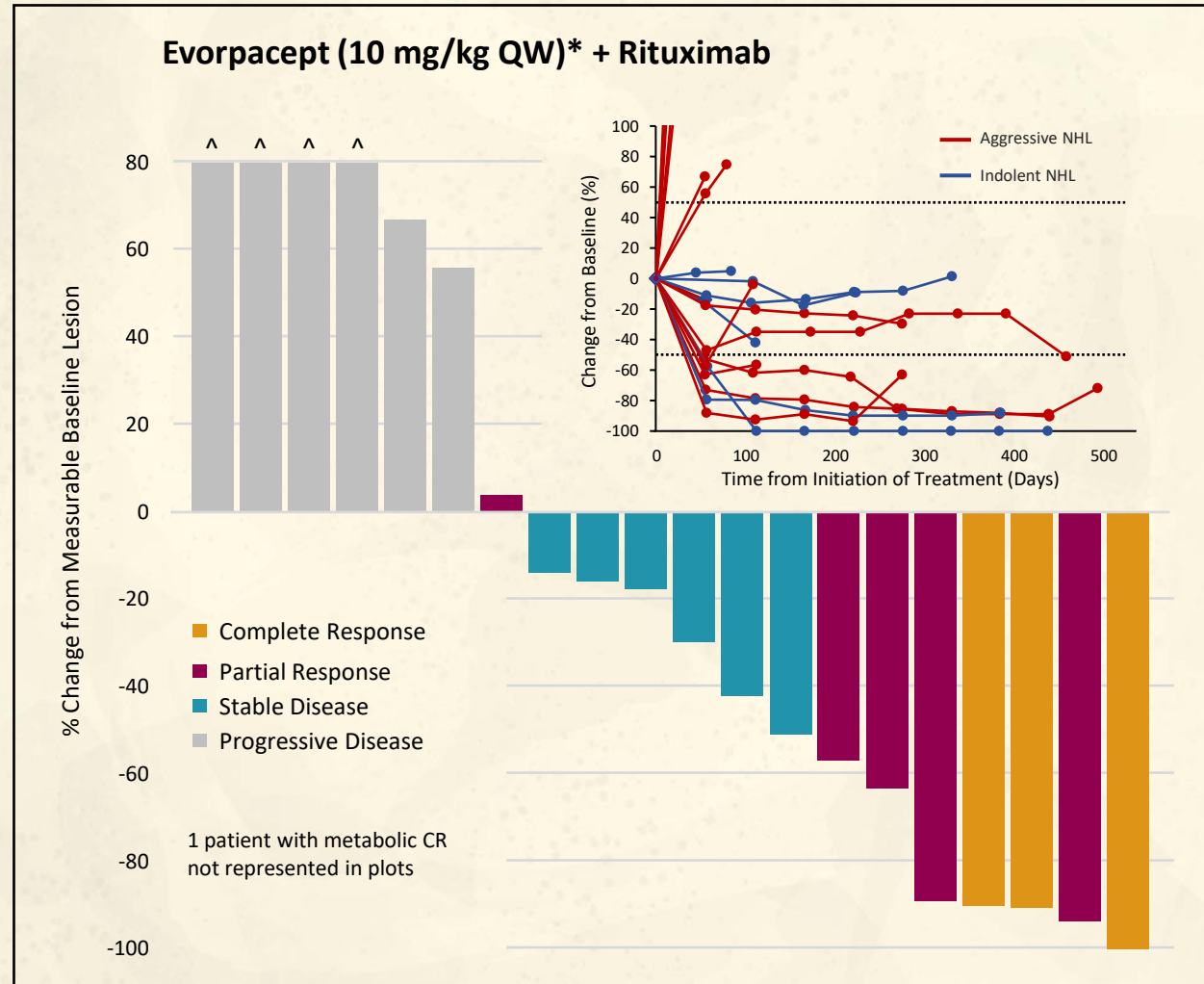
# ASPEN-01 NHL: PRELIMINARY CLINICAL TOLERABILITY

## evorpacept + Rituximab (N=33)

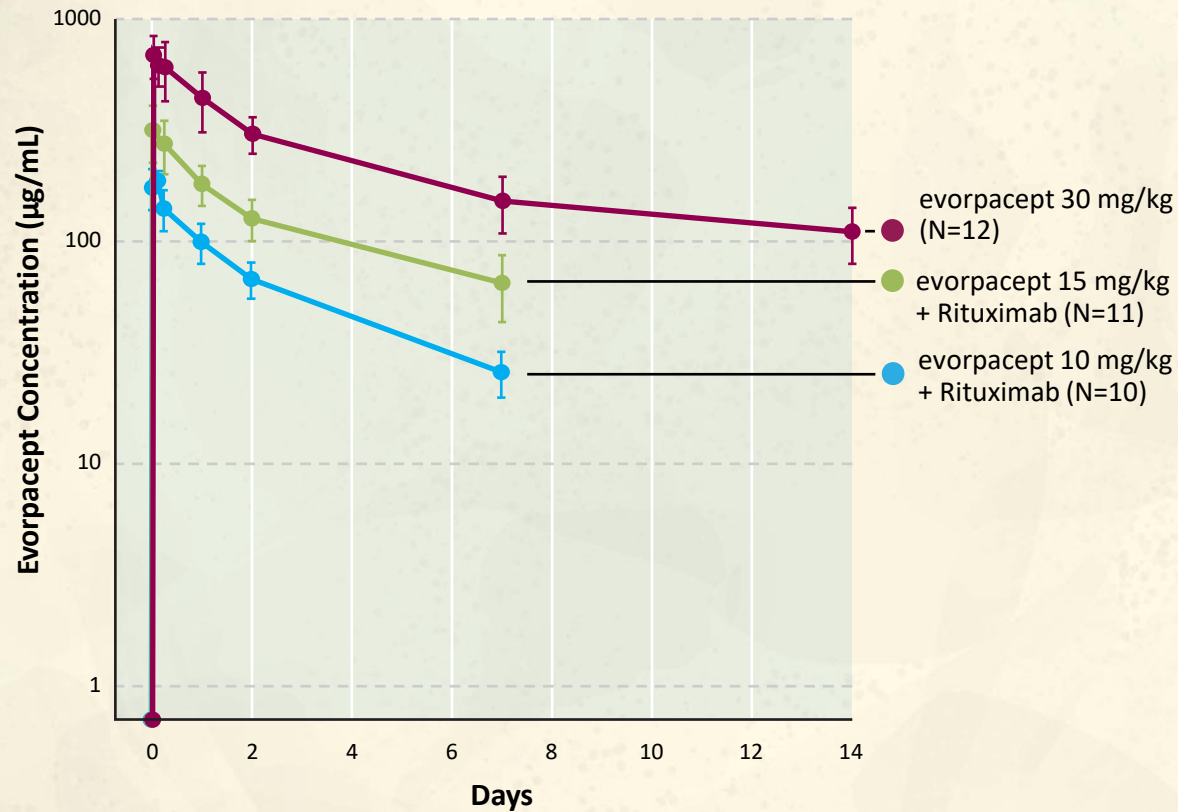
Treatment Related Adverse Event	Total n (%)	≥Grade 3 n (%)
Rash	8 (24.2)	—
Fatigue	4 (12.1)	—
Nausea	2 (6.1)	—
Neutrophil Count Decreased	2 (6.1)	2 (6.1)
Anemia	2 (6.1)	1 (3.0)
Myalgia	2 (6.1)	—
Pruritus	2 (6.1)	—

Data Cutoff: October 1, 2020

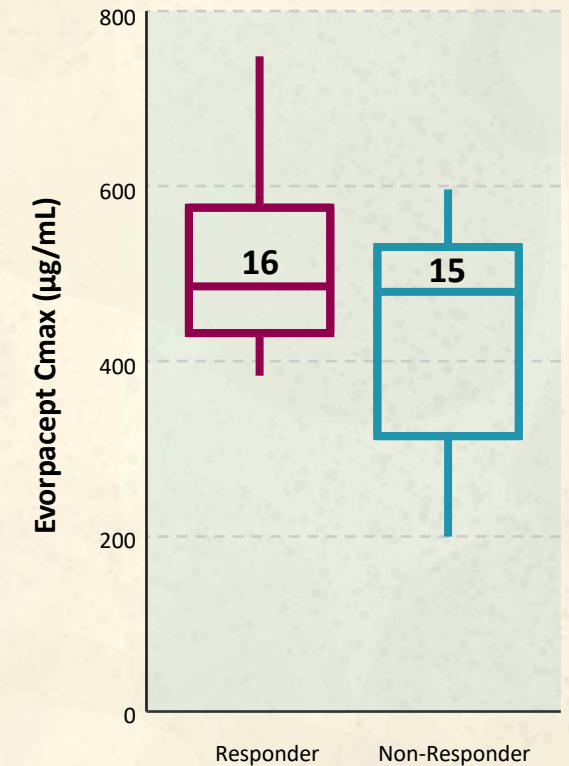
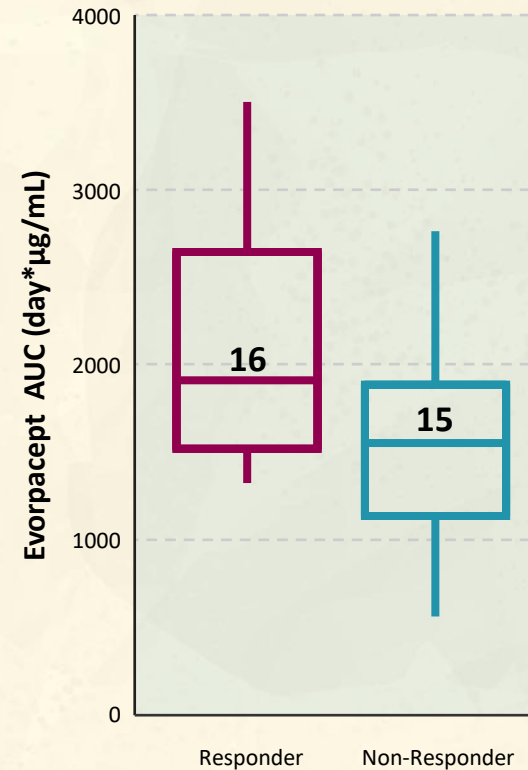
# ASPEN-01 NHL: CLINICAL ACTIVITY OF EVORPACEPT + RITUXIMAB BY PATIENT



