# ASPEN-06 Study in Patients with Gastric or Gastroesophageal Junction (GEJ) Cancer

Phase 2 Top Line Results
Conference Call

July 31, 2024

# Forward-looking statements

Certain information set forth in this presentation contains “forward-looking information”, under applicable laws collectively referred to herein as forward-looking statements. Except for statements of historical fact, information contained herein constitutes forward-looking statements and includes, but is not limited to the (i) results and cost and timing of our product development activities and clinical trials; (ii) completion of the Company’s clinical trials that are currently underway, in development or otherwise under consideration; (iii) our expectations about the timing of achieving regulatory approval and the cost of our development programs; (iv) projected financial performance of the Company; (v) the expected development of the Company’s business, projects, collaborations and joint ventures; (vi) execution of the Company’s vision and growth strategy, including with respect to future M&A activity and global growth; (vii) sources and availability of third-party financing for the Company’s research and development; (viii) future liquidity, working capital, and capital requirements; and (ix) industry trends. These and other risks are described more fully in ALX Oncology’s filings with the Securities and Exchange Commission (“SEC”), including ALX Oncology’s Annual Report on Form 10-K and other documents ALX Oncology files with the SEC from time to time.

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# ALX Oncology program update call

## Agenda

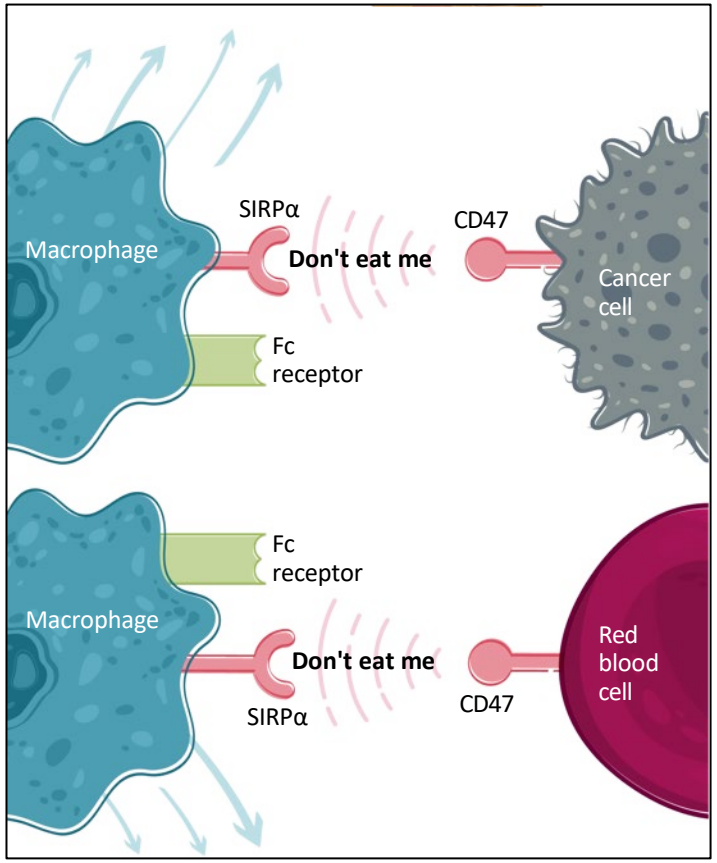
1. Welcome
2. Evorpacept Introduction and MOA
3. Gastric/GEJ cancer overview
4. ASPEN-06 Top line results
5. Closing remarks

