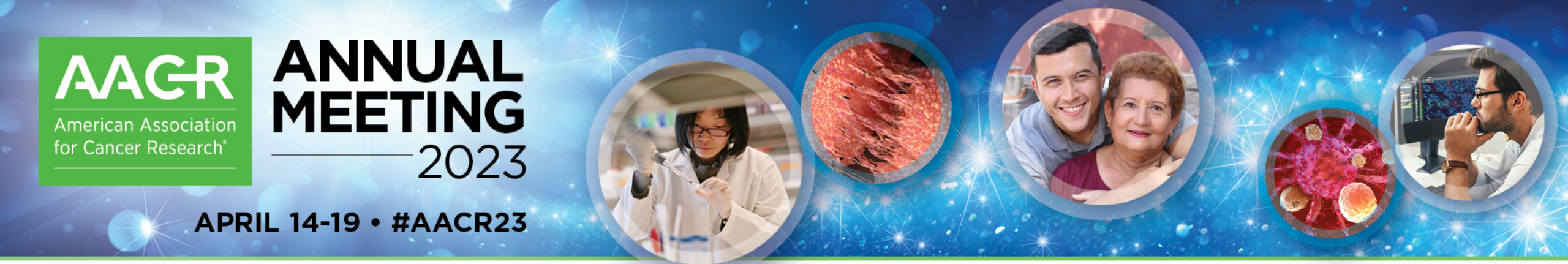

EO-3021: An antibody drug conjugate targeting CLDN18.2 expressing cancers

David Dornan, PhD
Elevation Oncology, Inc.

ELEVATION ONCOLOGY

Disclosure Information

David Dornan

I have the following relevant financial relationships to disclose:

Employee of: Elevation Oncology, Inc.

Consultant for: ReviR Therapeutics, Inc., Teon Therapeutics, Inc.

Stockholder in: Elevation Oncology, Inc.

I will discuss investigational use in my presentation: EO-3021/SYSA1801/CPO102 in the Treatment of CLDN18.2 Positive Advanced Malignant Solid Tumors

Claudin 18.2 Expression Profile Confers Selectivity for Therapeutic Intervention

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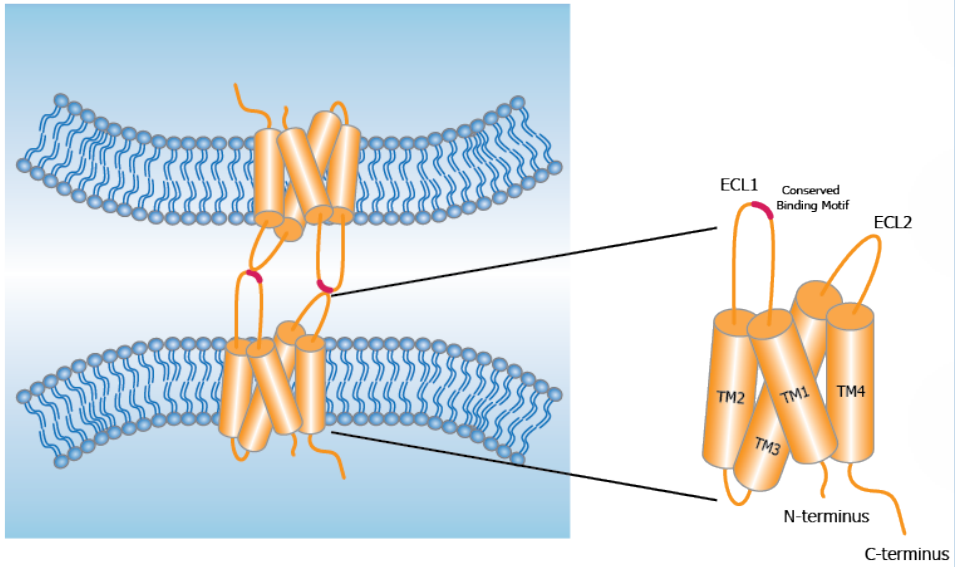
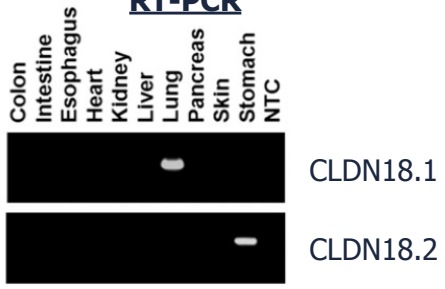
Claudin 18.2



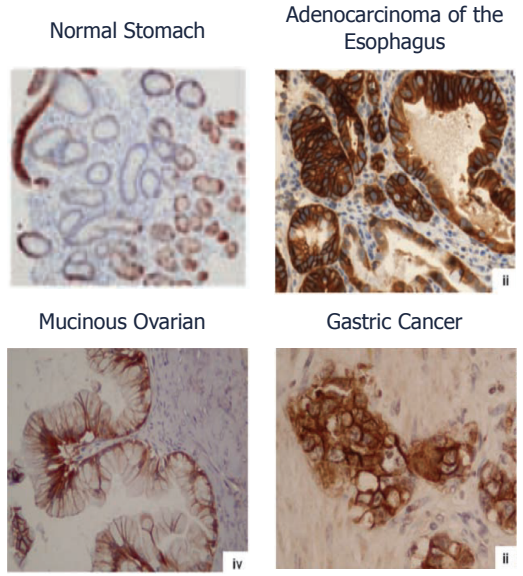
- Claudin 18.2 is part of a family of tight junction membrane proteins
- Claudin 18.2 expression in normal tissues is restricted to the gastric mucosa with basolateral localization
- During malignant transformation, changes in cell polarity may result in exposure of Claudin 18.2
- Claudin 18.2 is overexpressed in several types of cancers including gastric, pancreatic, esophageal, ovarian, and lung
- Claudin 18.2 expression has minimal overlap (<20%) with HER2 or PD-L1 expression in gastric cancer
- No approved therapies targeting Claudin 18.2

Tissue Distribution RT-PCR



Turechi et al. (2011)

CLDN18.2 Immunohistochemistry



Sahin et al. (2008)

Estimated Incidence of Claudin 18.2 in Solid Tumors

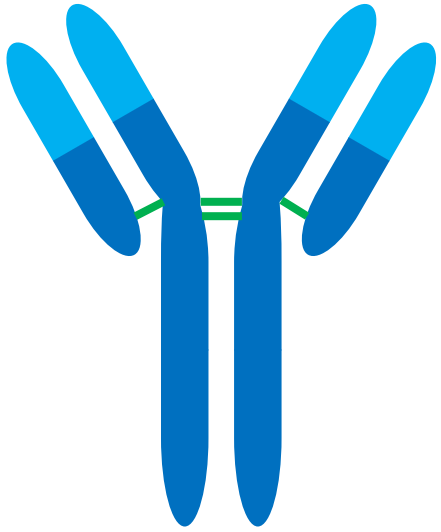
Cancer Type	Estimated New Cancer Cases		Claudin 18.2 expression per disease type (IHC)
	US Incidence[1]	Global Incidence[2]	
Gastric	26,500	1,090,000	77%[3] (adenocarcinoma)
Esophageal	21,500	604,000	78%[3] (adenocarcinoma)
Pancreatic	64,000	496,000	59-80%[3-5] (PDAC)
Ovarian	20,000	314,000	24%[3] (mucinous)
Lung	238,000	2,207,000	6%[6] (adenocarcinoma)

*Any level of expression (e.g., ≥1% cells with any staining intensity of CLDN18.2)
Abbreviations: US, United States; IHC, Immunohistochemistry; PDAC, Pancreatic ductal adenocarcinoma

[1]Siegel RL, et al. CA: A Cancer Journal for Clinicians. 2023; 73:1. [2]Sung H. et al. CA: A Cancer Journal for Clinicians. 2020; 71:3. [3]Sahin, et al. Clin Cancer Res. 2008 1;14(23):7624-34. [4]Wöll et al. Int J Cancer. 2014; 134(3). [5]Tanaka, et al. J Histochem Cytochem. 2011; 59(10): 942–952. [6]Micke, et al. Int J Cancer. 2014;135(9):2206-14.