# ASPEN-01 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**

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

HER2 GC Population	N	ORR	DOR (m) [95% CI]	PFS (m) [95% CI]	OS (m) [95% CI]	OS rate at 12 m	Follow up (m) [95% CI]
2L GC evorpaccept + Herceptin + Cyramza + paclitaxel	18	72%	14.8 [3.9–NR]	17.1 [5.4–NR]	17.1 [9.8–NR]	79%	14.5 [7.2–19.0]
≥2L Gastric ramucirumab/paclitaxel RAINBOW <sup>1</sup>	330	28%	4.4 [IQR 2.8–7.5]	4.4 [4.2–5.3]	9.6 [8.5–10.8]	40%	
≥2L Gastric trastuzumab/ram/paclitaxel <sup>2</sup>	50	52%	5.1 [3.3–6.9]	7.4 [6.5–8.3]	13.6 [9.6–17.5]	-	22.9
2L Gastric trastuzumab-deruxtecan DESTINY 02 <sup>3</sup>	79	38%	8.1 [4.1–NE]	5.5 [4.2–7.3]	-	-	5.7
≥3L Gastric trastuzumab-deruxtecan DESTINY 01 <sup>4</sup>	126	41%	11.3 [5.6–NE]	5.6 [4.3–6.9]	12.5 [9.6–14.3]	52%	
≥2L Gastric evorpaccept (10 mg/kg) + Herceptin	19	21%	8.7 [5.6; NR]	2.2 [1.9 ; 5.5]	8.1 [3.4 ; 12.6]	38%	27.0
≥3L Gastric Irinotecan or Paclitaxel DESTINY 01 Control Arm <sup>4</sup>	62	11%	3.9	3.5	8.4	29%	

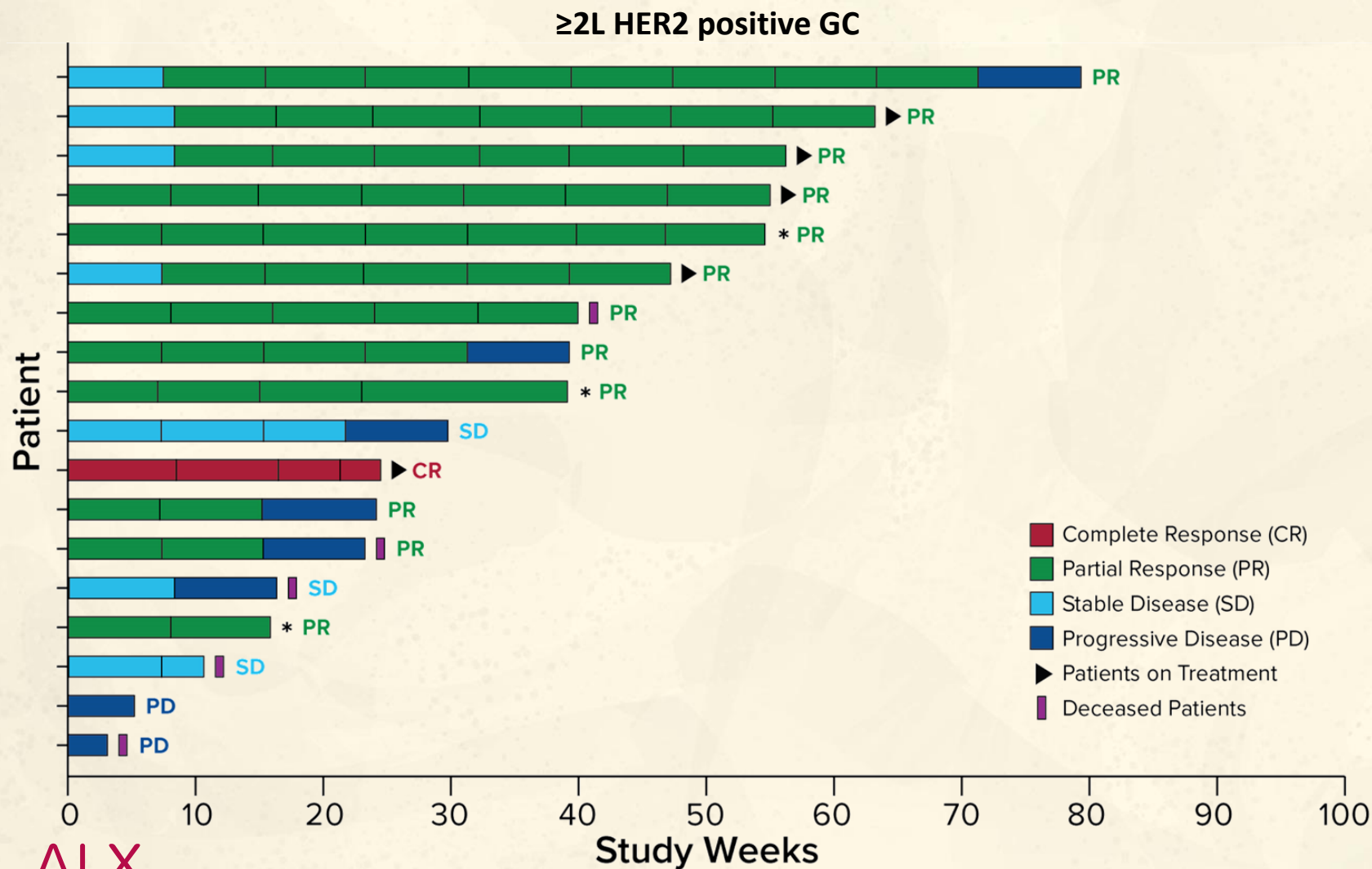
# ASPEN-01 PHASE 1B ≥2 LINE GC TRIAL: EVORPACEPT + HERCEPTIN + CYRAMZA + PACLITAXEL TREATMENT EMERGENT ADVERSE EVENTS

Grade Evorpacept Dose QW	Evorpacept + Trastuzumab + Ramucirumab + Paclitaxel (N=18) / Adverse Event, n (%)					
	ALL Causality			Evorpacept - related		
	G1-2	G3	G4	G1-2	G3	G4
Neutrophil Count Decreased	3 (17)	5 (28)	3 (17)	–	–	–
Epistaxis	9 (50)	–	–	–	–	–
Peripheral Neuropathy / Peripheral Sensory Neuropathy	8 (44)	1 (6)	–	–	–	–
Decreased Appetite	8 (44)	–	–	–	–	–
Fatigue	7 (39)	1 (6)	–	2 (11)	–	–
Anemia	3 (17)	4 (22)	–	1 (6)	–	–
Hypertension	–	6 (33)	–	–	–	–
Abdominal Pain / Abdominal Pain Upper	5 (28)	–	–	1 (6)	–	–
Headache	5 (28)	–	–	1 (6)	–	–
Stomatitis	5 (28)	–	–	1 (6)	–	–
Alanine Aminotransferase Increased	4 (22)	–	–	–	–	–
Alopecia	4 (22)	–	–	–	–	–
Aspartate Aminotransferase Increased	3 (17)	1 (6)	–	–	–	–
Asthenia	3 (17)	1 (6)	–	–	–	–
Diarrhea	4 (22)	–	–	3 (17)	–	–
Insomnia	4 (22)	–	–	–	–	–
Rash/Dermatitis Acneiform	4 (22)	–	–	4 (22)	–	–
Pruritis	3 (17)	–	–	2 (11)	–	–
Urticaria	3 (17)	–	–	3 (17)	–	–
Back Pain	2 (11)	–	–	1(6)	–	–
Diverticulitis	1 (6)	1 (6)	–	–	–	–
Dysphagia	1 (6)	1 (6)	–	–	–	–
Hypophosphatemia	1 (6)	1 (6)	–	–	–	–
Platelet Count Decreased	1 (6)	1 (6)	–	–	–	–
Hydronephrosis	–	1 (6)	–	–	–	–
Lymphocyte Count Decreased	–	1 (6)	–	–	1 (6)	–
Non-Cardiac Chest Pain	–	1 (6)	–	–	–	–
Urinary Tract Infection	–	1 (6)	–	–	–	–
Vision Blurred	1 (6)	–	–	1 (6)	–	–

Data Cutoff September 1, 2021

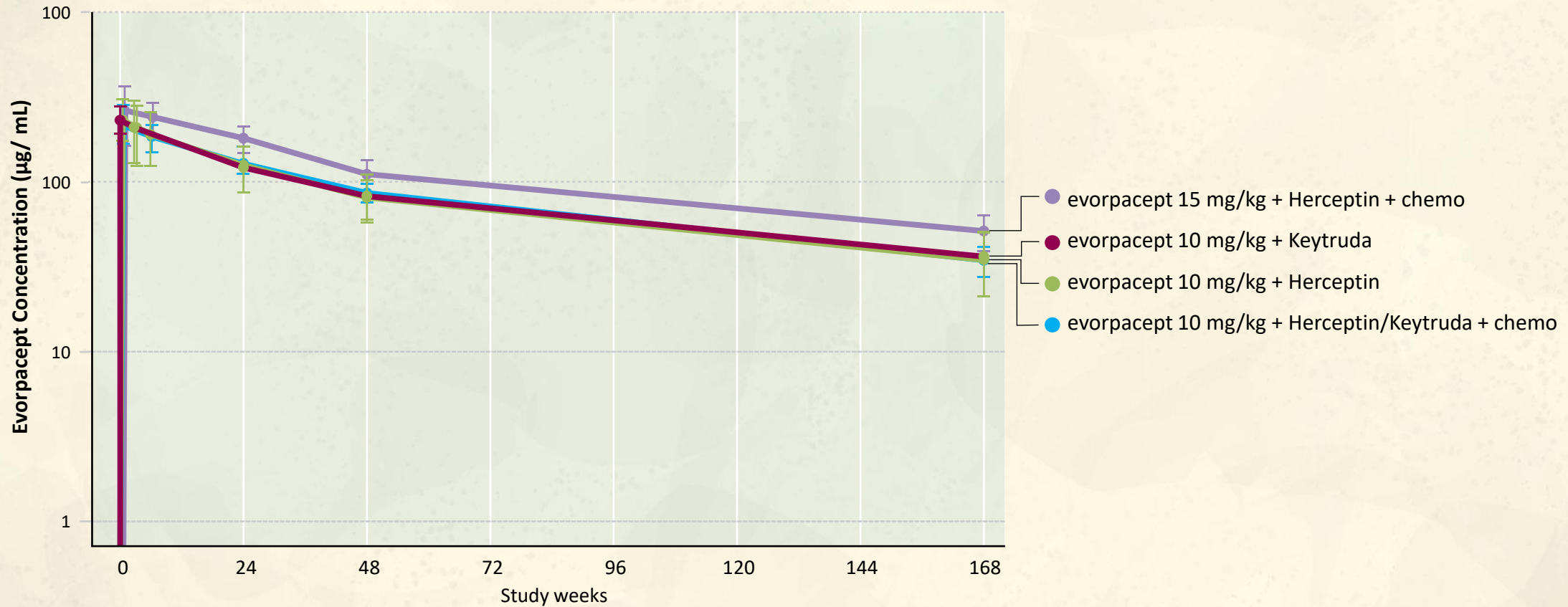
Evorpacept: 10 mg/kg (n=3) & 15 mg/kg (n=15); All TEAEs occurring in ≥4 patients. For cases of TEAEs Grade ≥3 and any TRAE, all AEs are listed irrespective of patient numbers.