## On the call

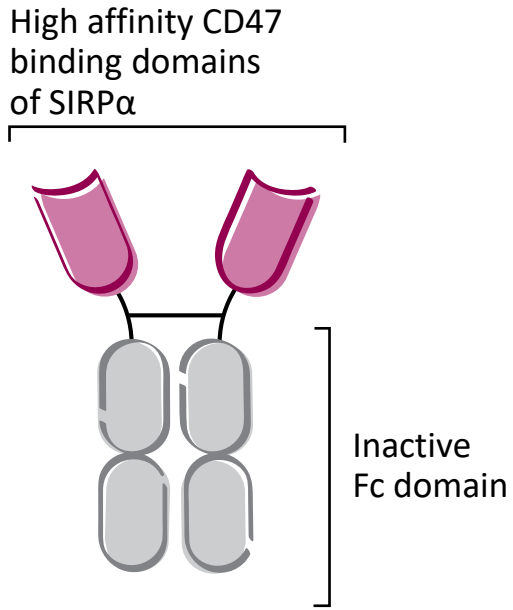
**Jason Lettmann**
CEO, ALX Oncology

**Dr. Sophia Randolph, MD, PhD**
CMO, ALX Oncology

# Evorpacept: A first-in-class approach to targeting CD47



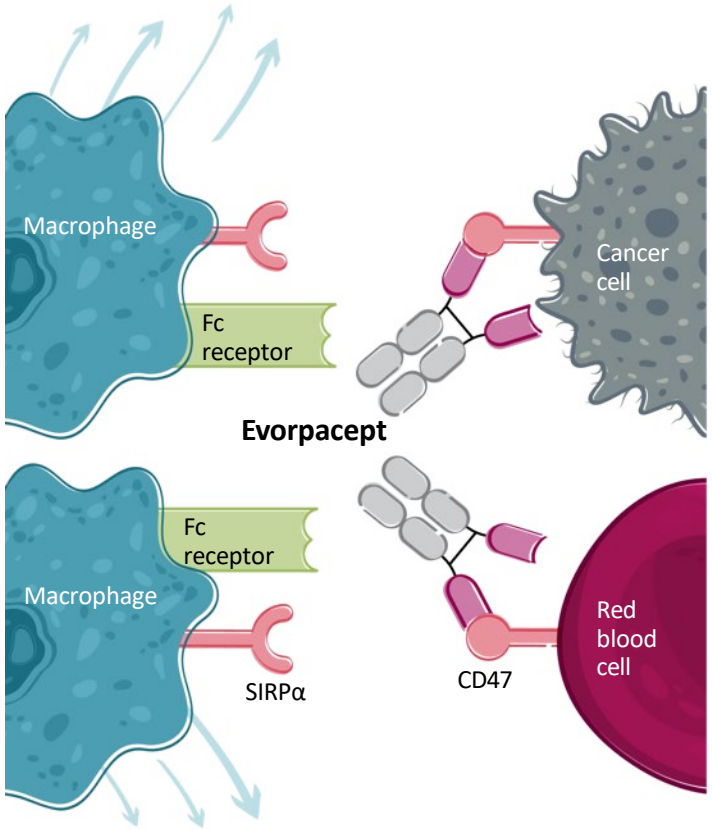

Target cells overexpress CD47 to evade destruction by macrophages



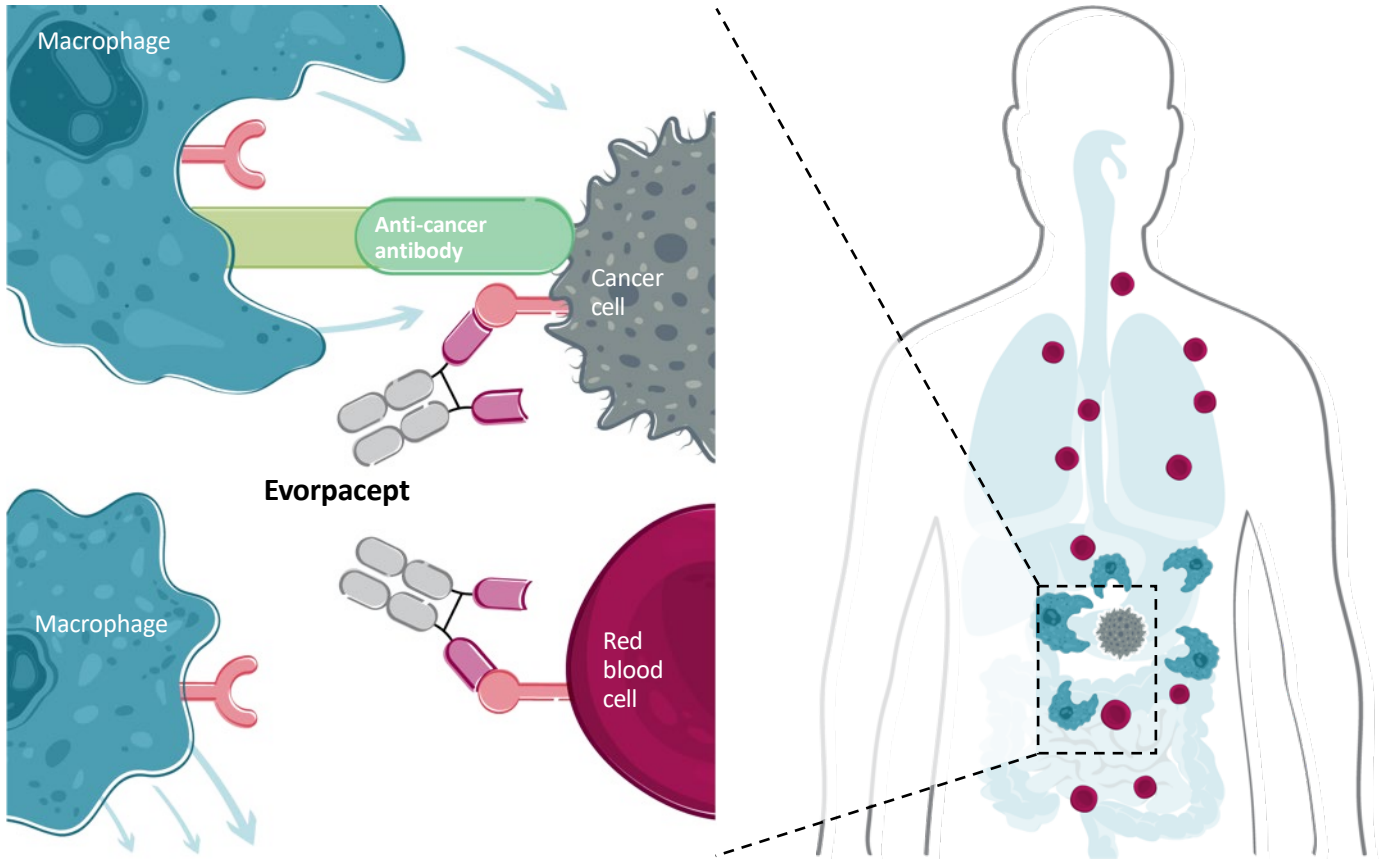

**Evorpacept**

A differentiated CD47 blocker

# Evorpacept targets the CD47 checkpoint

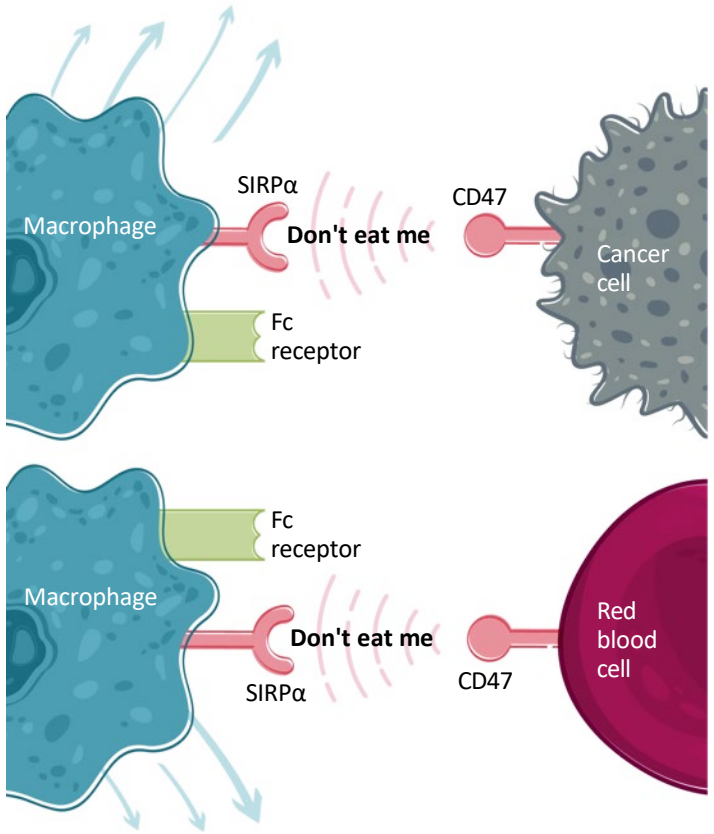



Complete CD47 blockade without targeting blood cells

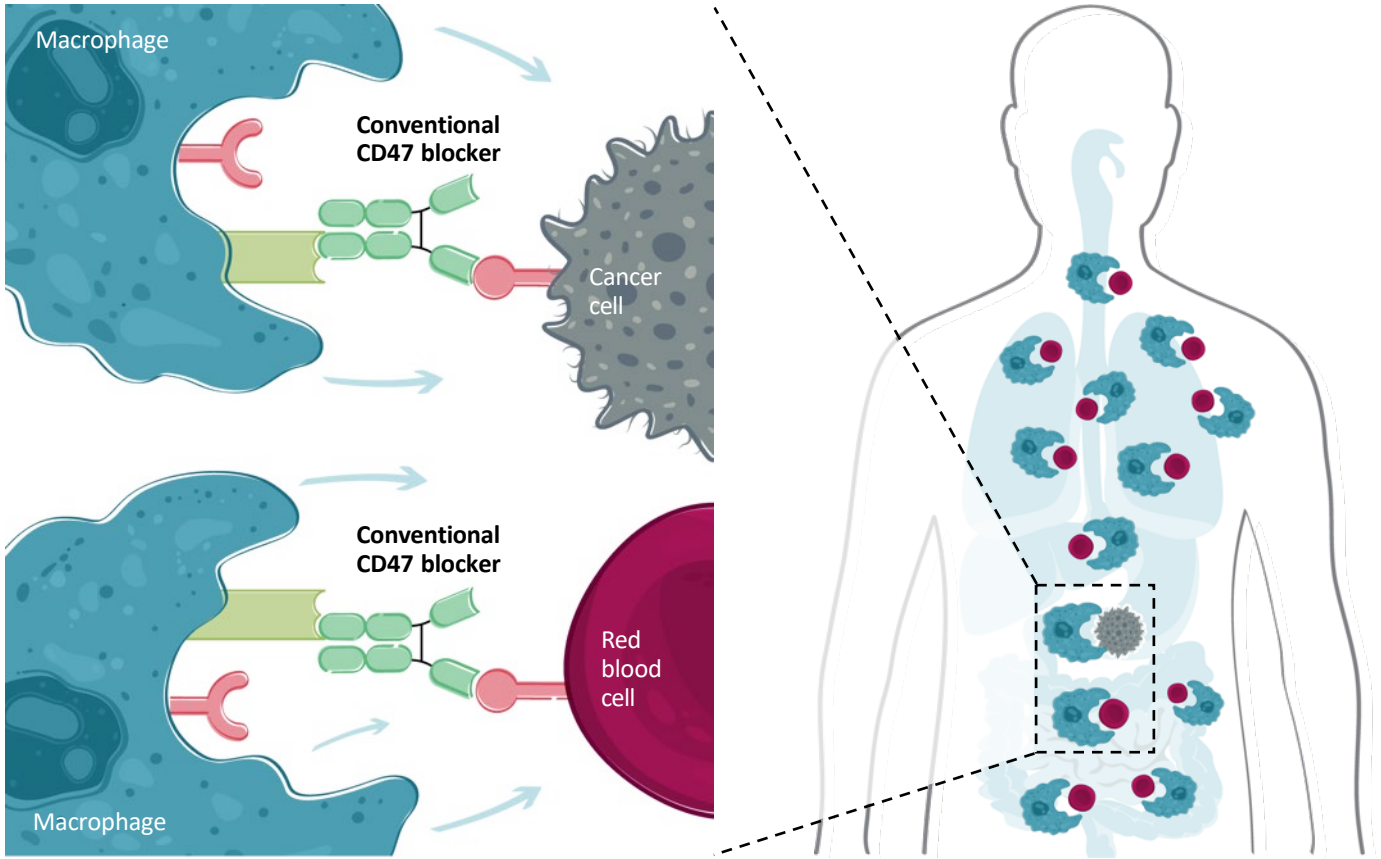



Combined with cancer therapy to specifically target cancer cells

# Conventional CD47 targeting is more toxic and less efficacious




CD47 is widely expressed in both healthy and cancer cells




Indiscriminate CD47 inhibition with an active Fc will target healthy cells

# ASPEN-06 demonstrates improvement in tumor response in patients with HER2+ gastric/GEJ cancer and validates evorpacept's mechanism with anti-cancer antibodies

- ✓ **ASPEN-06:** First prospective, randomized clinical study in solid tumors and the first randomized study demonstrating durable improvement vs. current standard of care in the CD47 space
- ✓ **ASPEN-06:** Evorpacept combination achieved a confirmed overall response rate of 40.3% compared to 26.6% for the control arm in the ITT population
- ✓ **ASPEN-06:** Median duration of response for evorpacept plus TRP was 15.7 months vs. 7.6 months for TRP control
- ✓ **ASPEN-06:** In patients with fresh HER2+ biopsies, evorpacept combination achieved a confirmed overall response rate of 54.8% compared to 23.1% for the control arm
- ✓ **ASPEN-06:** Evorpacept in combination with TRP was generally well tolerated and compared favorably with the TRP control arm

