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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, evorpacept, currently in phase 2 clinical trials

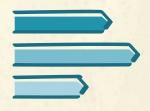


## **Evorpacept (myeloid checkpoint inhibitor) as a cornerstone therapy**

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

Ongoing 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 and equivalents of \$385.1M as of September 30, 2021.

Expected cash runway into 2024.

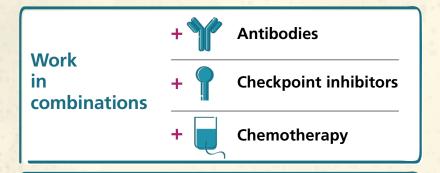
#### **Collaboration partners**

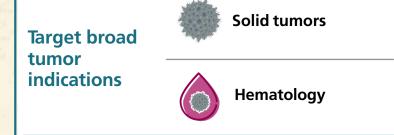
Merck, Eli Lilly, Zymeworks

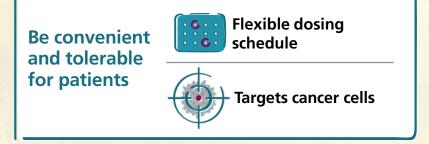


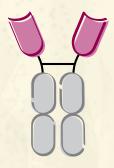
## **EVORPACEPT'S BROAD CLINICAL DATA SUPPORTS ITS DIFFERENTIATED POTENTIAL**

#### **Evorpacept was designed to:**





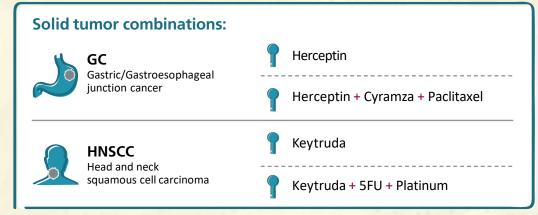


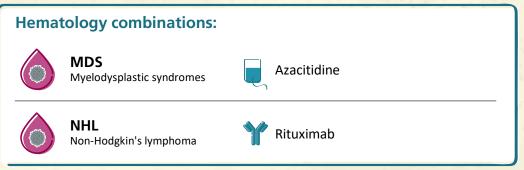


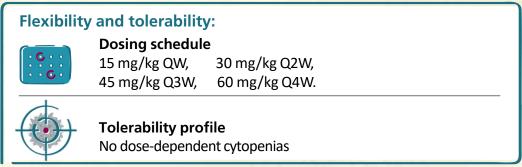
#### **Evorpacept:**

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

## Evorpacept's clinical data shows promising initial activity in:







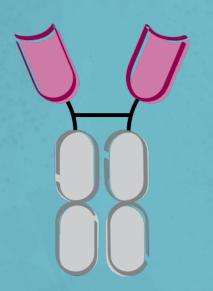


## **ALX PIPELINE**

	Indication		Combination Agent	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Fast Track	Collaboration Partner
			Keytruda (ASPEN-03)							<b>♦</b> MERCK
on Studies	IORS		Keytruda + 5FU + Platinum (ASPEN-04)							MERCK
	D TUM	GC Gastric/Gastroesophageal	Herceptin (ASPEN-01)							
mbination	SOLID	Junction Cancer	Herceptin + Cyramza + Paclitaxel (ASPEN-06)							Lilly
S		Breast Cancer	Zanidatamab							<b>zyme</b> works
rpacept	TATOLOGY	MDS Myelodysplastic Syndromes	Azacitidine (ASPEN-02)							
Evor		AML Acute Myeloid Leukemia	Azacitidine + Venclexta (ASPEN-05)							
	HEN	NHL Non-Hodgkin's Lymphoma	Rituximab (ASPEN-01)							
ALTA- 002*		Advanced Cancer								TALLAC

<sup>\*</sup>SIRPa Toll-like receptor agonist antibody conjugate (TRAAC)