# ASEPN-01 PHASE 1B $\geq 2$ LINE GC TRIAL: EVORPACEPT + HERCEPTIN + CYRAMZA + PACLITAXEL BEST OVERALL AND DURATION OF RESPONSE WHILE ON TREATMENT

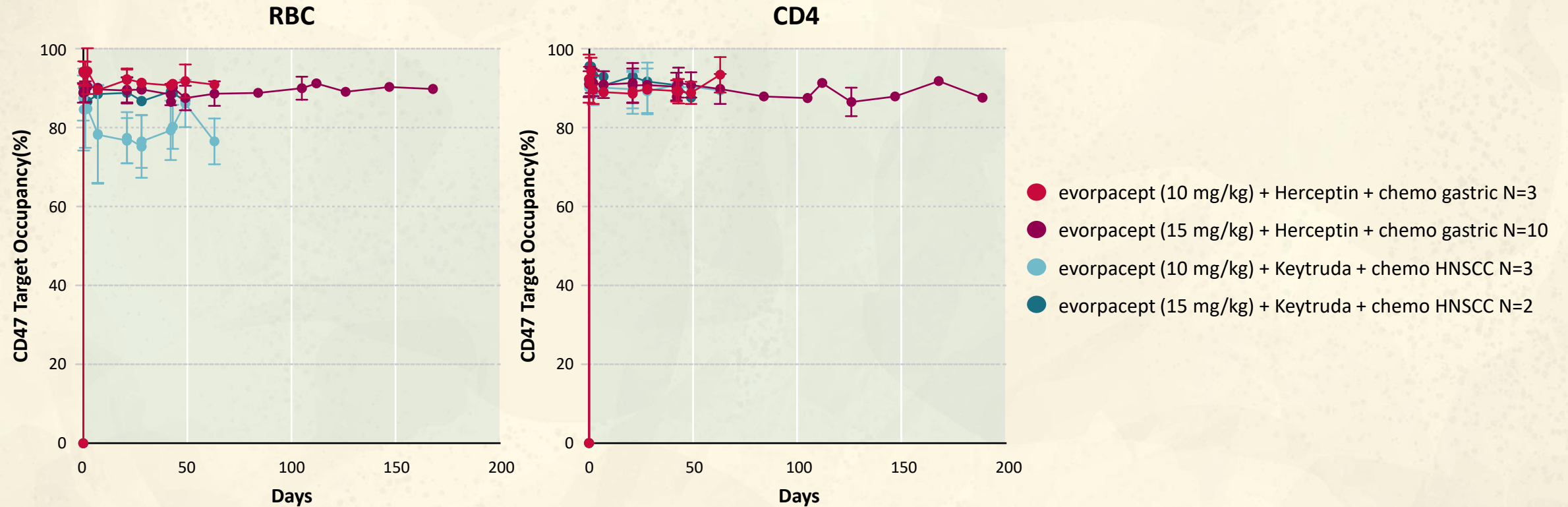




# EVORPACEPT PK FOLLOWING COMBINATION THERAPIES IS COMPARABLE WITH AND WITHOUT CHEMOTHERAPY



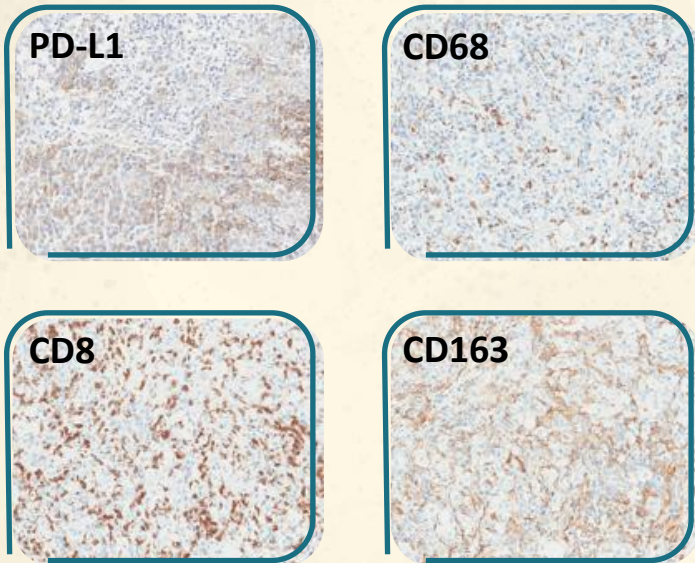
# NEAR COMPLETE CD47 TARGET OCCUPANCY IS MAINTAINED THROUGHOUT EVORPACEPT DOSING INTERVAL WHEN COMBINED WITH CHEMOTHERAPY CONTAINING REGIMENS



## PRE-TREATMENT IHC RESULTS IN HOT AND COLD TUMORS

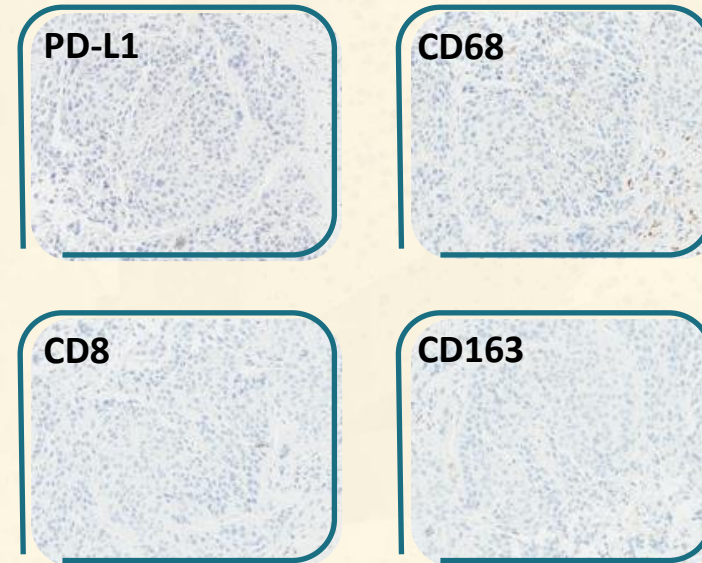
### HNSCC PATIENT 1 (PD-L1 POSITIVE) AND PATIENT 2 (PD-L1 NEGATIVE)

**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.



# ASPEN-01 PHASE 1B FIRST LINE HNSCC: EVORPACEPT + KEYTRUDA + 5FU/PLATINUM TREATMENT RELATED ADVERSE EVENTS

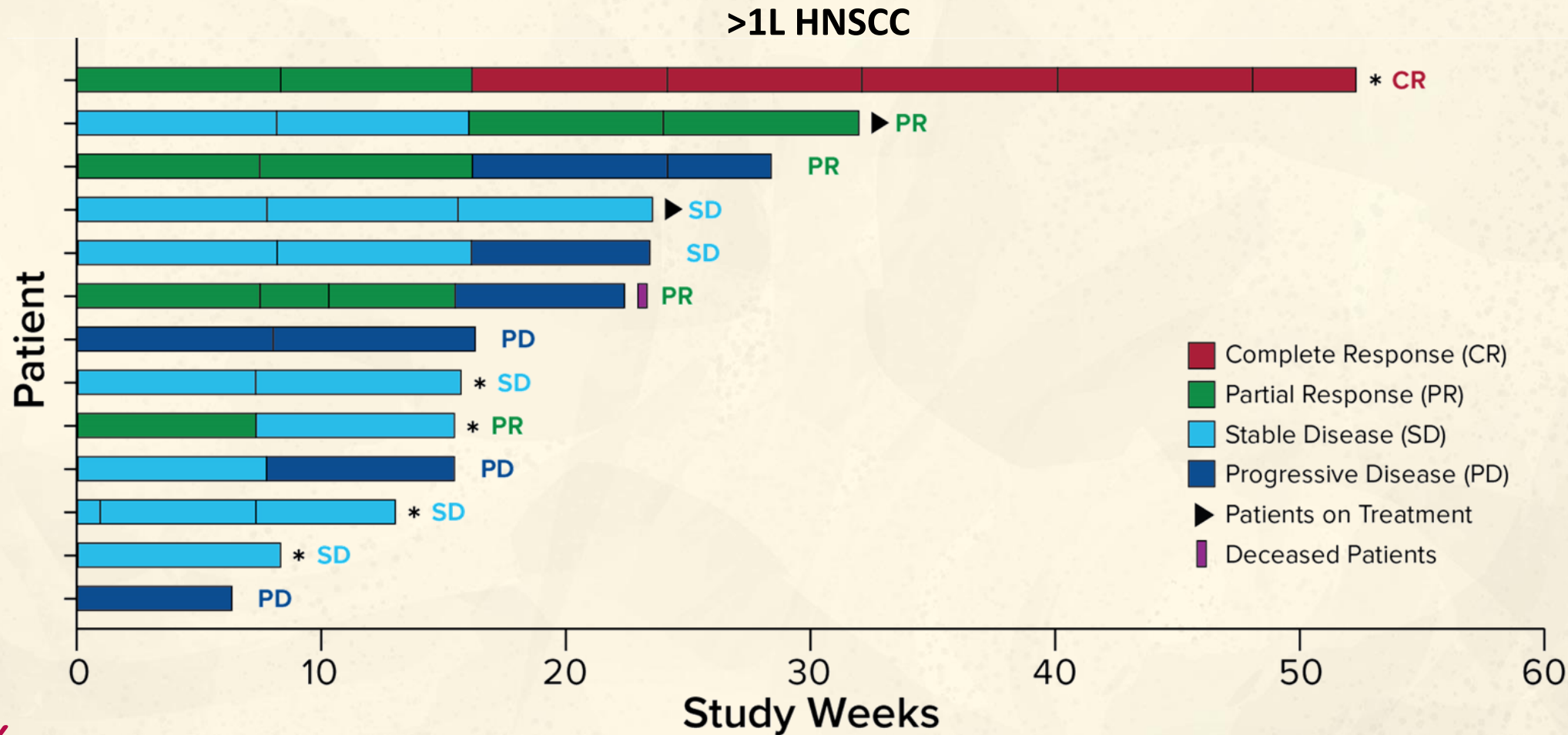
Evorpacept + Pembrolizumab + 5FU + Platinum (N=13) / Adverse Event, n (%)						
Grade	ALL Causality			Evorpacept - Related		
Evorpacept Dose QW	G1-2	G3	G4	G1-2	G3	G4
Anemia	4 (31)	4 (31)	–	–	1 (8)	–
Nausea	8 (62)	–	–	–	–	–
Stomatitis	7 (54)	1 (8)	–	–	–	–
Neutrophil Count Decreased / Neutropenia	2 (15)	5 (38)	–	1 (8)	–	–
Platelet Count Decreased /Thrombocytopenia	7 (54)	–	–	–	–	–
Fatigue	5 (38)	–	–	1 (8)	–	–
Alanine Aminotransferase Increased	3 (23)	1 (8)	–	–	–	–
Dysphagia	1 (8)	1 (8)	–	–	–	–
Hypersensitivity	1 (8)	–	1 (8)	–	–	1 (8)
Pneumonia	1 (8)	1 (8)	–	–	–	–
Pneumonitis	2 (15)	–	—	1 (8)	–	–
Candida Infection	–	1 (8)	–	–	–	–
Cardiac Tamponade	–	–	1 (8)	–	–	–
Headache	–	1 (8)	–	–	–	–
Pericarditis Constrictive	–	1 (8)	–	–	–	–
Supraventricular Tachycardia	–	1 (8)	–	–	–	–
Tracheal Obstruction	–	1 (8)	–	–	–	–

Data Cutoff September 1, 2021

Evorpacept: 10 mg/kg (n=3) & 15 mg/kg (n=10); All TEAEs occurring in ≥ 4patients. For cases of TEAEs Grade ≥3 and any TRAE, all AEs are listed irrespective of patient numbers.

