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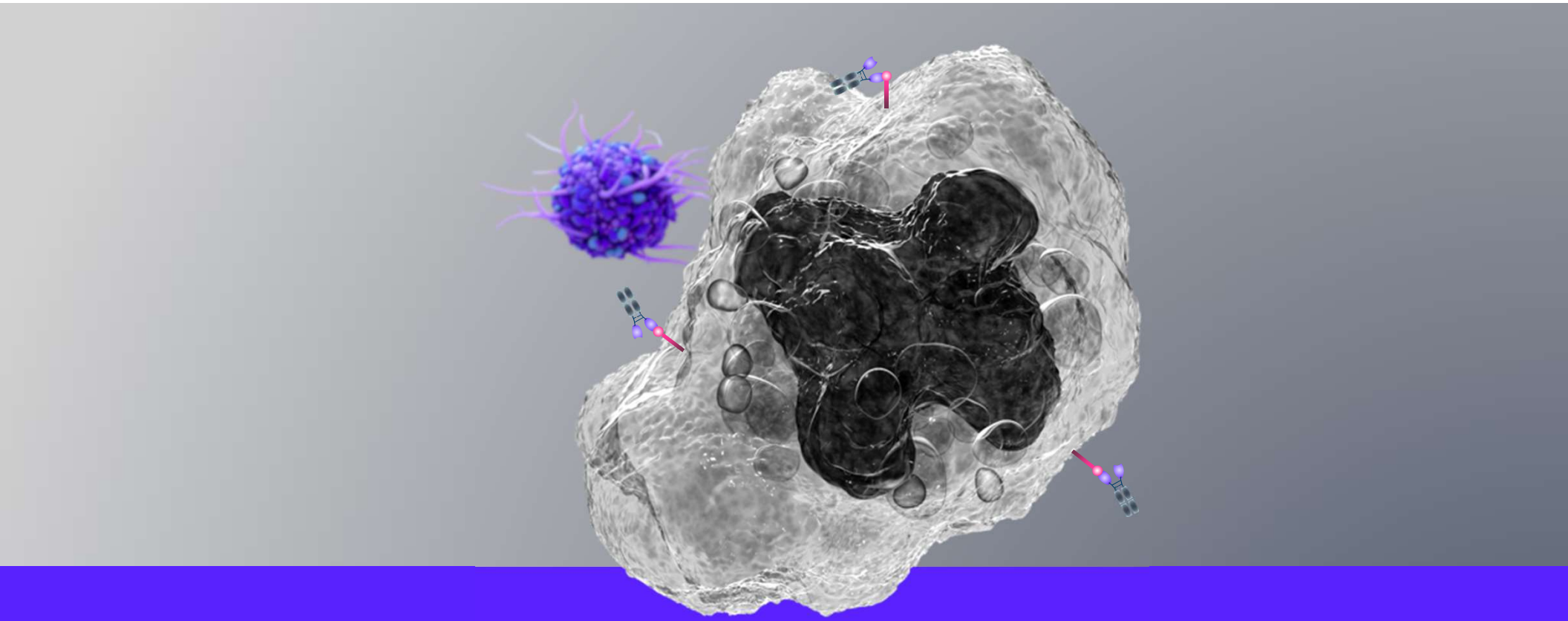

ALX™ ONCOLOGY

R&D Day 2025

Jason Lettmann | Chief Executive Officer

March 5, 2025

NASDAQ GS
ALXO

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Forward-Looking Statements

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What We Will Cover Today

1. ***Summarize the clinical data*** **that underpin our conviction in evorpacept's activity**
2. ***Lay out a clear and focused development strategy*** **with several paths to FDA registration**
3. ***Share the results of aggressive prioritization and cost-cutting*** **resulting in additional catalysts and extending our runway into Q4 2026**
4. ***Provide new guidance on upcoming data events*** **over next ~12-18 months across multiple clinical studies**

ALX has now demonstrated that combining evorpacept with anti-cancer antibodies is active and is advancing several trials forward to drive the program towards approval

Today's Presenters

Jason Lettmann
CEO, ALX Oncology

Jaume Pons, PhD
CSO, ALX Oncology

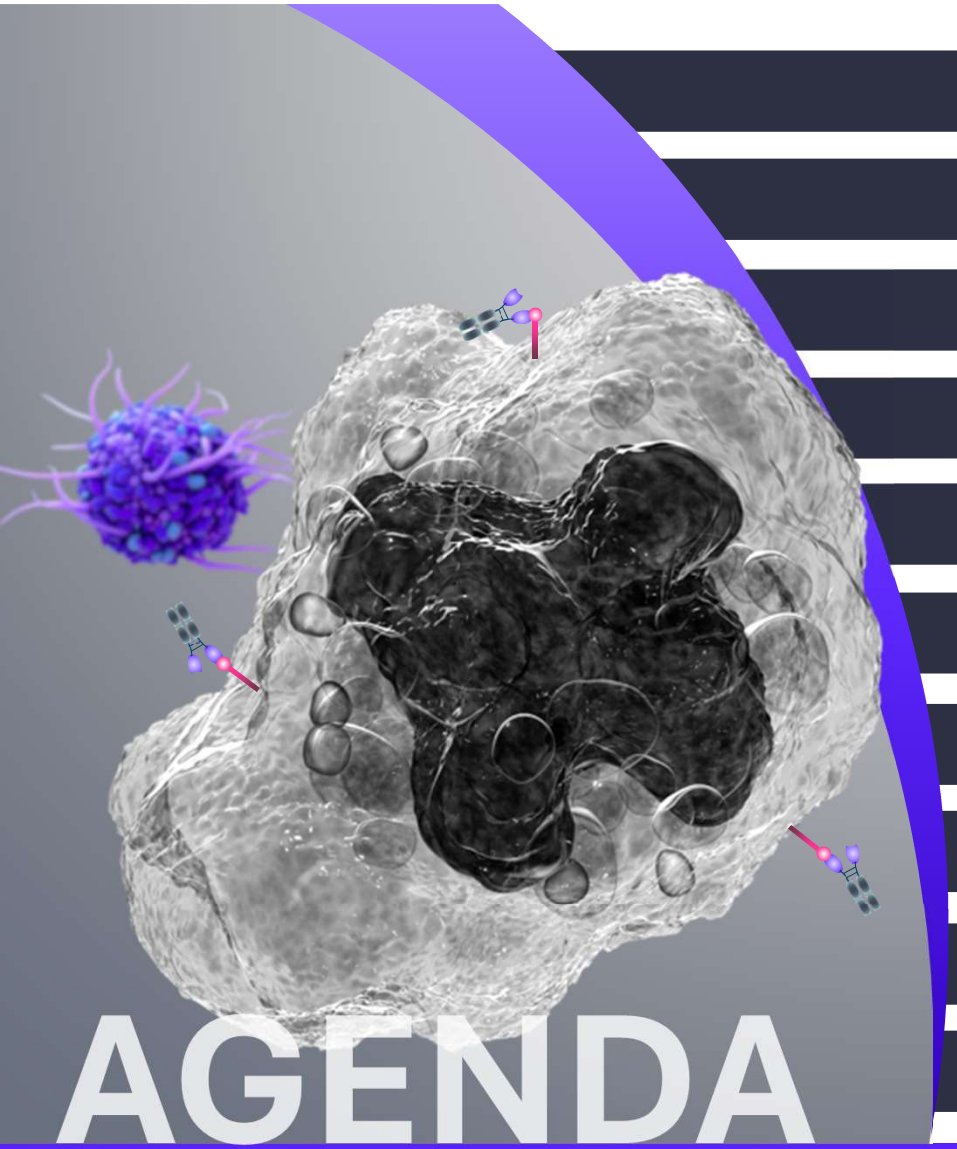
Alan Sandler, MD
CMO, ALX Oncology

Allison Dillon, PhD
CBO, ALX Oncology

Harish Shantharam, CFA
CFO, ALX Oncology

Paula R. Pohlmann, MD, MS, PhD
Associate Professor
Chief, Section of Breast Cancer Clinical Research
Department of Breast Medical Oncology
Department of Investigational Cancer Therapeutics
UT MDACC

Eric Van Cutsem, MD, PhD
Professor
Gastroenterology / Digestive Oncology
University Hospitals Gasthuisberg / Leuven & KU Leuven
Belgium



AGENDA

01 **Introduction**
Jason Lettmann, Chief Executive Officer

02 **History of Evorpacept and Preclinical Rationale**
Jaume Pons, PhD, Chief Scientific Officer

03 **Clinical Data in HER2+ Patient Populations**
Alan Sandler, MD, Chief Medical Officer

04 **New Breast Cancer Program**
Paula Pohlmann, MD, MD Anderson Cancer Center

05 **New Colorectal Cancer Program**
Eric Van Cutsem, MD, PhD, Univ Hospitals Belgium

06 **Antibody Combinations in Heme Malignancies**
Alan Sandler, MD, Chief Medical Officer

07 **Building the Evorpacept Franchise**
Allison Dillon, PhD, Chief Business Officer

08 **ALX2004**
Jaume Pons, PhD, Chief Scientific Officer

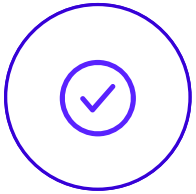
09 **Financial Updates and Milestones**
Harish Shantharam, Chief Financial Officer

10 **Concluding Remarks**
Jason Lettmann, Chief Executive Officer

Looking Back at Our 2024 Priorities

2024 Accomplishments	Results
Focus on execution: Deliver data from five clinical studies	• Delivered first positive randomized study in the CD47 space with the ASPEN-06 gastric data - oral presentation at ASCO GI 2025 • Delivered ASPEN-07 bladder data at ASCO 2024, evorpacept + zanidatamab breast data at SABCS 2024, and NHL data at AACR 2024 • Completed enrollment of ASPEN-03, 04 and 07, and announced first patient dosed in Sanofi study with Sarclisa
Drive what's next: Advance new evorpacept studies and ALX2004 into the clinic	• Drove indication selection and study launch for evorpacept antibody combinations in breast and colorectal cancers • Delivered IND-ready package for ALX2004 to support Q1 2025 IND submission
Build an A Team: Assemble world-class management team and board	• Added to leadership with new CMO Dr. Alan Sandler, new CFO Harish Shantharam, new CBO Dr. Allison Dillon, and several others in < one year • Added deep clinical and oncology strength to Board of Directors with Dr. Barbara Klencke and Dr. Chris Takimoto in Q4 2024

2025 Strategic Imperatives



EXECUTE ON EXISTING STUDIES

Deliver ASPEN-03 / ASPEN-04 data

Execute on ongoing studies

EXPAND INDICATIONS & DELIVER PIPELINE

Pursue additional studies in BC and CRC

Drive ALX2004 to IND clearance

RAISE ALX PROFILE & PARTNER

Deliver BD partnership/ strategic deals

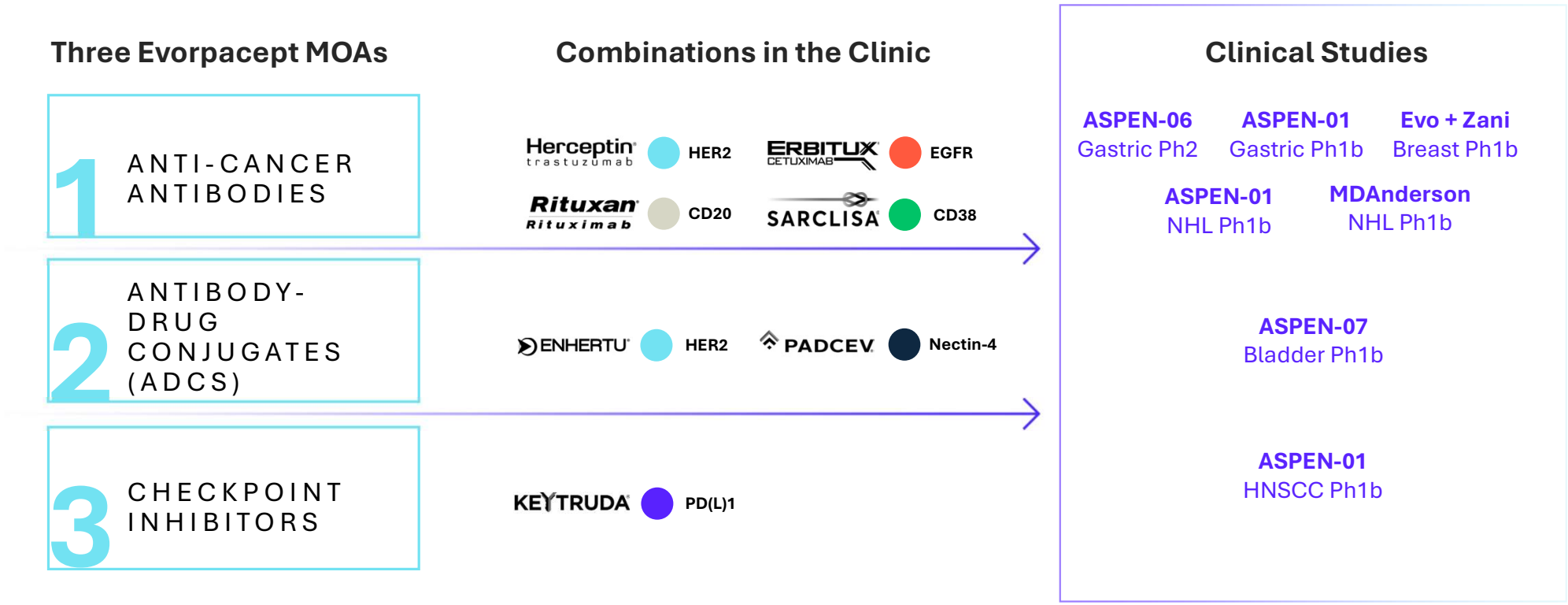
Expand and execute with existing partners

OPTIMIZE BUDGET & PRIORITIES

Deliver major catalysts on current cash

Manage budget to extend runway

Bold Vision for Evorpacept: Deliver First-In-Class, Universal Combination Agent

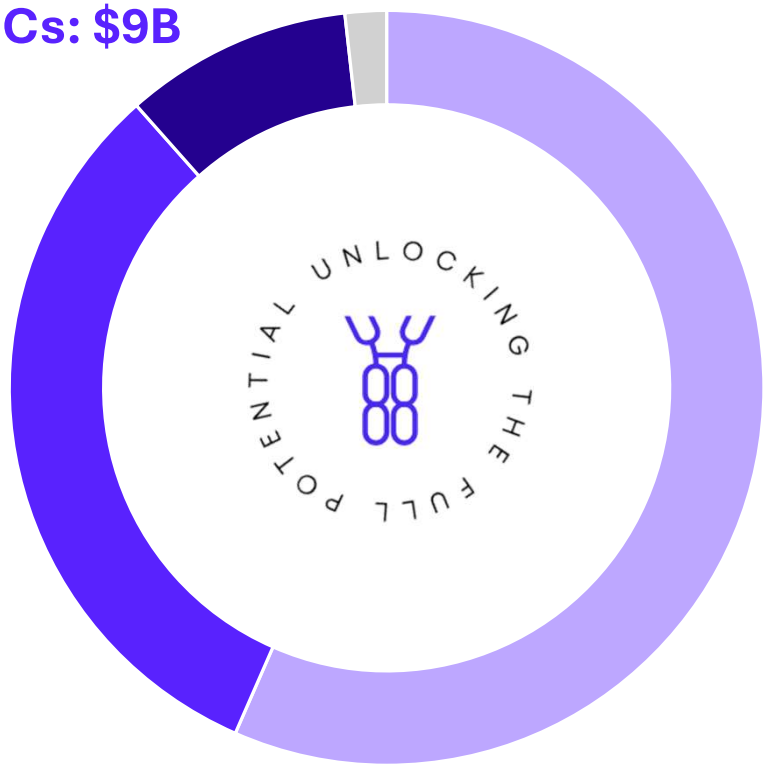


Evorpacept Is Designed to Enhance the Activity of the Majority of Biologics Used in Oncology Today

2023 Global Sales of Biologics in Oncology: $88B

ADCs: $9B

Anti-cancer antibodies: $28B

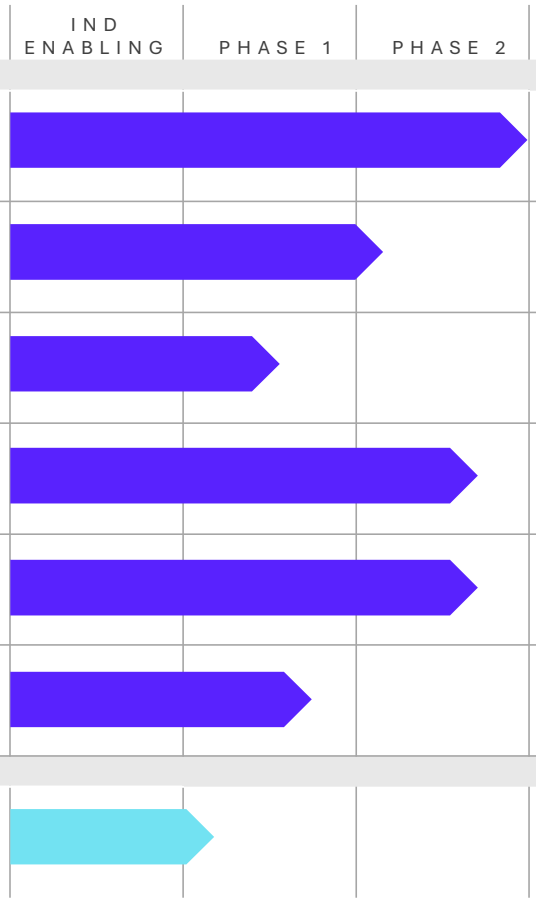


PD(L)1 inhibitors: $50B

Analysis based on GlobalData sales estimates

ALX Oncology is Pursuing a Robust Development Plan for Evorpacept

MODALITY /TARGET	PROGRAM	INDICATION	IND ENABLING	PHASE 1	PHASE 2	PHASE 3	STATUS
EVORPACEPT PROGRAMS							
Anti-cancer Antibodies	**ASPEN-06** Evorpacept, Herceptin®, CYRAMZA® + Paclitaxel[1]	2L or 3L Advanced HER2-Overexpressing Gastric/Gastroesophageal Junction (GEJ)					**Next steps pending FDA input**
	ASPEN-Breast Evorpacept, Herceptin® + chemotherapy	ENHERTU®-Experienced HER2-Positive Breast Cancer					**Launching Q1 '25, FPI mid-year '25**
	ASPEN-CRC Evorpacept, Erbitux® + chemotherapy	2L, EGFR-Naïve Metastatic Colorectal Cancer (CRC)					**Launching Q1 '25, FPI mid-year '25**
Checkpoint Inhibitors	**ASPEN-03** Evorpacept + KEYTRUDA®[2]	1L PD-L1 Positive Advanced HNSCC (Head and Neck Squamous Cell Carcinoma)					**Topline results Q2 '25**
	ASPEN-04 Evorpacept, KEYTRUDA®, 5FU + Platinum[2]	1L Advanced HNSCC					**Topline results Q2 '25**
ADCs	**ASPEN-07** Evorpacept + PADCEV®	Urothelial Cancer					**Data update Q2' 25**
ALX2004 PROGRAM							
ADC	Single-agent dose-escalation and expansion	EGFR-Expressing Solid Tumors					**Filing IND Q1 '25**



ALX Oncology retains worldwide rights to evorpacept.

1. Lilly supplies CYRAMZA® for ALX Oncology's ASPEN-06 program **2**. Merck supplies KEYTRUDA® for ALX Oncology's ASPEN-03 and ASPEN-04 programs

ALX Oncology is Pursuing a Robust Development Plan for Evorpacept: Non-ALX Sponsored Evorpacept Trials

MODALITY /TARGET	PROGRAM	INDICATION	IND ENABLING	PHASE 1	PHASE 2	PHASE 3	STATUS
EVORPACEPT PROGRAMS							
Anti-cancer Antibodies	Zanidatamab[1] + Evorpacept	HER2-Expressing Breast Cancer and Other Cancers					**Data presented at SABCS '24**
	SARCLISA® + Dexamethasone[2] + Evorpacept	RRMM (Relapsed or Refractory Multiple Myeloma)					**FPI Q3 '24, Currently Enrolling**
ADCs	ENHERTU® (I-SPY)[3] + Evorpacept	HER2-Positive HER2-Low Metastatic Breast Cancer					**Currently Enrolling**

ALX Oncology retains worldwide rights to evorpacept.

1. Jazz Pharmaceuticals sponsors zanidatamab clinical trial **2.** Quantum Leap Healthcare Collaborative sponsors I-SPY clinical trial **3.** Sanofi sponsors SARCLISA clinical trial

Upcoming milestone ASPEN-03 and ASPEN-04 Phase 2 Readout: 1L HNSCC

ASPEN-03 Phase 2 trial

Evorpacept + Keytruda

2:1

N≈118	N≈59
Evorpacept 45 mg/kg (Q3W) + Keytruda	Keytruda (Q3W)

Primary Endpoint

- ORR based on BICR vs historical control of pembro alone

ASPEN-04 Phase 2 trial

Evorpacept + Keytruda + chemo

2:1

N≈108	N≈54
Evorpacept 45 mg/kg (Q3W) + Keytruda + 5FU + cisplatin or carboplatin	Keytruda + 5FU + cisplatin or carboplatin (Q3W)

Primary Endpoint

- ORR based on BICR vs historical control of pembro + 5FU + platinum

Secondary analyses will include ORR between randomized arms

- Primary endpoint updated to be only ORR to support potential Accelerated Approval
- OS, PFS, and ORR between groups are secondary endpoints
- Results will be submitted to a medical meeting in 2H 2025

ASPEN-03 and ASPEN-04 TLR expected 2Q 2025

Unmet Need in HNSCC and Evorpacept's Potential

Need for agents in 1L HNSCC that:

... are **novel** and bring a different mechanistic approach to target

... **have demonstrated efficacy in randomized settings** given that single-arm trials have not consistently translated to larger pivotal trials

... **can address the entire 1L continuum of care** including both pembro and pembro + chemo

... **are IO agents** that can enable the "long tail" and ultimately benefit survival

Evorpacept's potential

- Drives a different MOA to cell killing via enhanced T-cell priming and activation
- With >300 patients enrolled, ASPEN-03/04 will be largest randomized trials in 1L HNSCC to read out since the LEAP study
- ASPEN-03/04 test evorpacept in combination with pembro +/- chemo
- Most advanced IO agent in development in 1L HNSCC with potential to be first IO drug approved since pembro in 2019

Combining Evorpacept With Anti-Cancer Antibodies Represents the Most De-Risked Path Forward and a Substantial Commercial Opportunity