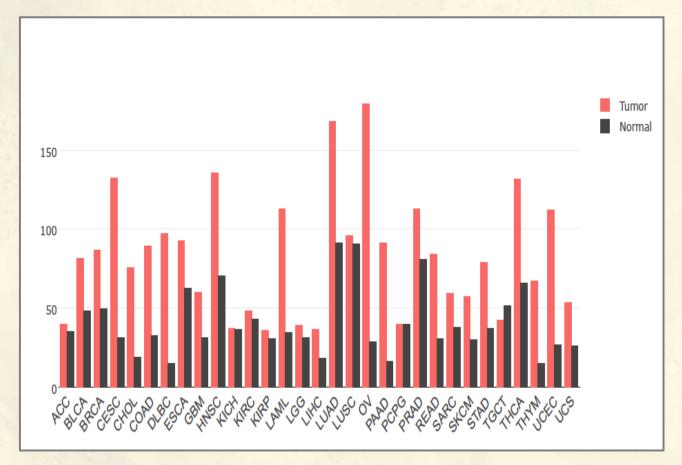


EVORPACEPT (ALX148)

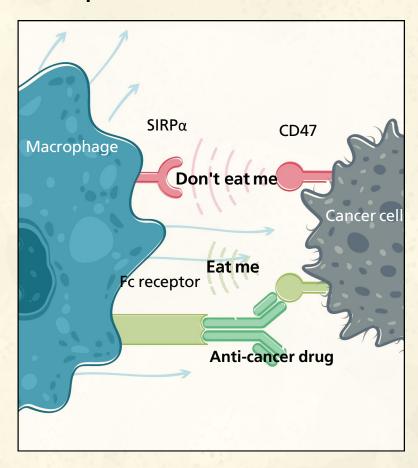


## CD47: TUMOR ASSOCIATED ANTIGEN (TAA)- MYELOID CHECKPOINT DUALITY

## **TAA-Expression levels on cancer and normal cells**



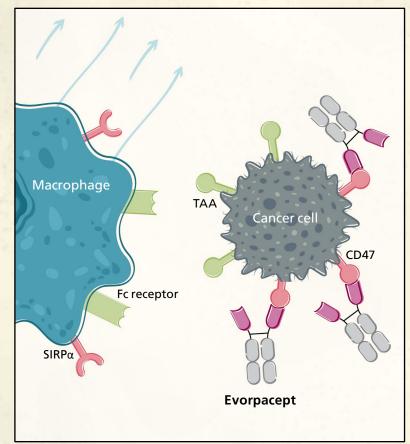
#### Checkpoint Mechanism: "do not eat me"



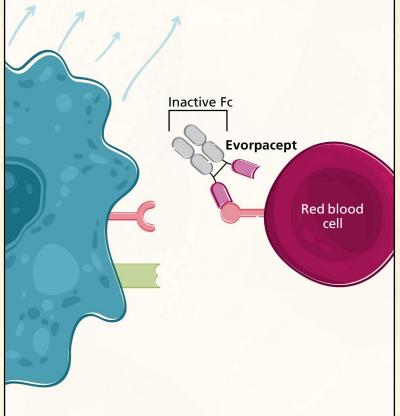


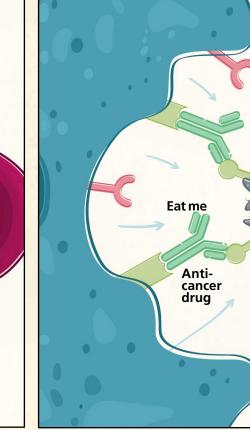
## TARGETING CD47 AS CHECKPOINT: ALX ONCOLOGY'S APPROACH

## It spares normal cells



Anti CD47 with inactive Fc binds and block CD47-SIRP $\alpha$  interaction





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



**Evorpacept** 

**Evorpacept** 

## **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

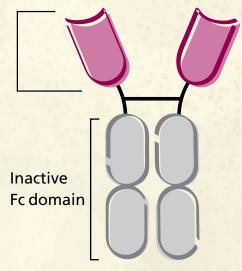
Presence of Fc domain ensures slow clearance and long half-life