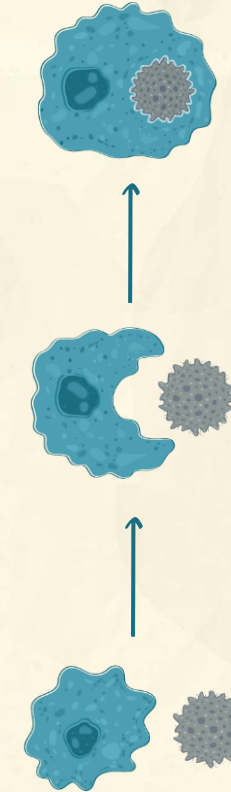
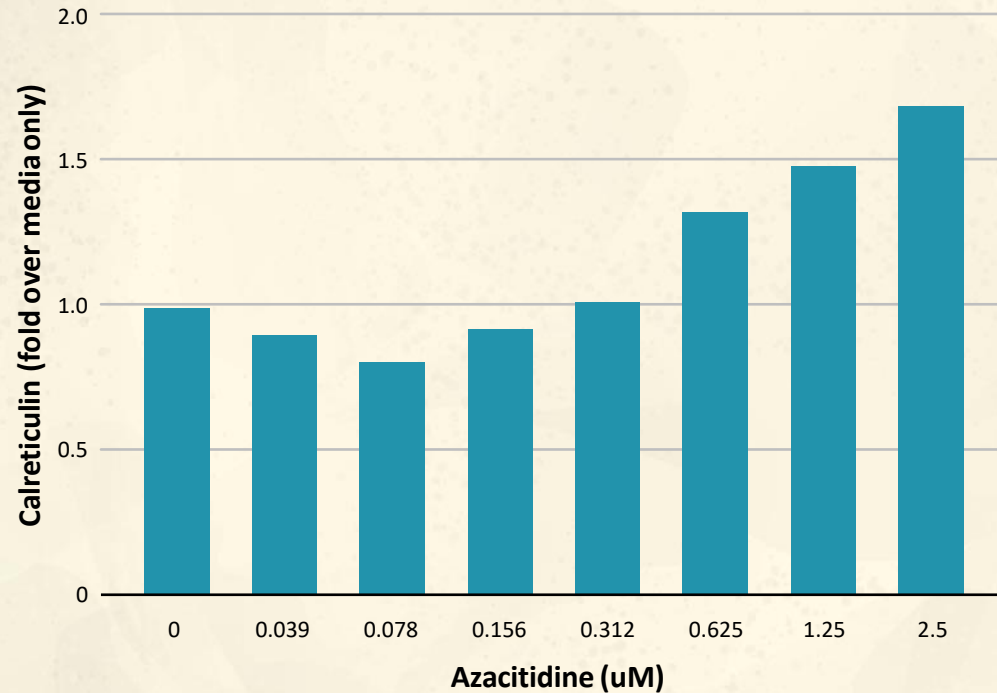


# ASPEN-01 PHASE 1B FIRST LINE HNSCC: EVORPACEPT + KEYTRUDA + 5FU/PLATINUM BEST OVERALL AND DURATION OF RESPONSE WHILE ON TREATMENT

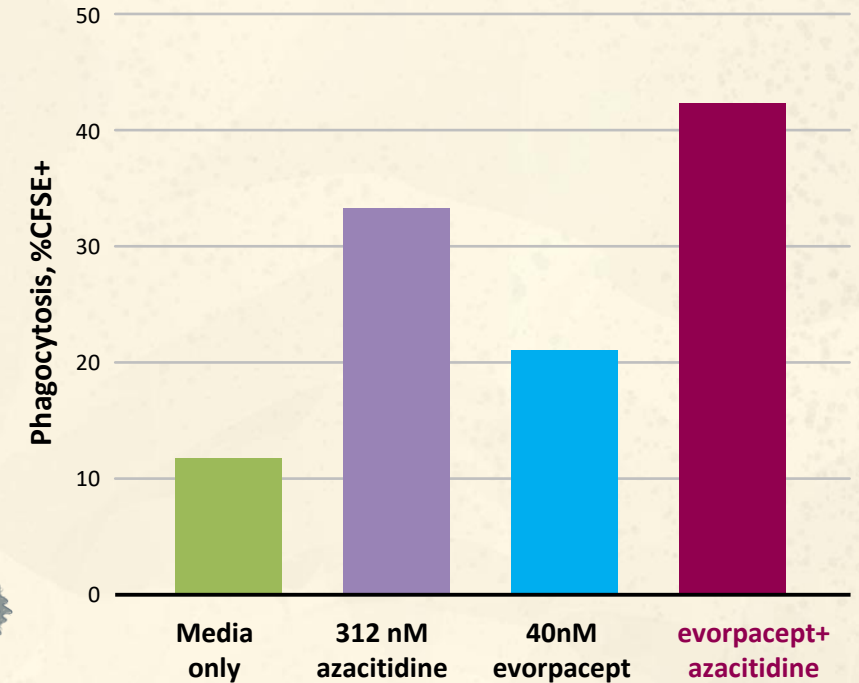


# PRECLINICAL: EVORPACEPT INCREASES PHAGOCYTOSIS OF BACKBONE MDS DRUG, AZACITIDINE

Calreticulin levels on HL60 Cells



Phagocytosis of HL60 Cells

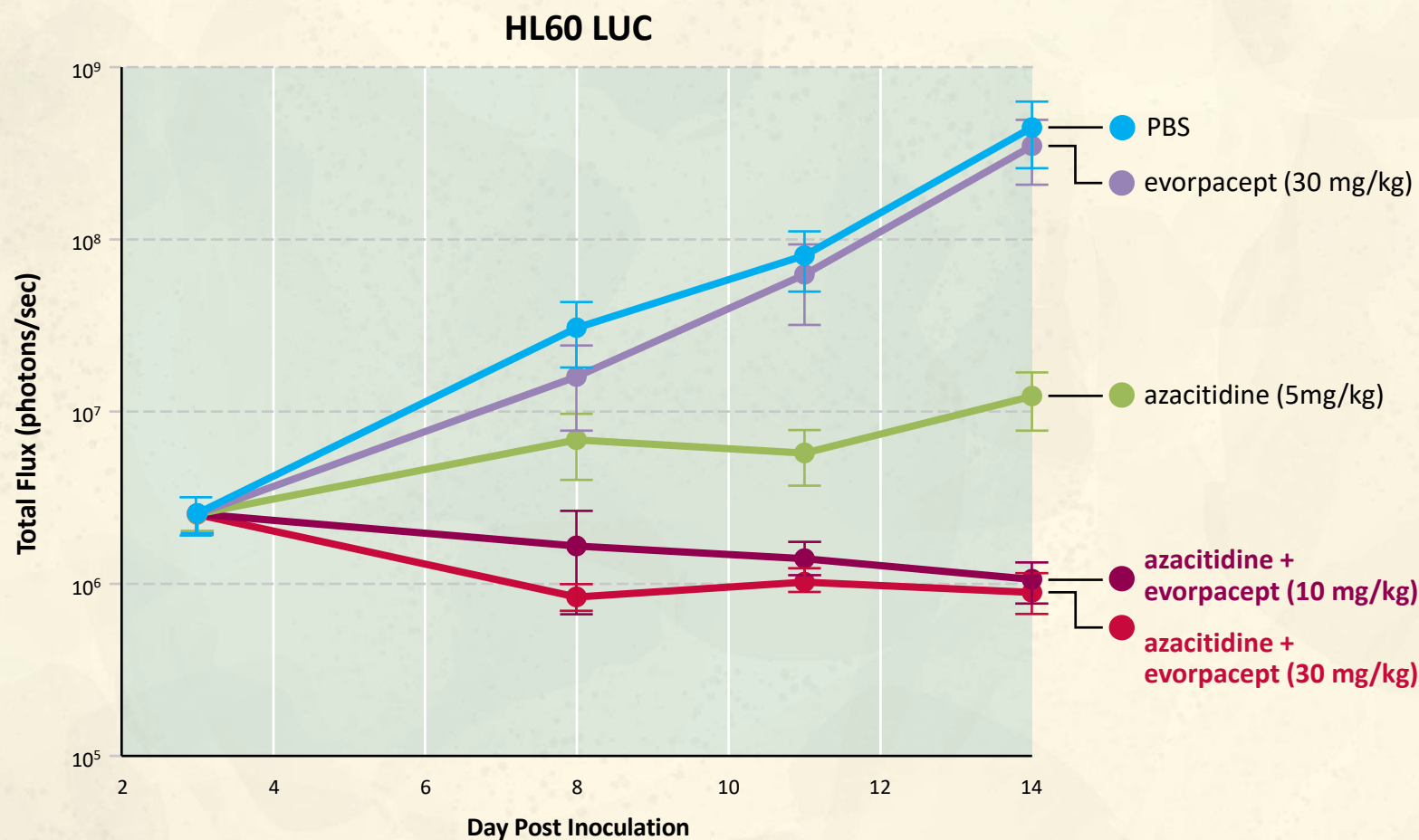


Azacitidine induces calreticulin display.