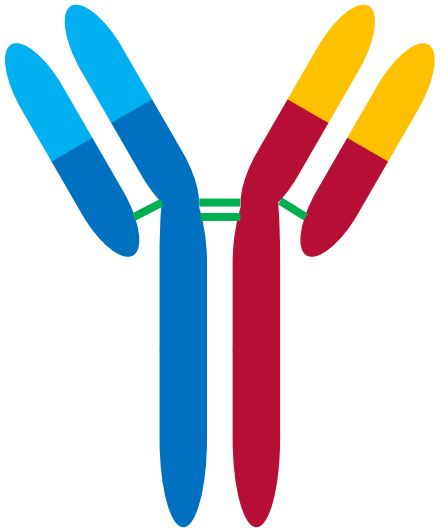
Examples of CLDN18.2 Targeted Therapy Modalities

Monoclonal mAbs



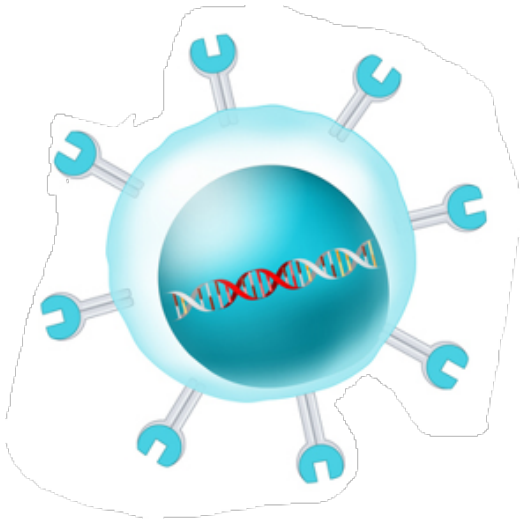
zolbetuximab
FL-301

Bispecific mAbs



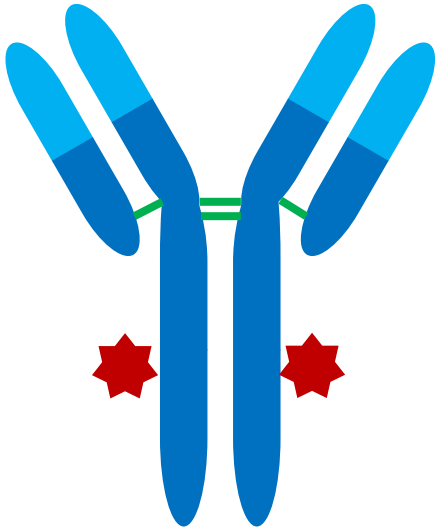
AMG-910 (CD3)
FL-302 (CD137)
PT886 (CD47)
Q-1802 (PD-L1)
TJ033721 (4-1BB)