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

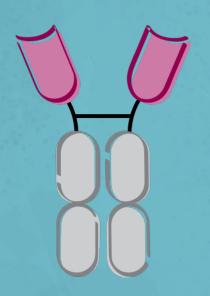


## **EVORPACEPT DEMONSTRATES CONSISTENT TOLERABILITY PROFILE**

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%)	-	-	- 1	5 (9.6%)	-	-	-
AST increased	-	-		- / - /	9 (17.3%)	-	-	-
Platelets decreased	-	-		- 11	4 (7.7%)	2 (3.8%)	-	-
ALT increased	-	-		<u>-</u>	7 (13.5%)	1 (1.9%)	-	-
Pruritus	2 (11.1%)	-	25 Ball -	14/1/ - 10/19	5 (9.6%)	-	-	-
Pyrexia	-	-		- V/// - V	3 (5.8%)	-	-	-
Decreased appetite	-	-	75.00 L	M 4.49. 13	2 (3.8%)	-	-	-
Anemia	1 (5.6%)	-	1 (7.7%)	1 (7.7%)	5 (9.6%)	1 (1.9%)	-	-
Infusion reaction	-	-	- \	- 1	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	-	-	-	- 19	3 (5.8%)	-	-	-
WBC decreased	-	-	27	-	3 (5.8%)	-	-	-
Myalgia	-	-	-		2 (3.8%)	-	-	-
Diarrhea	3 (16.7%)	-	-	-	-	-	-	-
Urticaria	3 (16.7%)	-		7.00 -	-	-	-	-
Lymphocyte count decreased	1 (5.6%)	1 (5.6%)		-	-	-	-	-
Headache	1 (5.6%)	-		3	-	-	-	-
Stomatitis	1 (5.6%)	-	<u>-</u>	- 10 m	-	-	-	-
Back pain	1 (5.6%)	-	-		-	-	-	-
Vision blurred	1 (5.6%)	-	-	-12	-	-	-	-
Abdominal pain / abdominal pain upper	1 (5.6%)	-	-		-	-	-	-
Hypersensitivity	-	-	1 (7.7%)	1 (7.7%)	-	-	-	-
Pneumonitis	-	-	1 (7.7%)	4 - 4 - 1 - 1	-	-	-	-
Constipation	-	-	-		-	-	3 (13.6%)	-
Vomiting	-	-	7, 3-7 ( <u>-</u> 1)		-	-	2 (9.1%)	-

ALX

Tolerability profile enables broad combination potential
For combination cohort of evorpacept plus Keytruda, treatment related adverse events occurring in >1 subject in all histologies at 10 & 15 mg/kg QW; data as of April 1, 2020. For combination cohorts of evorpacept plus Keytruda and