Three Evorpacept MOAs

1 ANTI-CANCER ANTIBODIES

Combinations in the Clinic

Herceptin trastuzumab — HER2

ERBITUX CETUXIMAB — EGFR

Rituxan Rituximab — CD20

SARCLISA — CD38

Clinical Studies

ASPEN-06
Gastric Ph2

ASPEN-01
Gastric Ph1b

Evo + Zani
Breast Ph1b

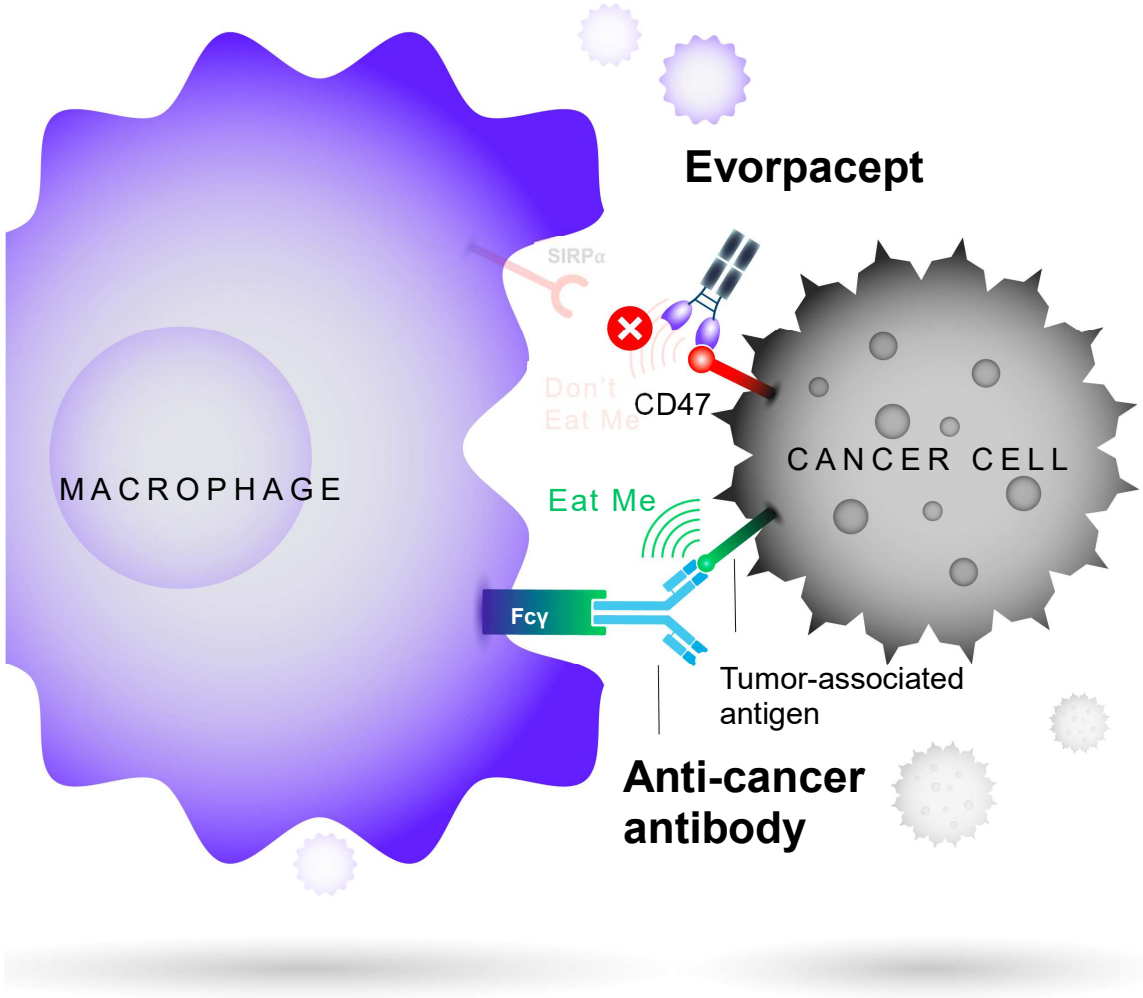
ASPEN-01
NHL Ph1b

MD Anderson
NHL Ph1b

TODAY'S FOCUS

The Evorpacept + Antibody Franchise

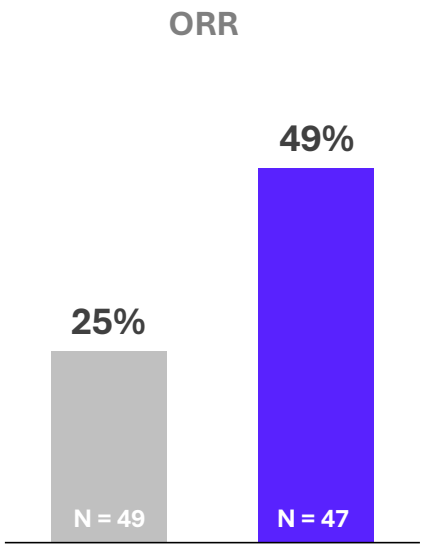
Evorpacept + Anti-Cancer Antibody Mechanism of Action



Evidence that Evorpacept Improves Upon Anti-Tumor Activity of Standard of Care Anti-Cancer Antibodies in Solid and Hematologic Tumors

Gastric

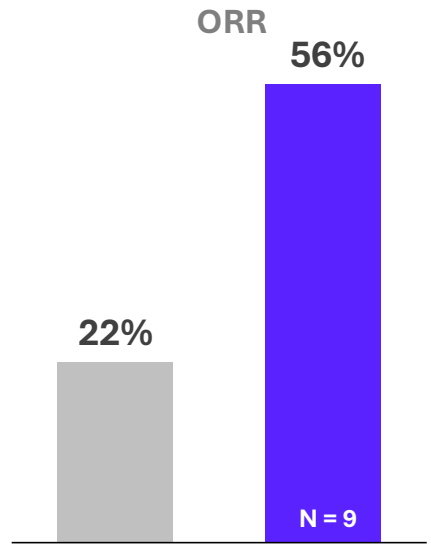
(HER2+ fresh biopsy or ctDNA+[1])



ASPEN-06, randomized Ph2

Breast

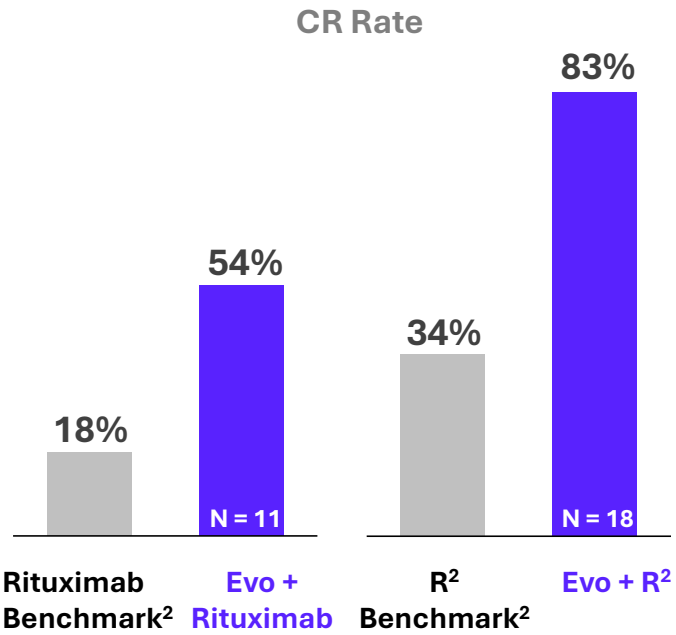
(R/R HER2+ by central assessment [4])



Phase 1b/2 Collaboration[4] and historic benchmark

NHL

(R/R Indolent)



ASPEN-01 Ph1b and historic benchmark

IST and historic benchmark

1. ASPEN-06 Dec 2, 2024 data cutoff in fresh HER2+ biopsy or ctDNA+ patients. 2. AUGMENT study, Leonard, *JCO*, 2019 3. Margenza prescribing information; 4. SABCS 2024 #PS8-09; HER2+ by central assessment
ORR = overall response rate; CR = complete response; IST = investigator-sponsored trial

The Evorpacept Opportunity in Breast Cancer

De-risked given positive data in two HER2-positive cancers

- **Positive randomized data in ASPEN-06 in gastric cancer with trastuzumab**
- **Positive data in evorpacept + zanidatamab study in HER2+ metastatic breast cancer**

Changing landscape drives opportunity in patients who have progressed on ENHERTU and/or other HER2-directed therapies

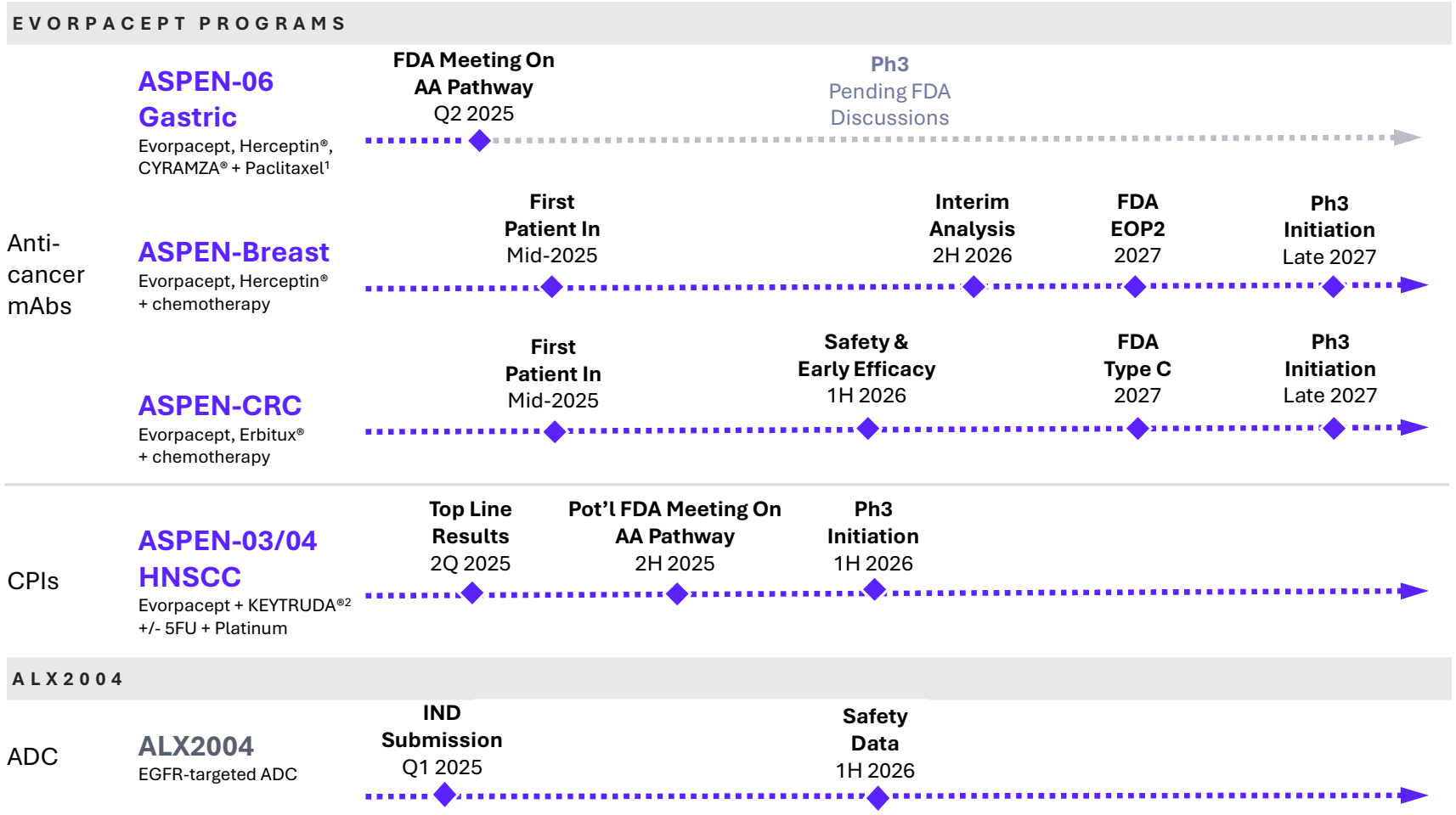
- **Active in patients who progressed on trastuzumab in gastric cancer**
- **Active in patients who progressed on ENHERTU and 5+ HER2-directed Tx in breast cancer**

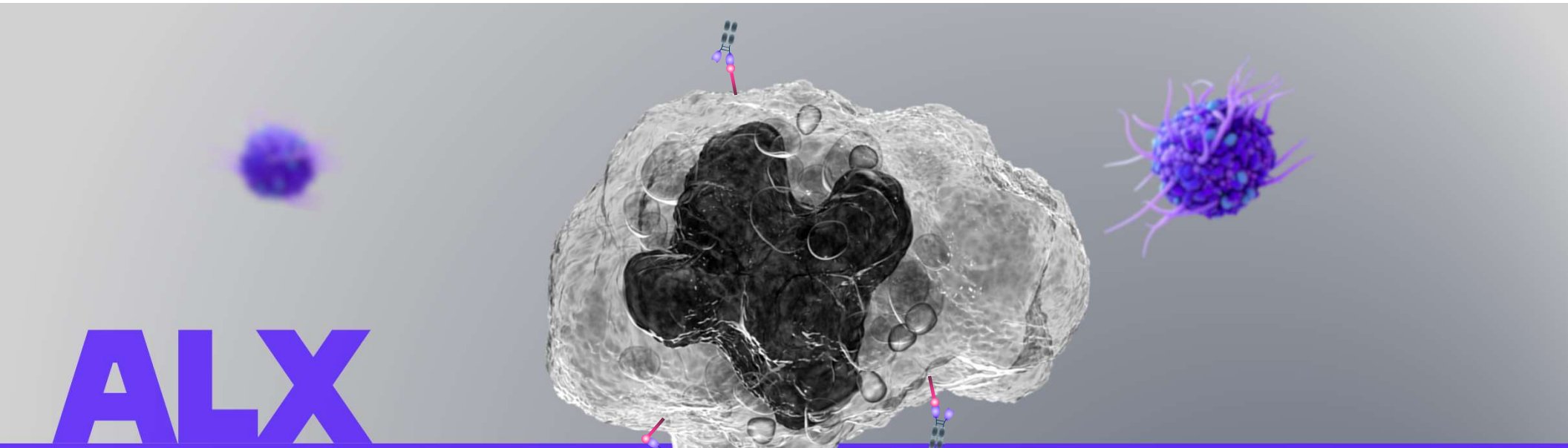
Significant peak sales potential and unique opportunity to move to earlier lines of care

- **2L+ HER2+ mBC represents a population of ~48k* patients**
- **1L HER2+ mBC and neoadjuvant setting represents a population of an additional ~120k* patients**

*In 7 major markets: US, EU5 (UK, Spain, Italy, Germany, France) and Japan; Source: Clarivate Market Forecast, gastroesophageal cancer, December 2024

ALX Is Focused On Aggressively Driving Several Paths to FDA Registration





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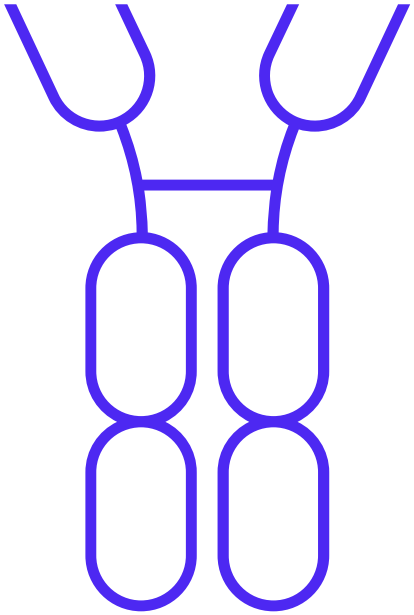
MECHANISM AND TARGET

History of Evorpacept and Preclinical Rationale

Jaume Pons, PhD
CSO, ALX Oncology

Evorpacept: Uniquely Designed to Offer a Differentiated Safety Profile and Robust Clinical Activity in Combination with Available Cancer Therapies

EVORPACEPT



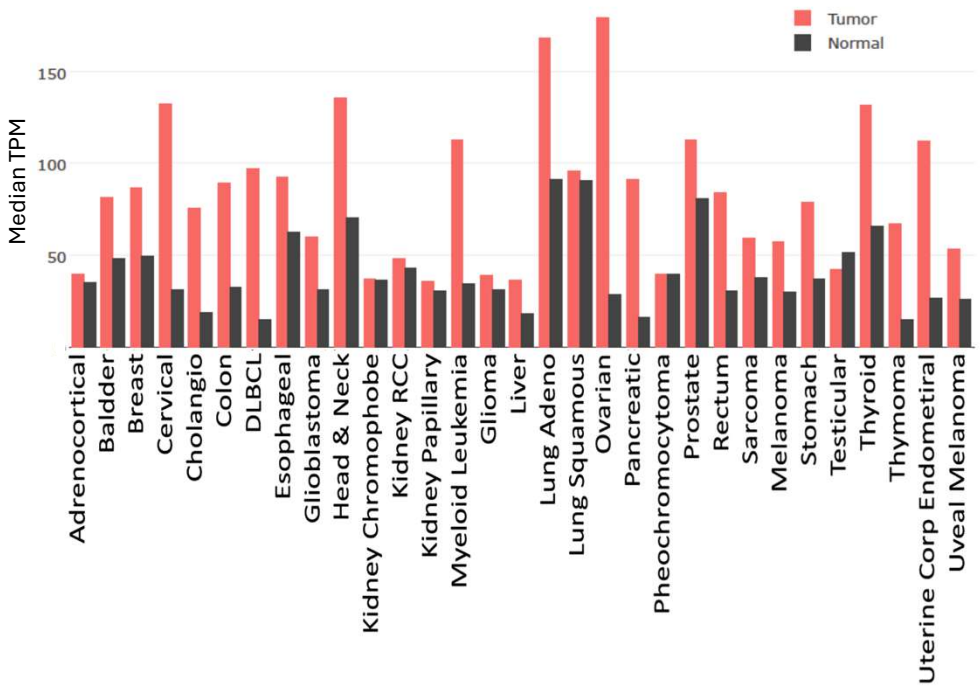
Higher affinity CD47 binding	Inactive Fc domain	Lower molecular weight	Antibody-like pharmacokinetics
More potently blocks CD47 signal on cancer cells	Less "sink effect" = more targeted No known dose-dependent cytopenia = higher dosing	Increased solid tumor penetration and higher effective dosing	Long half life = less frequent dosing and matching regimen with combinations

ROBUST CLINICAL ACTIVITY | **BEST-IN-CLASS SAFETY PROFILE** | **STRONG SOLID TUMOR ACTIVITY** | **BROAD COMBINATION POTENTIAL**

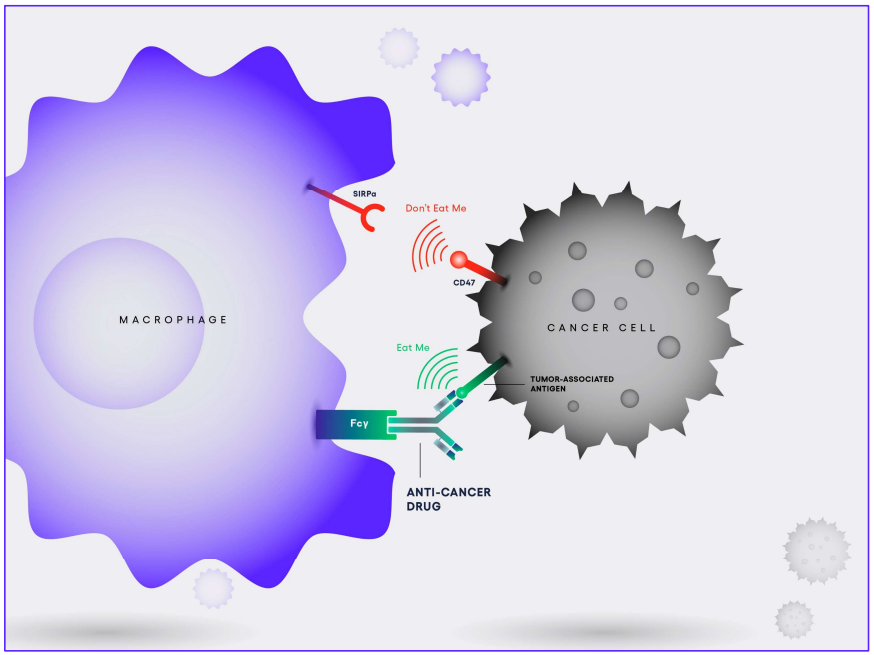
CD47 Is the Canonical Myeloid Checkpoint and Ubiquitously Expressed in Both Healthy Tissues and Tumors