# ASPEN-06: Registration strategy for evorpacept in HER2+ gastric/GEJ cancer

## Proof of principle

**ASPEN-01 Phase 1b**
**HER2+ gastric/GEJ cancer**

South Korea, USA

Patients: **R/R ≥2L** N=18 with prior HER2 targeted therapy + chemotherapy

Treatment:

Evo 10 and 15 mg/kg (QW) + T + R + P

Endpoint:

Safety of combination
Anti-cancer activity

## Proof of concept

**ASPEN-06 Randomized Phase 2**
**HER2+ gastric/GEJ cancer**

Asia, Australia, Europe and North America

Patients: **2L/3L** N=127 with prior HER2 targeted therapy + chemotherapy

Treatment (1:1 randomization):

Evo 30 mg/kg (Q2W) + T + R + P **vs.** Control: T + R + P

Endpoint:

Anti-cancer activity:
Primary endpoint: ORR
Secondary: DOR, PFS, OS, safety

## Registrational

**ASPEN-06 Randomized phase 3**
**HER2+ gastric/GEJ cancer**

Worldwide

Patients: **2L /3L** with prior HER2 targeted therapy + chemotherapy

Treatment (randomized):

Evo 30 mg/kg (Q2W) + T + R + P **vs.** Control: R + P

Endpoint:

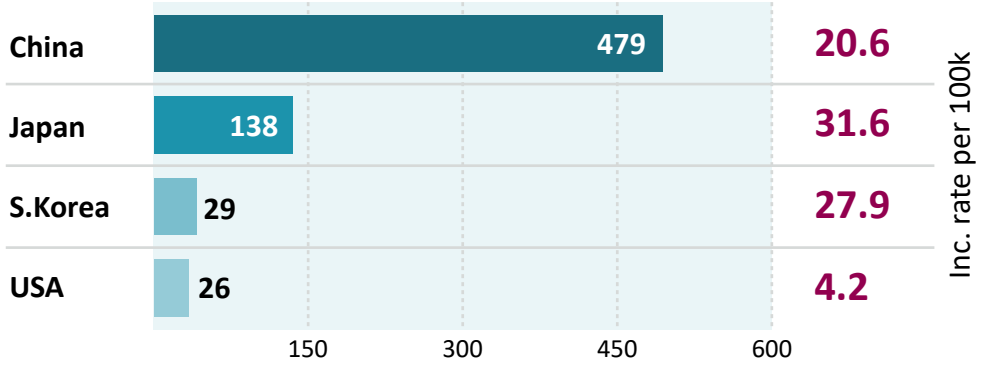
Anti-cancer activity: including OS, PFS, ORR, DOR

Legend:

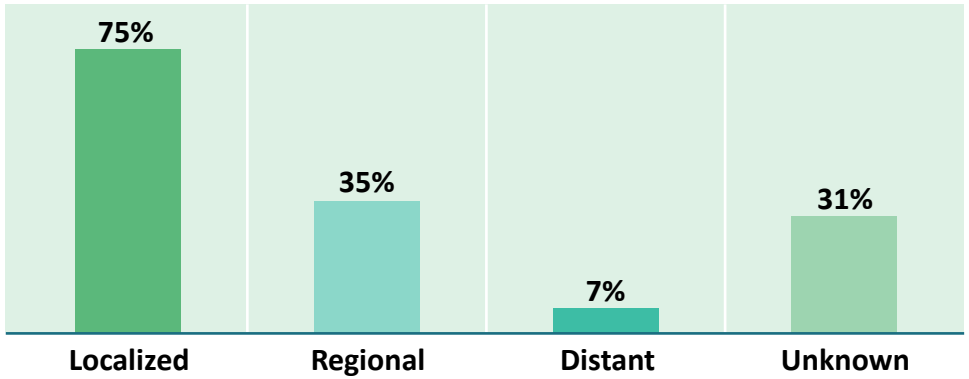
Evo Evorpacept  T Trastuzumab  R Ramucirumab  P Paclitaxel

# With a global unmet need, advanced gastric/GEJ cancer provides the initial population to clinically validate evorpacept's mechanism of action

## Annual new cases and ASR incidence per 100,000[1]




## 5-Year survival by stage at diagnosis in US[2]




## HER2+ treatment SOC by line of therapy

| | | | |
|---|---|---|---|
| 1st Line | Pembrolizumab (if CPS ≥ 1) + Trastuzumab + Fluoropyrimidine/Platinum (FP) doublet | Trastuzumab + FP doublet | |
| 2nd Line | Ramucirumab + Paclitaxel | Trastuzumab deruxtecan (only US/EUR) | Paclitaxel<br>Docetaxel<br>Irinotecan |
| 3rd Line | Trastuzumab deruxtecan (Asia) | Trifluridine /Tipiracil | Nivolumab<br>Irinotecan |

[1] WHO/IARC data accessed September 14, 2023 for most recent year, 2020; ASR = Age Standardized Rate;
[2] SEER Cancer Stats accessed September 14, 2023

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# Current HER2+ gastric/GEJ cancer standard of care reflects the need for novel combinations in 2L/3L

## HER2+ treatment benchmarks:

### RAINBOW[1] 2L

| | ORR (%) | DOR | PFS | OS |
|---|---|---|---|---|
| **Ramucirumab/Paclitaxel** N=330 | 27.9% | 4.4 months IQR 2.8–7.5 | 4.4 months 4.2-5.3 | 9.6 months 8.5-10.8 |
| **Paclitaxel** N=335 | 16.1% | 2.8 months IQR 1.4-4.4 | 2.9 months 2.8-3.0 | 7.4 months 6.3-8.4 |

THE LANCET Oncology — Volume 15, ISSUE 11, P1224-1235, October 2014

Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial

### DESTINY-Gastric01[2] 3L

| | | DOR | PFS | OS |
|---|---|---|---|---|
| **Trastuzumab deruxtecan** N=126 | 40.5% | 11.3 months 5.6-NE | 5.6 months 4.3-6.9 | 12.5 months 9.6-14.3 |
| **Physicians' choice** N=62 | 11.3% | 3.9 months 3.0-4.9 | 3.5 months 2.0-4.3 | 8.4 months 6.9-10.7 |

The NEW ENGLAND JOURNAL of MEDICINE — Volume 382: P2419-2430 June 2020

Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer – DESTINY-Gastric-01

**Both large, randomized studies demonstrated a survival benefit of ~1 year or less highlighting significant unmet medical need**

[1] Wilke et al, Lancet October 2014,
[2] Enhertu US product insert, and Shitara et al, NEJM June 18, 2020; NE could not be estimated

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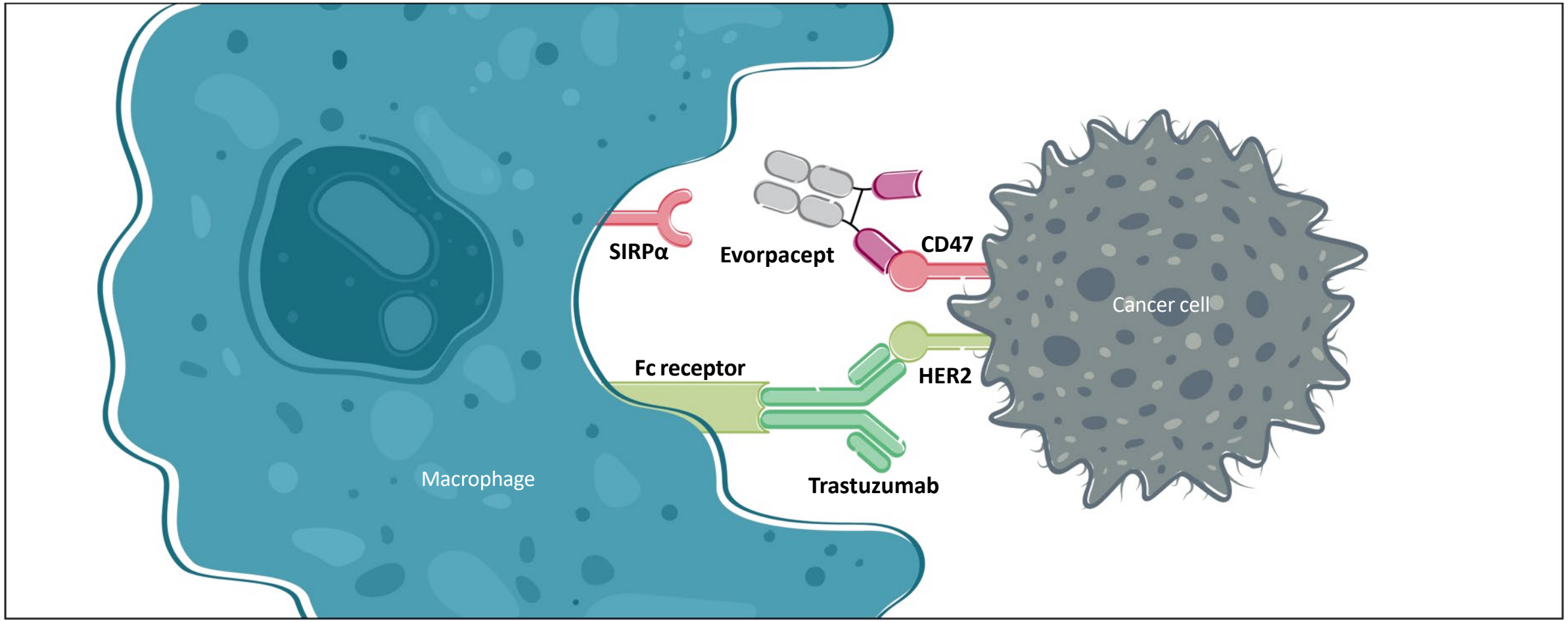
# Evorpacept + Trastuzumab (Herceptin) mechanism of action