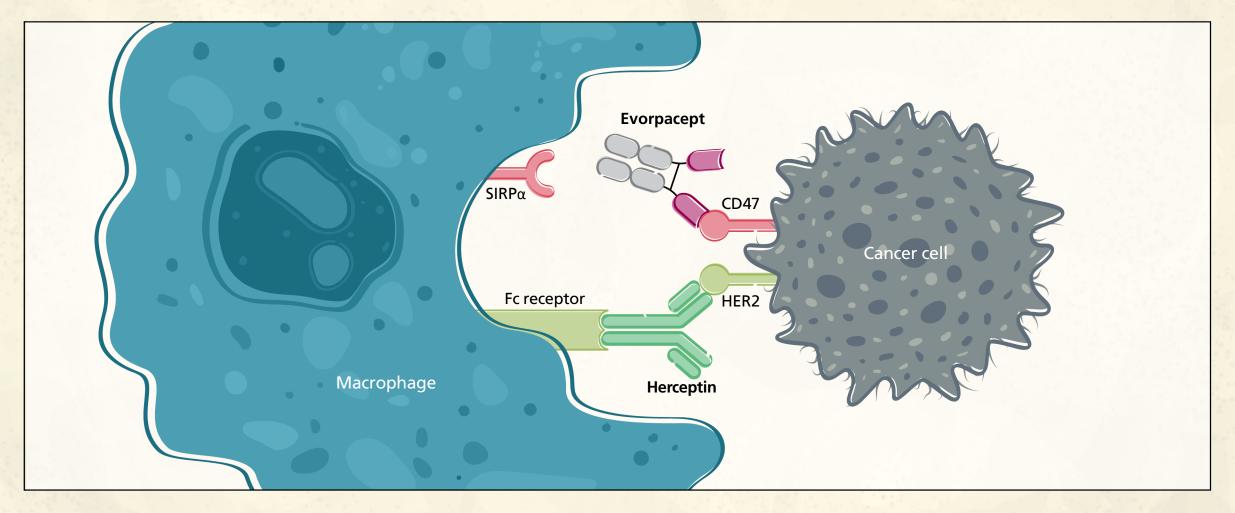


ASPEN-06: EVORPACEPT (ALX148) IN HER2+ GASTRIC/GEJ CANCER



## GC TRIAL: EVORPACEPT + HERCEPTIN MECHANISM OF ACTION





Evorpacept increases antibody dependent cellular phagocytosis in combination with Herceptin



## 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.

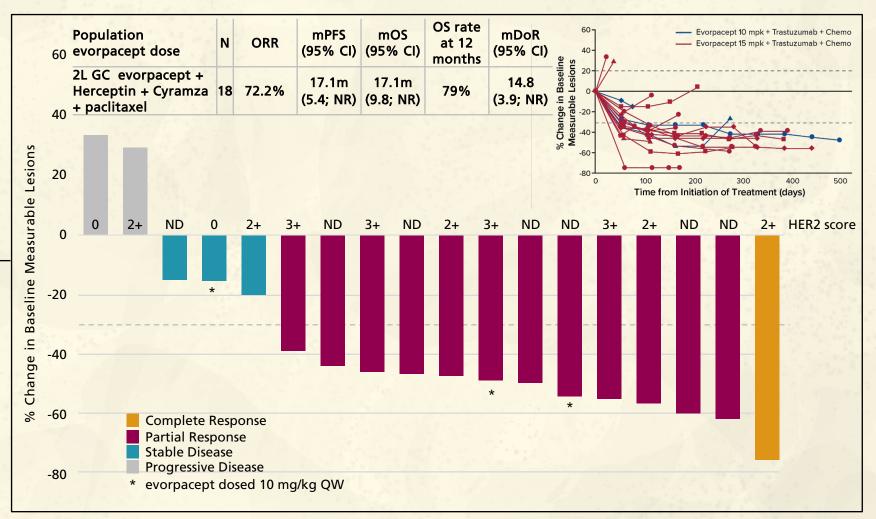


evorpacept 10 and 15 mg/kg (QW)

- + Herceptin
- + Cyramza
- + paclitaxel



- safety of combination
- anti-cancer activity





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

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



#### **Randomized Phase 2:**



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



evorpacept 30 mg/kg (Q2W)

- + Herceptin
- + Cyramza
- + paclitaxel

- + Herceptin
  - + Cyramza
  - + paclitaxel

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

VS.

#### **Randomized Planned Phase 3:**



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



evorpacept 30 mg/kg (Q2W)

- + Herceptin
- + Cyramza
- + paclitaxel

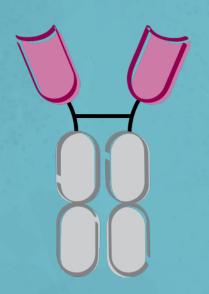
+ Cyramza

+ paclitaxel

VS.