CD47 as a tumor-associated antigen

CD47 expression levels from RNA sequencing

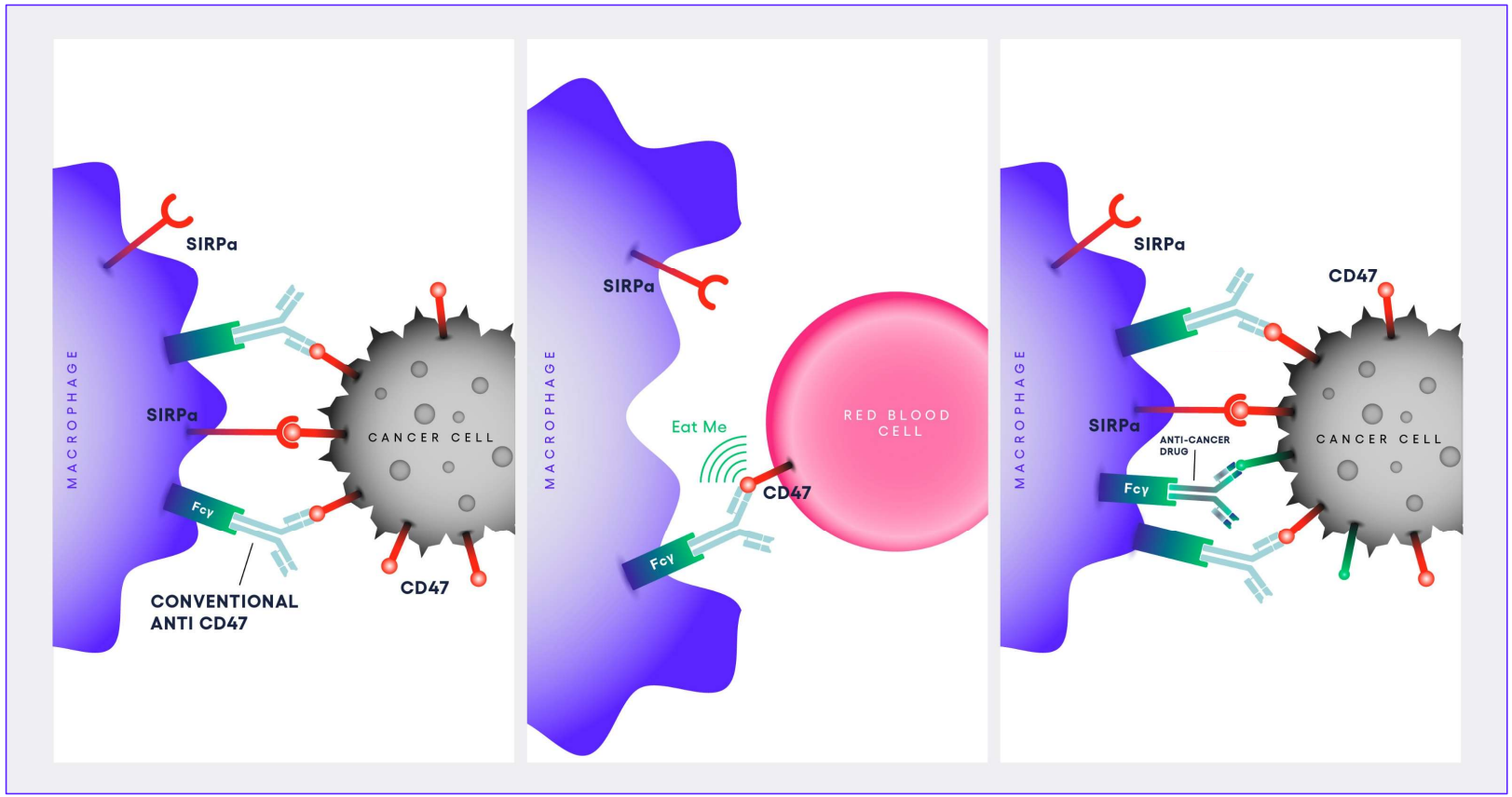


CD47 as a myeloid checkpoint

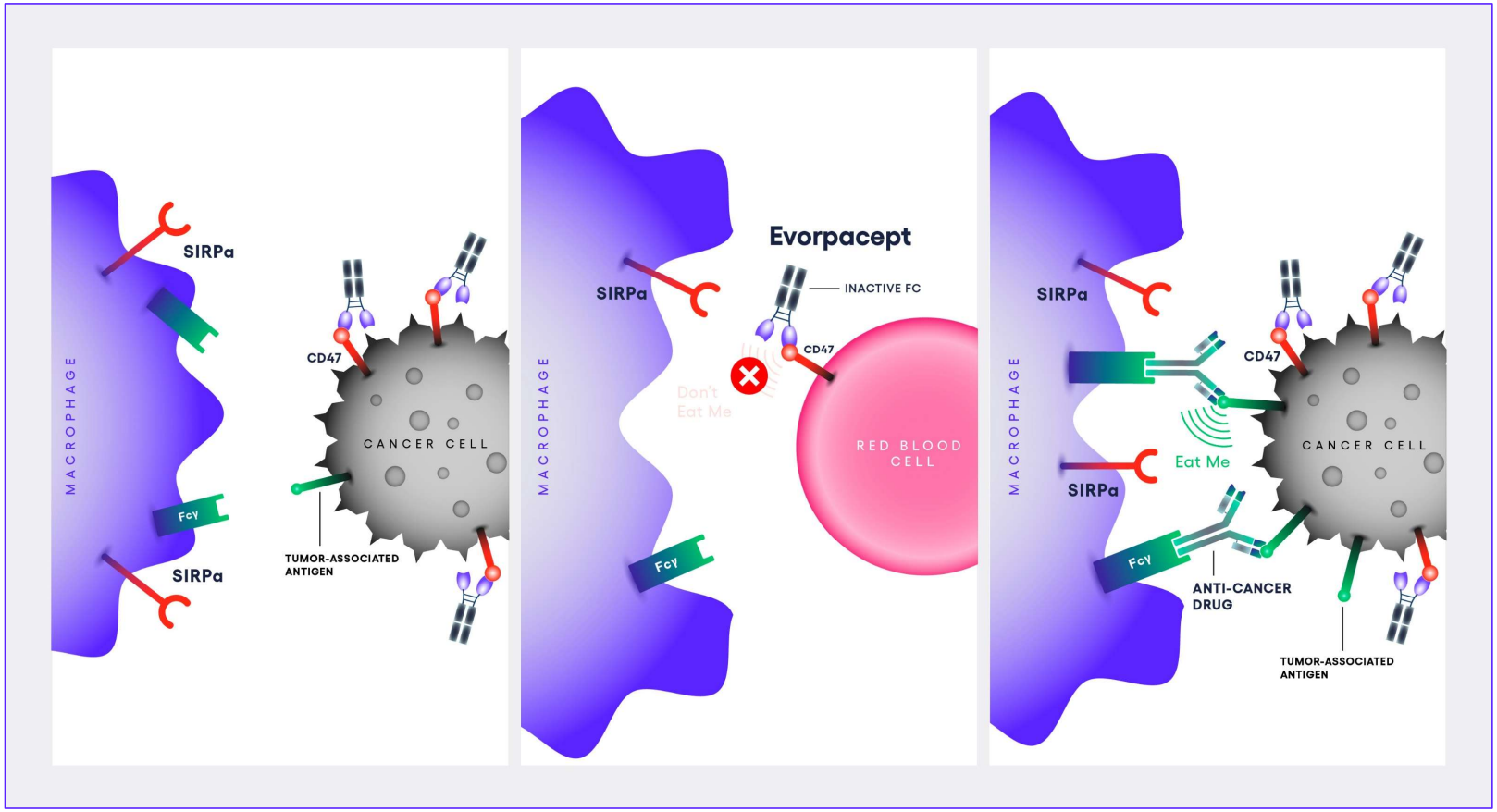


Tang, Z. et al, GEPIA, 2017; TPM = transcripts per million

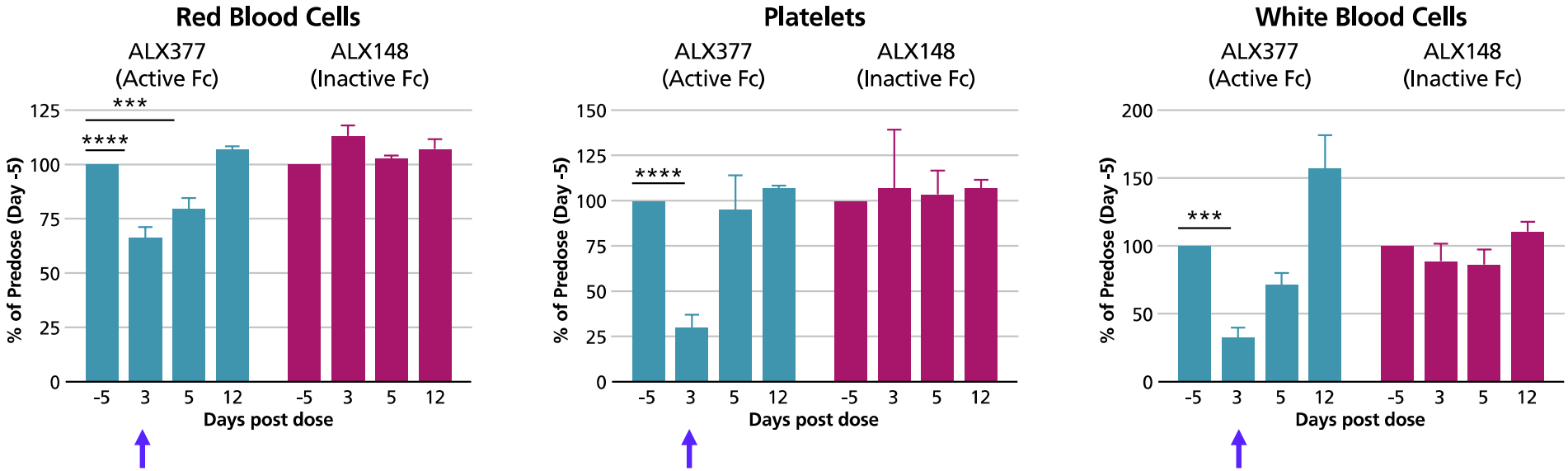
Traditional CD47 Blockers With Active FC Domains Were Limited by On-Target Cytopenias



Evorpacept Enables Antibody-Dependent Cellular Phagocytosis (ADCP) Without Inducing Cytopenias



Evorpacept (ALX148) Is Designed To Avoid the Cytopenias Caused by Traditional Approaches To Targeting CD47



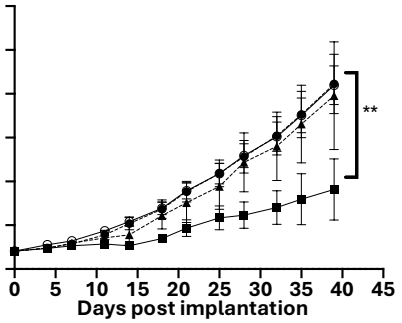
Inactive Fc is the core determinant of safety profile for a CD47-targeted agent as evidenced by decreased blood counts after initial dose with active Fc

CD-1 mice received 30 mg/kg IV single dose
***p<0.001, ****p<0.0001
Kauder, et al, 2018

Evorpacept Combined With Anti-Cancer Antibodies in a Range of Cancer Types

Solid tumors

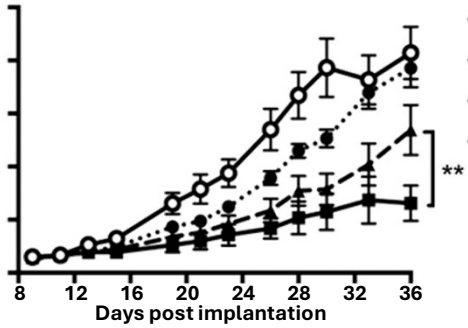
CRC PDOX22420 Model



PBS
Evorpacept
Cetuximab
Evorpacept + cetuximab

** p =0.0051, paired two-tailed t-test, N=5 mice/group
Cetuximab (3 mg/kg), every 7 days, 3 doses; evorpacept (30 mg/kg), every 4 days, 6 doses

OE19 HER2+ Gastric Model

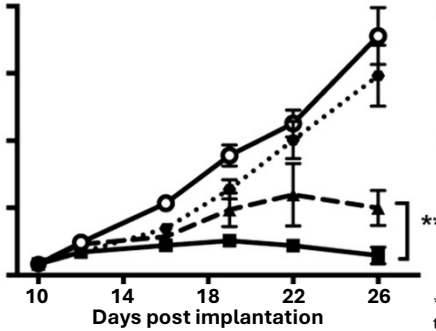


PBS
Evorpacept
Trastuzumab
Evorpacept + Trastuzumab

** p <0.01, two-tailed t-test, N=10 mice/group
Trastuzumab, twice/week, 6 doses; evorpacept, twice/week, 6 doses

Hematologic malignancies

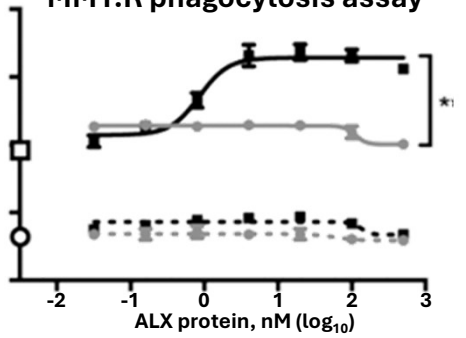
Raji NOD-SCID Model



PBS
Evorpacept
Rituximab
Evorpacept + rituximab

**** p < 0.0001, paired two-tailed t-test, N=10 mice/group

MM1.R phagocytosis assay



Evorpacept + daratumumab
Control + daratumumab
Evorpacept + isotype control
Control + isotype control

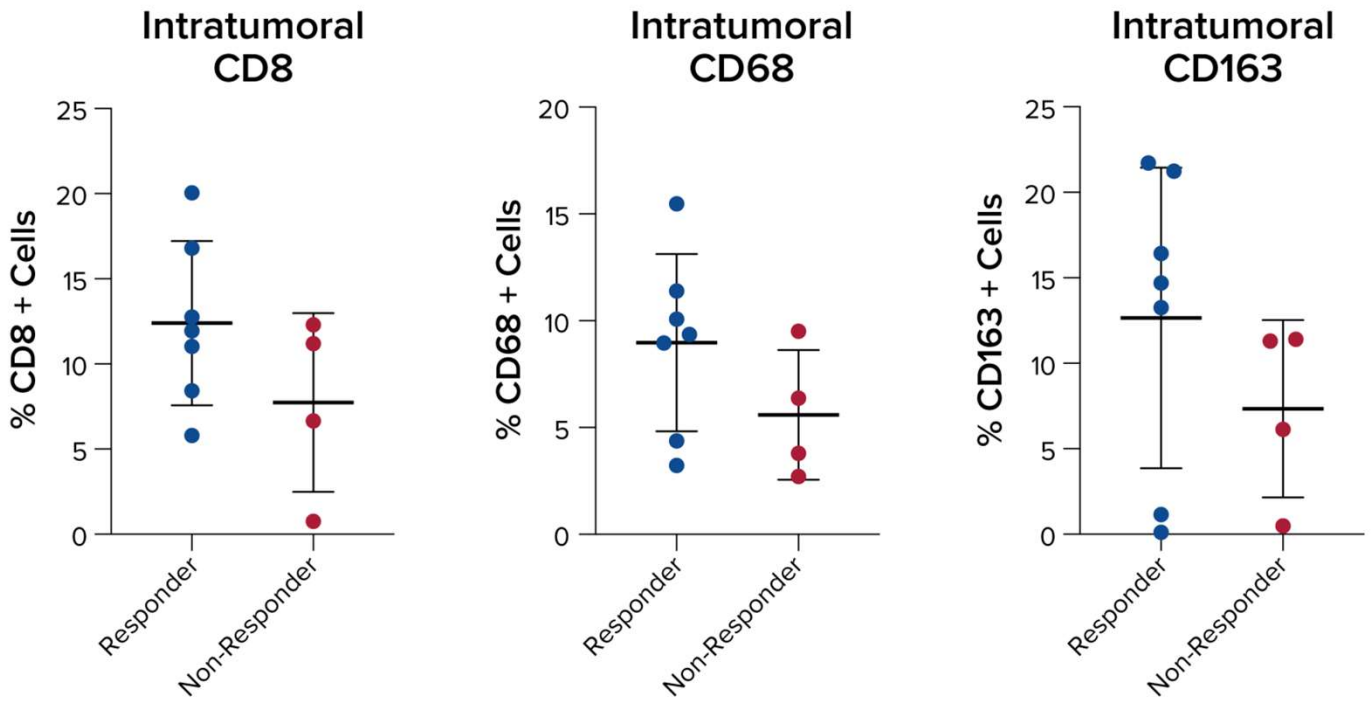
* p < 0.0001 one-way ANOVA compared to antibody alone

Kauder, et al, 2019; ALX unpublished research

Evorpacept unleashes macrophages to destroy cancer cells and the combined effect with an anti-cancer antibody potentiates the innate immune system, an underexploited pathway of tumor killing

Increased Tumor-Associated Macrophages and Infiltrating Lymphocytes Observed After Treatment with Evorpacept Combinations in Patients

Baseline tumor-infiltrating immune cells in responders and non-responders treated with evorpacept + trastuzumab, ramucirumab, and paclitaxel



Chung, et al, ESMO 2021

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CLINICAL DATA IN HER2+ PATIENT POPULATIONS

Gastric Cancer:
Trastuzumab + Evorpacept

Breast Cancer:
Zanidatamab + Evorpacept

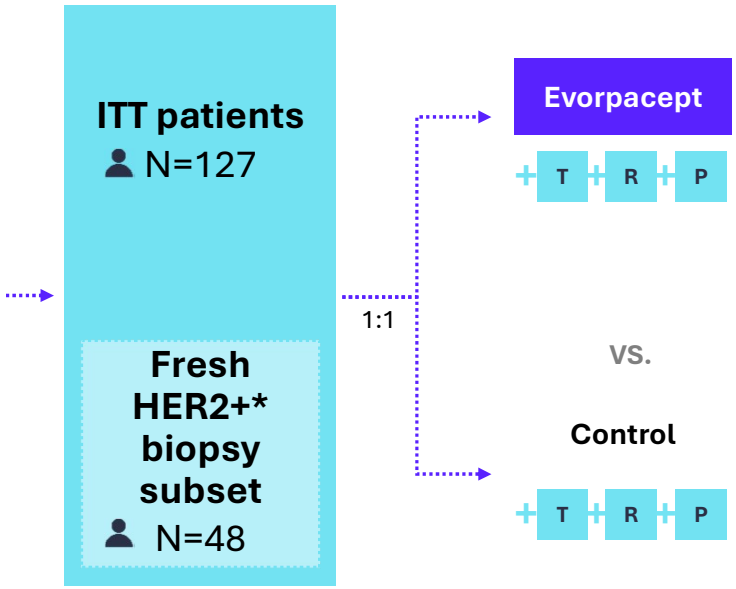
Alan Sandler, MD
CMO, ALX Oncology

ANTI-CANCER ANTIBODIES

ASPEN-06 Phase 2: Evorpacept Plus TRP in HER2+ Advanced/Metastatic GC/GEJ Adenocarcinoma

Key eligibility criteria

- HER2+ GC or GEJ that has progressed on or after prior HER2-directed therapy
- 2L or 3L
- Prior trastuzumab deruxtecan (ENHERTU) and/or checkpoint inhibitors allowed
- Prior CD47-agent, anti-SIRPα, or ramucirumab excluded



Primary endpoints in both ITT and fresh biopsy populations:

- Improvement in ORR** vs assumed historical control of 30% (Wilke et al, Lancet, October 2014)
- Improvement in ORR** over internal control (difference ≥ 10%)

Secondary endpoints

- DOR, PFS, OS

Exploratory endpoint

- ctDNA

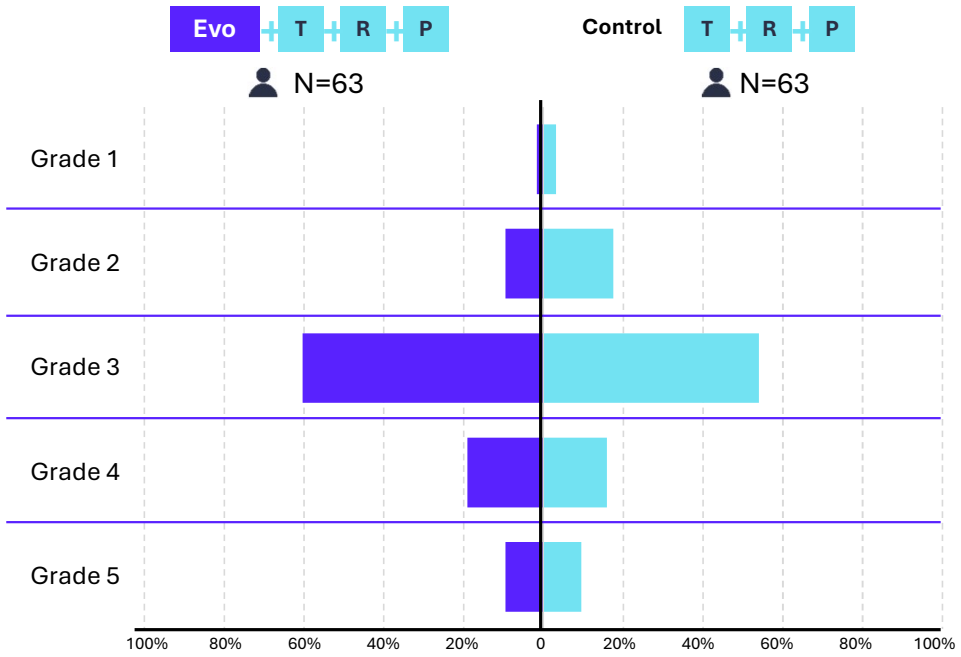
All patients enrolled received a prior HER2-targeted therapy (e.g., trastuzumab) and were enrolled with either a HER2+ fresh or archival biopsy

Evo Evorpacept (30 mg/kg IV Q2W) **T** Trastuzumab (6 mg/kg > 4 mg/kg Q2W) **R** Ramucirumab (8 mg/kg Q2W) **P** Paclitaxel (80 mg/m^2 on day 1, 8, 15 of 28-day cycle)

GC- gastric cancer, GEJ- gastroesophageal junction, TRP- trastuzumab, ramucirumab, paclitaxel; selected secondary and exploratory endpoints shown.
*Fresh HER2-positive is defined as biopsies that were HER2-positive after receiving prior HER2-targeted treatment
**Based on investigator assessment

ASPEN-06 Safety: Evo-TRP Was Generally Well Tolerated and ≥Grade 3 TEAEs Were Largely Balanced Across the Two Arms

All causality adverse events, by grade



- The incidence of adverse events due to any cause was comparable by arm
- There were 11 Grade 5 treatment emergent adverse events (four for ETRP; seven for TRP), only two of which were deemed to be treatment related: esophageal perforation (ETRP) and pneumopathy (TRP)

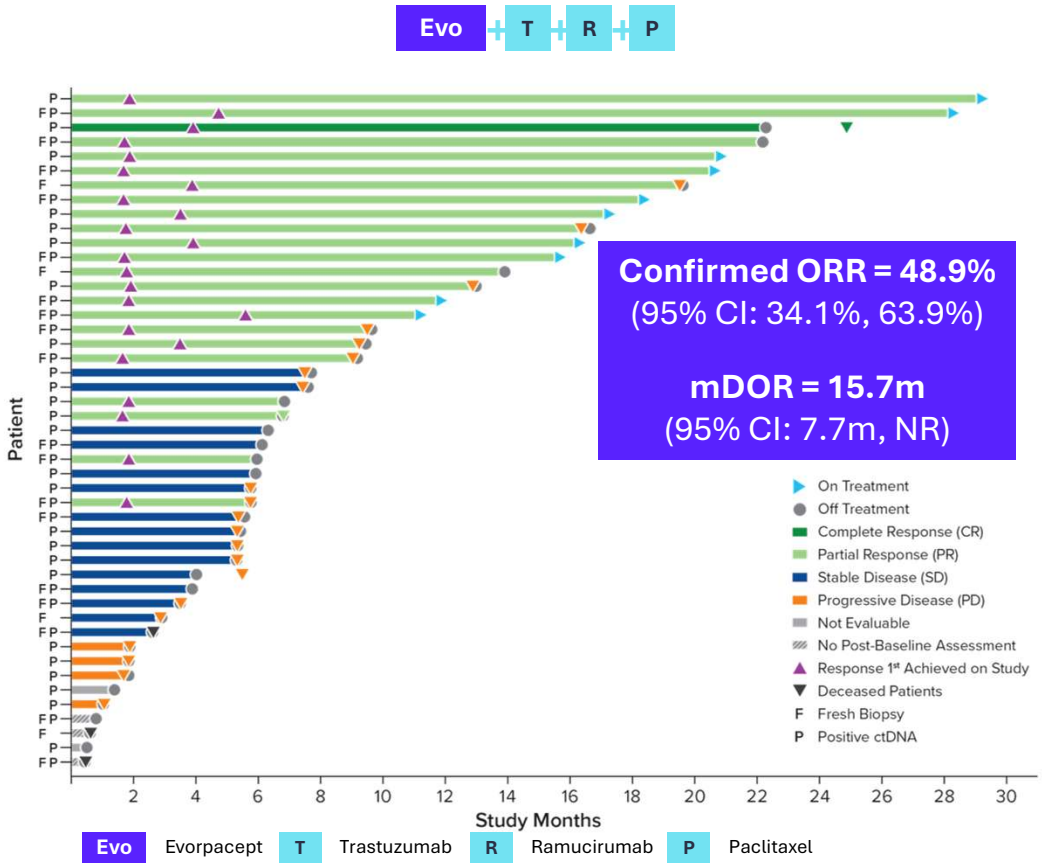
Evorpacept's safety profile was consistent with its prior experience in over 700 patients treated to date

Evo Evorpacept T Trastuzumab R Ramucirumab P Paclitaxel

All G5 TEAEs: ETRP (N=4): sepsis N=2, esophageal perforation N=1, respiratory failure N=1. TRP (N=7): sepsis N=1, pneumonia/pneumopathy/respiratory infection N=1 each, sudden death N=1, death from unknown cause N=1, esophageal hemorrhage N=1; data cutoff as of 02 Dec 2024

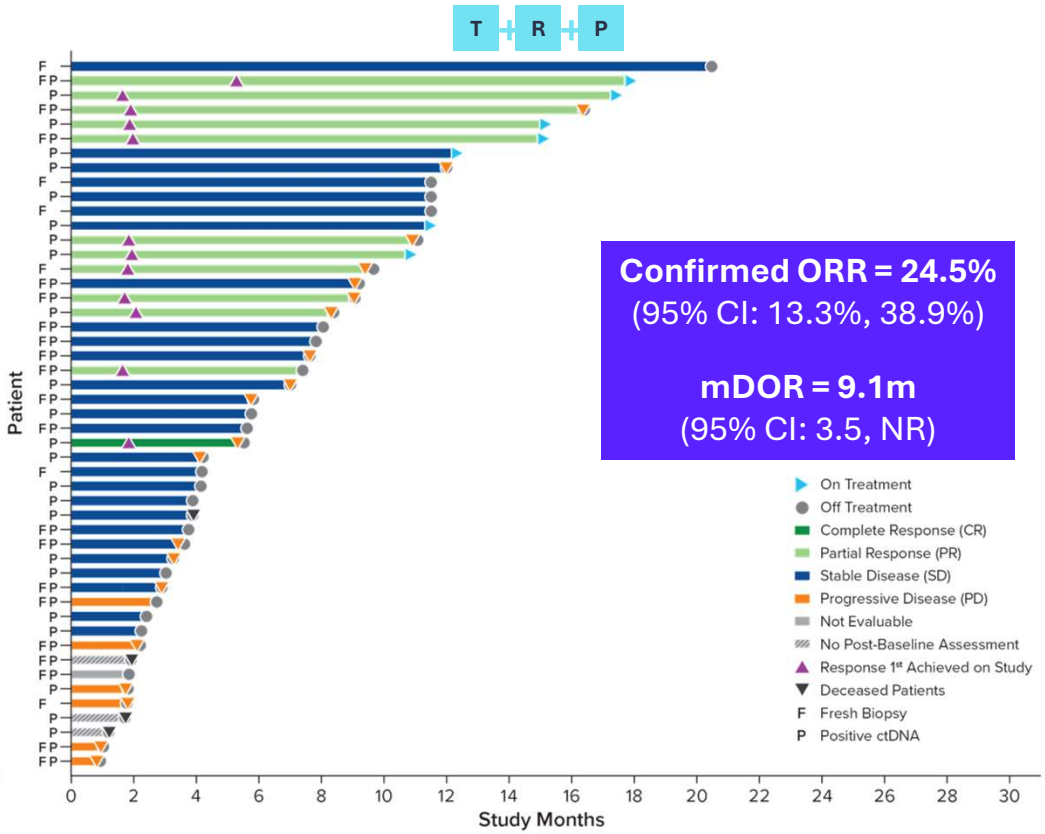
Evorpacept Demonstrated Durable Activity in Patients with HER2-Positivity Confirmed by Fresh Biopsy or ctDNA

Patients with HER2+ confirmed with fresh biopsy OR ctDNA+ (n=96)



Confirmed ORR = 48.9%
(95% CI: 34.1%, 63.9%)

mDOR = 15.7m
(95% CI: 7.7m, NR)



Confirmed ORR = 24.5%
(95% CI: 13.3%, 38.9%)