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

# ASPEN-02 PHASE 1B MDS: EVORPACEPT + AZACITIDINE PREVIOUSLY UNTREATED HR-MDS AND RELAPSED/REFRACTORY MDS ADVERSE EVENTS

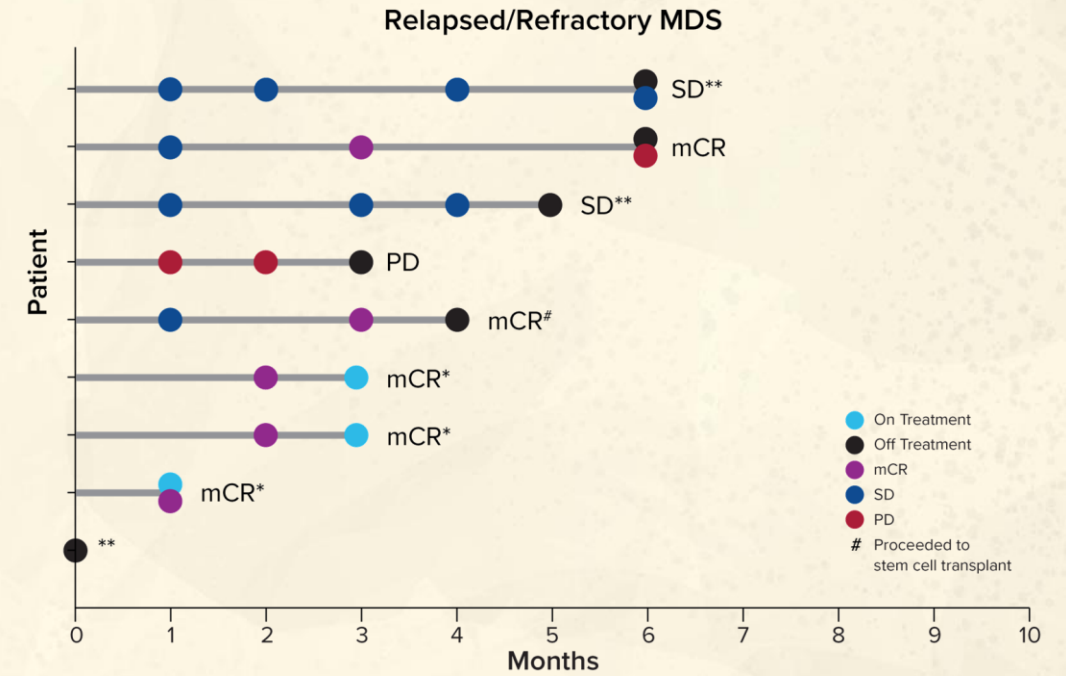
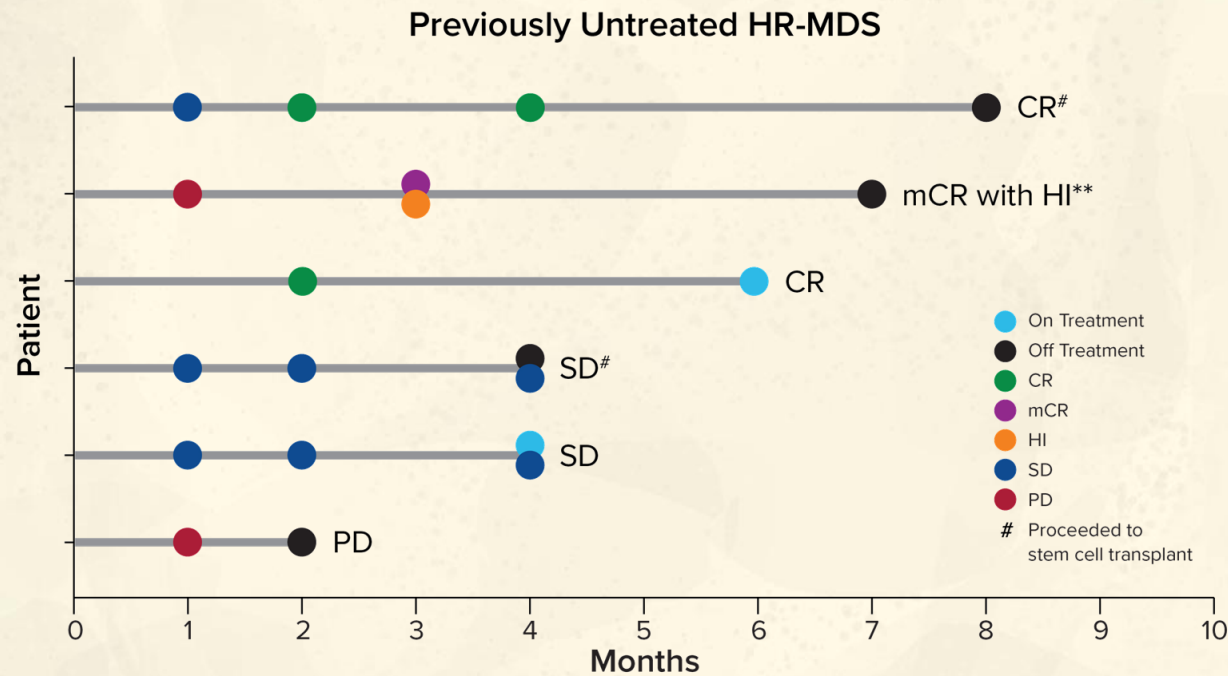
Adverse Event, n	20 mg/kg Q2W (N=3)		30 mg/kg Q2W (N=3)		60 mg/kg Q4W (N=16)		Total (N=22) All Grade n (%)
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4	
Blood Creatinine Increased	2	–	1	–	2	–	5 (23)
Constipation	1	–	1	–	2	1	5 (23)
Diarrhea	1	–	1	–	3	–	5 (23)
Fatigue	–	–	–	–	4	1	5 (23)
Neutropenia/Neutrophil Count Decreased	–	–	–	1	1	3	5 (23)
Anemia	1	1	1	–	–	1	4 (18)
Dizziness	–	–	1	–	3	–	4 (18)
Dyspnea	1	–	–	–	2	1	4 (18)
Febrile Neutropenia	–	2	–	–	–	2	4 (18)
Infusion Related Reaction	–	–	–	–	4	–	4 (18)
Nausea	–	–	1	–	3	–	4 (18)
Abdominal Pain	1	–	1	–	1	–	3 (14)
Contusion	1	–	1	–	1	–	3 (14)
Platelet Count Decreased	–	2	–	1	–	–	3 (14)
Pneumonia	–	1	–	–	–	2	3 (14)
Transfusion Reaction	2	–	–	–	1	–	3 (14)
Vomiting	1	–	–	–	2	–	3 (14)



# ASPEN-02 PHASE 1B MDS: EVORPACEPT + AZACITIDINE

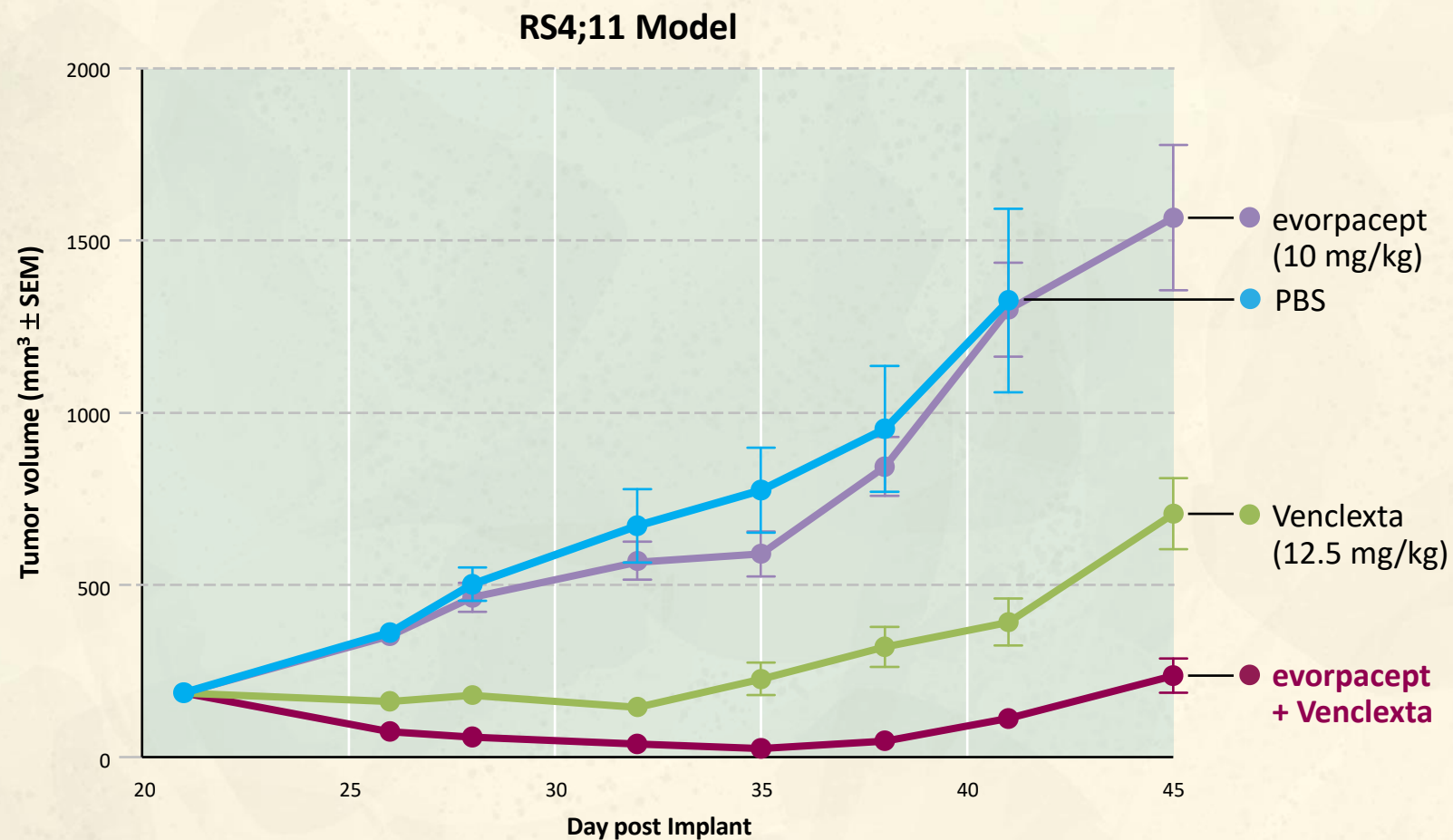
## PREVIOUSLY UNTREATED HR-MDS AND RELAPSED/REFRACTORY MDS

### DURATION OF RESPONSE

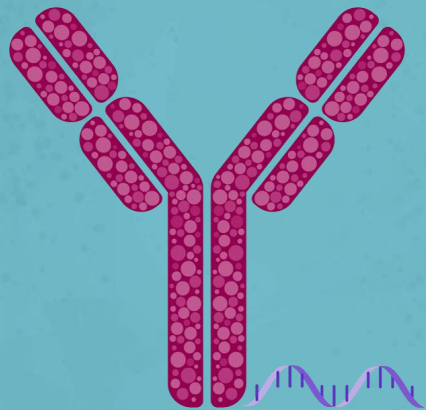


# EVORPACEPT INCREASES TUMOR INHIBITION OF VENCLEXTA

evorpacept  
in  
AML



Combination  
opportunity  
in AML



## 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.**

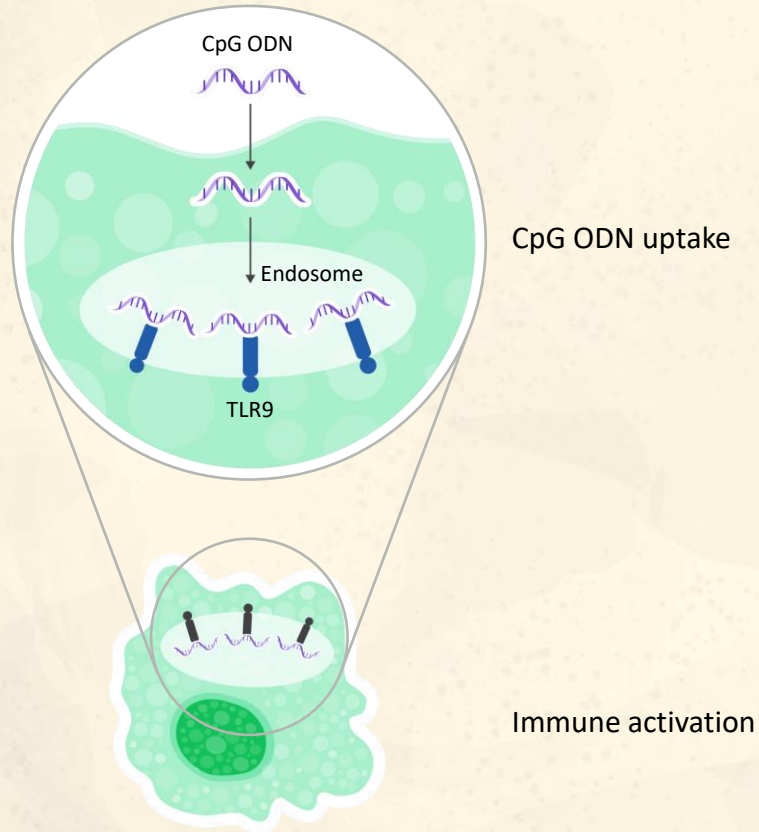
**SIRP $\alpha$  TRAAC simultaneously overrides “don’t eat me” signals by blocking CD47-SIRP $\alpha$  myeloid checkpoint pathway and induces TLR9-based immune activation in antigen presenting cells (APCs).**