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



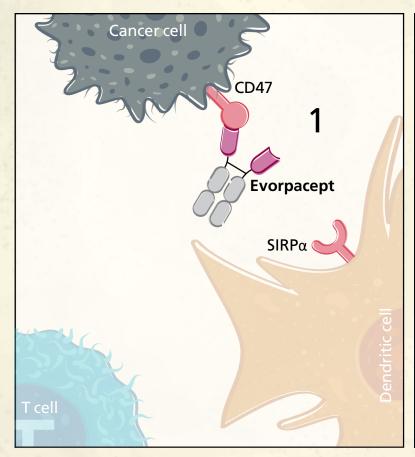


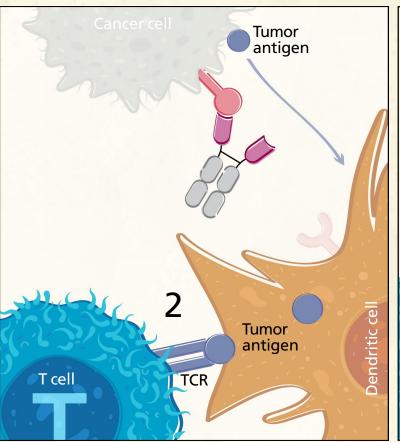
ASPEN-03 AND ASPEN-04: EVORPACEPT (ALX148) IN 1L HNSCC