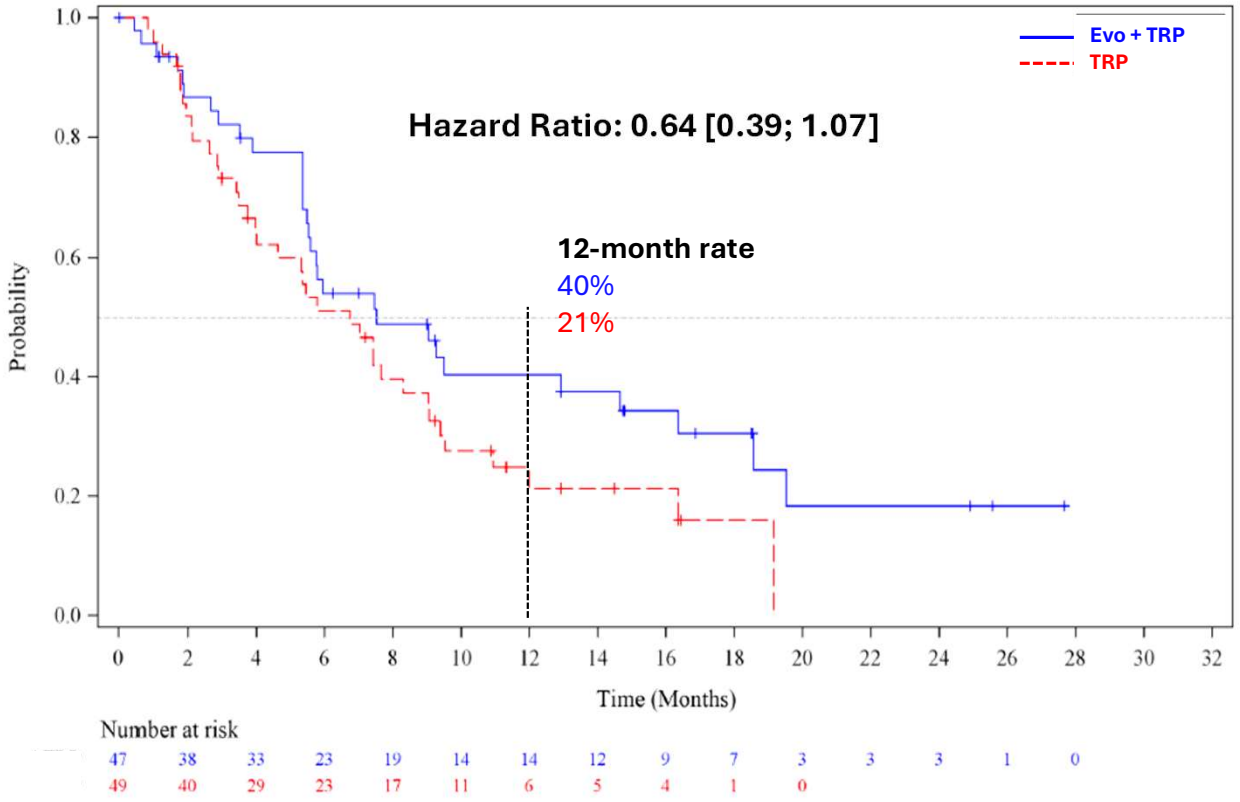
mDOR = 9.1m
(95% CI: 3.5, NR)

Evo Evorpacept T Trastuzumab R Ramucirumab P Paclitaxel

Seven patients treated with Evo+TRP and five patients treated with TRP had no post-baseline assessment or best response of NE; data cutoff as of 02 Dec 2024; NR = Not Reached

Improved Progression-Free Survival in Patients with Fresh Biopsy or HER2+ Positive ctDNA

Progression-free survival (PFS) based on investigator assessment
HER2+ confirmed with fresh biopsy OR ctDNA+ (n=96)



Number of patients with events
30 (63.8%)
37 (75.5%)

Number of patients censored
17 (36.2%)
12 (24.5%)

mPFS [95% CI]
7.5 [5.5-14.7]
6.7 [4.0-9.0]

Data cutoff as of 02 Dec 2024

ASPEN-06 Gastric Study:
Potential Lead Indication in a Biomarker-Selected Patient Population

- **Robust and Durable Clinical Activity in HER2+ Patients**
- **Validated Mechanism of Action with a Clear Biomarker**
- **Consistently Well-Tolerated with a Multidrug Regimen**
- **Active in Patients Who Have Progressed on Conventional HER2-Directed Therapy**
- **Evorpacept + TRP Compares Favorably to Benchmarks in ≥2L Treatment**

FDA meeting scheduled in Q2 to discuss ASPEN-06 results and possible path to Accelerated Approval; update planned in Q2

Phase 1b/2 Trial Evaluating Safety and Efficacy of Evorpacept Plus Zanidatamab in Patients Who Have Progressed on Prior HER2-Directed Therapy

Key eligibility criteria

Unresectable, locally advanced and/or metastatic HER2-expressing cancer

- HER2-positive breast cancer (IHC 3+ or IHC 2+/FISH-positive)
- ≥3 prior regimens, must include trastuzumab, pertuzumab and either T-DM1, tucatinib, or T-DXd
- Data were analyzed for all patients enrolled and based on central assessment

Treatment[1]

Evorpacept 30 mg/kg Q2W

\+ **Zanidatamab** 1200 mg (<70 kg) OR 1600 mg (≥ 70kg) Q2W

Expansion Cohort 1

HER2-positive mBC (n=21)

Summary of baseline characteristics in Cohort 1

- **Population represented heavily pretreated R/R population**
- Median of six prior therapies including multiple HER2-targeted therapies
- **Notably, 100% of patients had received prior ENHERTU**
- **Local assessment of HER2 in archived tumor samples was used for enrollment; when unavailable, patients could be enrolled based on central assessment**
- Data were analyzed for all patients enrolled and based on central assessment
- Of the 20/21 patients with local HER2 assessment, eight (40%) were confirmed HER2-positive by central assessment (one centrally HER2-positive patient did not have local assessment)

1. Mandatory IRR prophylactic treatment included corticosteroids, antihistamines, and acetaminophen. Study conducted by Jazz Pharmaceuticals

This study provides clinical data supporting further development of evorpacept with HER2-targeted agents in patients with breast cancer

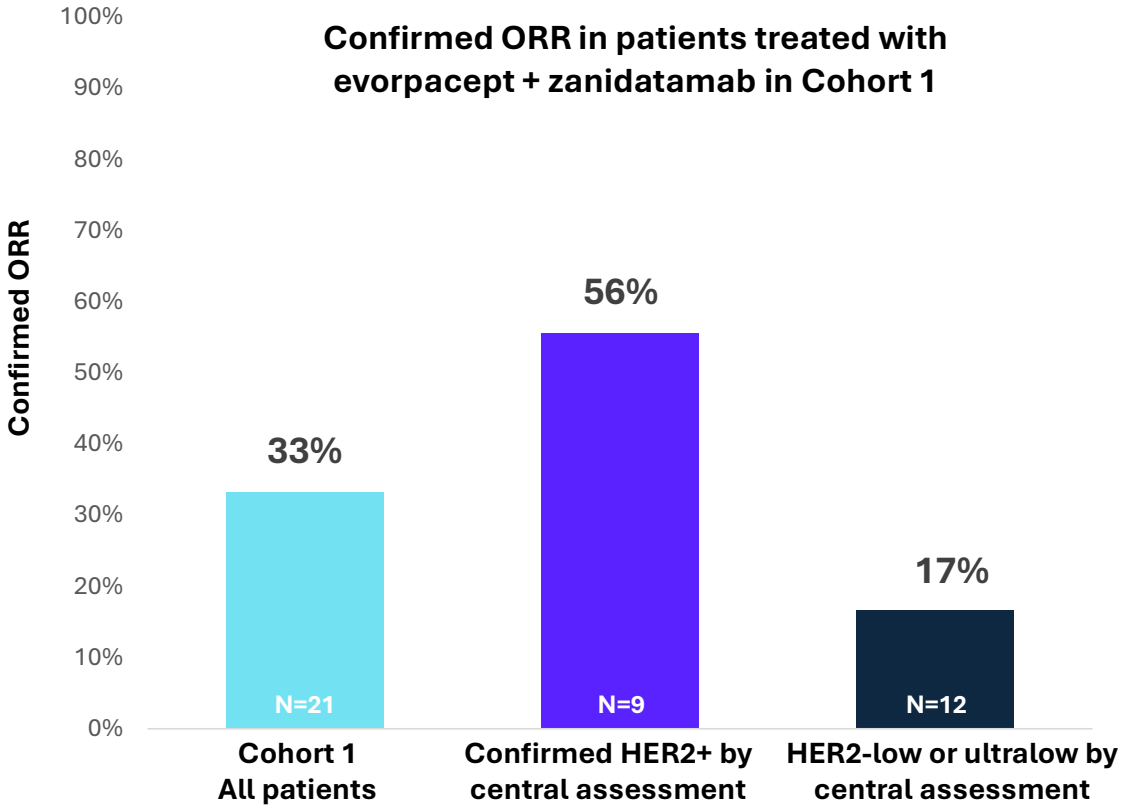
The Combination of Evorpacept and Zanidatamab was Well-Tolerated With a Manageable Safety Profile that is Consistent With Prior Experience With Each Agent

	All Patients (N=52)		
Any TRAE, n (%)	**45 (86.5)**		
Grade 1-2	38 (73.1)		
Grade 3	7 (13.5)		
Grade 4-5	0 (0)		
Serious TRAEs, n (%)	**3 (5.8)[b]**		
TRAEs leading to treatment discontinuation, n (%)	**2 (3.8)[c]**		
TRAEs leading to dose reductions, n (%)	**0 (0)**		
Treatment-related AESI, n (%)			
Left ventricular dysfunctional	1 (1.9)		
IRR	12 (23.1)		
Non-infectious pulmonary toxicities	0 (0)		
Most common TRAEs* n (%)	**Grade 1**	**Grade 2**	**Grade 3**
Diarrhea	20 (38.5)	9 (17.3)	3 (5.8)
Fatigue	9 (17.3)	7 (13.5)	1 (1.9)
Nausea	11 (21.2)	3 (5.8)	0 (0)
IRR	3 (5.8)	7 (13.5)	2 (3.8)

- **Most treatment-related adverse events were grade 1 or 2 (related to zanidatamab and/or evorpacept)**
- TRAEs of special interest included: one (1.9%) patient with grade 3 ejection fraction decreased and 12 (23.1%) patients with IRRs – all IRRs resolved; one patient had an IRR event after the dosing order was reversed to zanidatamab followed by evorpacept
- **No non-infectious pulmonary toxicities occurred**
- **There were no treatment-related deaths**

Data cutoff date 1 August 2024. **a.** TRAEs defined as events with an onset during or after receipt of the first dose of study treatment within 30 days after the last dose and were determined as related to zanidatamab and/or evorpacept by the investigators. **b.** Two additional events (diarrhea and LVEF decreased) occurred outside the 30-day window for TRAEs. **c.** Both events were grade 3 IRRs that resolved following treatment discontinuation. **d.** Defined as LVEF <50% with absolute decrease of ⩾10 percentage points below pretreatment baseline and/or grade ⩾2 heart failure. **e.** Grades 1-3 occurring in ⩾20% of patients or ⩾2 patients.
AESI, adverse event of special interest; IRR, infusion-related reaction; LVEF, left ventricular ejection fraction; TRAE, treatment-related adverse event.
Montero. et. al. SABCS 2024, Poster Spotlight Presentation. Abstr #SESS-2007

Breast Cancer Patients With Confirmed HER2-Positivity Had the Greatest Benefit From Evorpacept + Zanidatamab



Strongest efficacy in confirmed HER2+

- ORR of 55.6% (5/9)
- mDOR NE (range: 5.5-25.9m)
- mPFS = 7.4m (95% CI: 0.6, NE)

Compares favorably to benchmark

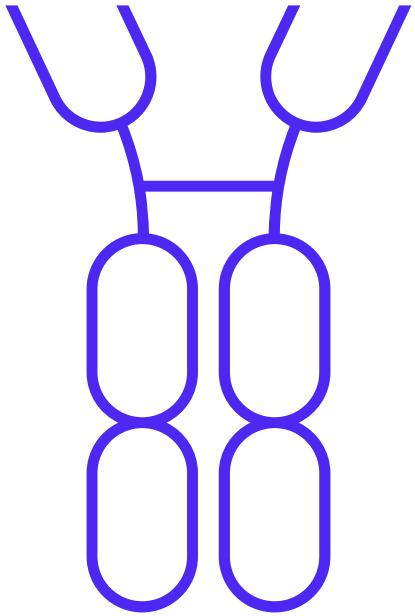
- SOPHIA study (n=536) of margetuximab + chemo vs. trastuzumab + chemo (ORR: 22% vs. 16%)

Median follow-up (range) was 9.6 (0.6, 29.7) months, with six patients on treatment at data cutoff as of August 1, 2024; HER2-Low/Ultralow = IHC1+, IHC2+ / ISH-, IHC 0

1. *JAMA Oncol*. 2021;7(4):573-584. doi:10.1001/jamaoncol.2020.7932
Montero. et. al. SABCS 2024, Poster Spotlight Presentation. Abstr #SESS-2007

Two Studies Demonstrate the Power of Evorpacept Engaging the Innate Immune Response and Further Validate Its Mechanism With Anti-Cancer Antibodies, Particularly in HER2+ Tumors

EVORPACEPT



- **Robust and Durable Clinical Activity in HER2+ Gastric/GEJ and Breast Cancer**
- **Validated Mechanism of Action with a Clear Biomarker**
- **Consistently Well-Tolerated with HER2-Targeted Agents**
- **Active in Patients Who Have Progressed on Conventional HER2-Directed Therapy**

ALX

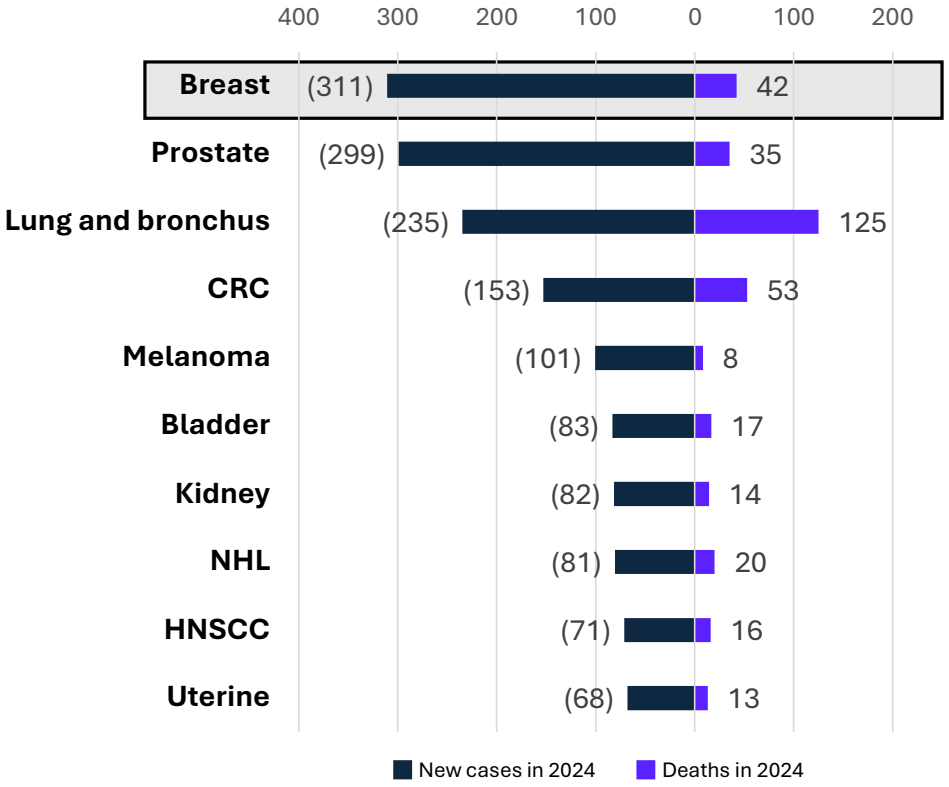
NEW BREAST CANCER PROGRAM

ASPEN-Breast

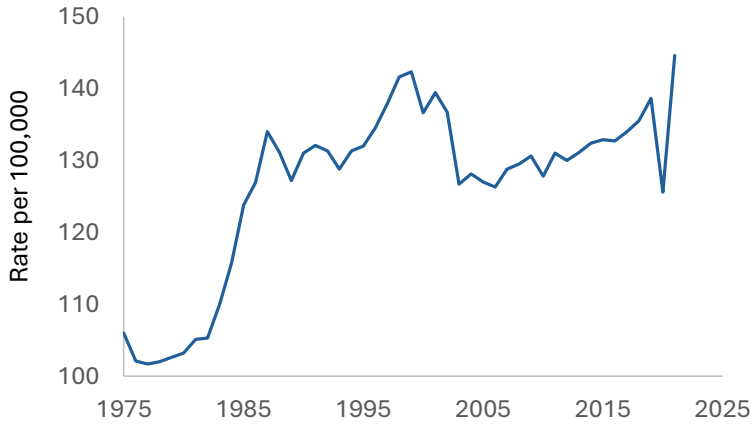
Paula R. Pohlmann, M., MS., PhD
Associate Professor
Chief, Section of Breast Cancer Clinical Research
Department of Breast Medical Oncology
Department of Investigational Cancer Therapeutics
UT MDACC

Breast Cancer Remains an Area of High Unmet Need Despite Recent Advancements in Early Metastatic Lines of Therapy

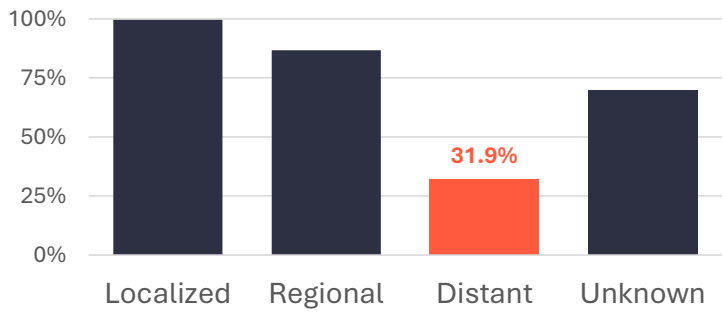
US top 10 types of cancer by estimated new cases in 2024 (thousands)



Breast cancer represents 15.5% of all new cancer cases in the US and rates are rising



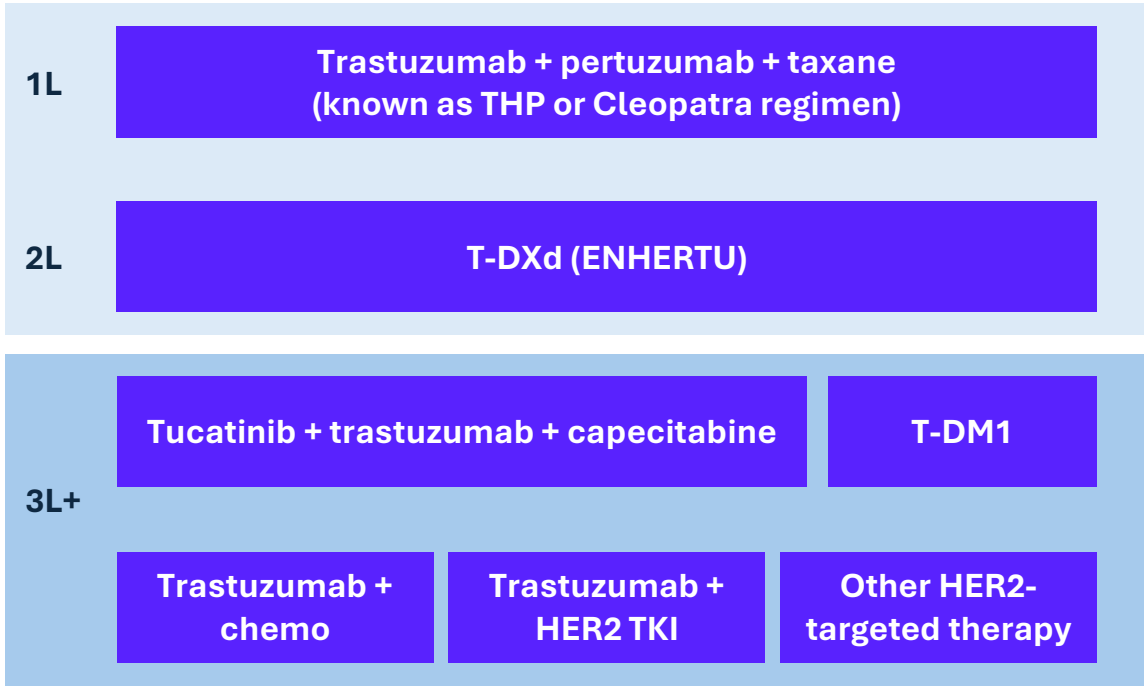
5-year relative survival in breast cancer



American Association for Cancer Research: Head and Neck Cancers; SEER cancer stat facts accessed February 2025; CRC = colorectal cancer; NHL = non-Hodgkin lymphoma

Recent Advancements in 1L and 2L Treatment Have Increased the Need for Effective Therapies in T-DXd Experienced Patients

Today's HER2+ metastatic cancer treatment paradigm

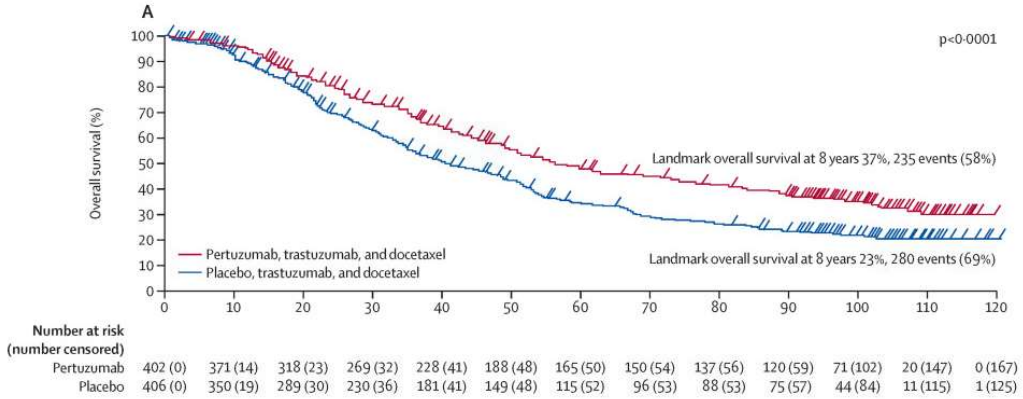


- Current SOC is 1st line THP followed by Enhertu for patients with no or stable CNS disease
- Options for patients that progress on T-DXd are increasingly important
- Current therapies used in the post T-DXd setting are approved based on pre T-DXd era trials
- Ongoing DESTINY-Breast09 Phase 3 trial of 1L T-DXd +/- pertuzumab could change treatment paradigm

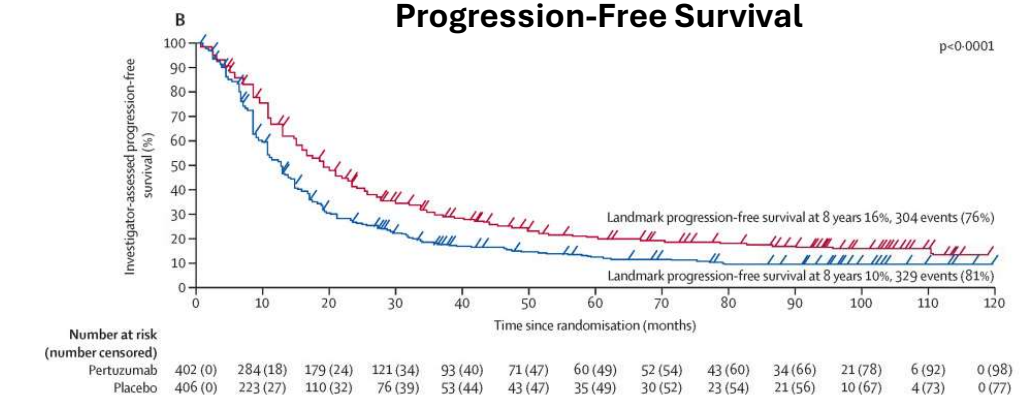
Adapted from NCCN guidelines v1.2025

Established THP as the Standard of Care in First-Line Metastatic Disease in HER2+ Breast Cancer

Overall Survival



Progression-Free Survival



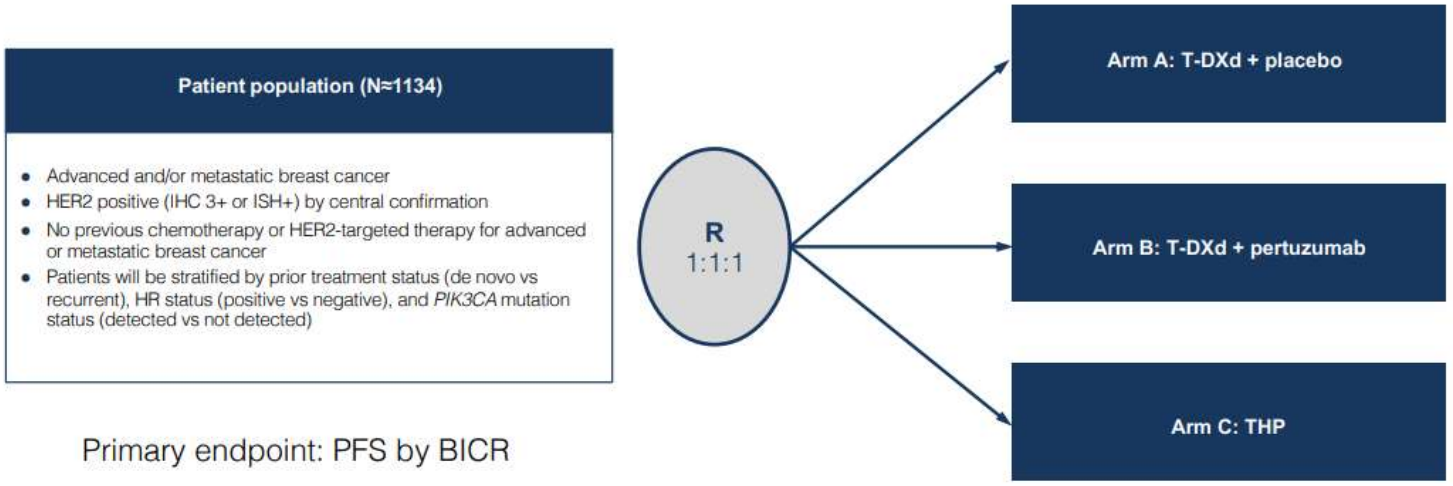
- CLEOPATRA study (n=808) established docetaxel + trastuzumab + pertuzumab (THP) as 1L standard of care

Baselga J et al. NEJM 2012; Swain S et al. NEJM 2015; Swain S et al. Lancet Oncol 2020

DESTINY-Breast 09 Is an Ongoing Challenge to 1L CLEOPATRA and May Establish T-DXd (ENHERTU) as the New 1L Standard of Care

DESTINY-Breast09: A Phase 3 Trial of T-DXd Alone or in Combination With Pertuzumab in First-Line HER2+ MBC

Will moving T-DXd earlier in disease course further increase its efficacy?