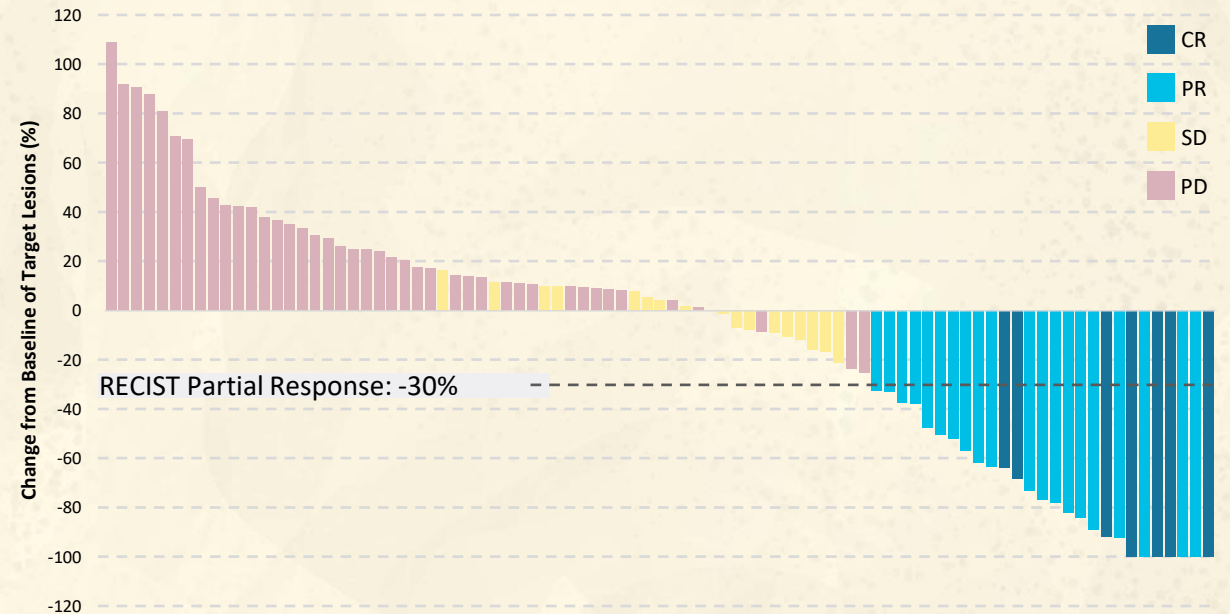
# TOLL-LIKE RECEPTOR 9 (TLR9): A KEY INNATE PATHWAY

## 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



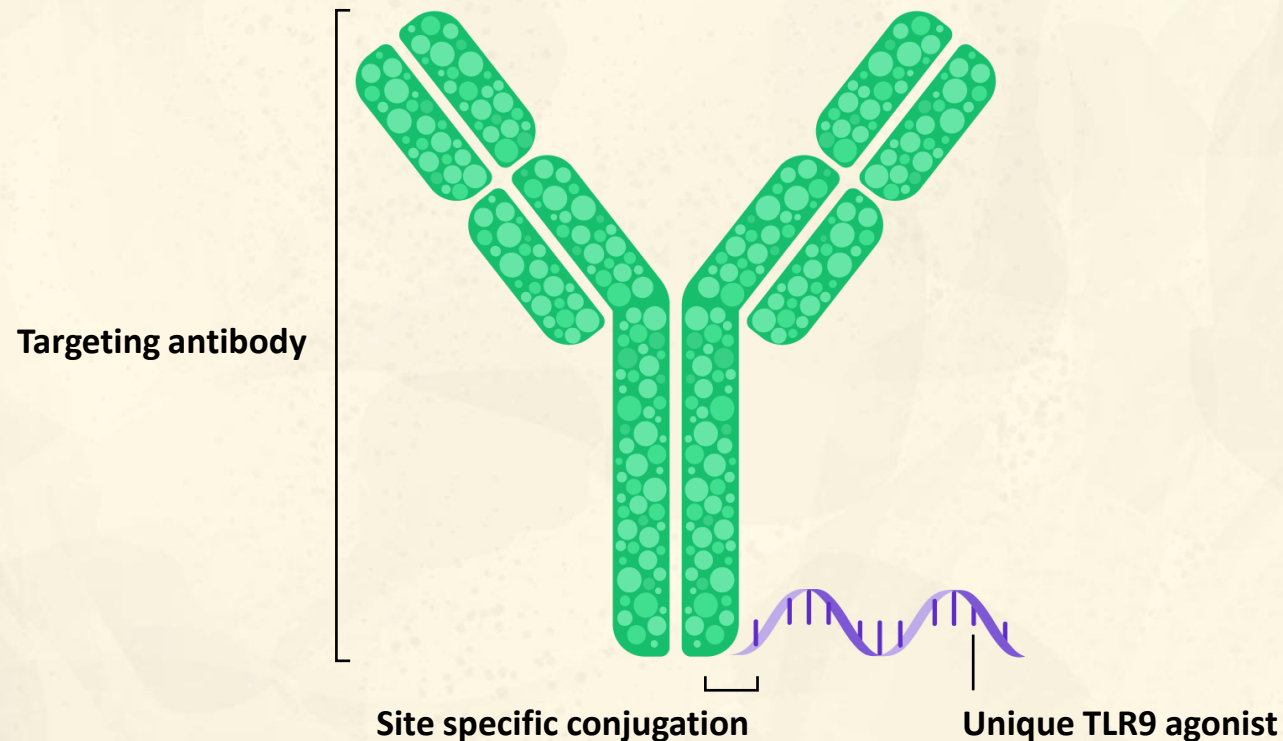
CMP-001 (Checkmate) + Pembrolizumab in Anti-PD-1 Refractory Melanoma, <sup>1-4</sup>Checkmate, S1 2020.

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

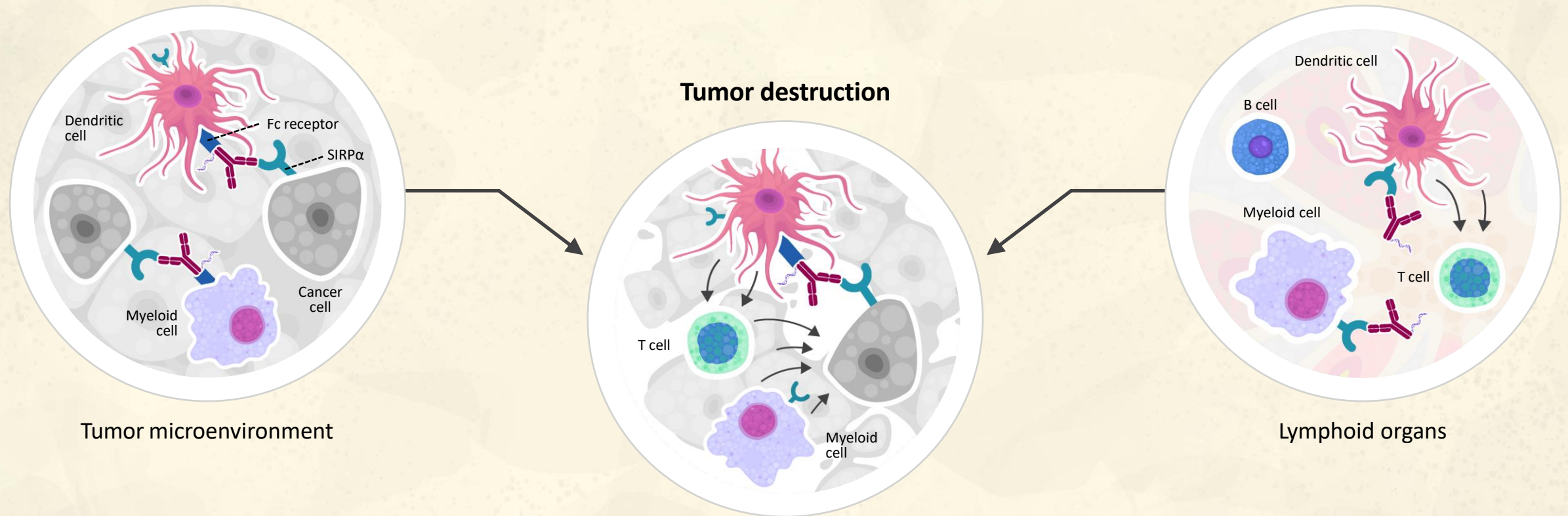
## ANTIBODY DIRECTS TLR9 AGONIST (T-CPG) TO SPECIFIC IMMUNE CELLS

**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



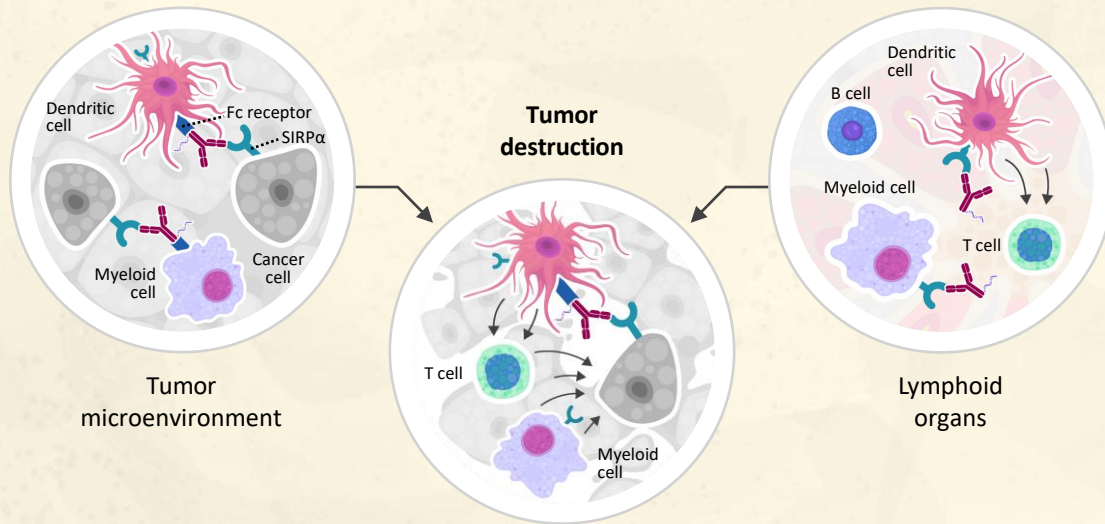
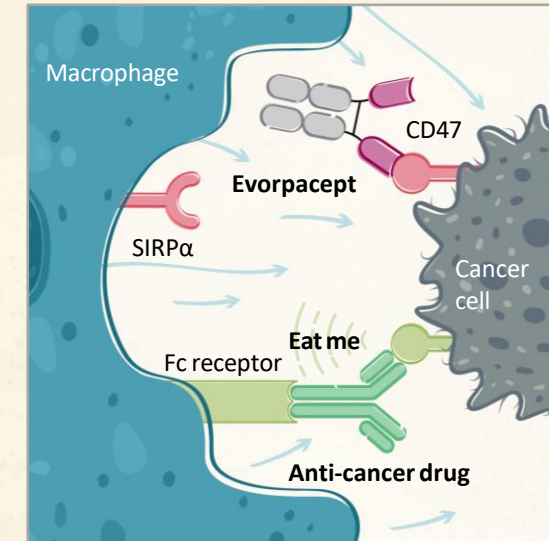
- SIRP $\alpha$  TRAAC binding to myeloid cells targets TLR9 activation in myeloid cells that matter (e.g. dendritic cells).
- SIRP $\alpha$  expression on tumor cells enables tumor microenvironment localization of SIRP $\alpha$  TRAAC.
- SIRP $\alpha$  TRAAC blocks CD47-SIRP $\alpha$  myeloid checkpoint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