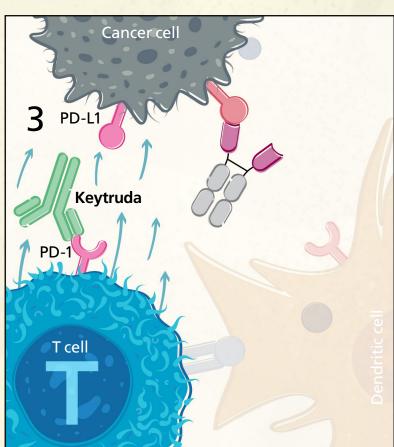


## HNSCC TRIAL: EVORPACEPT + KEYTRUDA MECHANISM OF ACTION







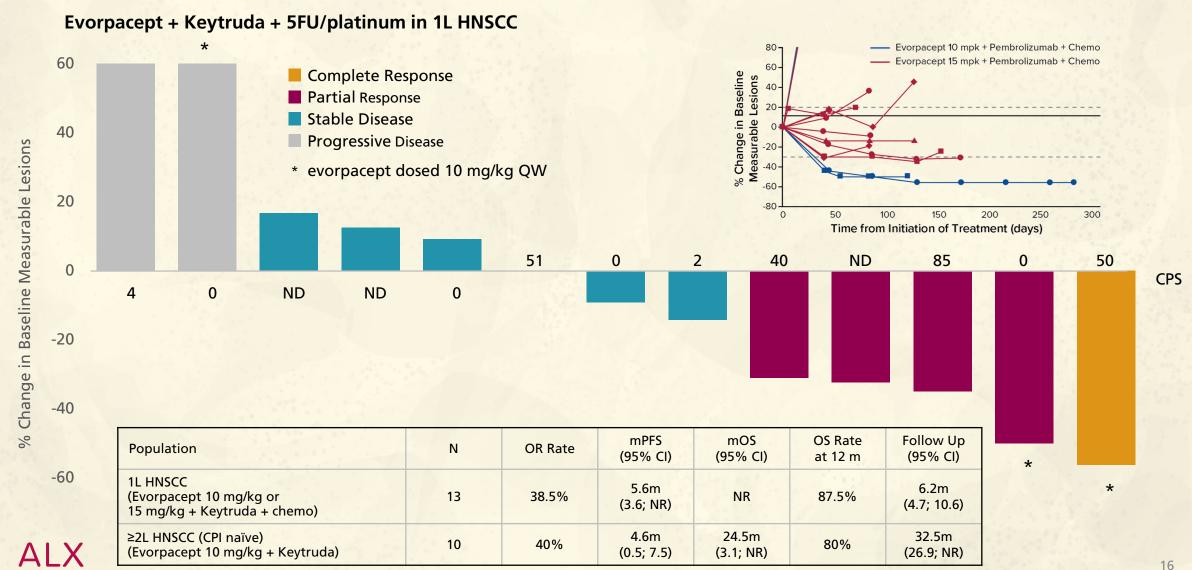




**Evorpacept activates dendritic cells and enhances cross-priming of T cells** 

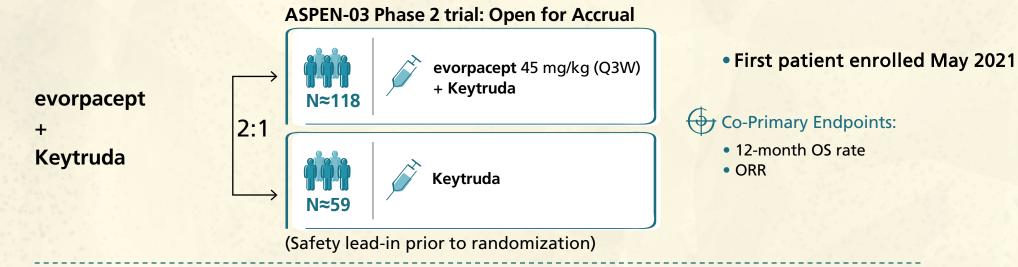
## PHASE 1B HNSCC: EVORPACEPT + KEYTRUDA + 5FU/PLATINUM FIRST LINE CHECKPOINT NAIVE