CAR T-cell



CT041
LCAR-C18S
LY011

Antibody Drug Conjugates

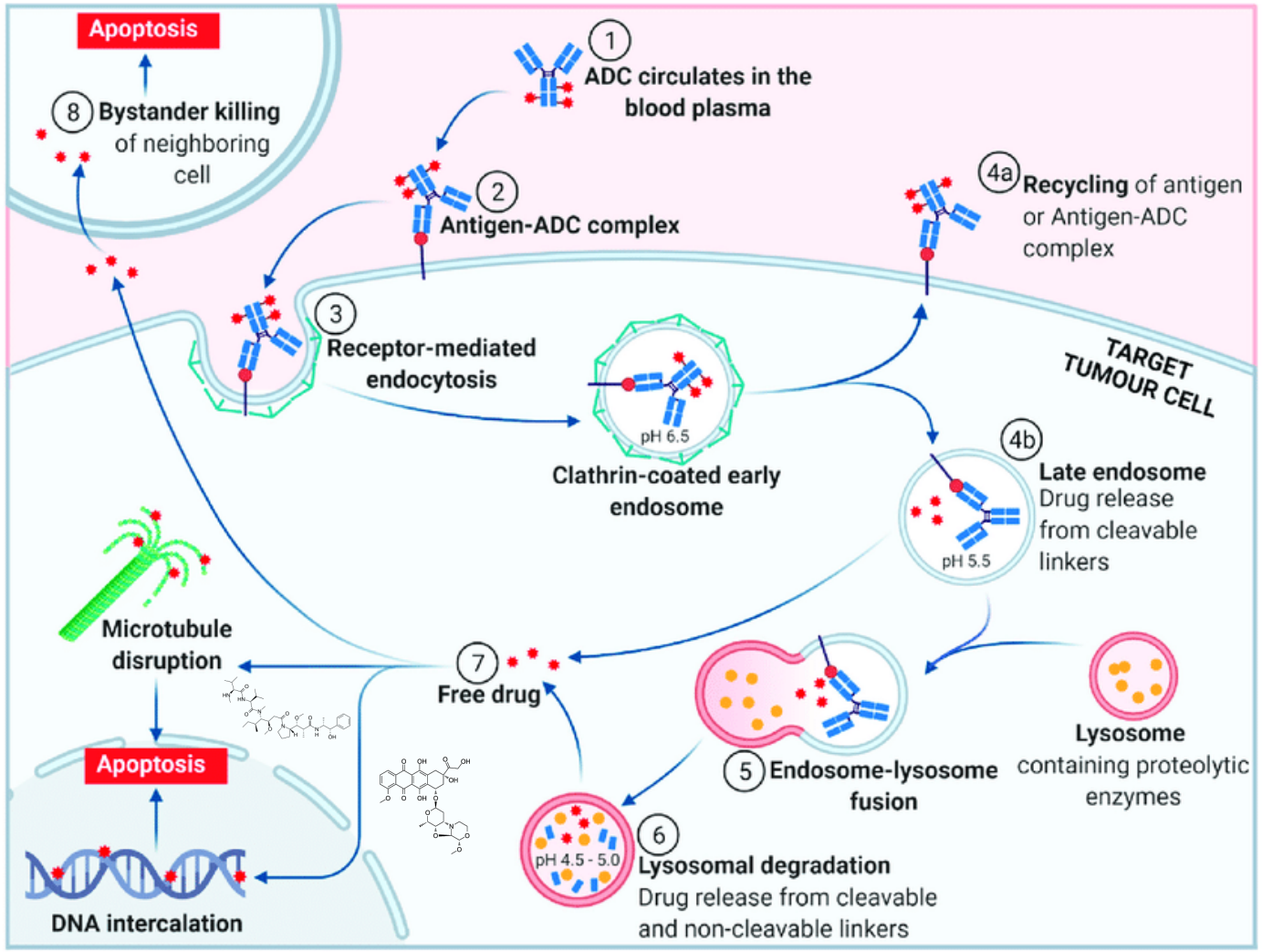


EO-3021/SYSA1801/CPO102
CMG901
RC118
LM302
SOT102
SKB315
TORL-2-307
JS107
IBI343

Abbreviations: mAb, monoclonal antibody

Not an exhaustive list of all publicly disclosed programs

Mechanism of Action for Antibody Drug Conjugates



Modified from Tong et al. (2021) https://doi.org/10.3390/molecules26195847

EO-3021 mAb is Specific for CLDN18.2 over CLDN18.1

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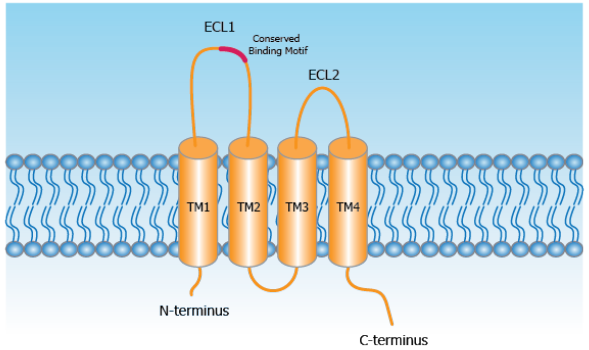
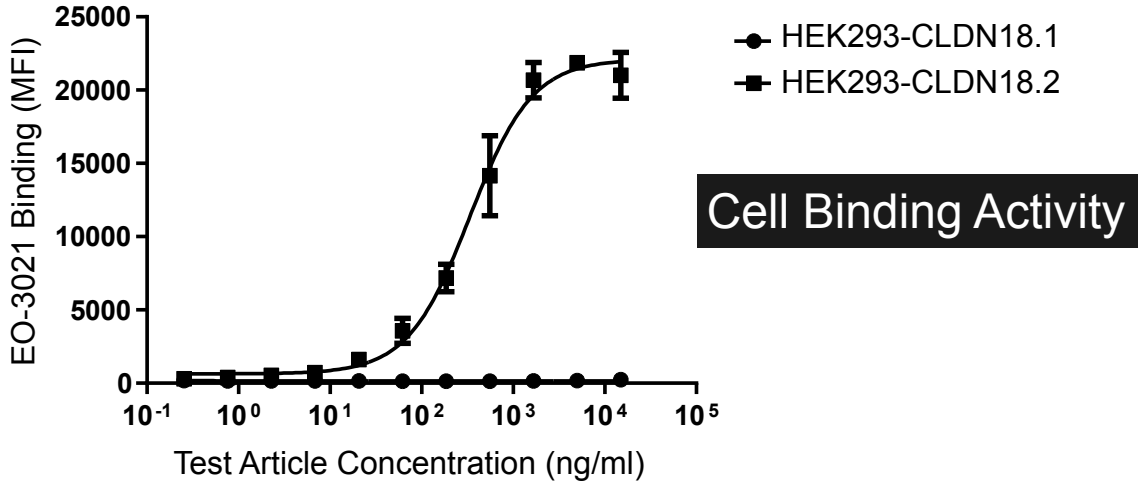


27					45	47				56					65					80	
M	D	Q	W	S	T	Q	D	L	Y	N	N	P	V	T	A	V	F	N	Y	Q	CLDN18.2 ECL1
M	D	M	W	S	T	Q	D	L	Y	D	N	P	V	T	S	V	F	Q	Y	E	CLDN18.1 ECL1

G	L	W	R	S	C	V	R	E	S	S	G	F	T	E	C	R	G	Y	F	T	L	L	G	L	P	A	M	L	Q	A	V	R
G	L	W	R	S	C	V	R	Q	S	S	G	F	T	E	C	R	P	Y	F	T	I	L	G	L	P	A	M	L	Q	A	V	R

EO-3021 mAb:

- Fully Human mAb
- IgG1 Isotype
- Kd = 0.6 nM for CLDN18.2
- No binding to CLDN18.1



Cell Binding Activity

Abbreviations: ECL1, Extracellular Loop 1; ECL2, Extracellular Loop 2; IgG1, immunoglobulin G1; TM, Transmembrane

EO-3021 is ADCC and CDC Competent: Modest Differences Relative to Unconjugated mAb

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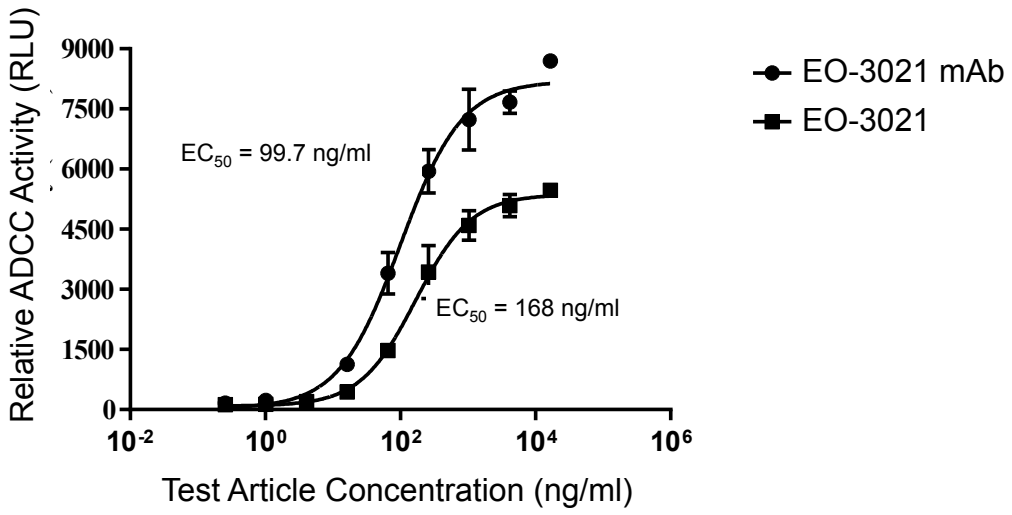
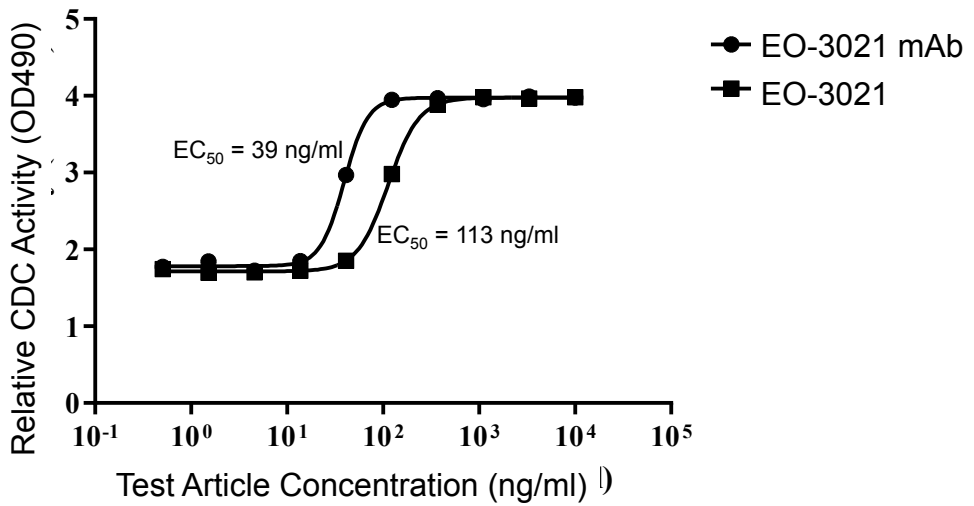
ADCC



HEK293-CLDN18.2 + Jurkat/FCGR3A-NFAT

CDC



CHO-K1-CLDN18.2 + human serum complement

Abbreviations: ADCC, antibody dependent cellular cytotoxicity; CDC, complement dependent cytotoxicity

EO-3021-Mediated Endocytosis and Reduction of Cell Viability is Dependent on CLDN18.2 Expression