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

# ASPEN-06 Study Design: Evorpacept in combination with trastuzumab, ramucirumab, and paclitaxel in patients with advanced HER2-overexpressing gastric/GEJ adenocarcinoma

**Key eligibility criteria:**

HER2+ advanced or metastatic gastric or gastroesophageal junction adenocarcinoma that has progressed on or after prior HER2-directed therapy

**2nd line or 3rd line**

✗ No prior treatment:
Anti-CD47 agent, an anti-SIRP agent or ramucirumab.

✓ Prior treatment ok:
Trastuzumab deruxtecan (Enhertu) and checkpoint inhibitors

**ASPEN-06 randomized phase 2**

N=127

Treatment (1:1 randomization):

Evo 30 mg/kg (Q2W) + T + R + P

vs.

Control: T + R + P

Endpoint:

Primary: ORR
Secondary: DOR, PFS, OS, safety

**Interim analysis (N=54)**

Presented Q4-2023

**Final analysis (N=127)**

Two primary objectives:

- Evo-TRP ORR of a 50% improvement over an assumed RP control of 30%
- Evo-TRP ORR compared to TRP arm at a clinically meaningful delta of >10%

In two prespecified HER2+ populations:

- Full intent to treat population (n=127)
- Subset of patients with “fresh” HER2+ biopsy after prior anti-HER2 treatment (n=48)

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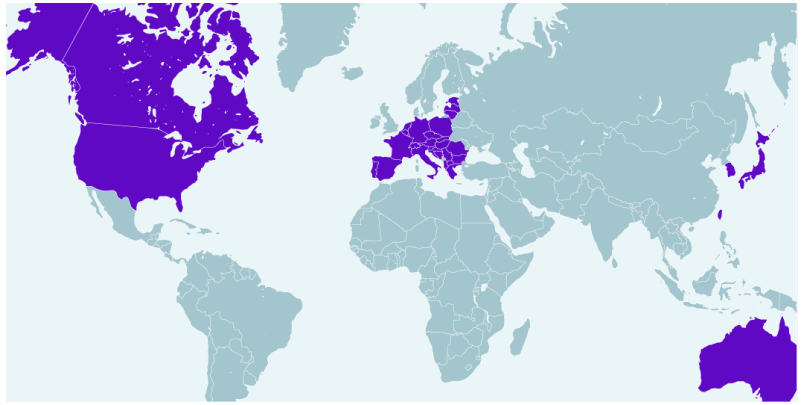
# ASPEN-06 Demographics: ASPEN-06 was a robust, global randomized study reflective of current standards of care in gastric cancer

**Study sites:**



**ASPEN-06**
91 trial sites activated in 13 countries in Asia, Australia, Europe and North America.

N=127

**Study regimen dose administration:**

| | | |
|---|---|---|
| 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/m²**<br>Days: 1, 8, 15 of 28-day cycle |

- All patients enrolled received a prior HER2-targeted therapy (eg, trastuzumab)
- Several stratification factors were used and were generally well-balanced across the two arms:
  - Cancer type (ie, Gastric vs GEJ)
  - Time of biopsy (ie, fresh vs archival)
  - Asia region
  - Treatment line (ie, 2nd vs 3rd line)
  - HER2 IHC score (IHC3+ or IHC2+/ISH+)
  - Prior Enhertu
- Study randomized n=127 vs targeted n=122 due to patients in screening at time of study end

Data Cutoff as of 24 May 2024

# ASPEN-06 Demographics: The study was generally well-balanced across several key factors although there were differences from the interim population to the final analysis

**Study population:**

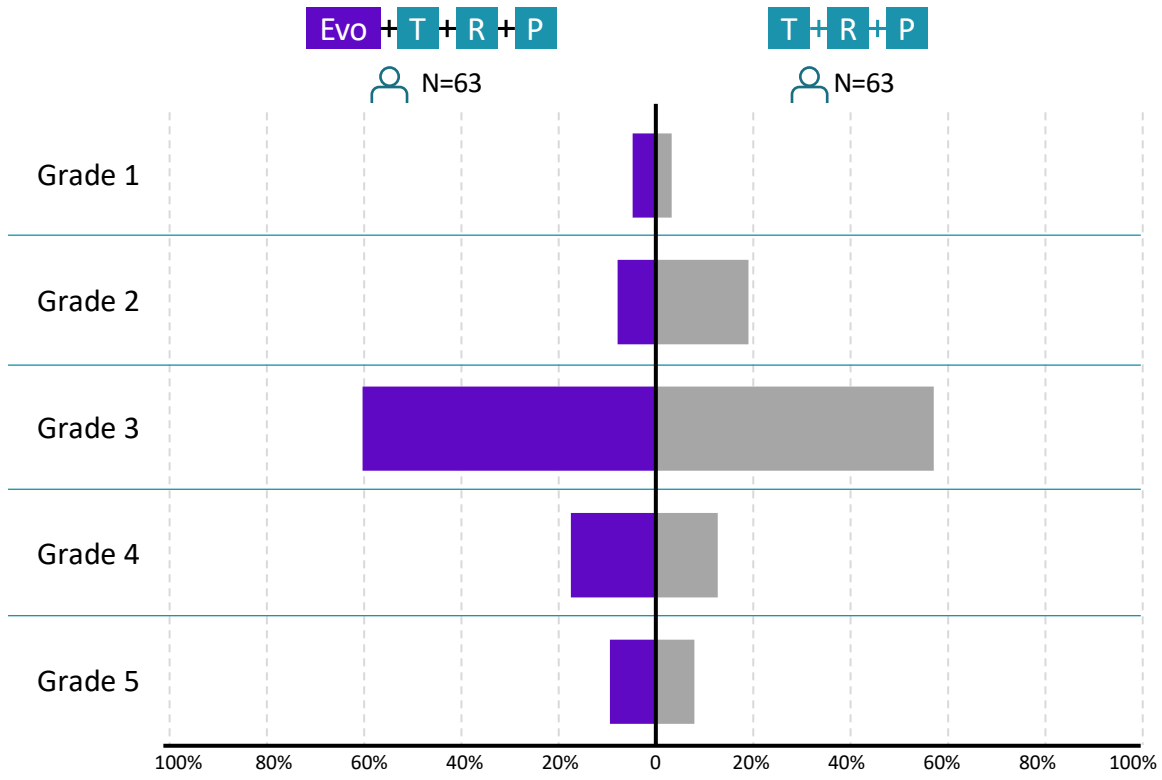
| | | Evo + T + R + P N=63 | Control: T + R + P N=64 |
|---|---|---|---|
| Median age, years (range) | | 64 (34-81) | 63 (31-86) |
| Sex, n% | Male | 55 (87.3%) | 48 (75.0%) |
| | Female | 8 (12.7%) | 16 (25.0%) |
| Race, n% | Asian | 31 (49.2%) | 31 (48.4%) |
| | White | 19 (30.2%) | 19 (29.7) |
| | Other | 1 (1.6%) | 4 (6.3%) |
| | Unknown | 12 (19.0%) | 10 (15.6%) |
| ECOG PS, n% | 0 | 30 (47.6%) | 27 (42.2%) |
| | 1 | 33 (52.4%) | 37 (57.8%) |
| GEJ, n% | | 15 (23.8%) | 20 (31.3%) |