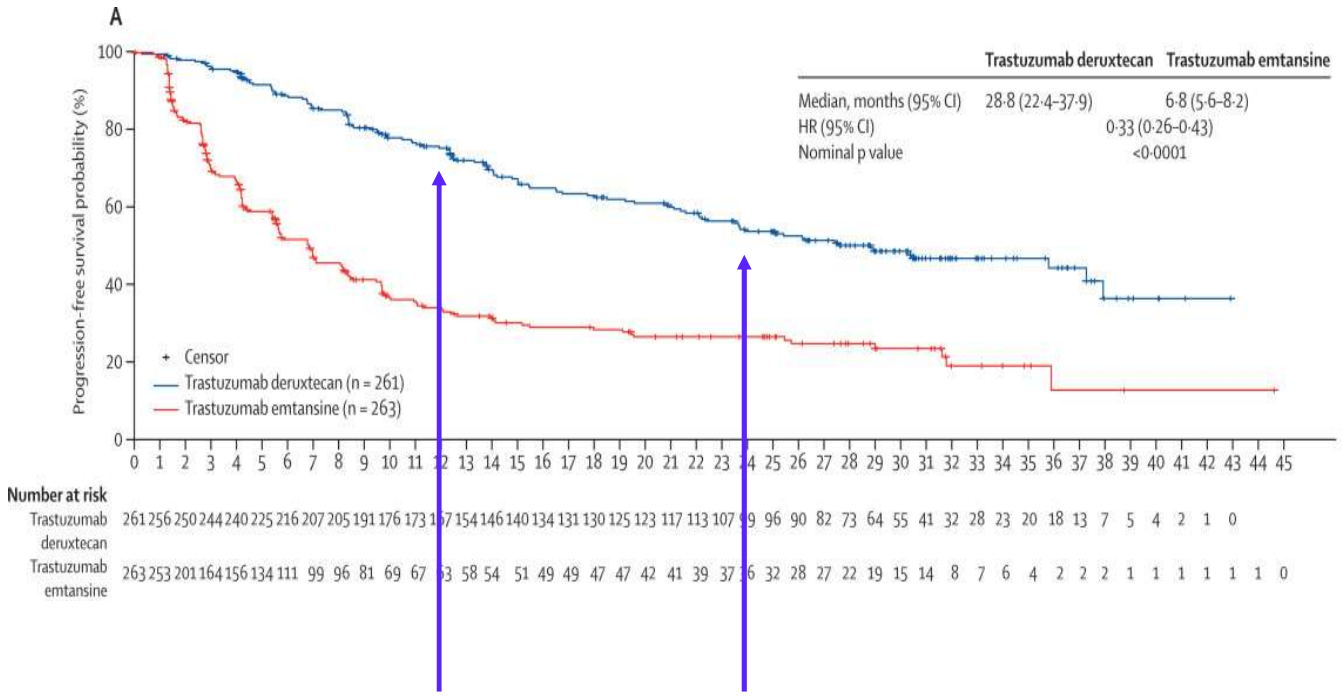
Primary endpoint: PFS by BICR

Cleopatra regimen

NCT04784715

Tolaney et al, SABCS 2021

Why Do We Need More Novel Anti-HER2 Treatment Options?



- Regardless of ENHERTU in 1L or 2L, patients will still progress and need new options in later lines
- Lack of post-ENHERTU data supporting the effectiveness of KADCYLA and/or TUKYSA® potentially creates a new, large market opportunity with no standard of care

With Destiny Breast03, ENHERTU was established as SOC in 2L mBC but …

~25% of patients progressed at 1 year and ~50% progressed at 2 years

Adapted from 1. Cortes J, et al N Engl J Med 2022; 2. Hurvitz et al, GS2-02 SABCS 2022.
From: Pohlmann PR Spotlight Discussion SABCS 2022

There Are No IO Agents Currently Approved With a Broad Label for HER2-Positive mBC

MAbs/Bispecifics	ADCs	TKIs	IO

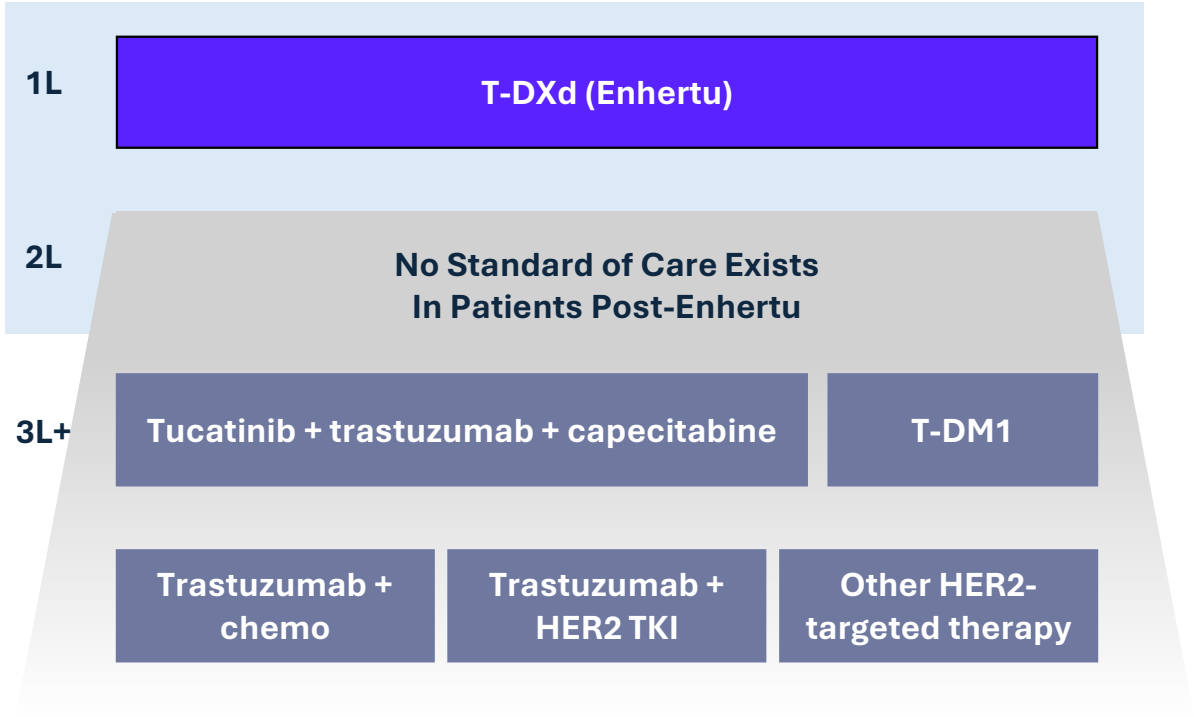
• Currently approved
  • Trastuzumab
  • Pertuzumab
  • Margetuximab
• In development
  • Zanidatamab
	• Currently approved
	  • T-DXd
	  • T-DM1
	• In development
	  • ARX-788
		• Currently approved
		  • Lapatinib
		  • Neratinib
		  • Tucatinib
		• In development
		  • AST-1306
			• Currently approved
			  • Pembrolizumab/ dostarlimab *(only approved for MSI-H or dMMR patients)*
			• In development
			  • **Evorpacept**

Adapted from Pohlmann PR et al. CCR Focus

There are no IO agents currently approved with a broad label for HER2-positive mBC

As ENHERTU May Move to First Line, Second Line Plus Is an Unknown Given That There Are No HER2-Targeted Agents With Data in a Post-ENHERTU Population

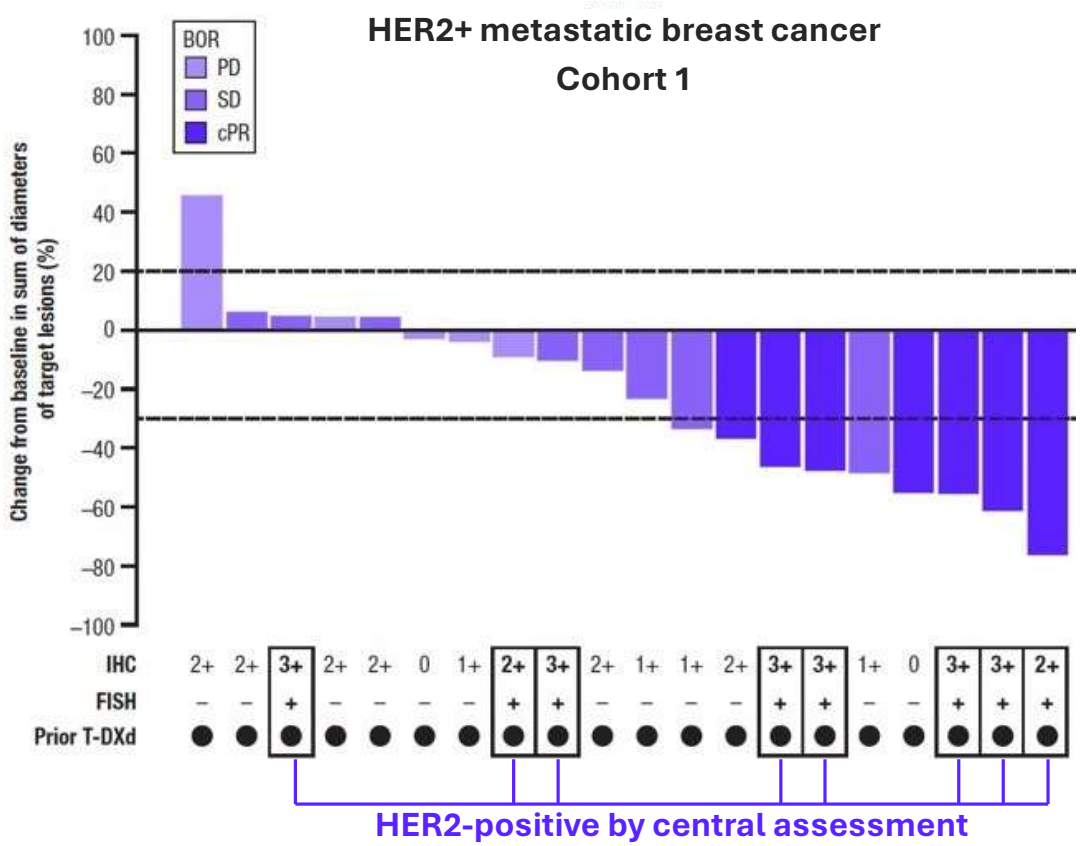
Future HER2+ metastatic cancer treatment paradigm



- Significant unmet need exists and will increase for patients that have progressed on T-DXd
- Evorpacept has demonstrated activity in post-Enhertu patients
  - Evorpacept + zanidatamab showed promising antitumor activity in patients with heavily pretreated HER2-positive mBC including after progression on prior T-DXd

Adapted from NCCN guidelines v1.2025

Evorpacept + Zanidatamab Had an ORR of 55.6% in Patients Who Had Confirmed HER2-Positivity and All Had Prior ENHERTU



- Patients with heavily pre-treated HER2-positive breast cancer had benefit from evorpacept + zanidatamab
- Patients had a **median of six prior lines** of therapy
- **All** patients had received **prior ENHERTU** and **prior trastuzumab**

Montero. et. Al. SABCS 2024, Poster Spotlight Presentation. Abstr #SESS-2007

Dotted lines indicate 20% increase and 30% decrease in sum of diameters of target tumors. Treated patients without a post-baseline assessment are not shown (1/21 patient in cohort 1).

BOR, best overall response; PR, confirmed partial response; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; PD, progressive disease; PR, partial response; SD, stable disease; T-DXd, trastuzumab deruxtecan.

Data cut off date 1 August 2024.

Unmet Need in mBC and Evorpacept's Potential

Need for agents in the HER2+ BC space that:

... are **novel** and bring a different mechanistic approach to target HER2 expression

... **have demonstrated activity in post-HER2-directed** tx settings following both ADCs and mAbs

... **can supplement and enhance standard of care** rather than replace the backbone therapies

... **are safer than ADCs,** which can have off-target payload-driven toxicities

... **are IO agents** that can enable the "long tail" and ultimately benefit survival

Evorpacept's Potential

- Drives a different MOA to cell killing via enhanced ADCP vs payload-based ADCs or kinase-driven mAbs/ bispecifics
- Demonstrated activity post-tras in gastric and following 4+ lines of HER2-directed therapy in breast
- Designed to work synergistically with central therapies in BC like Herceptin
- Safety profile is differentiated versus both approved and emerging ADCs
- Potential to be 1st and only IO therapeutic for all HER2+ BC patients

Now Advancing Two Clinical Studies in Breast Cancer: Evorpacept + Herceptin in 2L+ BC Post-ENHERTU and Evo + ENHERTU in Late-Line mBC

ALX ONCOLOGY ASPEN – Breast

Ph2 Randomized mBC Study of Evorpacept + Trastuzumab + Chemo

Locally advanced or metastatic HER-2 positive breast cancer following prior ENHERTU

Treatment

Evorpacept +
Trastuzumab +
Physician's Choice Chemotherapy

First Patient Will be Dosed Mid-year 2025

QLHC Quantum Leap Healthcare Collaborative Pre-ISPY NCT05868226

Ph 1b Single-Arm mBC Study of Evorpacept + ENHERTU

N=30 Unresectable or metastatic HER2-positive or HER2-low breast cancer

Treatment

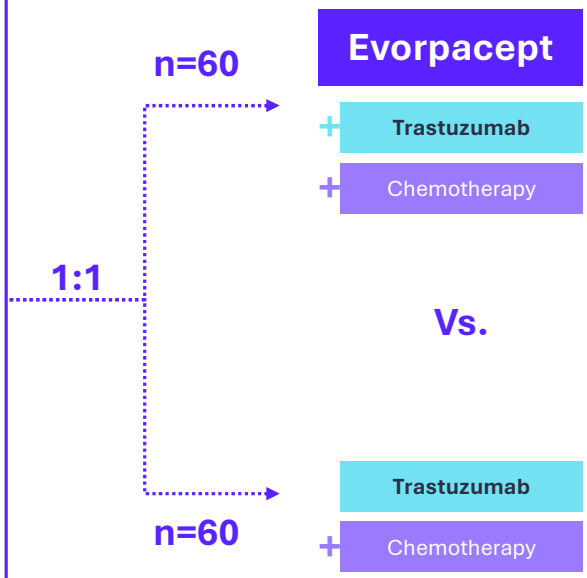
Evorpacept 30 mg/kg every two weeks (Q2W) or 45 mg/kg every three weeks (Q3W)
+
ENHERTU (trastuzumab deruxtecan) 5.4 mg/kg every three weeks (Q3W)

Currently Enrolling, Update Expected by EOY

Proposed Randomized Phase 2 Trial of Evorpacept and Trastuzumab and Chemotherapy in Patients With HER2+ Metastatic Breast Cancer

Key eligibility criteria

- HER2+ mBC (IHC3+ or IHC2+/ISH+) with measurable disease per RECIST 1.1
- Prior T-DXd
- All approved treatments are allowed post T-DXd therapy
- No CNS metastases or previously treated and stable CNS metastases
- Post Enhertu biopsy
- ECOG 0-1



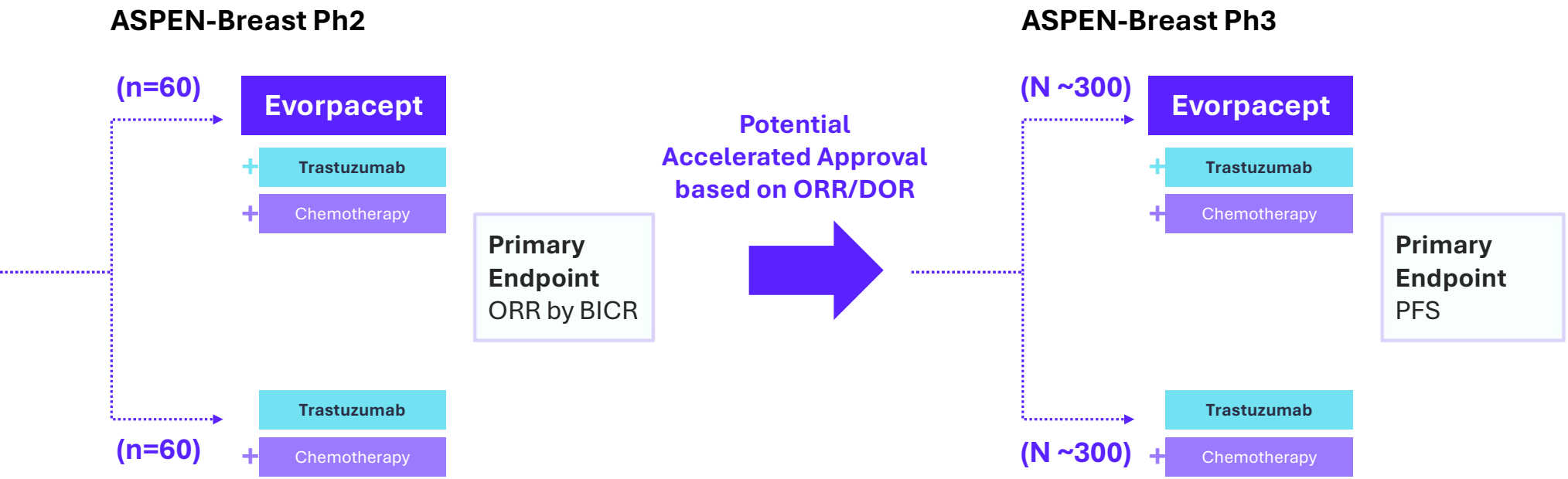
Primary Endpoints

- ORR by BICR

Secondary Endpoints

- PFS
- DOR
- OS

Path to Registration in Breast Cancer



Randomized Ph2 FPI anticipated mid-year 2025
Interim analysis anticipated 2H26

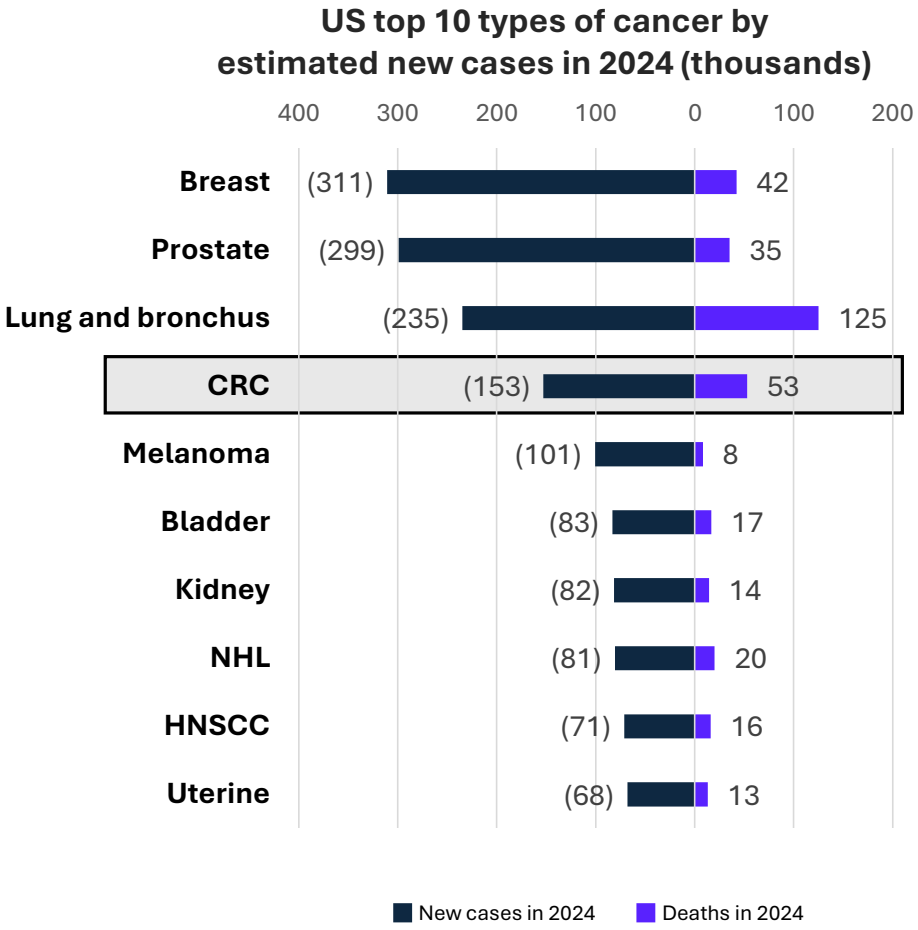
ALX

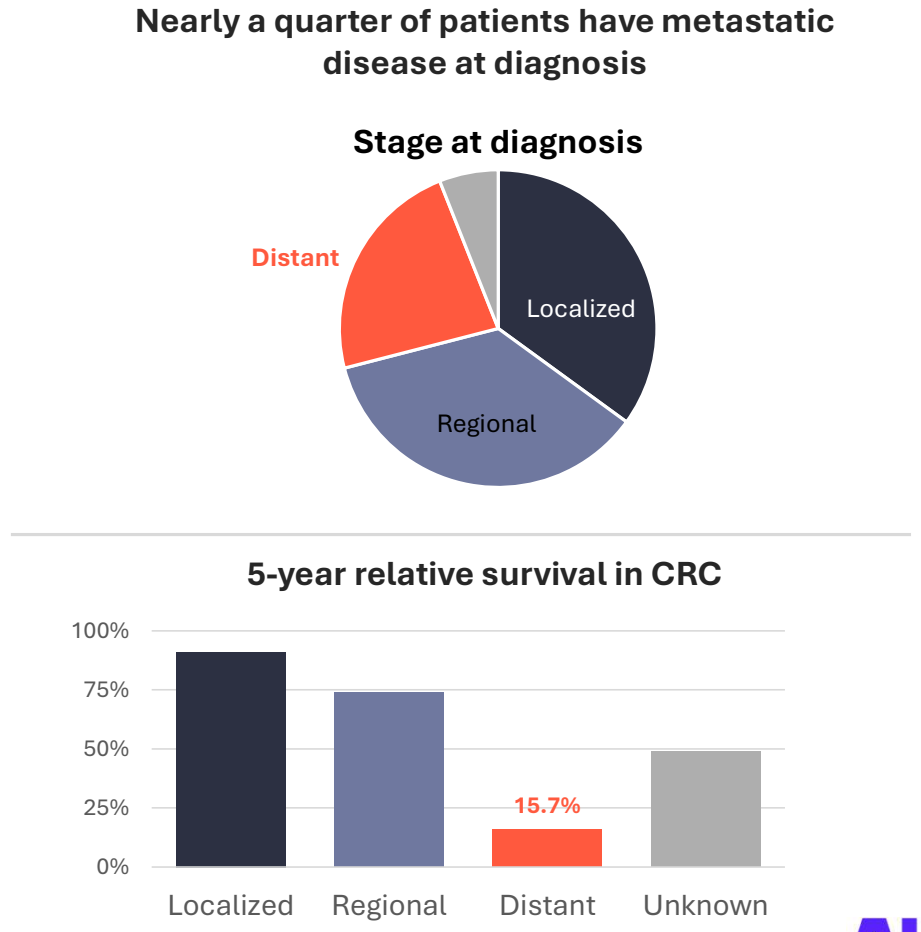
NEW COLORECTAL CANCER PROGRAM

ASPEN-CRC

Eric Van Cutsem, MD, PhD
Professor
Gastroenterology / Digestive Oncology
University Hospitals Gasthuisberg / Leuven & KULeuven
Belgium