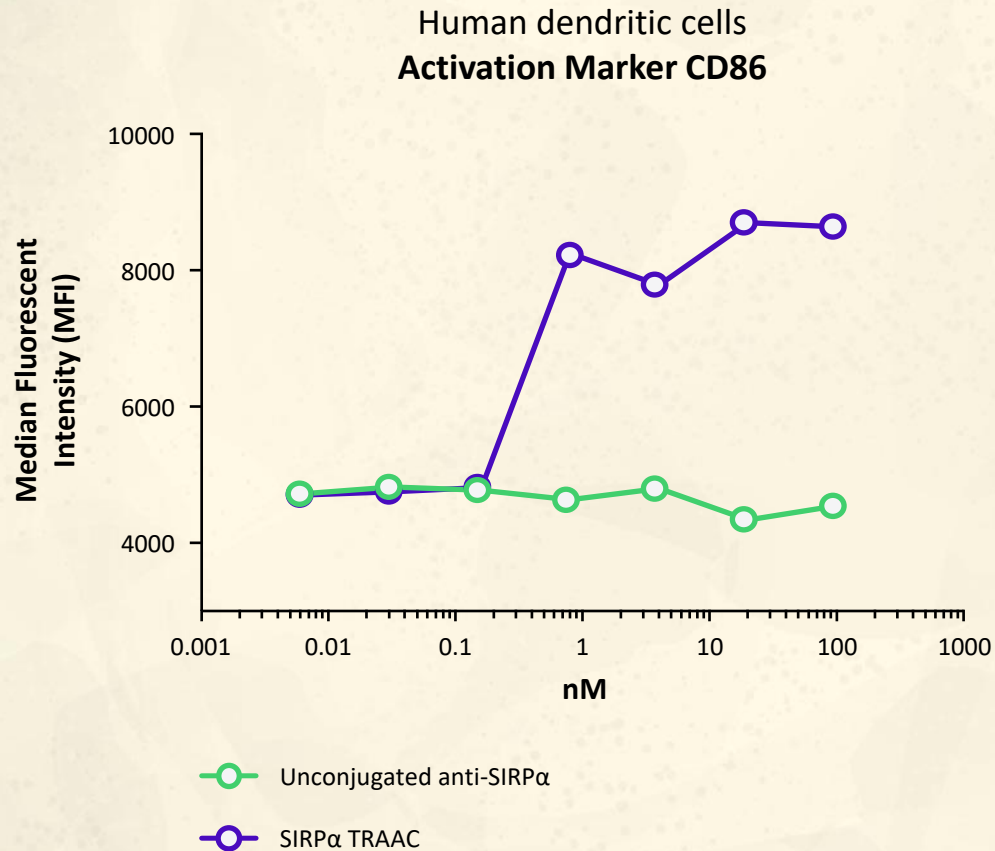


SIRP $\alpha$  TRAAC is an agonistic molecule that directly activates dendritic cells and initiates a coordinated innate and adaptive immune response against cancer.

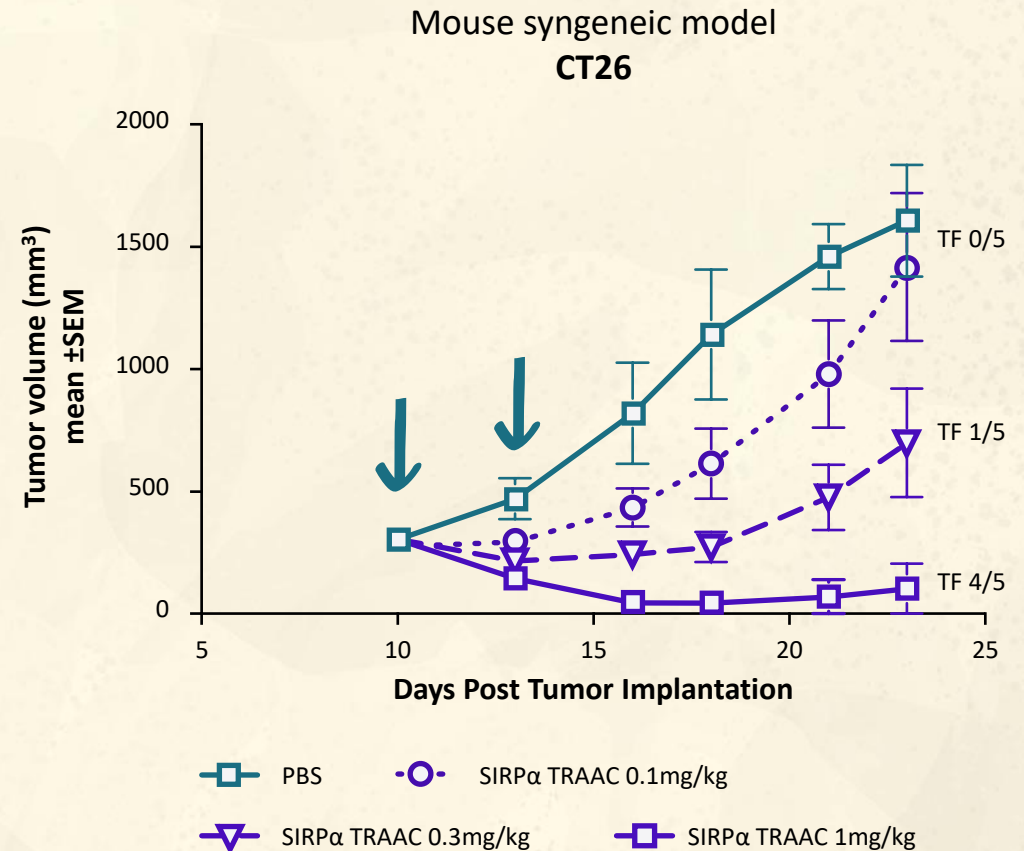
In the case of agonistic molecules (TLR9 agonist), constant blockade is not required.



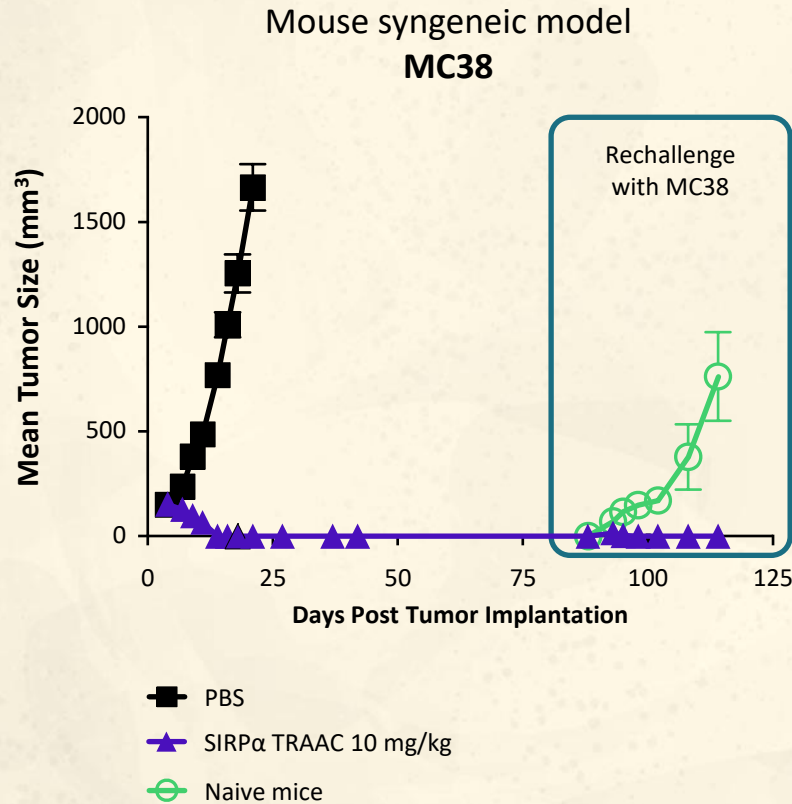
# SIRP $\alpha$ TRAAC INDUCES POTENT AND SELECTIVE IMMUNE ACTIVATION AND LEADS TO POTENT SINGLE AGENT ACTIVITY IN TUMOR MODELS