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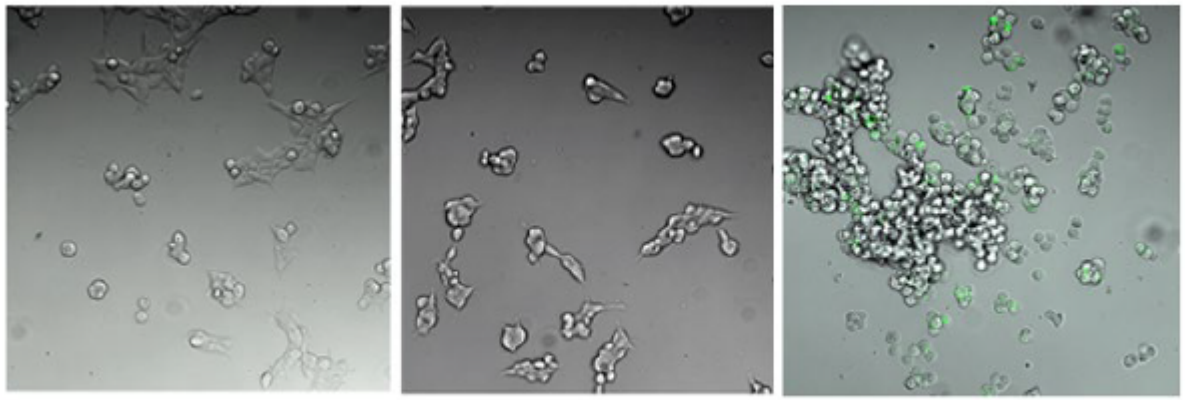
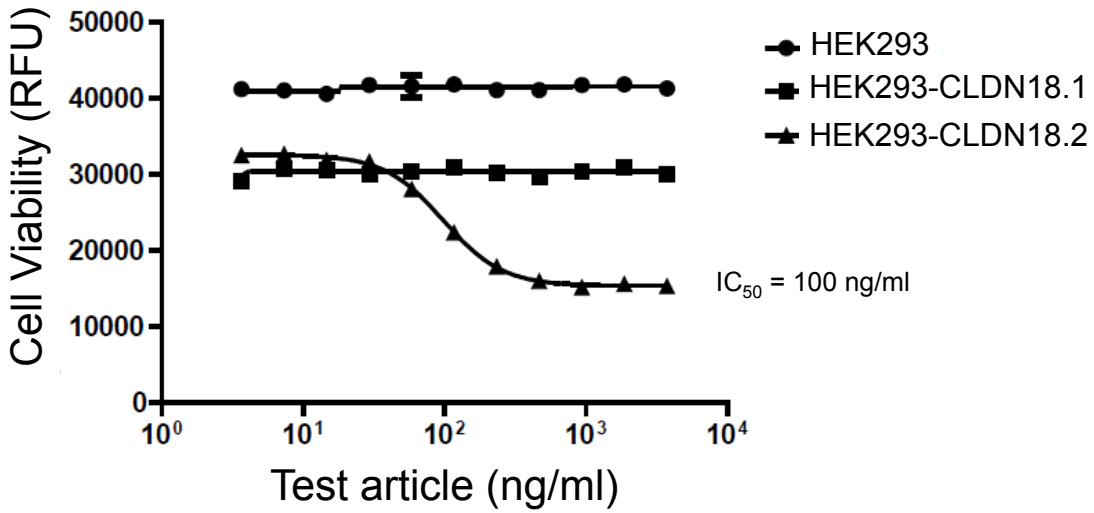
Endocytosis of Fluorescent Labeled EO-3021



HEK293 HEK293-CLDN18.1 HEK293-CLDN18.2

EO-3021 Tx (2 μg/ml) labeled with Zenon pHrodo iFL, 24-hour incubation

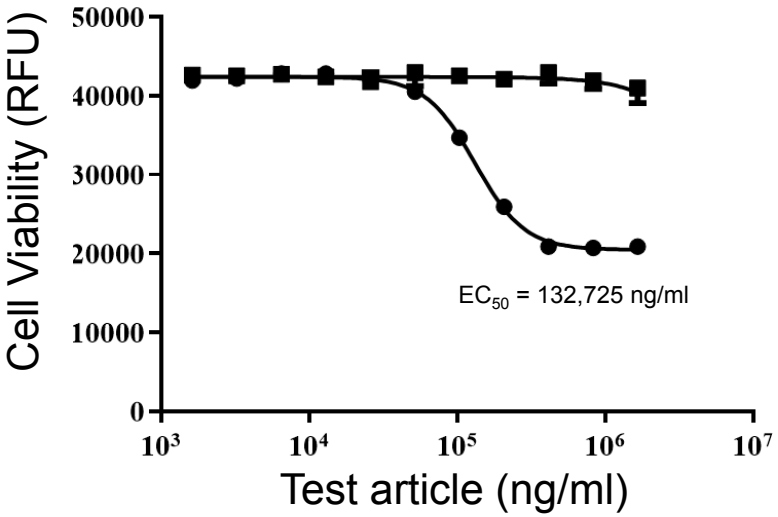
EO-3021 Impact on Cell Viability



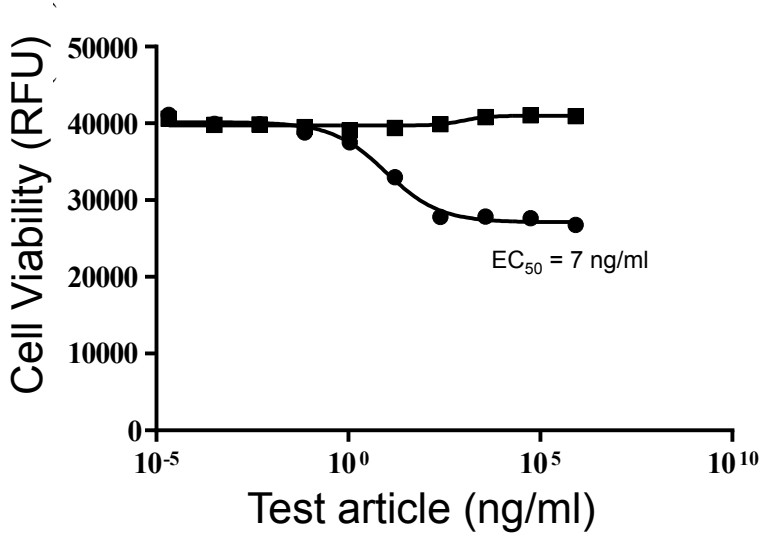
EO-3021 Tx (varying concentration), 72-hour incubation, resazurin assay

EO-3021 in vitro Activity More Notable in Cell Lines with Medium or High Levels of CLDN18.2 Expression

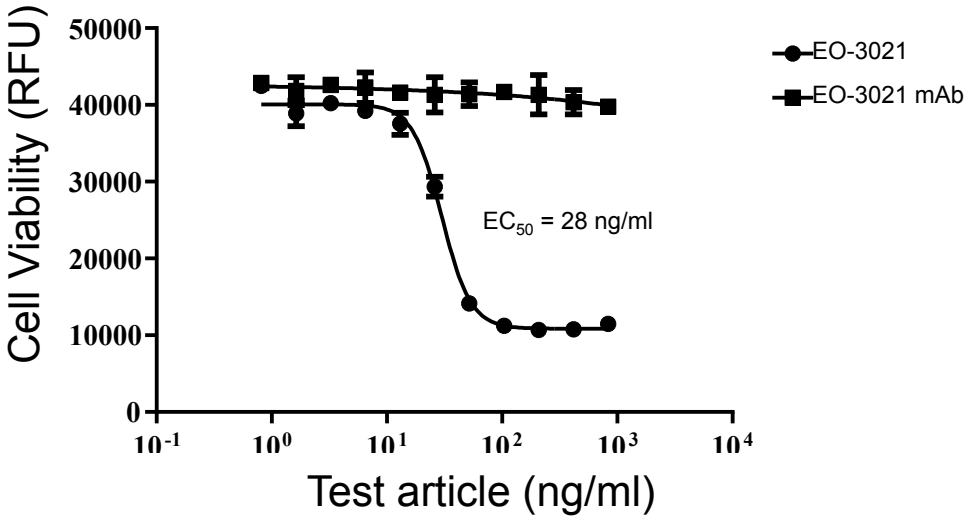
Pancreatic Cancer PATU8988S CLDN18.2 Low