CRC Is the Second Highest Cause of Cancer Deaths in the US

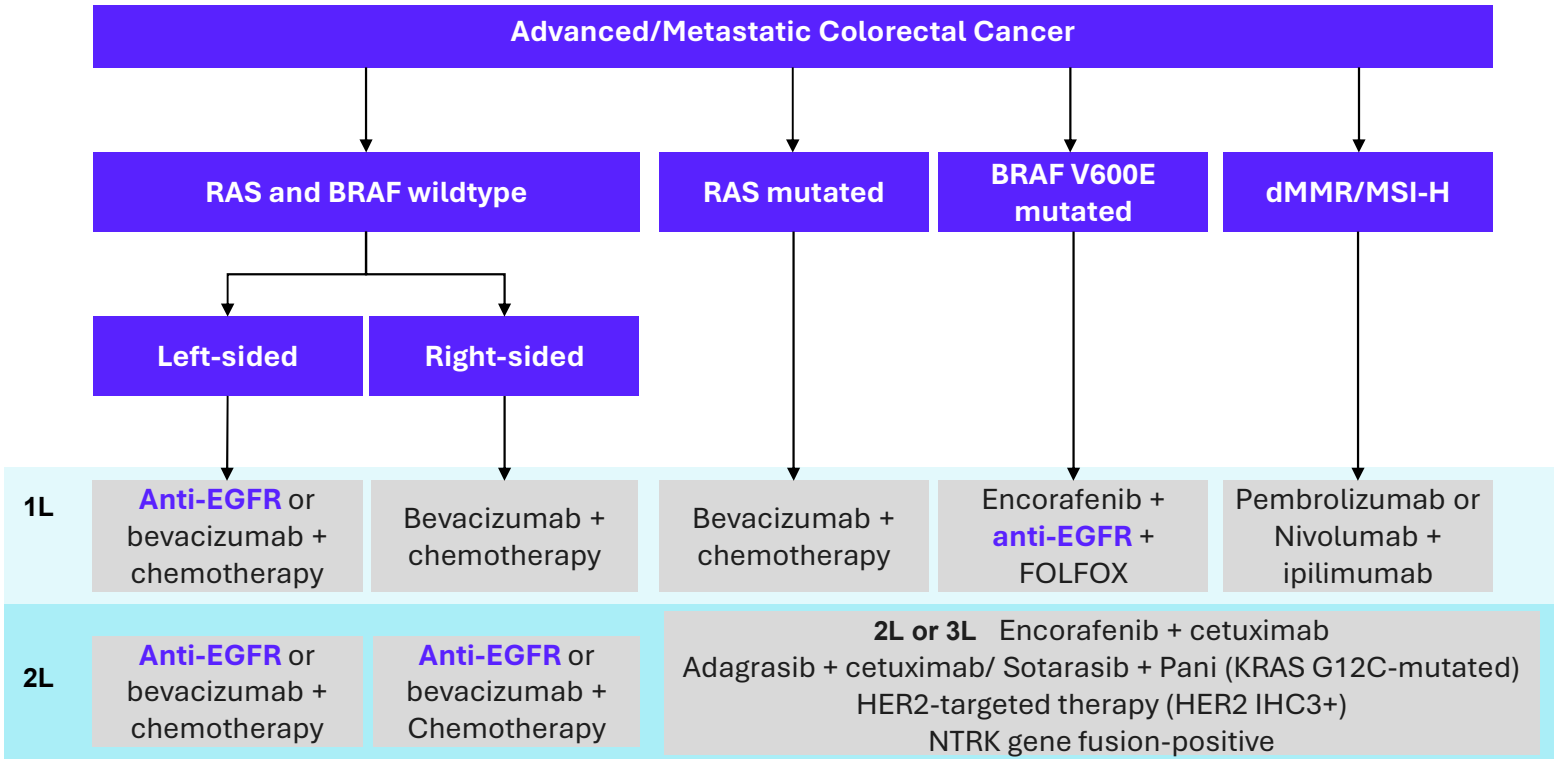




SEER cancer stat facts accessed February 2025; CRC = colorectal cancer; NHL = non Hodgkin lymphoma

Standards of Care for Metastatic CRC Without Actionable Biomarkers Is Largely Unchanged Since the Approvals of Cetuximab and Bevacizumab

Current treatment paradigm for metastatic patients



- Anti-EGFR therapy is standard-of-care in patients with left-sided, RAS/BRAF wildtype tumors
- In 2L treatment, mPFS is ~4 months
- In RAS and BRAF-mutated tumors, EGFR is still expressed, but the ERK pathway is activated downstream of EGFR
- EGFR is also expressed in right-sided tumors, but anti-EGFR treatment is ineffective

NCCN guidelines v1.2025; ESMO Metastatic Colorectal Cancer Living Guidelines; Cunningham, et al, NEJM 2004

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cetuximab Monotherapy and Cetuximab plus Irinotecan in Irinotecan-Refractory Metastatic Colorectal Cancer

David Cunningham, M.D., Yves Humblet, M.D., Ph.D., Salvatore Siena, M.D., David Khayat, M.D., Ph.D., Harry Bleiberg, M.D., Ph.D., Armando Santoro, M.D., Danny Bets, M.Sc., Matthias Mueser, M.D., Andreas Harstrick, M.D., Chris Verslype, M.D., Ph.D., Ian Chau, M.B., B.S., and Eric Van Cutsem, M.D., Ph.D.

ABSTRACT

BACKGROUND
The epidermal growth factor receptor (EGFR), which participates in signaling pathways that are deregulated in cancer cells, commonly appears on colorectal-cancer cells. Cetuximab is a monoclonal antibody that specifically blocks the EGFR. We compared the efficacy of cetuximab in combination with irinotecan with that of cetuximab alone in metastatic colorectal cancer that was refractory to treatment with irinotecan.

METHODS
We randomly assigned 329 patients whose disease had progressed during or within three months after treatment with an irinotecan-based regimen to receive either cetuximab and irinotecan (at the same dose and schedule as in a prestudy regimen [218 patients]) or cetuximab monotherapy (111 patients). In cases of disease progression, the addition of irinotecan to cetuximab monotherapy was permitted. The patients were evaluated radiologically for tumor response and were also evaluated for the time to tumor progression, survival, and side effects of treatment.

RESULTS
The rate of response in the combination-therapy group was significantly higher than that in the monotherapy group (22.9 percent [95 percent confidence interval, 17.5 to 29.1 percent] vs. 10.8 percent [95 percent confidence interval, 5.7 to 18.1 percent], P=0.007). The median time to progression was significantly greater in the combination-therapy group (4.1 vs. 1.5 months, P<0.001 by the log-rank test). The median survival time was 8.6 months in the combination-therapy group and 6.9 months in the monotherapy group (P=0.48). Toxic effects were more frequent in the combination-therapy group, but their severity and incidence were similar to those that would be expected with irinotecan alone.

CONCLUSIONS
Cetuximab has clinically significant activity when given alone or in combination with irinotecan in patients with irinotecan-refractory colorectal cancer.

From the Royal Marsden Hospital, London and Surrey, United Kingdom (D.C., I.C.); Saint-Luc University Hospital, Université Catholique de Louvain, Brussels (Y.H.); Ospedale Niguarda Ca' Granda, Milan (S.S.); Hôpital Salpêtrière, Paris (D.K.); Institut Jules Bordet, Brussels (H.B.); Istituto Clinico Humanitas, Rozzano-Milano, Italy (A.S.); Merck, Amsterdam (D.B.); Merck, Darmstadt, Germany (M.M., A.H.); and University Hospital Gasthuisberg, Leuven, Belgium (C.V., E.C.). Address reprint requests to Dr. Cunningham at the Department of Medicine, Royal Marsden Hospital, Downs Rd., Sutton, Surrey SM2 5PT, United Kingdom, or at david.cunningham@icr.ac.uk.

N Engl J Med 2004;351:337-45.
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Table 2. Rates of Radiologic Response.*

Subgroup and Variable	Cetuximab plus Irinotecan	Cetuximab	P Value
Intention-to-treat population			
No. of patients	218	111	
Response — no. (%)			
Complete response	0	0	
Partial response	50 (22.9)	12 (10.8)	
Stable disease	71 (32.6)	24 (21.6)	
Progressive disease	68 (31.2)	59 (53.2)	
Could not be evaluated	29 (13.3)	16 (14.4)	
Overall response†	50 (22.9 [17.5–29.1])	12 (10.8 [5.7–18.1])	0.007
Disease control‡	121 (55.5 [48.6–62.2])	36 (32.4 [23.9–42.0])	<0.001
Subgroup with progression during or within 4 wk after prestudy irinotecan			
No. of patients	135	71	
Response — no. (%)	34 (25.2 [18.1–33.4])	10 (14.1 [7.0–24.4])	0.07
Subgroup with prior oxaliplatin therapy			
No. of patients	135	71	
Response — no. (%)	30 (22.2 [15.5–30.2])	6 (8.5 [3.2–17.5])	0.01

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cetuximab and Chemotherapy as Initial Treatment for Metastatic Colorectal Cancer

Eric Van Cutsem, M.D., Ph.D., Claus-Henning Köhne, M.D., Erika Hitre, M.D., Ph.D., Jerzy Zaluski, M.D., Chung-Rong Chang Chien, M.D., Anatoly Makhson, M.D., Ph.D., Geert D'Haens, M.D., Ph.D., Tamás Pintér, M.D., Robert Lim, M.B., Ch.B., György Bodoky, M.D., Ph.D., Jae Kyung Roh, M.D., Ph.D., Gunnar Folprecht, M.D., Paul Ruff, M.D., Christopher Stroh, Ph.D., Sabine Tejpar, M.D., Ph.D., Michael Schlichting, Dipl.-Stat., Johannes Nippgen, M.D., and Philippe Rougier, M.D., Ph.D.

ABSTRACT

BACKGROUND

We investigated the efficacy of cetuximab plus irinotecan, fluorouracil, and leucovorin (FOLFIRI) as first-line treatment for metastatic colorectal cancer and sought associations between the mutation status of the *KRAS* gene in tumors and clinical response to cetuximab.

METHODS

We randomly assigned patients with epidermal growth factor receptor–positive colorectal cancer with unresectable metastases to receive FOLFIRI either alone or in combination with cetuximab. The primary end point was progression-free survival.

RESULTS

A total of 599 patients received cetuximab plus FOLFIRI, and 599 received FOLFIRI alone. The hazard ratio for progression-free survival in the cetuximab–FOLFIRI group as compared with the FOLFIRI group was 0.85 (95% confidence interval [CI], 0.72 to 0.99; P=0.048). There was no significant difference in the overall survival between the two treatment groups (hazard ratio, 0.93; 95% CI, 0.81 to 1.07; P=0.31). There was a significant interaction between treatment group and *KRAS* mutation status for tumor response (P=0.03) but not for progression-free survival (P=0.07) or overall survival (P=0.44). The hazard ratio for progression-free survival among patients with wild-type–*KRAS* tumors was 0.68 (95% CI, 0.50 to 0.94), in favor of the cetuximab–FOLFIRI group. The following grade 3 or 4 adverse events were more frequent with cetuximab plus FOLFIRI than with FOLFIRI alone: skin reactions (which were grade 3 only) (in 19.7% vs. 0.2% of patients, P<0.001), infusion-related reactions (in 2.5% vs. 0%, P<0.001), and diarrhea (in 15.7% vs. 10.5%, P=0.008).

CONCLUSIONS

First-line treatment with cetuximab plus FOLFIRI, as compared with FOLFIRI alone, reduced the risk of progression of metastatic colorectal cancer. The benefit of cetuximab was limited to patients with *KRAS* wild-type tumors. (ClinicalTrials.gov number, NCT00154102.)

From the University Hospital Gasthuisberg, Leuven (E.V.C., S.T.); and Imelda Ziekenhuis, Bonheiden (G.D.) — both in Belgium; Klinikum Oldenburg, Oldenburg (C.-H.K.); Universitätsklinikum Carl Gustav Carus, Dresden (G.F.); and Merck, Darmstadt (C.S., M.S., J.N.) — all in Germany; Országos Onkológiai Intézet, Budapest (E.H.); Petz Aladár County Teaching Hospital, Gyõr (T.P.); and St. László Hospital, Budapest (G.B.) — all in Hungary; Wielkopolskie Centrum Onkologii, Poznan, Poland (J.Z.); Chang Gung Memorial Hospital, Taoyuan, Taiwan (C.-R.C.C.); Moscow City Oncology Clinical Hospital 62, Moscow (A.M.); National University Hospital, Singapore, Singapore (R.L.); Yonsei University College of Medicine, Seoul, South Korea (J.K.R.); University of Witwatersrand, Johannesburg, South Africa (P. Ruff); and Hôpital Ambroise Paré, Boulogne, France (P. Rougier). Address reprint requests to Dr. Van Cutsem at the University Hospital Gasthuisberg, Digestive Oncology Unit, Herestraat 49, 3000 Leuven, Belgium, or at eric.vancutsem@uz.kuleuven.ac.be.

N Engl J Med 2009;360:1408-17.
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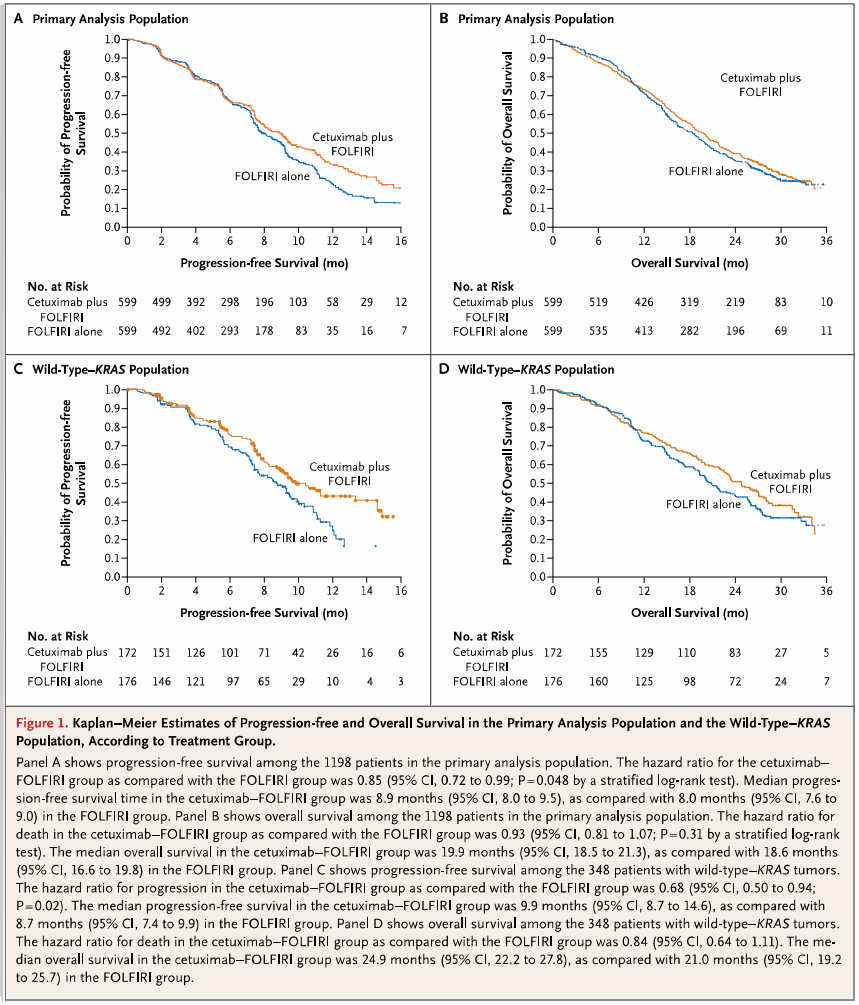
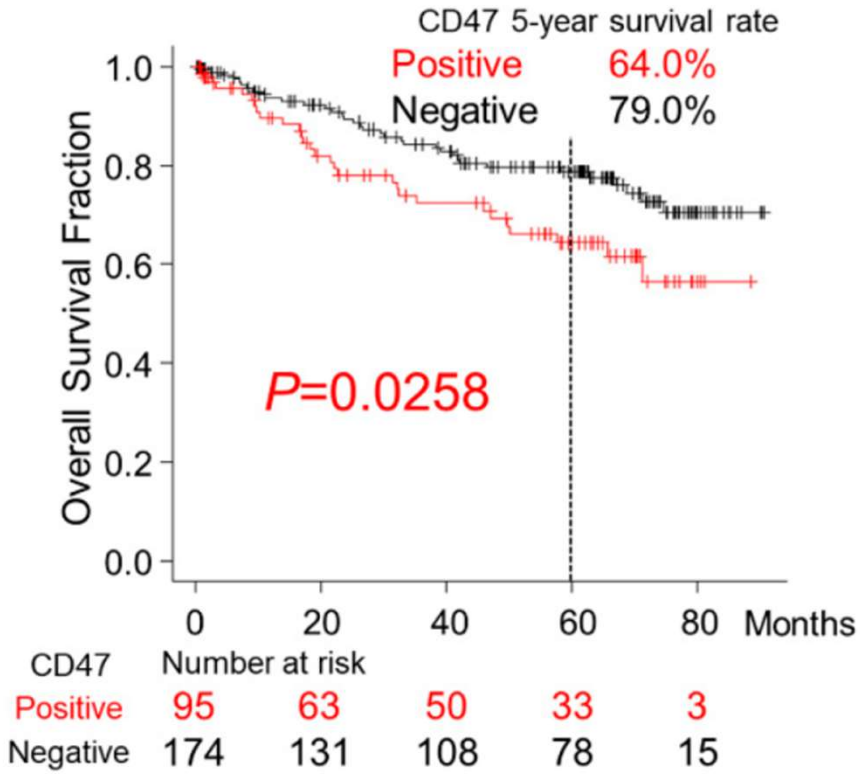


Figure 1. Kaplan–Meier Estimates of Progression-free and Overall Survival in the Primary Analysis Population and the Wild-Type–*KRAS* Population, According to Treatment Group.

Panel A shows progression-free survival among the 1198 patients in the primary analysis population. The hazard ratio for the cetuximab–FOLFIRI group as compared with the FOLFIRI group was 0.85 (95% CI, 0.72 to 0.99; P=0.048 by a stratified log-rank test). Median progression-free survival time in the cetuximab–FOLFIRI group was 8.9 months (95% CI, 8.0 to 9.5), as compared with 8.0 months (95% CI, 7.6 to 9.0) in the FOLFIRI group. Panel B shows overall survival among the 1198 patients in the primary analysis population. The hazard ratio for death in the cetuximab–FOLFIRI group as compared with the FOLFIRI group was 0.93 (95% CI, 0.81 to 1.07; P=0.31 by a stratified log-rank test). The median overall survival in the cetuximab–FOLFIRI group was 19.9 months (95% CI, 18.5 to 21.3), as compared with 18.6 months (95% CI, 16.6 to 19.8) in the FOLFIRI group. Panel C shows progression-free survival among the 348 patients with wild-type–*KRAS* tumors. The hazard ratio for progression in the cetuximab–FOLFIRI group as compared with the FOLFIRI group was 0.68 (95% CI, 0.50 to 0.94; P=0.02). The median progression-free survival in the cetuximab–FOLFIRI group was 9.9 months (95% CI, 8.7 to 14.6), as compared with 8.7 months (95% CI, 7.4 to 9.9) in the FOLFIRI group. Panel D shows overall survival among the 348 patients with wild-type–*KRAS* tumors. The hazard ratio for death in the cetuximab–FOLFIRI group as compared with the FOLFIRI group was 0.84 (95% CI, 0.64 to 1.11). The median overall survival in the cetuximab–FOLFIRI group was 24.9 months (95% CI, 22.2 to 27.8), as compared with 21.0 months (95% CI, 19.2 to 25.7) in the FOLFIRI group.

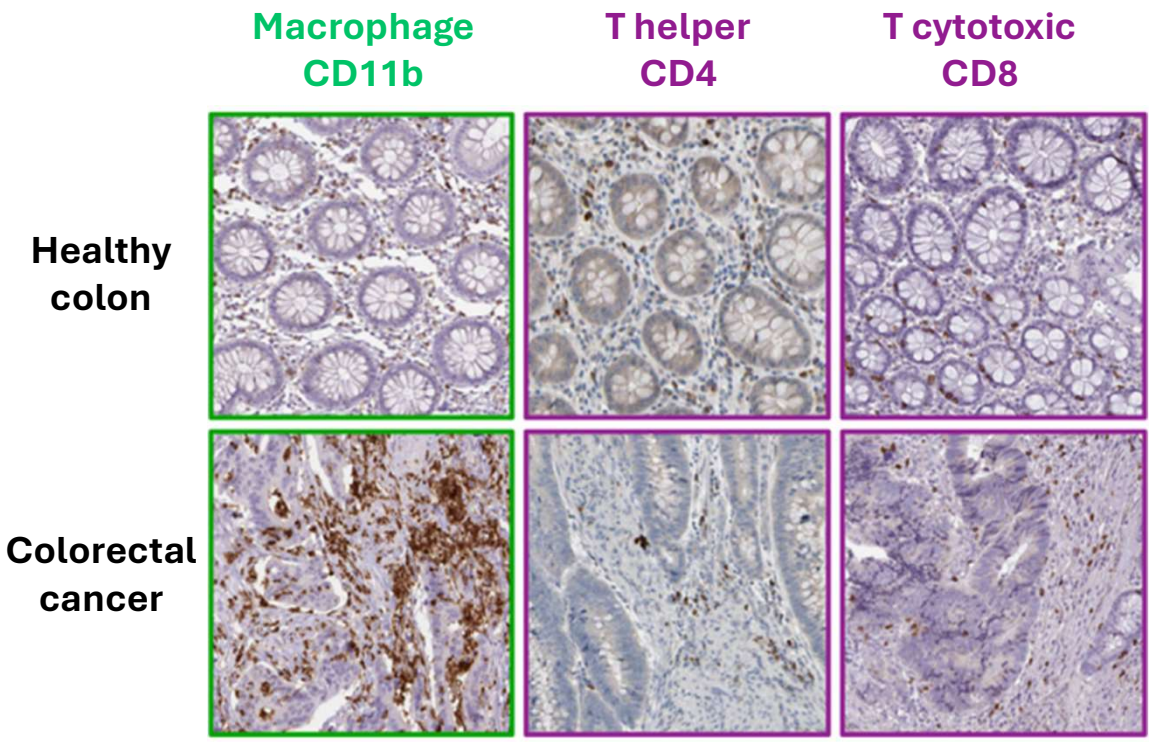
Evorpacept May Benefit Patients With CRC by Blocking CD47, Given That CD47 Expression Is a Negative Prognostic Factor for Patients With mCRC



- CD47 is overexpressed in CRC cells compared to heathy tissue
- Decreased CD47 expression is prognostic for improved survival in patients with CRC based on data showing that patients with CD47-positive CRC had significantly worse survival than patients with CD47-negative disease[1]