- Demographics and the stratification factors were generally well-balanced across each arm
- Some patient characteristics differed between the interim analysis (n=54) and post-interim populations (n=73)
  - Post-interim analysis, fewer patients were enrolled with a fresh biopsy (46% had a fresh biopsy at interim vs. 32% post-interim)
  - Evo-TRP patients enrolled post-interim analysis had characteristics of more aggressive disease (ie, higher ECOG, faster time to initial progression, and a shorter prior disease course)
- Patients with a recent HER2+ biopsy had a recent biopsy at a median of only 1.1 months before dosing (vs. 14.1 months for archival patients)

Data Cutoff as of 24 May 2024

# ASPEN-06 Safety: Evorpacept in combination with TRP was well tolerated with a safety profile consistent with that of the backbone TRP therapy

**All causality adverse events, by grade**




- Evo-TRP was generally well tolerated
- The incidence of adverse events due to any cause was comparable by arm
- There were no on study treatment-related deaths on either arm
- Evorpacept's safety profile was consistent with its prior experience in over 500 patients treated to date

Data Cutoff as of 24 May 2024

# ASPEN-06 Safety: Evo-TRP was generally well-tolerated as grade 3-5 TEAEs were largely balanced across the two arms

**Summary of treatment-emergent adverse events grades 3-5**
(with frequency >5% on either arm)

| | Evo + T + R + P N=63 | | | | T + R + P N=63 | | | |
|---|---|---|---|---|---|---|---|---|
| **Grade** | **3** | **4** | **5** | **Total** | **3** | **4** | **5** | **Total** |
| Neutrophil count decreased | 11 (17.5%) | 7 (11.1%) | - | **18 (28.6%)** | 12 (19.0%) | 4 (6.3%) | - | **16 (25.4%)** |
| Anemia | 13 (20.6%) | - | - | **13 (20.6%)** | 11 (17.5%) | - | - | **11 (17.5%)** |
| Neutropenia | 11 (17.5%) | 3 (4.8%) | - | **14 (22.2%)** | 7 (11.1%) | 1 (1.6%) | - | **8 (12.7%)** |
| White blood cell count decreased | 7 (11.1%) | - | - | **7 (11.1%)** | 6 (9.5%) | - | - | **6 (9.5%)** |
| Febrile neutropenia | 1 (1.6%) | - | - | **1 (1.6%)** | 2 (3.2%) | 2 (3.2%) | - | **4 (6.3%)** |
| Hypertension | 6 (9.5%) | - | - | **6 (9.5%)** | 4 (6.3%) | - | - | **4 (6.3%)** |
| Sepsis | 2 (3.2%) | - | 2 (3.2%) | **4 (6.3%)** | 2 (3.2%) | - | 1 (1.6%) | **3 (4.8%)** |
| Asthenia | 2 (3.2%) | - | - | **2 (3.2%)** | 4 (6.3%) | - | - | **4 (6.3%)** |

Data Cutoff as of 24 May 2024

# ASPEN-06 Efficacy: Evorpacept achieved a 52% improvement in ORR over the TRP control arm with a median DOR of more than 15 months

| | Evo + T + R + P | Control: T + R + P |
|---|---|---|
| **Full study population** (ITT) | N=63 | N=64 |
| **Confirmed Objective Response** (ORR) | **40.3%** | **26.6%** |
| **Median Duration of Response** (mDOR) | **15.7 months** [11.0 – NE] | **7.6 months** [6.3 – NE] |

- In the full ITT population (N=127), Evo-TRP ORR of 40.3% compared favorably to an assumed RP control ORR of 30% (p=0.095)
- Evo contributed a clinically meaningful benefit of >10% magnitude of improvement in ORR over the TRP arm
- When compared to the observed TRP ORR of 26.6%, a p value of p=0.027 was observed
- Evo-TRP's durability of response was more than double that observed with TRP
- Activity of evorpacept + TRP compares favorably to ramucirumab + paclitaxel (28% ORR, 4.4 mo DOR)[1] as well as to trastuzumab-deruxtecan (40.5% ORR, 11.3 mo DOR)[2]

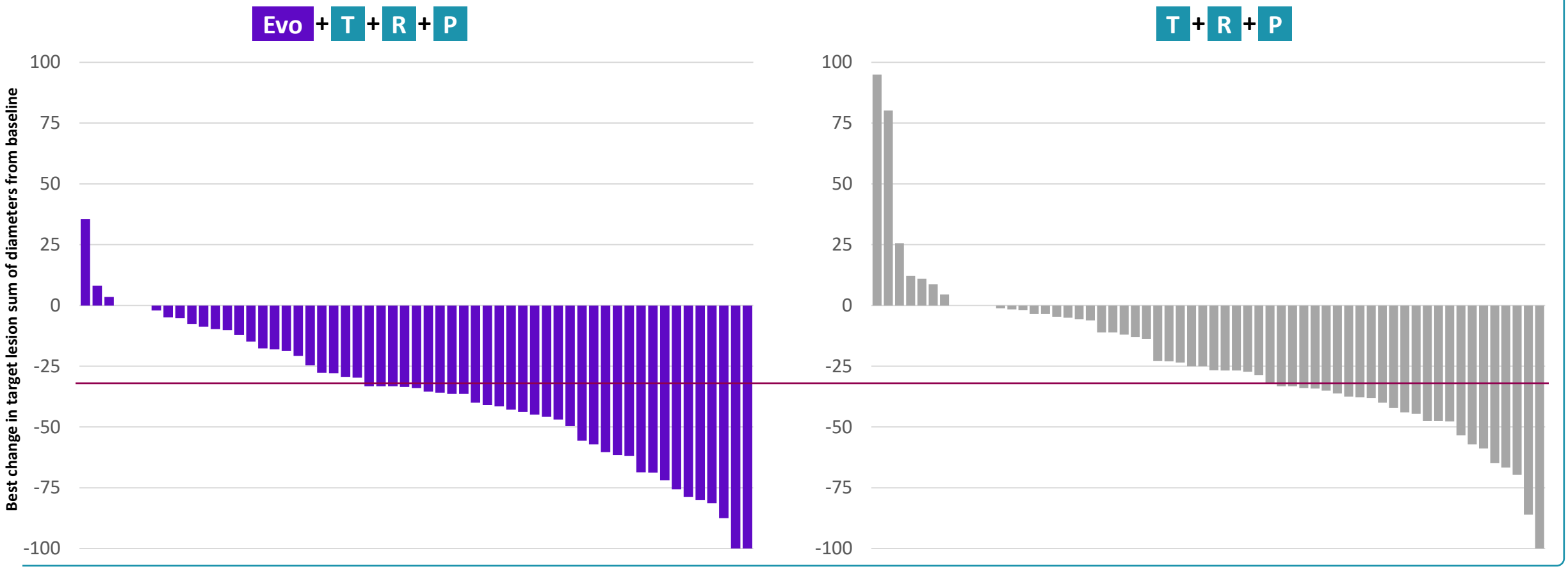
Data Cutoff as of 24 May 2024

[1] Wilke et al, Lancet October 2014,

[2] Enhertu US product insert, and Shitara et al, NEJM June 18, 2020; NE not estimable