Gastric Cancer NCI-N87-18.2 CLDN18.2 Medium HER2 Amplified



Pancreatic Cancer BxPC3-18.2 CLDN18.2 High

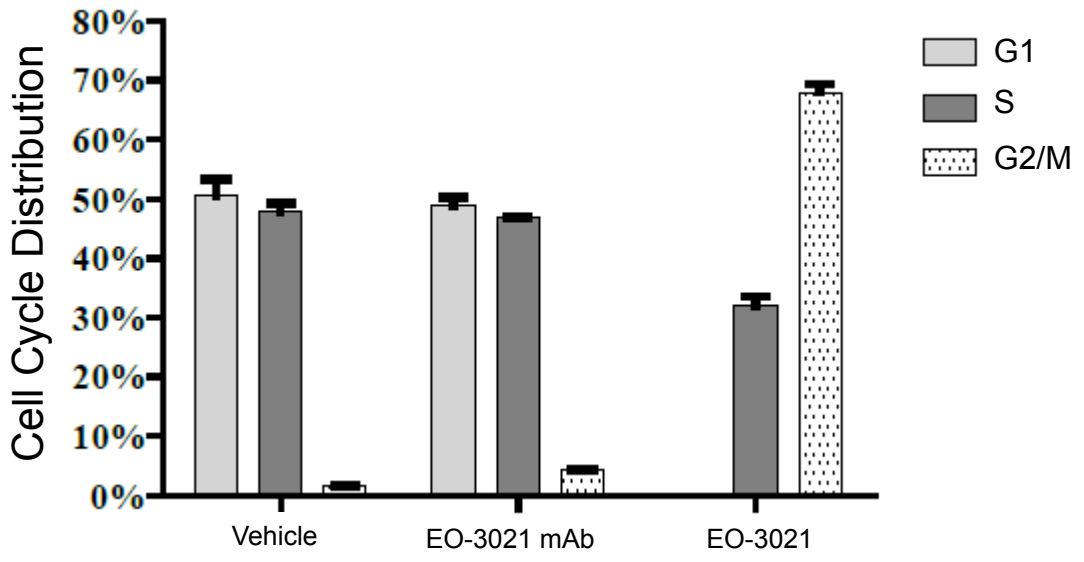


Approximately 15% of CLDN18.2 expressing gastric cancers co-express HER2[7]

[7]Schuler MH et al. J Clin Oncol. 2017. 35:15_suppl 4038-4038.

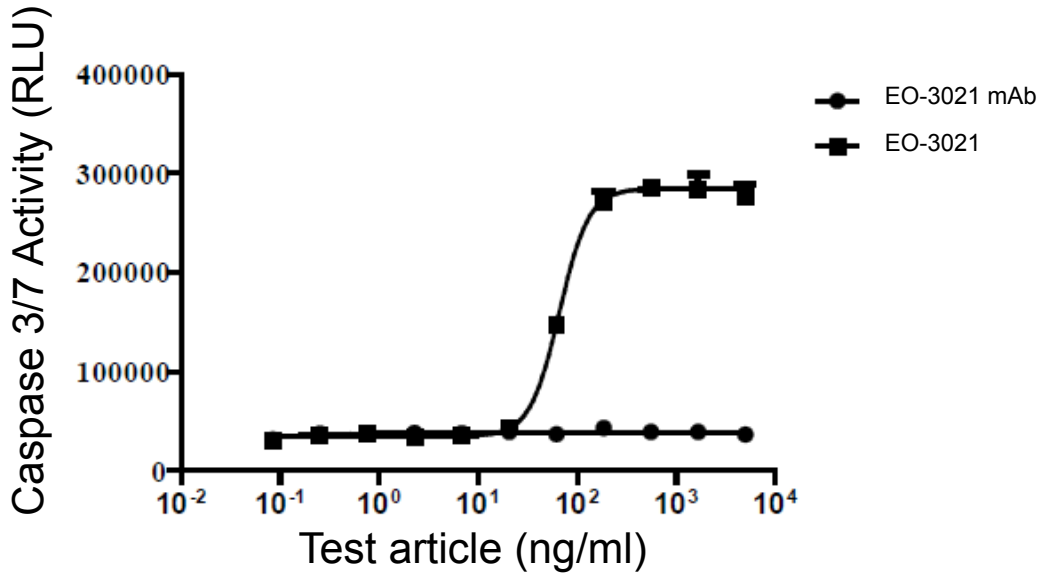
EO-3021 Promotes G2/M Cell Cycle Arrest and Activates Caspase 3/7

Cell Cycle Distribution Post-Tx



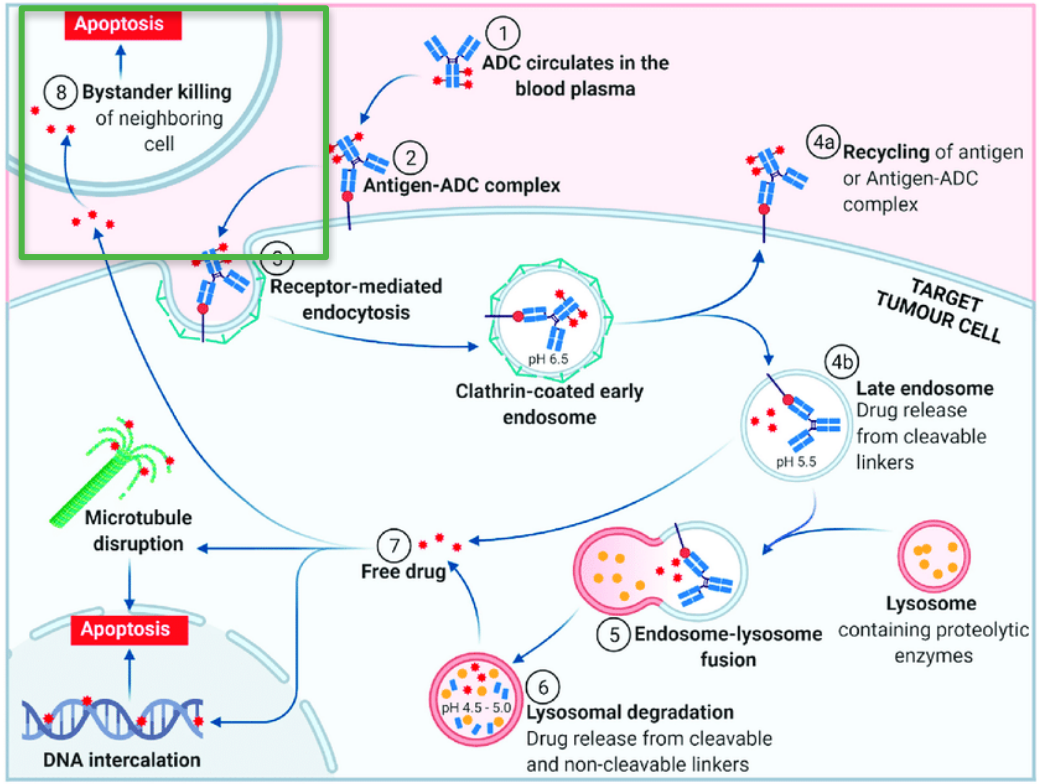
BxPC3-CLDN18.2, 600 ng/ml Tx, 66±3 hours