1. Sugimura-Nagata et al., Int J. Mol Sci. 2021:22(2690)

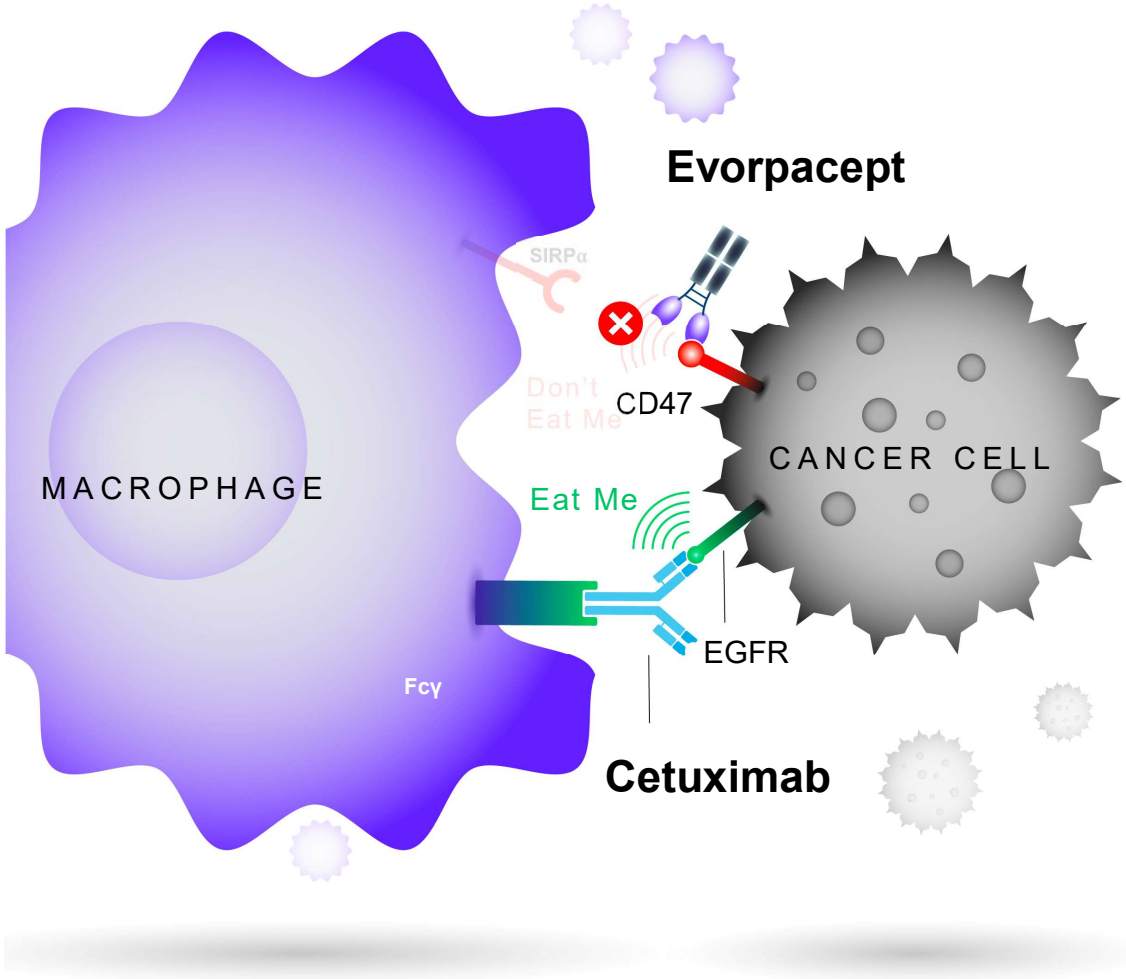
Macrophages Are Highly Present in Colon Cancer, but Are Inhibited by CD47



- Current immune checkpoint inhibitors target T cells, which are largely absent in colorectal cancer
- Evorpacept targets CD47, the checkpoint for macrophages that is overexpressed in CRC compared to heathy tissue
- Macrophages are generally the most abundant immune cell type in cancers and the most profuse leukocyte in the colon
- By targeting CD47, evorpacept may show activity in tumors historically classified as “cold” due to the absence of T cells

Tape, Trends in Cancer, 2017

Evorpacept + Cetuximab Mechanism of Action in CRC



Unmet Need in Metastatic CRC and Evorpacept's Potential

Need for agents in the CRC space that:

… are **novel** and bring a different mechanistic approach by combining with EGFR-targeted antibodies

… **leverage the importance of macrophages in CRC** vs. prior T-cell driven approaches

… **can improve the efficacy of cetuximab**, the SOC for CRC

… have a **manageable, well-tolerated safety profile** which could be used earlier in 1L or 2L EGFR-naïve patients

… **are IO agents** that can provide long-term survival benefit

Evorpacept's Potential

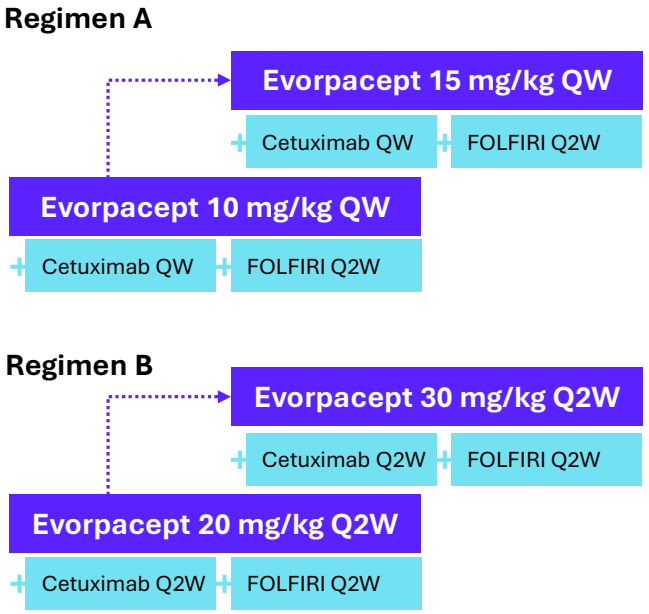
- Potential to build on promising ASPEN-06 gastric data in a similar tumor type
- Uniquely designed to activate macrophages that are highly abundant in CRC
- Designed to work synergistically and add ADCP on top of cetuximab's ADCC-driven tumor killing
- Safety profile allows for combining with multiple therapeutic options and in earlier lines
- Potential to be a novel IO drug for 2L CRC patients

ASPEN-CRC: Evorpacept + Cetuximab + FOLFIRI in Patients With 2L Metastatic Colorectal Cancer

Key eligibility criteria

- Histologically-confirmed left-sided metastatic CRC
- KRAS/NRAS/BRAF wild type
- pMMR/MSS
- Progression on or after first-line oxaliplatin-based SOC therapy
- No prior anti-EGFR treatment
- No prior irinotecan-based therapy
- ECOG 0 or 1

Dose escalation and optimization (N~ 40-60)



Primary Objectives

- Safety and tolerability
- Recommended Phase 2 dose (RP2D)
- Recommended regimen

Secondary Objectives

- Anti-tumor activity including ORR, DCR, DOR, PFS, and OS

Dosing: Cetuximab; QW 400 mg/m^2 loading -> 250 mg/m2 or Q2W 500 mg/m^2 FOLFIRI; irinotecan + leucovorin + 5FU

ORR = objective response rate, DCR = disease control rate, DOR = duration of response, PFS = progression-free survival, OS = overall survival

Path to Registration in Previously Treated Colorectal Cancer

ASPEN-CRC Phase 1b/2 (N~40-60)

Evorpacept
+ Cetuximab
+ FOLFIRI

Primary endpoints
- Safety
- Tolerability
- RP2D
- Dosing regimen

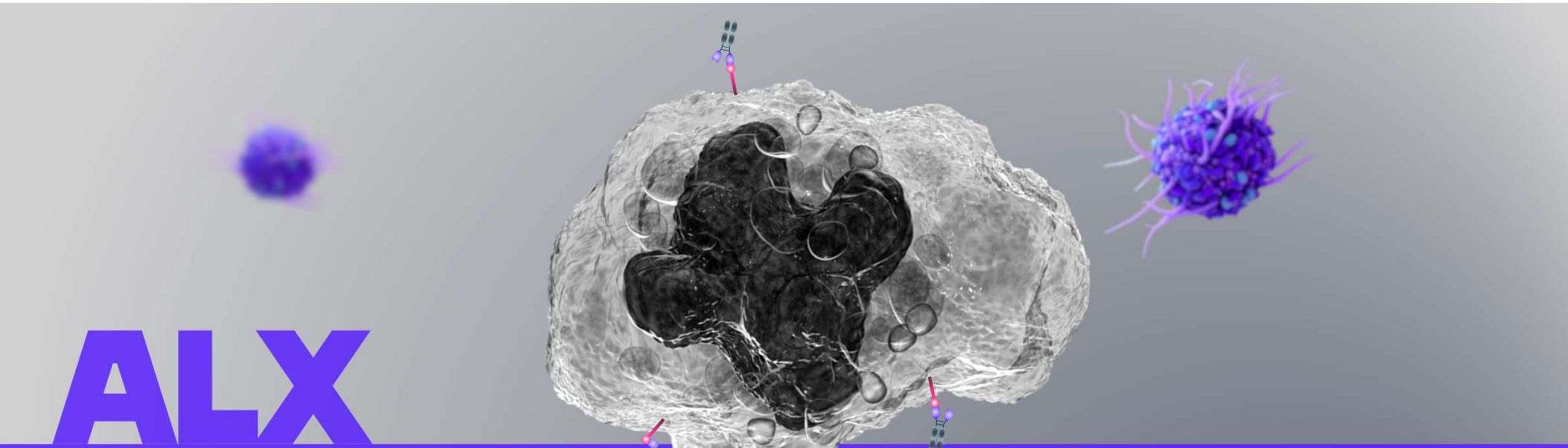
ASPEN-CRC Phase 3 (N~500)

Evorpacept
+ Cetuximab
+ FOLFIRI

Cetuximab
+ FOLFIRI

Primary endpoint
- OS

Ph1b/2 FPI anticipated mid-year 2025
Safety and initial efficacy anticipated 1H '26



ALX

ANTIBODY COMBINATIONS IN HEME MALIGNANCIES

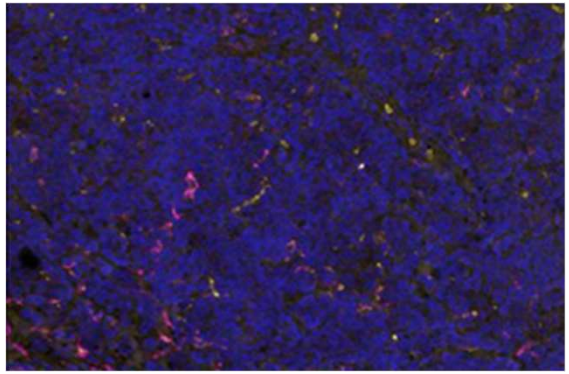
NHL: Rituxan + Evorpacept

Multiple Myeloma: SARCLISA + Evorpacept

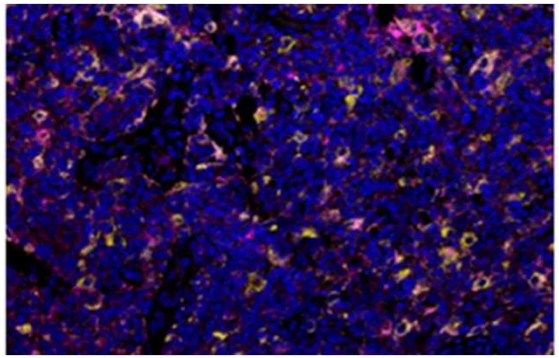
Alan Sandler, MD
CMO, ALX Oncology

SIRPα-Positive Macrophages Increase at Time of Progression After R^2 in Patients With Follicular Lymphoma (FL)

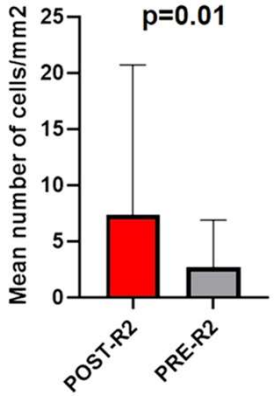
CSF1-R+ SIRPα+ M before R^2



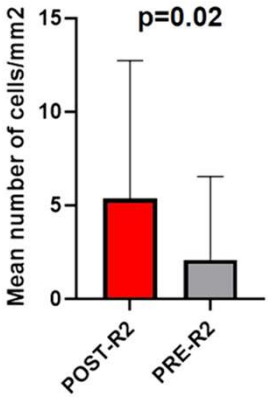
CSF1-R+ SIRPα+ M after R^2



CD163+ SIRPα+ M



CSF1-R+ SIRPα+ M



- Rituximab + lenalidomide (R^2) is the standard-of-care therapy for patients with relapsed FL, with a 34% CR rate
- RELEVANCE (N=517) trial demonstrated activity of R^2 in frontline FL was similar to standard-of-care rituximab + chemotherapy

Marques-Piubelli M et al, Blood Adv 2022; Strati, et al, AACR 2024 #10285; Leonard, et al, JCO 2019; Morschhauser, et al, NEJM 2018

ASPEN-01 Phase 1b Clinical Trial of Evorpacept + the CD20-Targeted Antibody Rituximab in Aggressive and Indolent NHL

Phase 1b clinical trial of evorpacept + rituximab in patients with aggressive or indolent NHL

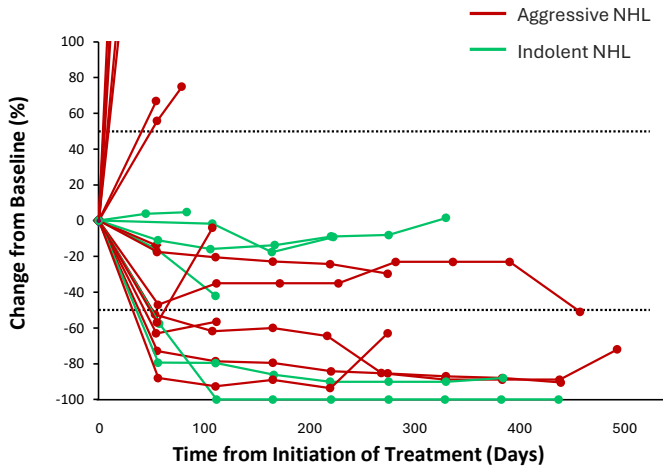
Cohorts

Relapsed/refractory NHL, prior regimen with Rituximab

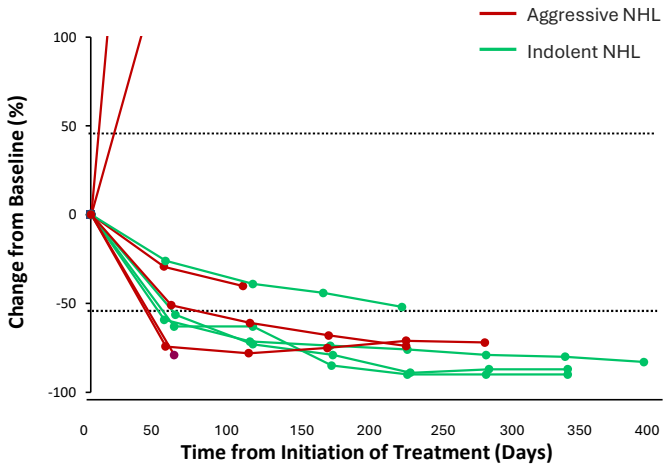
Treatment

Evorpacept 10 or 15 mg/kg once a week (QW)
+
Rituximab 375 mg/m^2 once a week for four weeks, once monthly for eight months

Evorpacept (10 mg/kg QW) + Rituximab



Evorpacept (15 mg/kg QW) + Rituximab



In indolent NHL, evorpacept + rituximab achieved:

- ORR = 72% (8/11)
- CR = 54% (6/11)
- Evorpacept + rituximab demonstrated favorable impact when compared to single-agent rituximab benchmarks of 18% CR and 53% ORR from AUGMENT pivotal study of rituximab + lenalidomide in indolent NHL

Data cutoff: October 1, 2020; Response evaluable patients; responses include metabolic response per Lugano Response Criteria.
Leonard, et al, JCO, 2019

Phase 1/2 IST of Evorpacept + R2 in Indolent and Aggressive Relapsed or Refractory B-cell Non-Hodgkin Lymphoma

Key eligibility criteria

Phase 1

- Adult patients with relapsed refractory B-NHL
- ≥2 prior lines of systemic therapy for patients with aggressive B-NHL or 1 for patients with indolent B-NHL
- No prior lenalidomide

Phase 2

- Adult patients with previously untreated indolent B-NHL

Phase 1 (R/R)

Presented at AACR 2024

N=3

Evo 30 mg/kg (Q2W) + R Weekly on cycle 1 & Q4W on cycles 2-6 + L Day 1-21 on cycles 1-6

N=17

Evo 60 mg/kg (Q4W) + R + L

Phase 2 (1L)

Recruiting

N=24

Evo 60 mg/kg (Q4W) + R + L

Primary Outcomes

- Phase 1: Safety and RP2D
- Phase 2: CR rate

Secondary Outcomes

- ORR
- PR
- DoR
- PFS
- OS
- AEs

Enrolled: n=18 patients with indolent lymphomas (n=15 with follicular and n=3 with marginal zone), all of whom had prior anti-CD20 targeted therapy

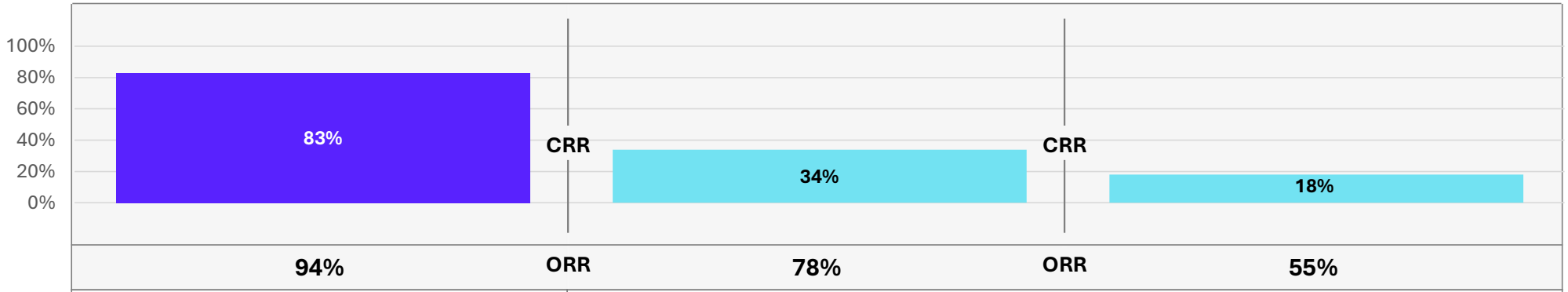
Evo Evorpacept R Rituximab L Lenalidomide

Investigator Sponsored Trial. P. Strati. AACR 2024, Oral Presentation. Abstr #CT037; Indolent = Follicular Lymphoma and Marginal Zone Lymphoma; Aggressive = Diffuse Large B-cell Lymphoma and Mantle Cell Lymphoma; CR = Complete response; PR = Partial response; ORR = Objective response rate; DoR= Duration of response; PFS = Progression free survival; AEs = Adverse events; IST = Investigator Sponsored Trial; RP2D = recommended phase 2 dose

Evorpacept-Based Regimen Compares Favorably to Benchmark Trial

R^2 in iNHL

Evo + R^2 Ph1/2 MDACC IST	R^2 AUGMENT	Placebo + Rituximab
N=18	N=178	N=180



MD Anderson Sponsored
P. Strati. AACR 2024, Oral Presentation. Abstr #CT037

Data Cutoff as of December 2023

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Volume 37, Number 14
March 2019

AUGMENT: A Phase III Study of Lenalidomide Plus Rituximab Versus Placebo Plus Rituximab in Relapsed or Refractory Indolent Lymphoma

Data coming 2Q 2025 at major medical meeting

R2 = Lenalidomide + Rituximab; N = Response Evaluable Patients; Indolent = Follicular Lymphoma and Marginal Zone Lymphoma; CRR = Complete response rate; ORR = Objective response rate; IST = Investigator Sponsored Trial

Ongoing Trial of Evorpacept + the CD38-Targeted Antibody SARCLISA (Isatuximab) Sponsored by Sanofi

Key eligibility criteria

- Relapsed or refractory multiple myeloma, two or more prior therapies
- Prior therapy with proteasome inhibitor (PI) and immunomodulatory drug (IMiD)
- Anti-CD38 therapy naïve or at least 12 months after last dose
- No prior anti-CD47
- ECOG 0 or 1

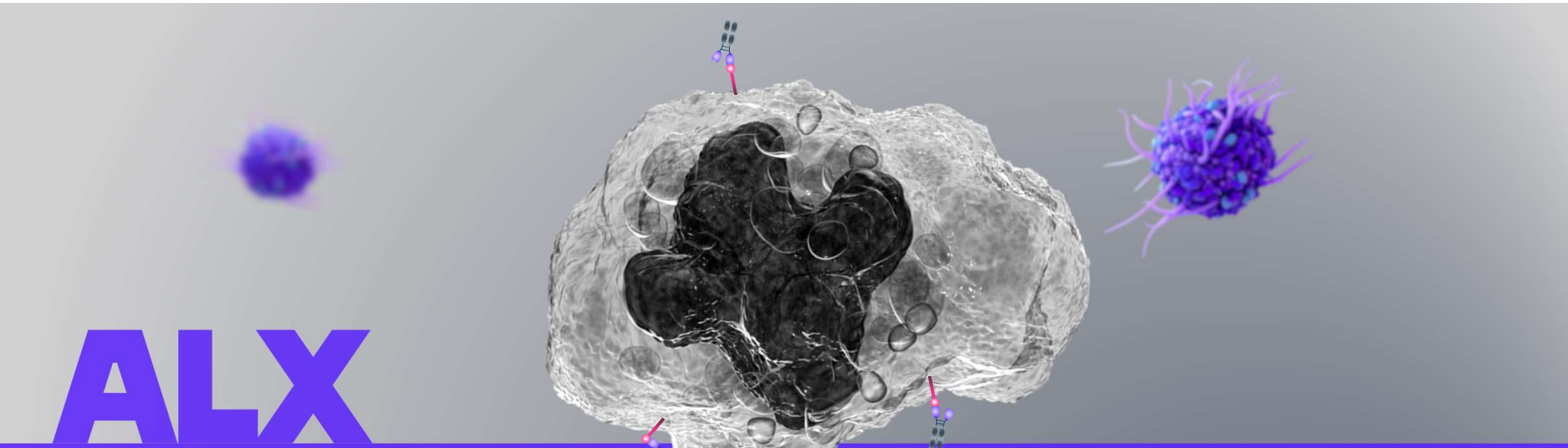
sanofi

Phase 1/2 Multiple Myeloma Study (UMBRELLA Trial)

Experimental	Active Comparator
Evorpacept + **SARCLISA (isatuximab)** + pomalidomide + dexamethasone	**SARCLISA (isatuximab)** + pomalidomide + dexamethasone

First patients dosed September 2024, currently enrolling

Multiple myeloma trial sponsored by Sanofi with ALX collaboration



ALX

BUILDING THE EVORPACEPT FRANCHISE

Commercial Opportunity

Allison Dillon, PhD
CBO, ALX Oncology

Building the Evorpacept Franchise

Lead indications with potential for accelerated approval

HER2+ gastric cancer
~12,000*
2L+ HER2+ patients

- Biomarker-driven patient population identified
- Pending FDA feedback on AA path

HNSCC
~57,000*
1L patients

- Addresses 1L patients with HNSCC irrespective of PD-L1 expression
- Expansion opportunity into other pembrolizumab-based standards of care

*7 major markets: US, EU5 (UK, Spain, Italy, Germany, France) and Japan
Source: Clarivate Market Forecast, gastroesophageal cancer, December 2024

Building the Evorpacept Franchise

Lead indication with potential for accelerated approval

2L+ HER2+ gastric cancer

1L HNSCC

~69,000*

Current wave of development

Metastatic Breast Cancer

~48,000*

2L+ HER2+ patients

2L CRC

~60,000*

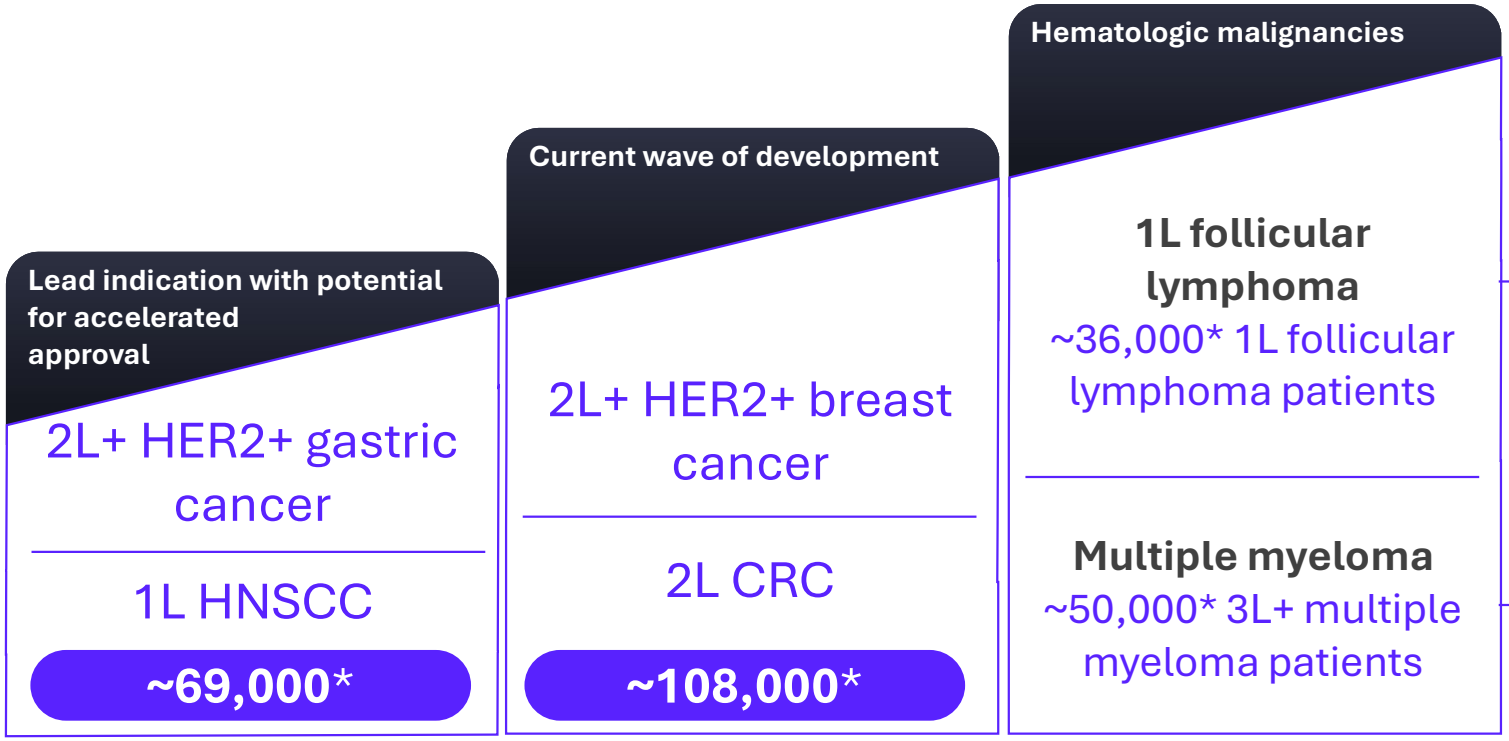
2L RAS/BRAF wildtype patients

- Derisked by multiple evorpacept clinical trials
- Urgent area of unmet need for HER2+ breast cancer patients
- Expansion opportunities in multiple lines of therapy, (neo)adjuvant setting, and with additional HER2-targeted