# Substantial tumor shrinkage is seen in ASPEN-06 HER2+ gastric/GEJ cancer patients receiving Evo-TRP compared to TRP

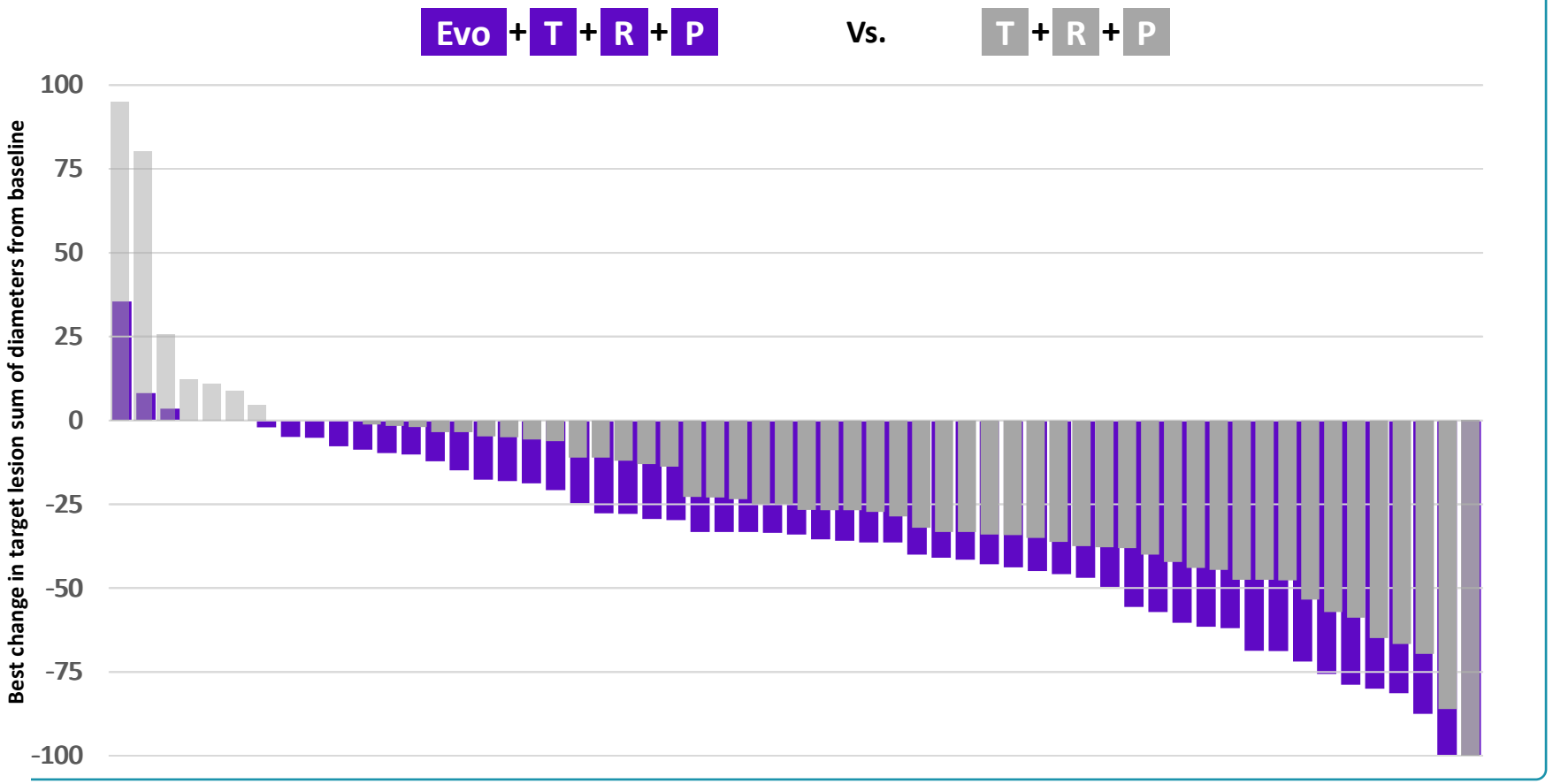
**ASPEN-06 Randomized Phase 2**




Data Cutoff as of 24 May 2024

# Deeper and durable responses across the Evo-TRP arm support evorpacept's mechanism and is consistent with that of an I-O agent

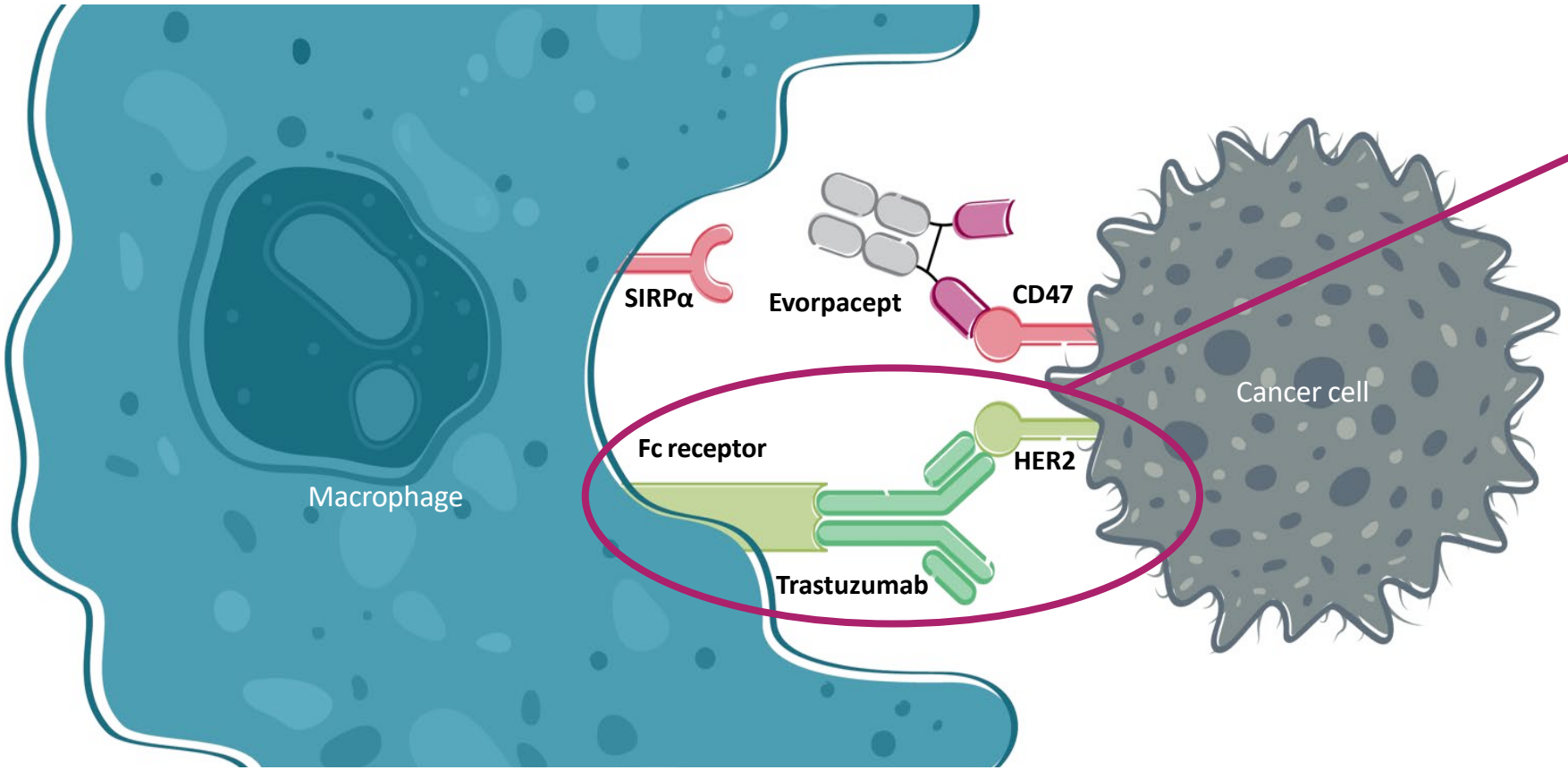
**ASPEN-06 Randomized Phase 2**




- Evorpacept provided broad benefit across the entire trial population
- Deeper and consistent tumor shrinkage in the Evo-TRP arm demonstrates the added contribution of evorpacept to the TRP backbone

Data Cutoff as of 24 May 2024

# Given evorpacept's MOA, HER2+ expression is an important biomarker of response




**When combining with trastuzumab, evorpacept's MOA depends on HER2 receptor expression in order to drive maximum phagocytosis against cancer cells**

# ASPEN-06 Efficacy: Evorpacept more than doubled tumor response in patients with fresh HER2+ biopsies indicating that HER2+ expression is a key biomarker

| Patients with fresh HER2+ biopsy | Evo + T + R + P<br>N=22 | Control: T + R + P<br>N=26 |
|---|---|---|
| Confirmed Objective Response (ORR) | **54.8%** | **23.1%** |

- Evo contributed an ORR delta of 31.7% over the TRP arm
- When compared to the observed TRP ORR of 23.1%, Evo-TRP demonstrated a significant p-value of <0.025 (p=0.0038) in an exploratory analysis