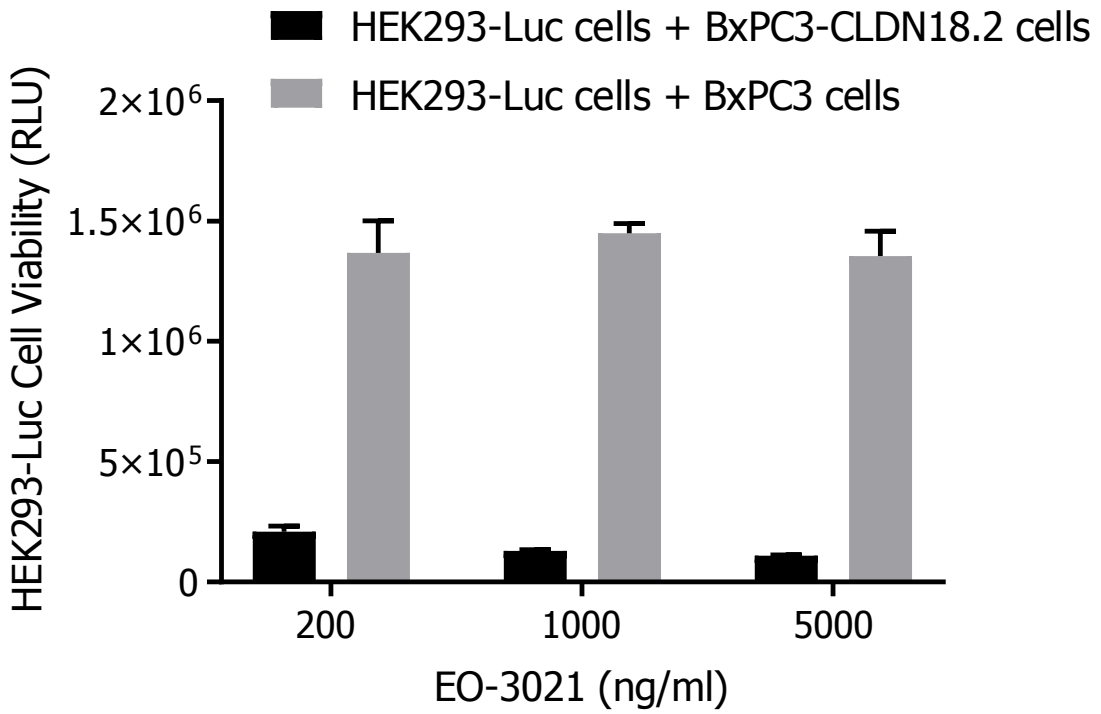
Caspase 3/7 Activity Post-Tx



BxPC3-CLDN18.2, 24±3 hours

EO-3021 Demonstrates Bystander Effect on CLDN18.2 Negative Cells





HEK-293-Luc cells co-cultured with either BxPC3-CLDN18.2 (Ag positive) or BxPC3 (Ag negative) cells and Tx for 96 hours

Abbreviations: Ag, antigen

Single Dose of EO-3021 Confers Tumor Regressions in CLDN18.2 High Expressing Xenograft Model

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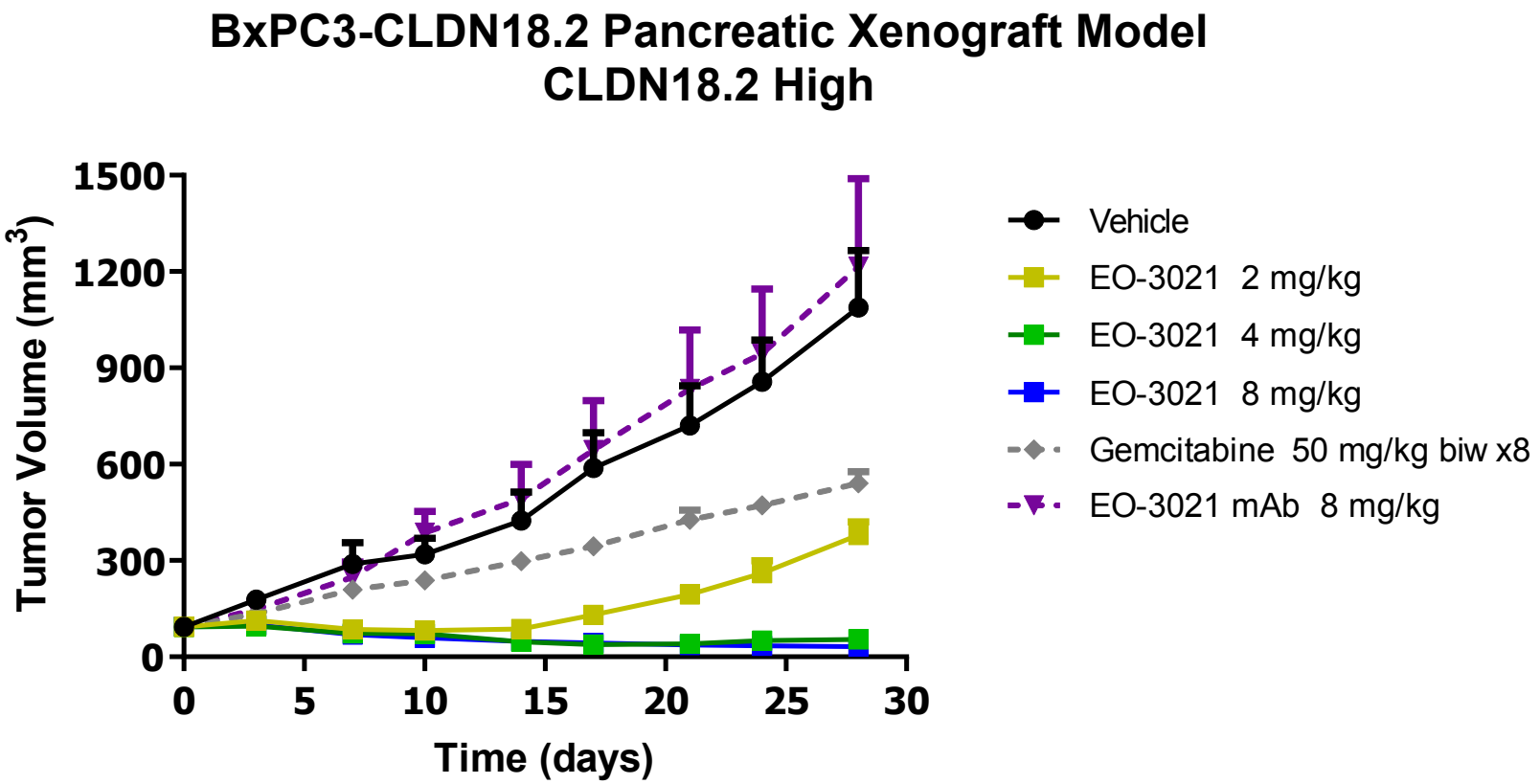

Nu/nu mice were administered single dose of Tx, unless otherwise indicated. Dosing initiated on Day 0.

Single Dose of EO-3021 Confers Tumor Regressions in CLDN18.2 Medium Expressing Xenograft Model