- Potential to be first new treatment for second-line wild-type CRC patients
- Potential expansion of evorpacept + EGFR into patients with right-sided tumors

*7 major markets: US, EU5 (UK, Spain, Italy, Germany, France) and Japan
Source: Clarivate Market Forecast, gastroesophageal cancer, December 2024

Building the Evorpacept Franchise

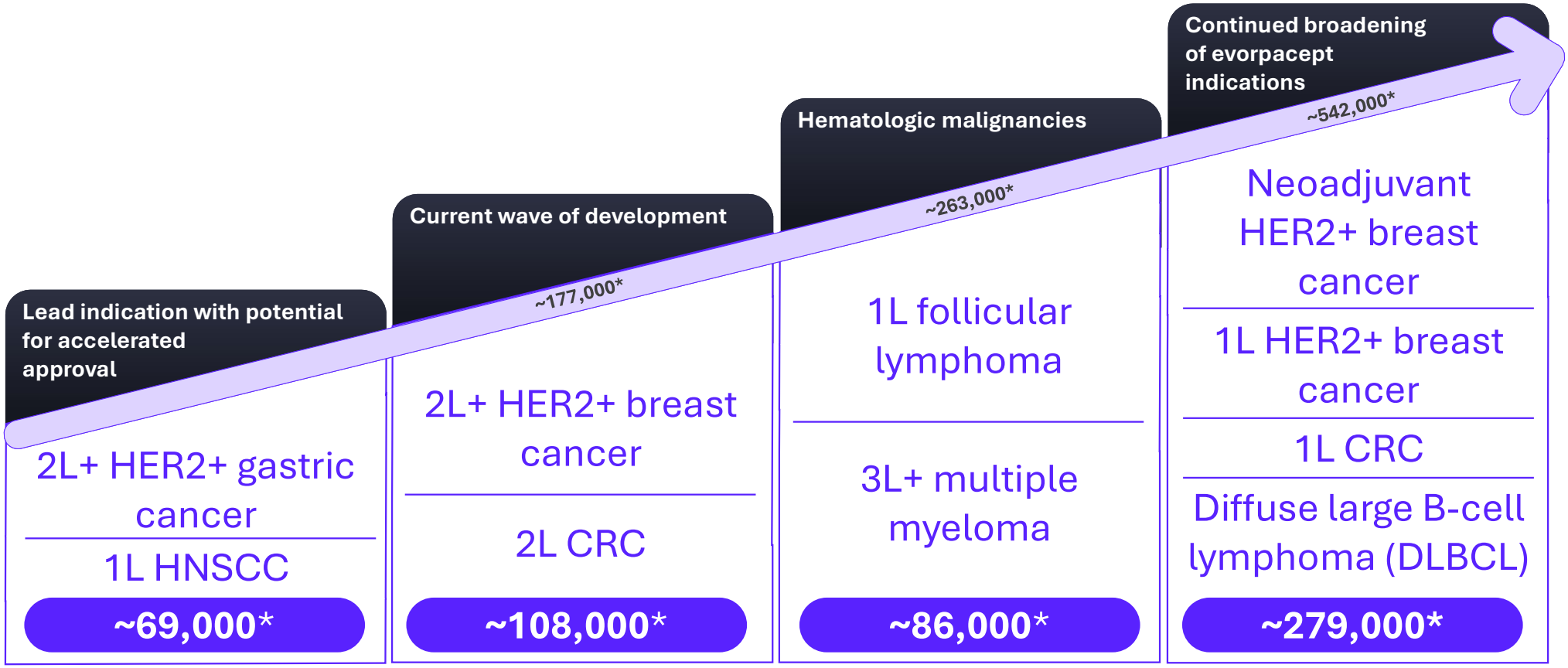


- Building on potentially best-in-class activity from Ph1b trials
- Significant opportunity for expansion with rituximab-based standards of care in B-cell lymphomas

- Ongoing Sanofi-sponsored trial in combination with isatuximab

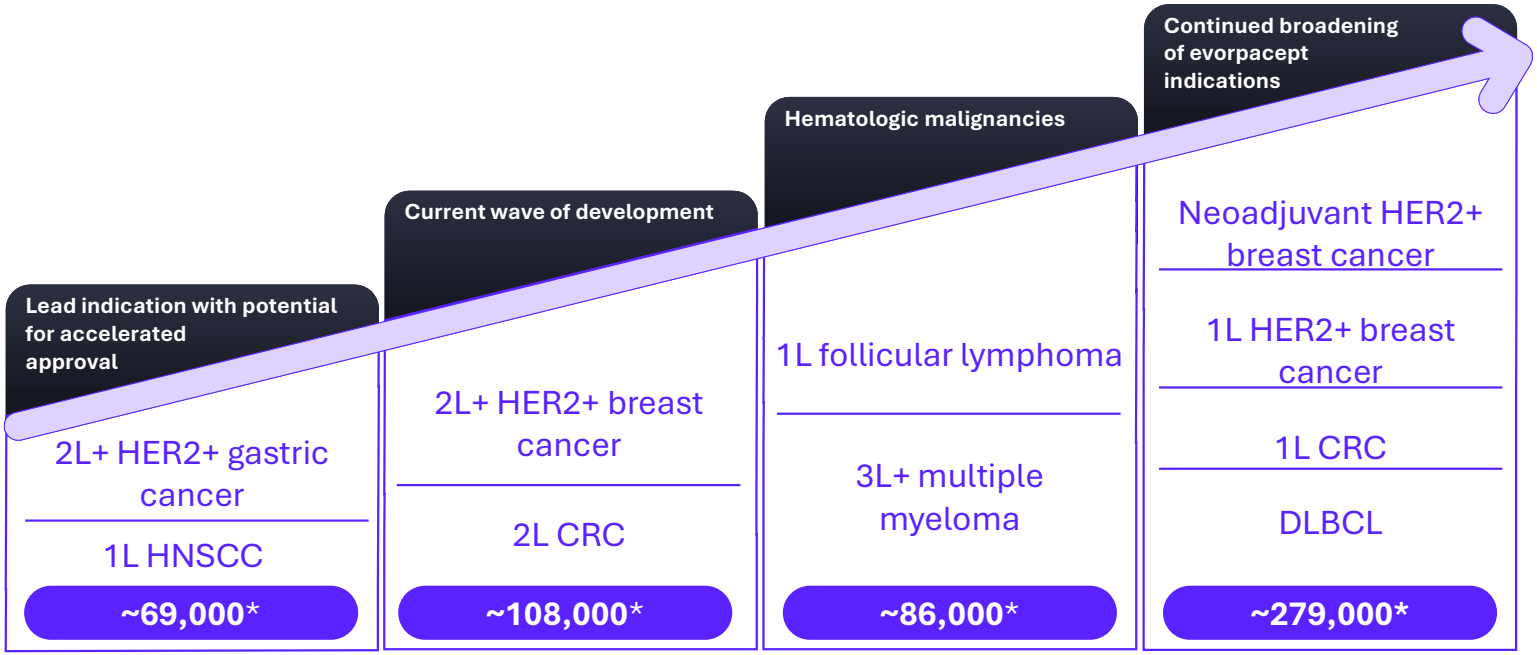
*7 major markets: US, EU5 (UK, Spain, Italy, Germany, France) and Japan
Source: Clarivate Market Forecast, gastroesophageal cancer, December 2024

Building the Evorpacept Franchise



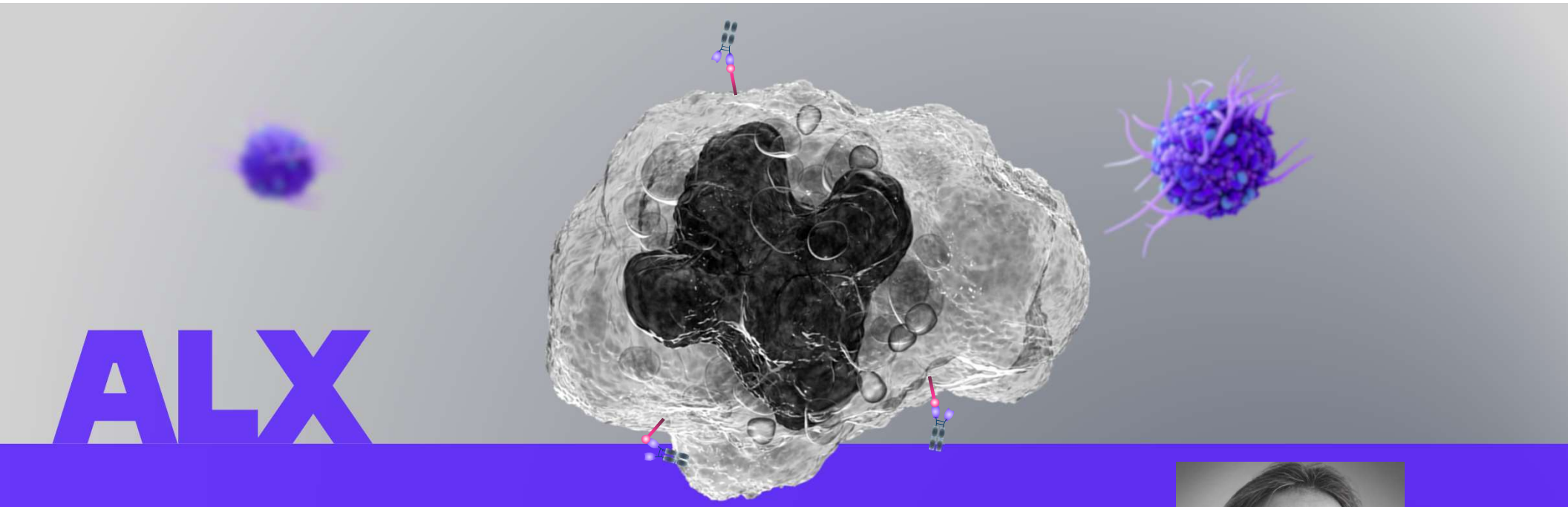
*7 major markets: US, EU5 (UK, Spain, Italy, Germany, France) and Japan
Source: Clarivate Market Forecast, gastroesophageal cancer, December 2024

Building the Evorpacept Franchise



*7 major markets: US, EU5 (UK, Spain, Italy, Germany, France) and Japan
Source: Clarivate Market Forecast, gastroesophageal cancer, December 2024

Ongoing studies for evorpacept target over 250,000 patients in the US, EU5, and Japan



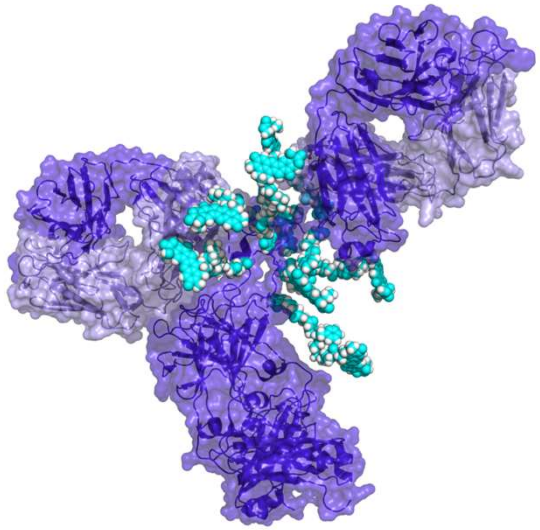
ALX

ALX2004

New Antibody-Drug Conjugate Clinical Candidate

Jaume Pons, PhD
CSO, ALX Oncology

ALX2004: First Drug Candidate That Was Internally Developed Using ALX's Linker-Payload Platform



ALX2004

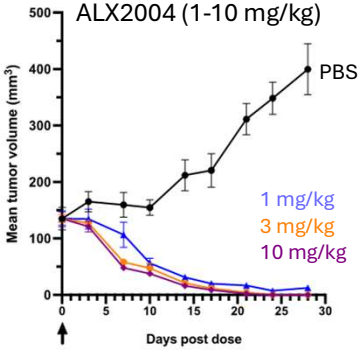
EGFR-targeted ADC with proprietary topoisomerase I inhibitor payload

IND filing Q1 2025

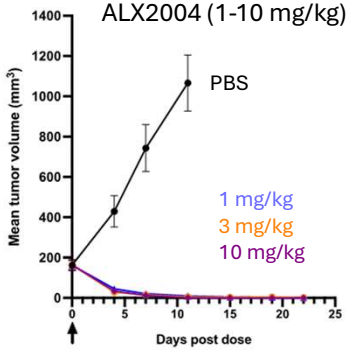
- EGFR-binding epitope distinct from cetuximab and panitumumab
- Affinity tuned to maximize therapeutic window
- Enhanced bystander effect compared to DXd
- Linker with improved ADC stability compared to DXd
- Uniform drug loading DAR 8 and well-behaved physico-chemical properties
- IP: patent applications covering multiple classes of payloads, payload linkers, and ADCs

ALX2004 Shows Potent Anti-Tumor Activity in Multiple Clinically Relevant Xenograft Models

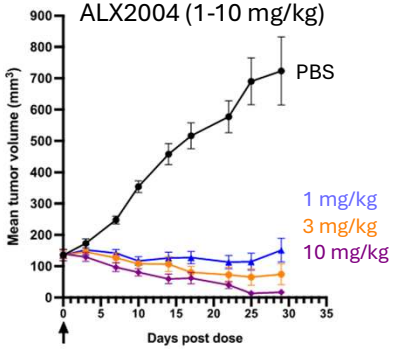
TNBC (MDA-MB-468)
ALX2004 (1-10 mg/kg)



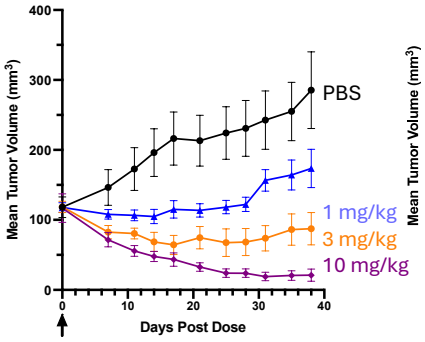
NPC (FaDu)
ALX2004 (1-10 mg/kg)



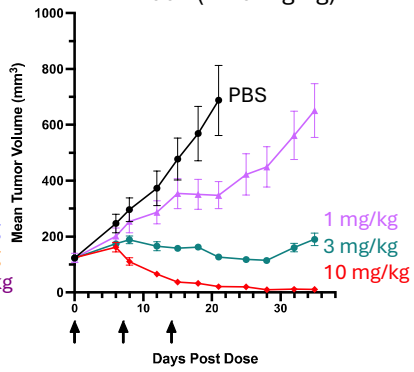
PDAC (CFPAC-1)
ALX2004 (1-10 mg/kg)



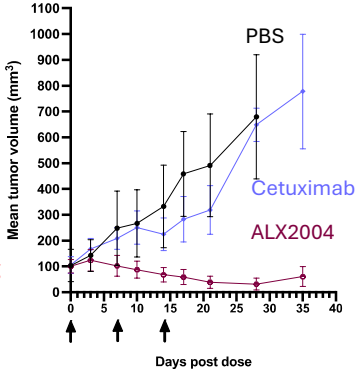
NSCLC (HCC827)
ALX2004 (1-10 mg/kg)



CRC (COLO205)
ALX2004 (1-10 mg/kg)



PDAC (CFPAC-1)
Cetuximab vs. ALX2004



ALX2004 designed to optimize ADC-based mechanisms of anti-tumor activity:

- Topoisomerase I inhibition
- Increased linker stability to maximize payload delivery to tumor cells
- Increased bystander effect
- Effector function and signaling inhibition from anti-EGFR antibody

ALX Data on File; TNBC = triple negative breast cancer; NPC = nasopharyngeal carcinoma; PDAC = pancreatic ductal adenocarcinoma; NSCLC = non small cell lung cancer; CRC = colorectal cancer

ALX2004 Has the Potential To Be a Best- and First-in-Class EGFR ADC

Need exists for novel ADCs that:

… are **pursuing targets with limited competition and room to differentiate**

… leverage **validated targets** and/or established pathways to mitigate biology risk

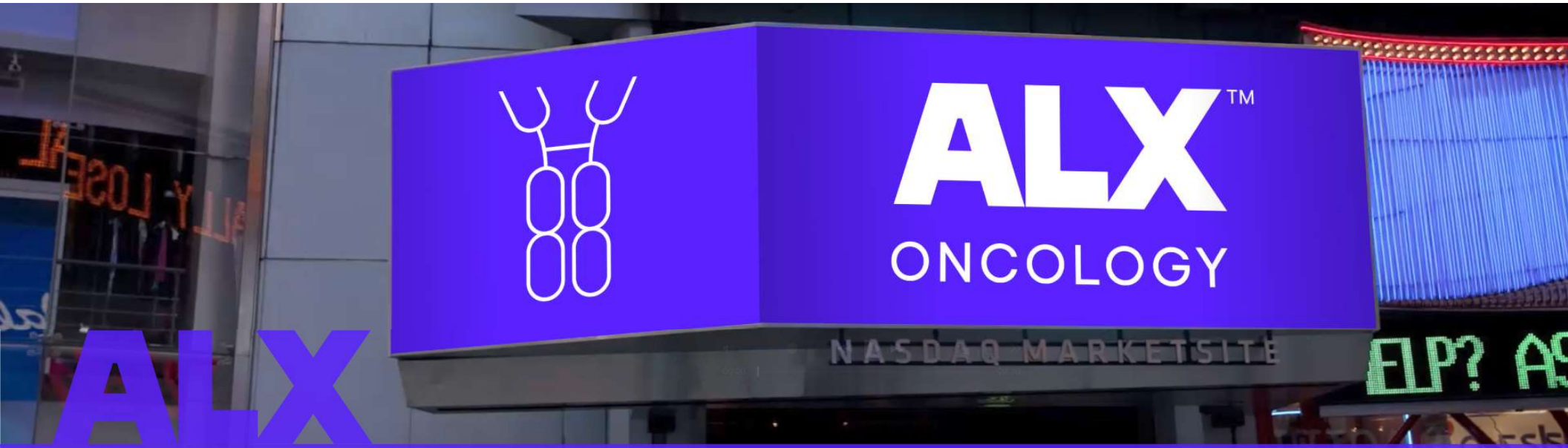
… **utilize clinically validated payloads** that are known to be highly efficacious in the clinic

… **have the potential to be significantly de-risked in early clinical studies**

ALX2004's Potential

- Approved EGFR therapies and most clinical candidates rely on signaling blockade
- No approved EGFR ADCs and only one other EGFR topo-based ADC in the clinic
- HER2/3 topo-1 ADC clinical success (e.g., ENHERTU) may support EGFR (HER1) ADCs potential
- Topo-1 is a highly validated payload
- ALX2004 addresses EGFR tubulin ADC failures through optimized affinity, payload, stability, and tumor penetration
- Combines direct cytotoxicity and bystander effect, signaling blockade, and immune stimulation (ADCC, ADCP, ICD)

ALX will host R&D Call focused on ALX2004 in Q2 2025



FINANCIAL UPDATES AND MILESTONES

Upcoming Catalysts

Harish Shantharam, CFA
CFO, ALX Oncology

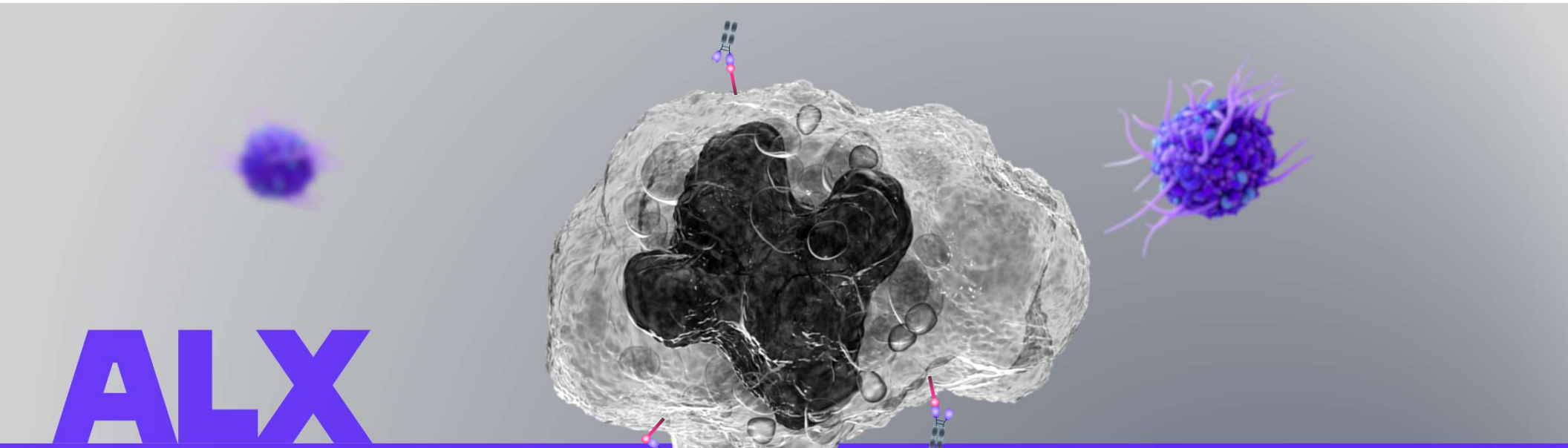
Key Milestones

PROGRAM	TRIAL	INDICATION	UPDATE	TIMELINE
Evorpacept (anti-cancer antibody w/ active Fc)	**ASPEN-06**	Gastric / GEJ	Accelerated Approval pathway – FDA feedback	2Q 2025
	ASPEN-Breast	HER2+ Breast Cancer	Interim analysis	2H 2026
	ASPEN-CRC	CRC	Safety and early efficacy	1H 2026
Evorpacept (w/checkpoint inhibitors)	**ASPEN-03**	HNSCC	Topline results	2Q 2025
	ASPEN-04	HNSCC	Topline results	2Q 2025
Evorpacept (w/ADC)	**ASPEN-07**	Bladder Cancer	Data update	2Q 2025
	I-SPY	Breast Cancer	Data update	2H20 25
ALX2004	**Pre-clinical**	-	IND submission	1Q 2025
	Ph1a/1b	Multiple	Safety data	1H 2026

Financial and Business Update

- $131.3M of cash, cash equivalents and investments as of Dec 31, 2024.

- Our strategic prioritization and resource optimization efforts enables us to extend cash runway guidance into Q4 2026.
  - Focused spend on Evorpacept anticancer antibody program (GC/ BC / CRC) and ALX 2004
  - Gated phase 3 spend while awaiting ASPEN-03/04 results and ASPEN-06 FDA meeting
  - ~30% reduction in force with substantial decrease in preclinical research investments and optimized spend across functions



Concluding Remarks

Jason Lettmann
CEO, ALX Oncology

Today's Key Messages

1. ***Evorpacept is an active IO agent*** **that has now demonstrated activity in six clinical trials to date**
2. ***Pursuing a focused development strategy*** **with several paths to FDA registration across both evorpacept and ALX2004**
3. ***Extended runway into Q4 2026*** **due to aggressive prioritization and cost-cutting**
4. ***Several major catalysts over next 12 to 18 months*** ***across active trials in major oncology indications***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