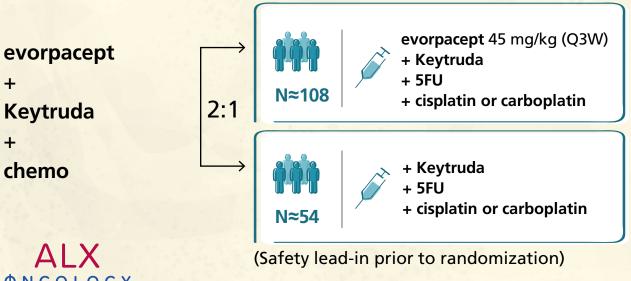
## evorpacept **HNSCC**

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

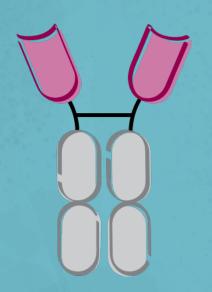


**ASPEN-04 Phase 2 trial: Open for Accrual** 

First patient enrolled July 2021



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

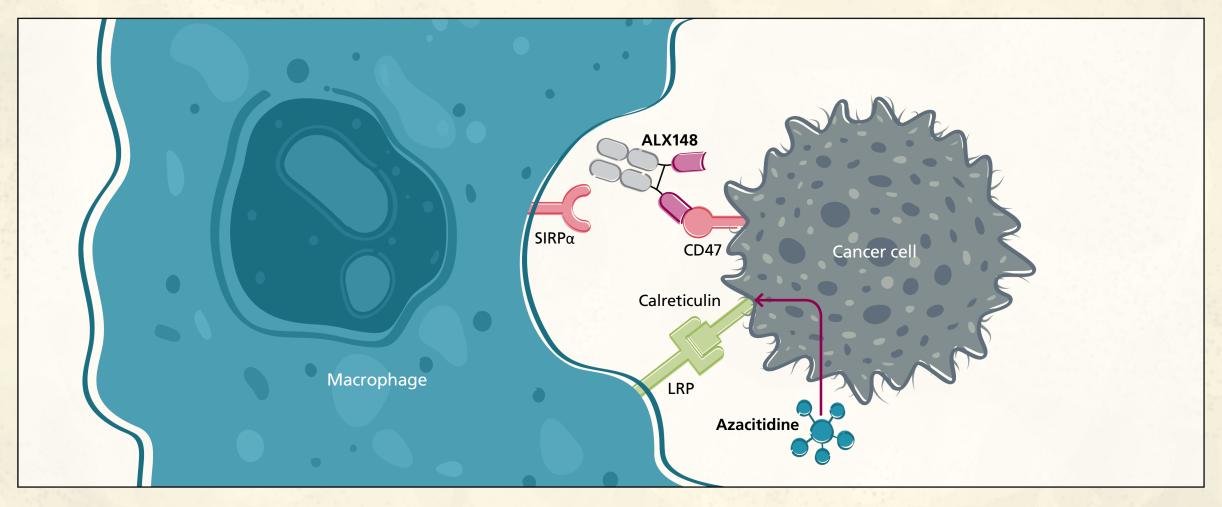


# **EVORPACEPT (ALX148) IN HEMATOLOGIC MALIGNANCIES**



## MDS TRIAL: ALX148 + AZACITIDINE MECHANISM OF ACTION





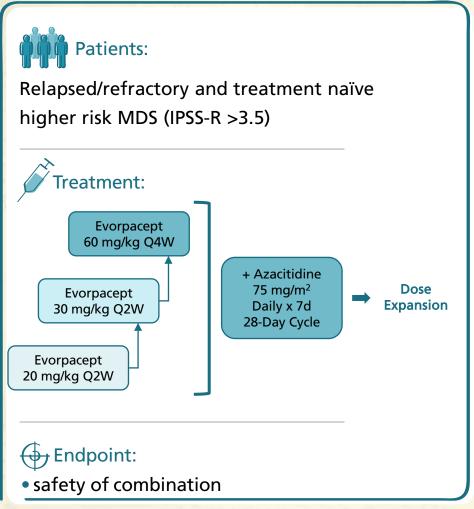




## MDS TRIAL: DESIGN AND PATIENT BASELINE CHARACTERISTICS



## **Phase 1 Design**



#### **Patient Baseline Characteristics**

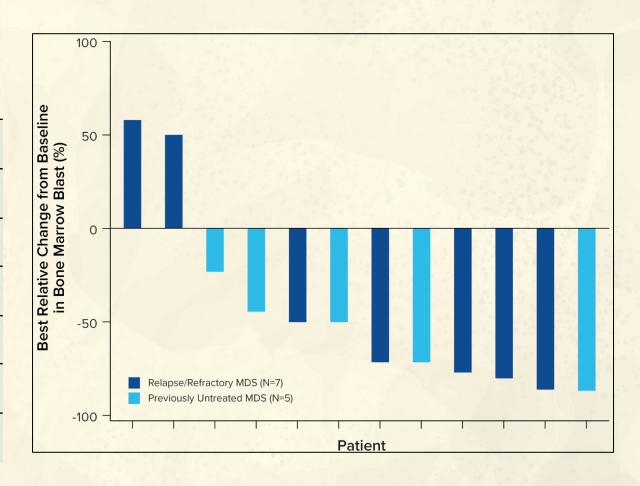
		evorpacept + azacitidine (N=22)
Median age, years (range)		70.5 (56 – 81)
Sex, n	F	8
	M	14
Race, n	White	17
	Black	4
	Unknown	1
ECOG PS, n	0	6
	1	16
	2	0
MDS Status, n	Previously untreated HR-MDS	9
	Therapy related	6
	Relapsed/Refractory MDS	13
	<ul> <li>Prior HMA treatment</li> </ul>	13
IPSS-R Score	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	Very Good	0
Diagnosis, n (%)	Good	2 (9%)
	Intermediate	0
	Poor	2 (9%)
	Very Poor	8 (36%)
	Not Available	10 (45%)

## 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)#	
ORR	3 (50%)	3 (60%)	5 (56%)*	
CR	2 (33%)	2 (40%)	0	
PR	0	0	0	
Marrow CR	1 (17%) with HI	1 (20%) with HI	5 (56%)*	
н	0	0	0	
SD	2 (33%)	1 (20%)	2 (22%)	
PD	1 (17%)	1 (20%)	1 (11%)	





Data Cutoff 25Oct2021; Response evaluable population (n=15); \*includes 3 unconfirmed responses; #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.