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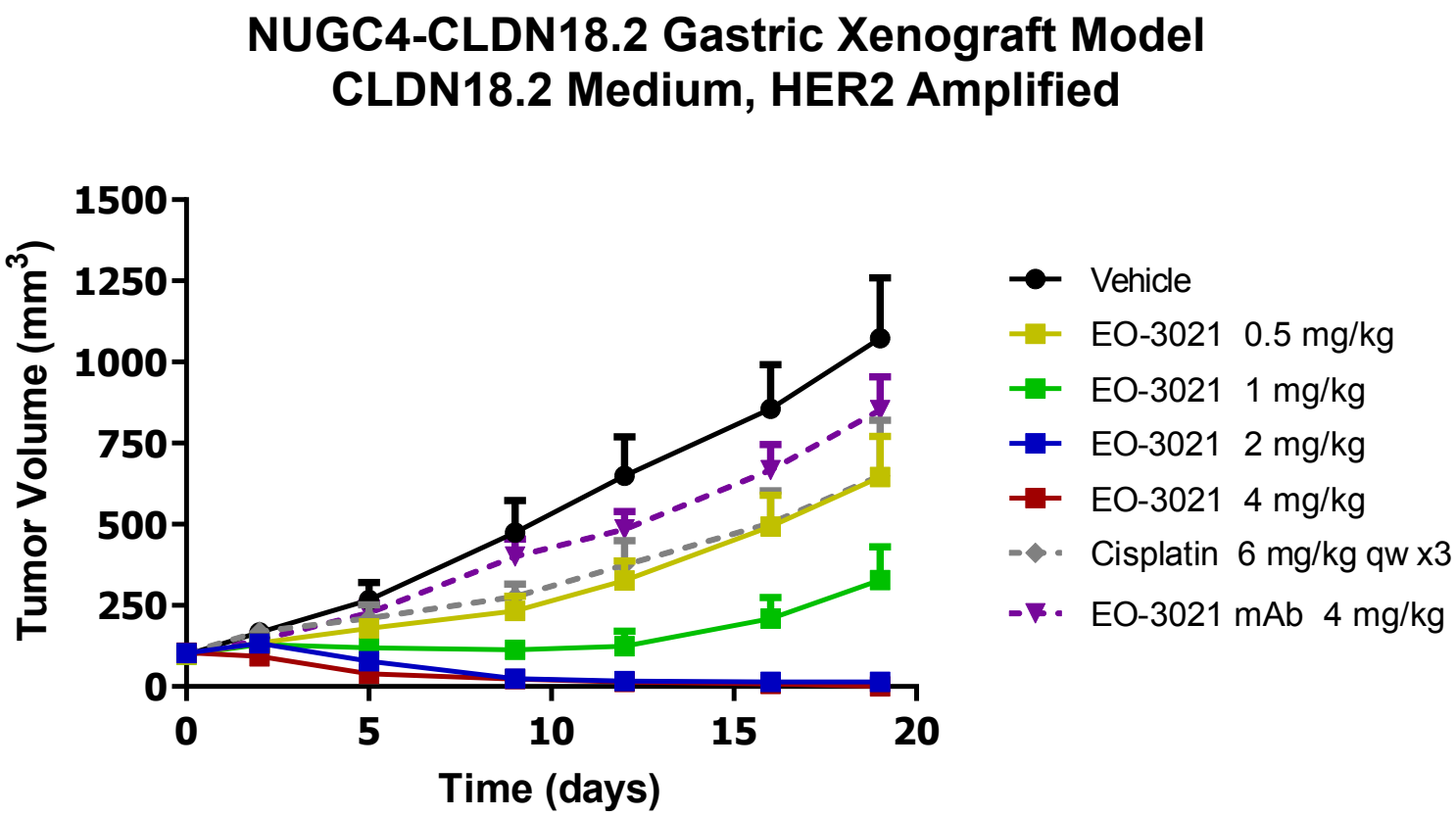

Nu/nu mice were administered single dose of Tx, unless otherwise indicated. Dosing initiated on Day 0.

Single Dose of EO-3021 Confers Tumor Regressions in CLDN18.2 Low Expressing Xenograft Model

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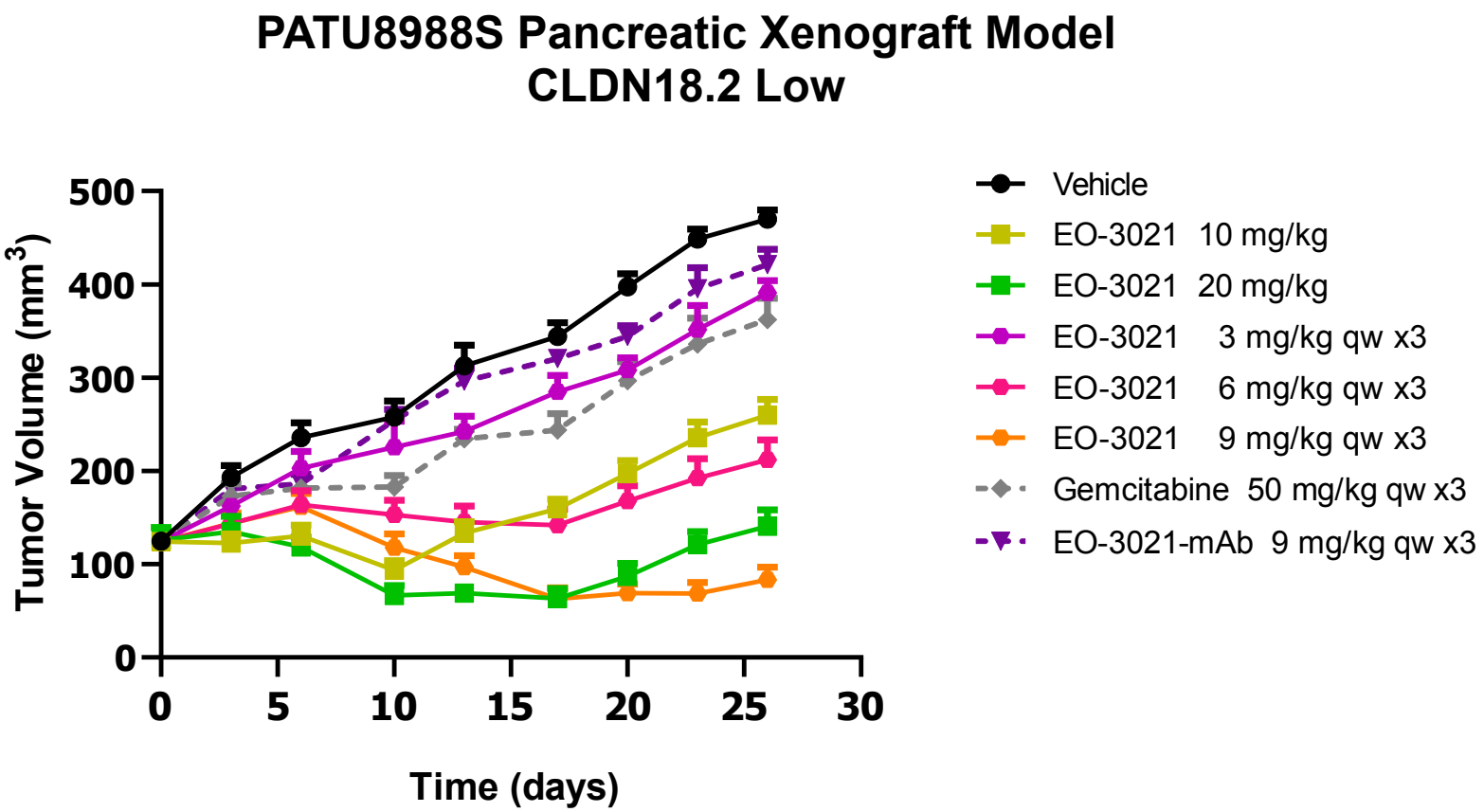
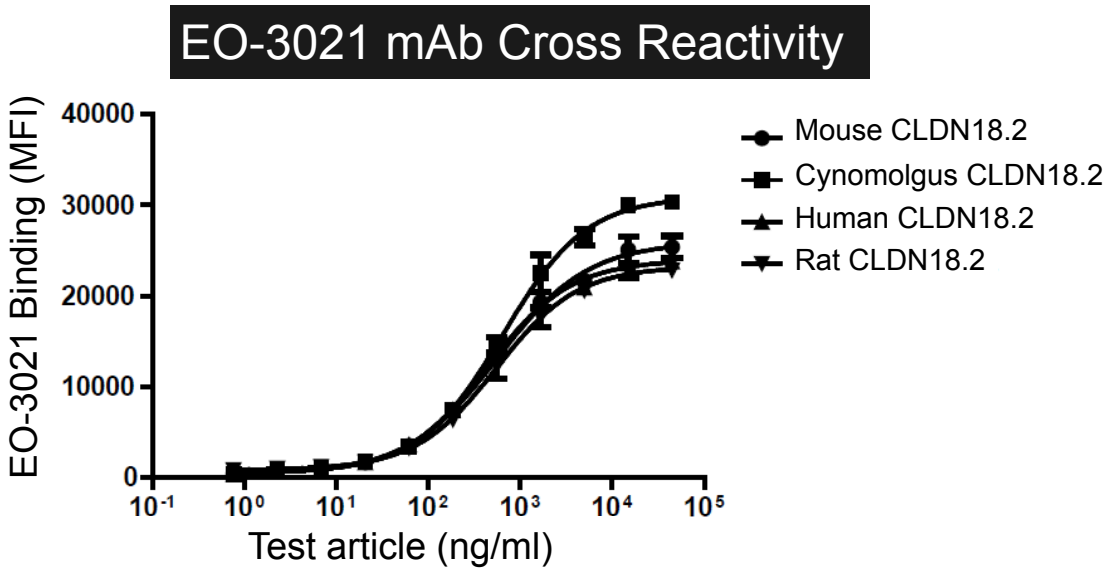


Nu/nu mice were administered single dose of Tx, unless otherwise indicated. Dosing initiated on day 0.