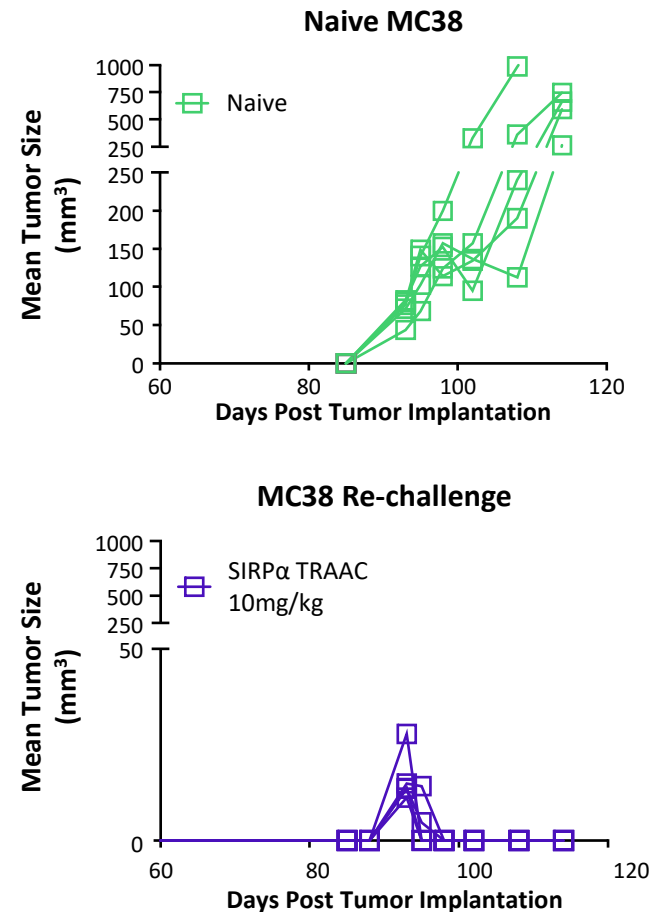
Harrabi et al., SITC, 2020



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

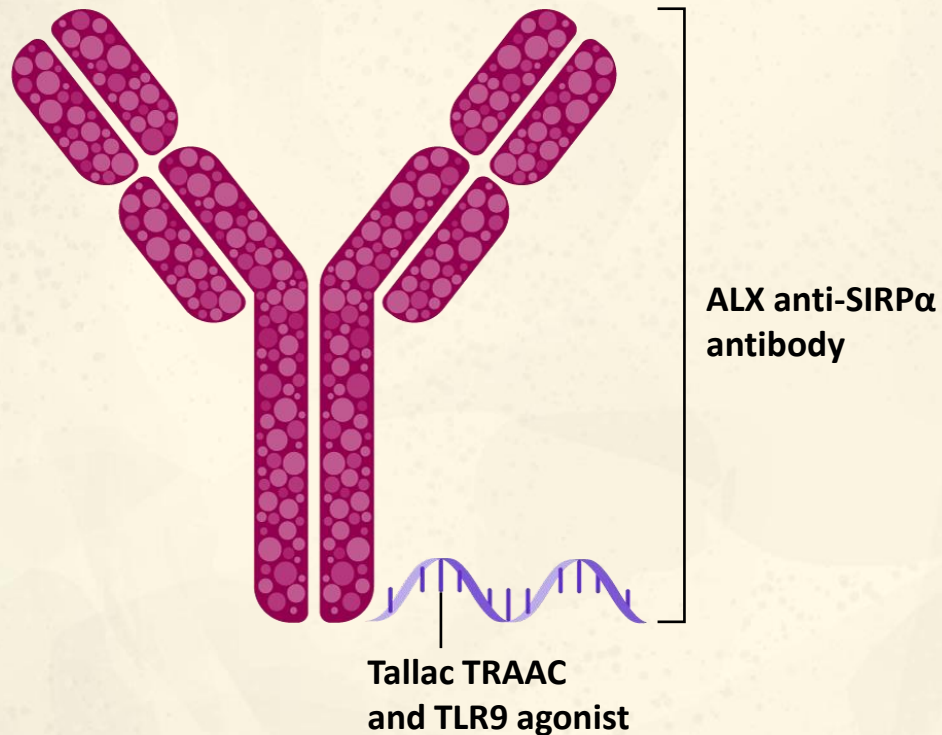


Harrabi et al., SITC, 2020



- 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.

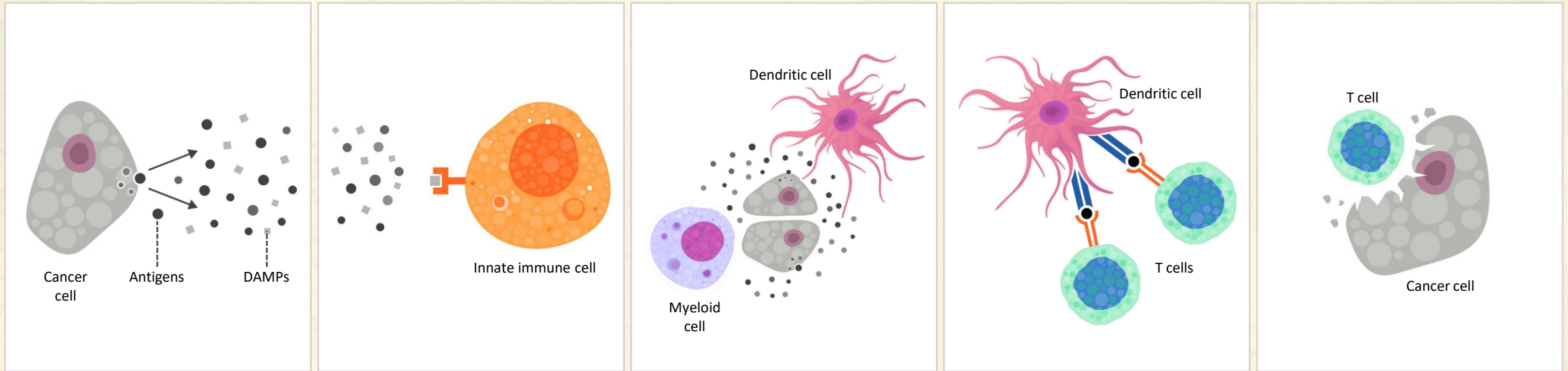
## ALTA-002: TARGETING IMMUNE ACTIVATION TO WHERE IT MATTERS



- 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 beginning of 2023

# 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**

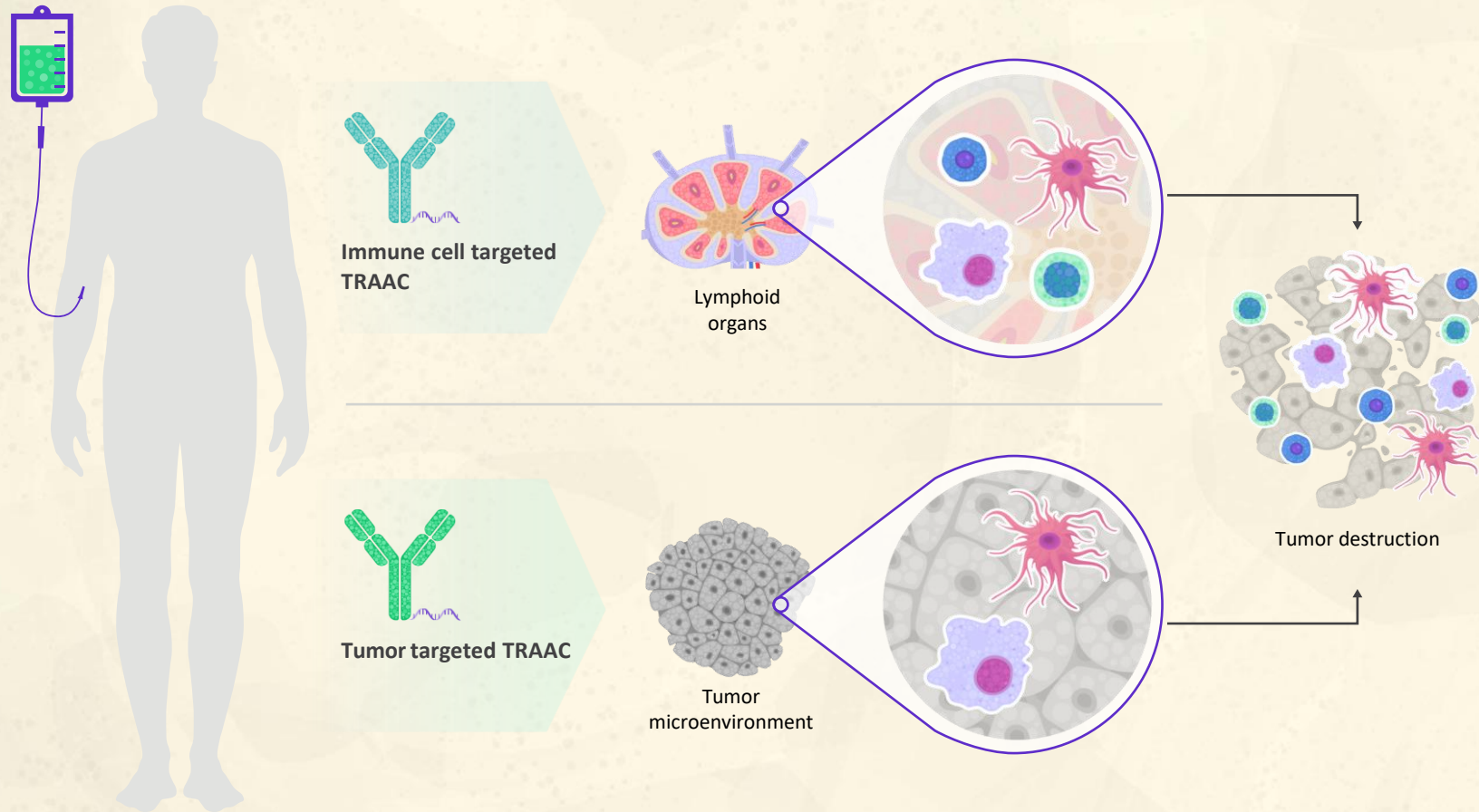
**5. Recognition and elimination of tumor by T cells**

- 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.

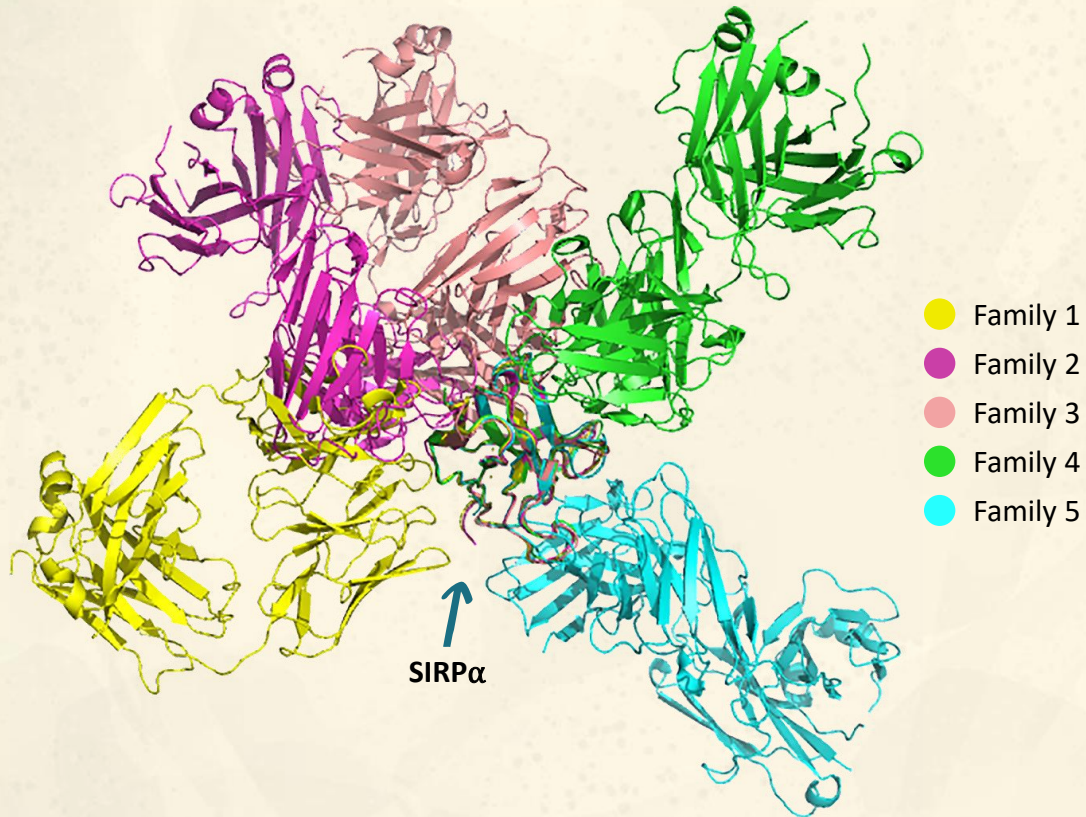
DAMPs: damage-associated molecular patterns  
PAMPs: pathogen-associated molecular patterns  
PRRs: pattern recognition receptors



# 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