## 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)



#### evorpacept

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

azacitidine



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



#### (<del>)</del> 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.

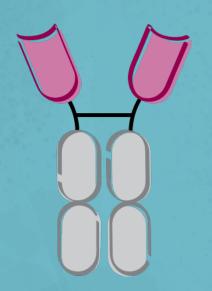
azacitidine



#### (<del>))</del> Endpoint:

• complete response rate (CRR)





# **EVORPACEPT (ALX148) CLINICAL ACTIVITY ACROSS INDICATIONS**



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

Population	≥2L HE	R2+ GC	1L HI	NSCC		INSCC Naïve)
Combination (N-evaluable)	+ Cyramza	+ Herceptin + paclitaxel :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 untre myelodysplastic with TP53	Relapsed / refractory MDS	
Combination	Evorpacept + azacitidine	Magrolimab + azacitidine¹	Evorpacept + azacitidine
N-evaluable	5	4	9
CR	2	2	-
mCR	1 with HI	1	5*
SD	1		2

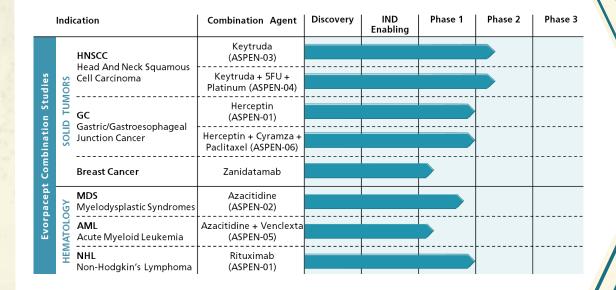
#### **ASPEN-01**

Population	≥2L aggressive non-Hodgkin's lymphoma			
Combination	Evorpacept + Rituximab²	Magrolimab + Rituximab³		
N-evaluable	21	38		
ORR	8	11		
(%)	(38%)	(29%)		
CR	1	2		
(%)	(5%)	(5%)		
PR	7	9		
(%)	(33%)	(24%)		

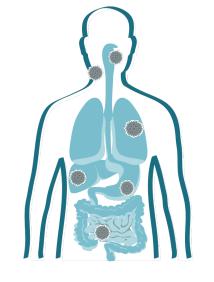


## **EVORPACEPT IS DESIGNED TO BE A CORNERSTONE OF CANCER TREATMENTS**

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



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 anticancer modalities



## 2022 FOCUSED ON DRIVING CLINICAL DEVELOPMENT

	Completed	2022	2023	2024
	ASPEN-01 (Phase 1b) Updated gastric/GEJ and HNSCC trial data at SITC	ASPEN-06 Initiation (Phase 2/3) Randomized gastric/GEJ cancer trial	ASPEN-06 (Phase 2) Randomized gastric/GEJ cancer trial readout	ASPEN-03 (Phase 2) Randomized HNSCC trial readout with pembrolizumab
	ASPEN-02 (Phase 1a) Initial MDS trial readout at ASH	ASPEN-02 (Phase 1b)  MDS dose optimization trial readout	ASPEN-05 (Phase 1a) AML trial readout	ASPEN-04 (Phase 2) Randomized HNSCC trial readouts with pembrolizumab and chemo
	ASPEN-03 Initiation (Phase 2) Randomized HNSCC trial with pembrolizumab	Ongoing collaborations (Zymeworks) and Investigator Sponsored Trials (NHL)		
Evorpacept	ASPEN-04 Initiation (Phase 2) Randomized HNSCC trial with pembrolizumab and chemo			
	ASPEN-05 Initiation (Phase 1a) AML trial			
Preclinical pipeline	Built pipeline through ScalmiBio acquisition and Tallac collaboration	Select clinical development candidates from preclinical pipeline	File IND for ALTA-002	