Nonclinical Toxicology and PK Summary of EO-3021



- EO-3021 mAb is cross reactive with major toxicology species
- NHP PK is dose proportional with $t_{1/2}$ ~7 days
- General toxicology profile across species (cyno and rat) is consistent with either MMAE payload or CLDN18.2 targeting in the stomach
- Pharmacology/toxicology integrated data suggest EO-3021 can achieve doses in humans that result in anti-tumor activity

Abbreviations: MMAE, monomethyl auristatin E; NHP, non-human primates; PK, pharmacokinetics; $t_{½}$, half-life

EO-3021/SYSA1801 Activity in a Patient with Gastric Cancer

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- **Patient:** 47-year-old female with gastric cancer
- **Metastases:** lymph nodes
- **Prior therapy:** XELOX (oxaliplatin + capecitabine) with immunotherapy
- **EO-3021 treatment:** 1.0 mg/kg IV Q3W x 12 cycles (ongoing)
- **Target Lesion:** Retroperitoneal lymph node
- **RECIST v1.1**: Best overall response of confirmed partial response (66.7% maximal tumor reduction)
- **Duration of response:** ~11 months (ongoing)
- **Clinical Trial:** Phase I (NCT05009966)

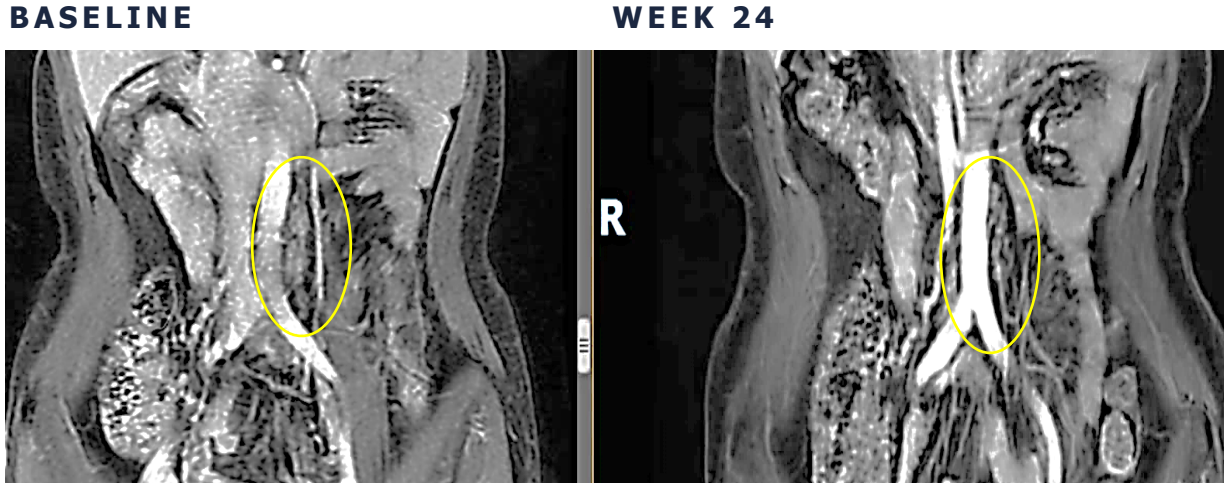
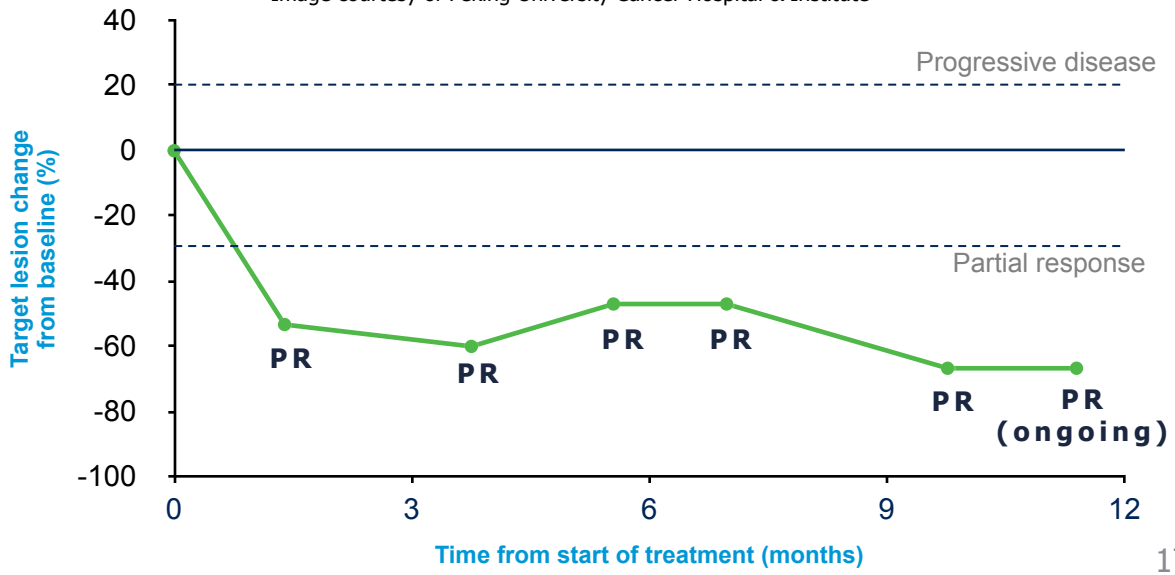


Image courtesy of Peking University Cancer Hospital & Institute



EO-3021 is under investigation in a clinical trial and has not been approved for any indication by a regulatory administration

EO-3021 Summary

- Antibody drug conjugate composed of a fully human IgG1 CLDN18.2 selective mAb conjugated at Q295 with a vcMMAE linker payload to give DAR2
- Promotes cell killing of cell lines expressing CLDN18.2 and a consequential bystander effect on CLDN18.2 negative cells
- Robust in vivo activity in xenografts with varying levels of CLDN18.2
  - Single dose tumor regressions in models with varying levels of CLDN18.2 with a lower minimal efficacious dose in models with medium and high levels of CLDN18.2 relative to models with low CLDN18.2
- Pharmacology/toxicology integrated data suggest EO-3021 can achieve doses in humans that results in anti-tumor activity
- Confirmed PR (66.7% reduction) with 11 months (and ongoing) duration of response in a patient living with metastatic gastric cancer in an ongoing Phase I clinical trial (NCT05009966)
- Elevation Oncology sponsored Phase I trial to initiate in US 2H 2023

Acknowledgements

CSPC

- Mo Dan
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- Shawn Leland
- Joe Ferra

Peking University Cancer Hospital & Institute

- Yakun Wang
- Jifang Gong
- Lin Shen