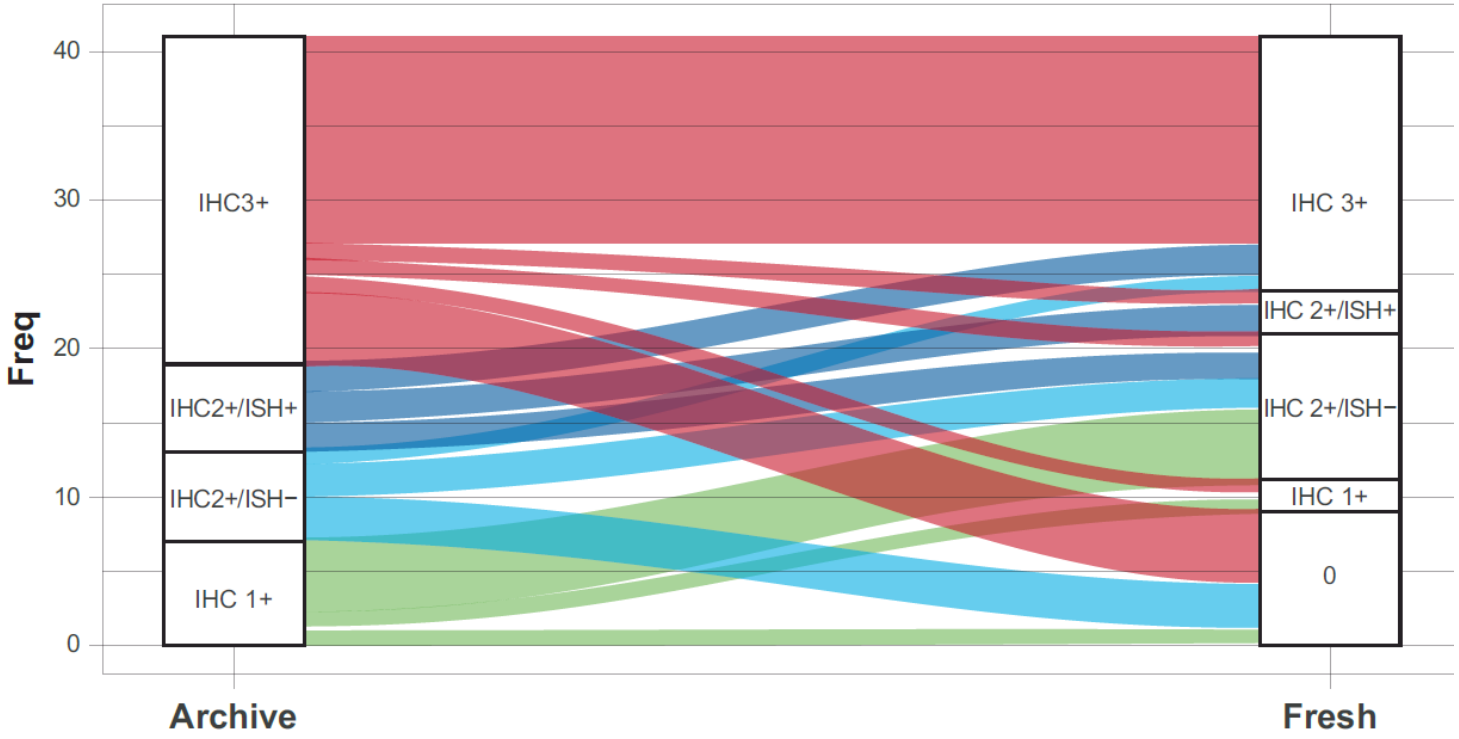
Data Cutoff as of 24 May 2024

[1] Wilke et al, Lancet October 2014,

[2] Enhertu US product insert, and Shitara et al, NEJM June 18, 2020;

# HER2 Expression is Highly Variable in Gastric Cancer

HER2+ status between matched archive and fresh biopsy samples



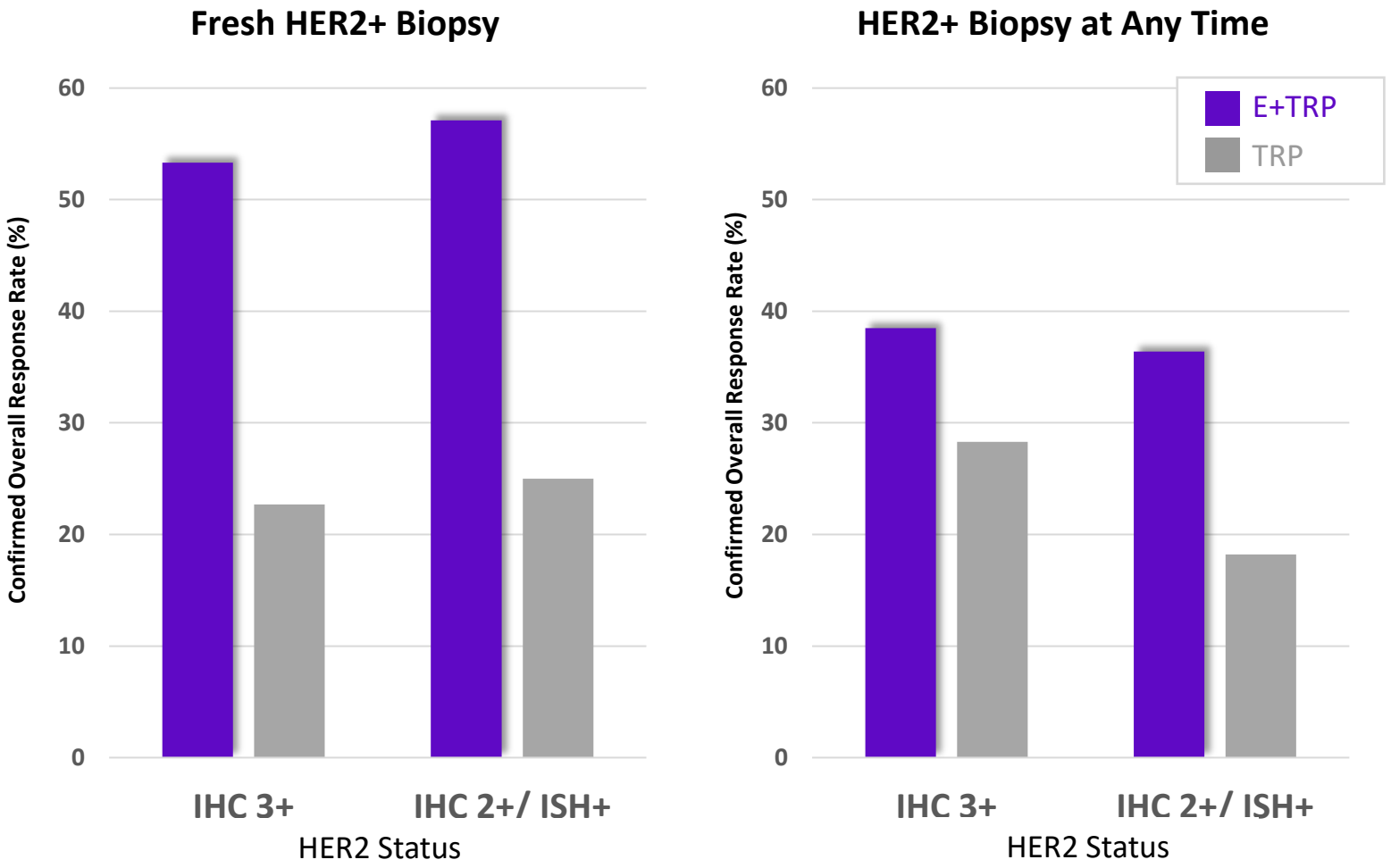

**"…decreased HER2 expression following treatment with trastuzumab or other HER2-targeted agents has been observed in 16–32% of patients."(1)**

- HER2 expression can change due to:
  - Loss of HER2 expression following HER2-targeted treatment[1]
  - Highly variable HER2 expression within the tumor[1]
- HER2 expression in gastric is also particularly variable vs other tumor types like breast[1,2]
- Confirming HER2-positivity with a fresh biopsy results in a more enriched HER2-positive population


(1) Shitara, et al, Nature Medicine, 2024; (2) Yamaguchi, JCO, 2022

# Response to TRP was not correlated to IHC score or fresh biopsy suggesting that HER2+ patients have become resistant to trastuzumab but are sensitive to evorpacept + trastuzumab

**ASPEN-06 Randomized Phase 2**

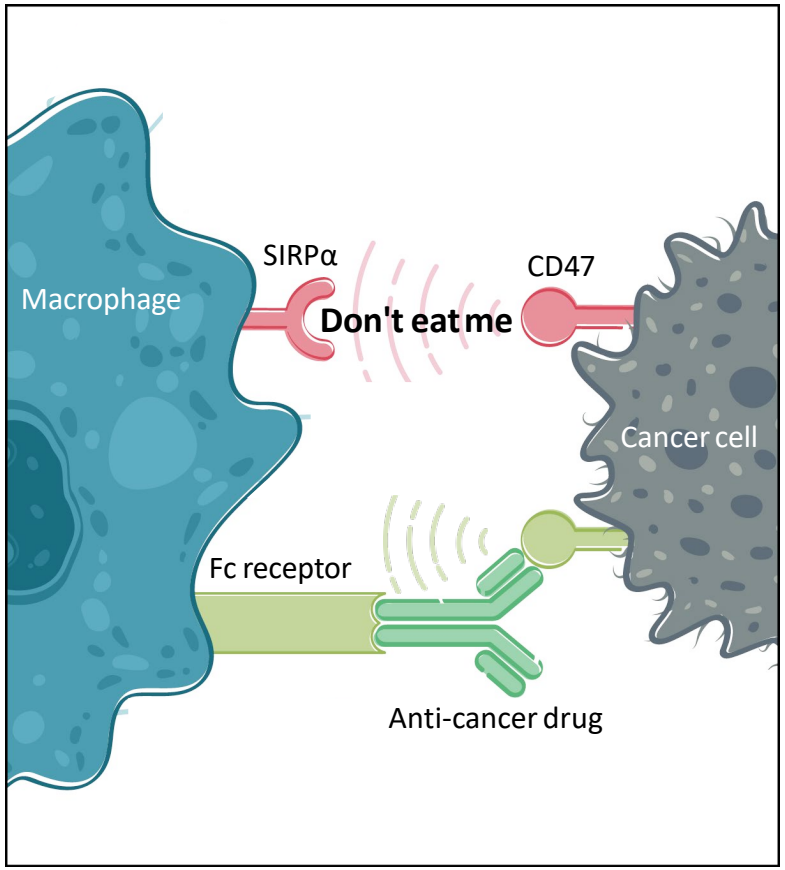



- HER2 positivity as confirmed on a recent biopsy was correlated with increased activity on the evorpacept arm
- Patients who have been re-treated with trastuzumab do not see additional benefit regardless of HER2 expression
- Response to trastuzumab on the control arm did not improve with a more recent HER2 biopsy

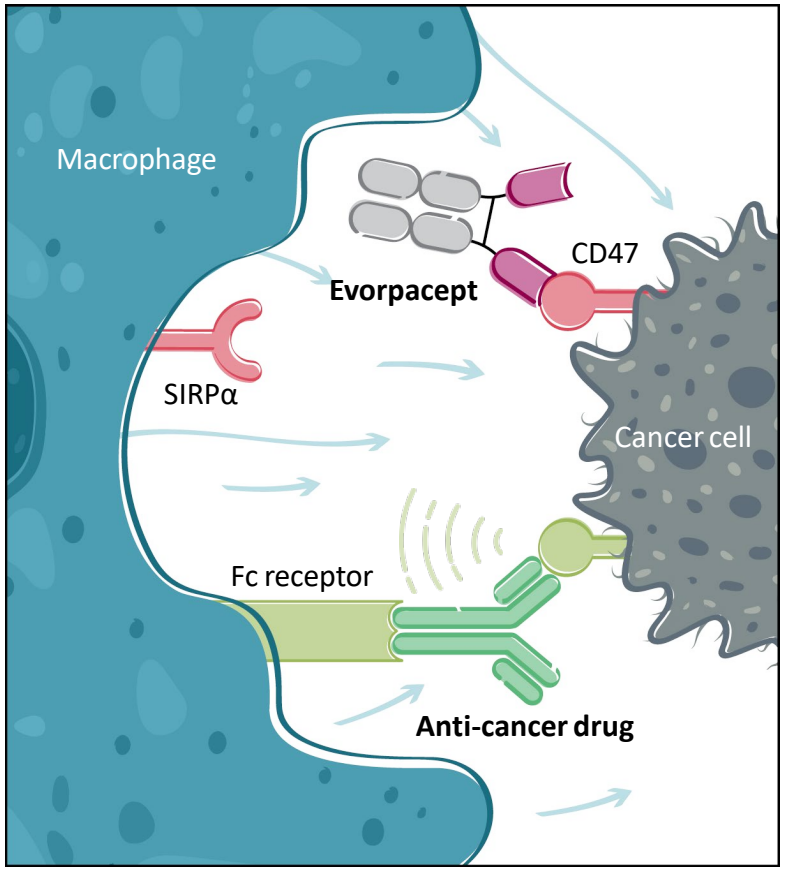
Data Cutoff as of 24 May 2024

# Evorpacept's mechanism translates into the clinic as these data illustrate how the MOA is fundamentally different from that of trastuzumab

T + R + P




Evo + T + R + P




- Without blockade of CD47, phagocytosis of cancer cells will not occur which is consistent with the ASPEN-06 data
- When combined with evorpacept's CD47 blockade, an Fc-active antibody will drive phagocytosis
- As patients develop resistance to HER2 directed therapy, evorpacept's novel MOA utilizes the innate immune response to uniquely drive tumor killing

# Summary: Evorpacept demonstrates the power of engaging the innate immune response in combination with TRP in patients with HER2+ gastric/GEJ cancer

## Robust and Durable Clinical Activity

The addition of evorpacept to TRP demonstrated an ORR of 40.3% and DOR of 15.7 months compared to the TRP control ORR of 26.6% and DOR of 7.6 months

## Validated Mechanism of Action

Evorpacept drove a 54.8% ORR in patients with fresh HER2+ biopsies vs. 23.1% in control, a delta of 31.8%, indicating that HER2+ expression is a key biomarker and validating evorpacept's unique MOA

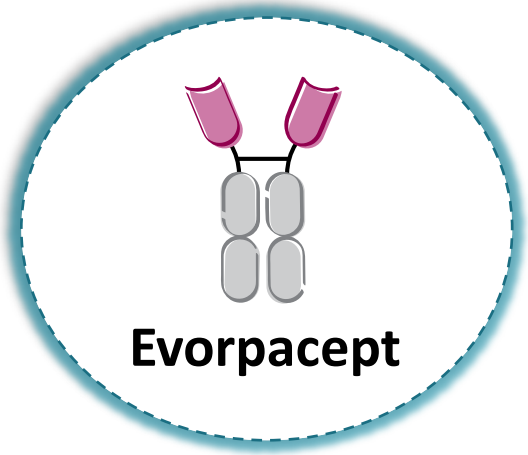
## Well-Tolerated

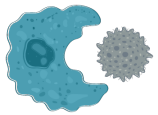
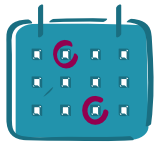
ASPEN-06 randomized data confirms that evorpacept can be combined with TRP with a favorable safety profile that was consistent with data from the >500 patients treated with evorpacept to date

## Novel IO agent

The only CD47 agent to demonstrate both durable improvement in overall response rate and a well-tolerated safety profile in a prospective randomized study

# Evorpacept's differentiated design results in differentiated safety and clinical activity

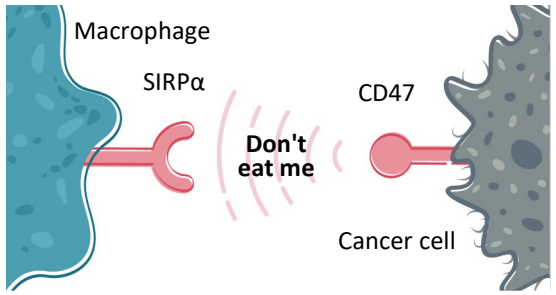


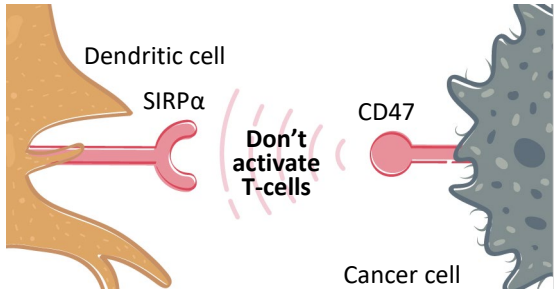

| | | |
|---|---|---|
| Higher affinity CD47 binding |  | More potently blocks CD47 signal on cancer cells |
| Inactive Fc domain |  | Less "sink effect" = more targeted<br>No known dose dependent cytopenia = higher dosing |
| Lower molecular weight |  | Increased solid tumor penetration and higher effective dosing |
| Antibody-like pharmacokinetics |  | 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

# Validated approach and our path to success

## 2 potential "First-In-Class" mechanisms of action




## 5 positive clinical readouts across multiple studies

- Ph2 Gastric/GEJ cancer randomized interim data with TRP
- Ph1b NHL data with Rituxan
- Ph1b Gastric/GEJ cancer data with TRP
- Ph1/2 IST NHL data with $R^2$
- Ph1b ≥2L Head and Neck cancer (HNSCC) data with Keytruda
- Ph1b 1L HNSCC data with Keytruda + chemotherapy

## 9 ongoing studies in new indications and combinations

**Anti-cancer antibodies:**

- ☐ Ph2 Gastric/GEJ cancer study with TRP
- ☐ Ph1b Multiple myeloma study with Sarclisa
- ☐ Ph1b Non-Hodgkin lymphoma IST
- ☐ Ph1b Breast cancer study with zanidatamab

**Antibody drug conjugates:**

- ☐ Ph1b Urothelial carcinoma study with Padcev
- ☐ Ph1b Breast cancer study (I-Spy) with Enhertu

**Checkpoint inhibitors:**

- ☐ Ph2 1L HNSCC randomized study with Keytruda
- ☐ Ph2 1L HNSCC randomized study with Keytruda + chemotherapy
- ☐ Ph2a 2L Ovarian cancer study with Keytruda + chemotherapy IST

**ASPEN-06 data de-risks and supports evorpacept in combination with any fc-active antibody across multiple tumor types**

ALX ONCOLOGY

# THANK YOU