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## **Preclinical characterization of IPH45, a novel topoisomerase I inhibitor ADC targeting Nectin-4 for the treatment of Nectin-4 expressing tumors**

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# Disclosure Information

## Nicola Beltraminelli

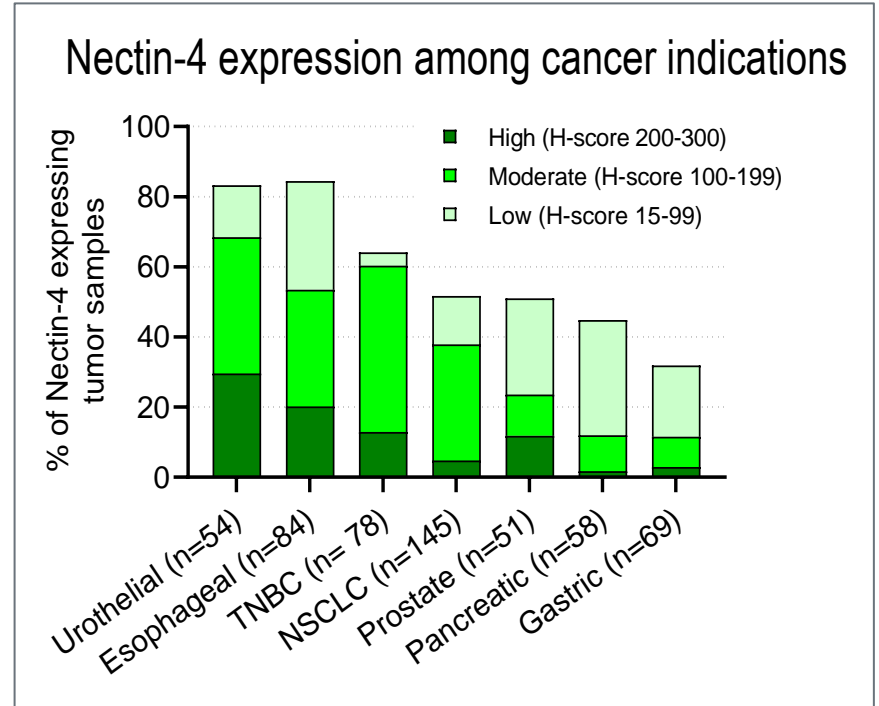
I have the following relevant financial relationships to disclose:

Employee and shareholder of Innate Pharma

Stock option holder of HiFiBiO Therapeutics

# Nectin-4 is a validated ADC target with opportunities for novel indications

- Enfortumab vedotin (EV, PADCEV®) is approved for locally advanced and metastatic urothelial carcinoma.
- EV is associated with skin toxicity and peripheral neuropathy leading to dose interruptions (61%), dose reductions (34%) and discontinuations (17%) (EV-301 study)
- There are limited data available on safety and efficacy beyond UC (EV-202 study)
- The limited expression of Nectin-4 in healthy tissues and its expression in several solid tumors with high medical need opens opportunities for treatments with a different modality

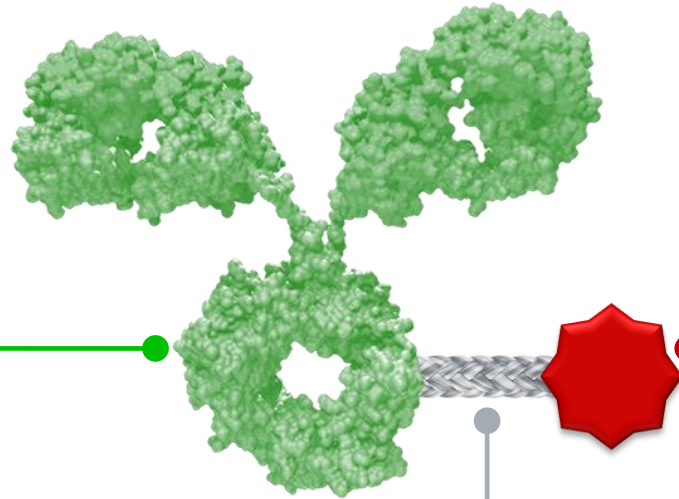


# IPH45 is a novel and differentiated Nectin-4 ADC

## Binder

### Proprietary humanized anti-Nectin-4 Antibody

- High affinity
- Non-overlapping epitope of EV (no competition for binding)
- Fc-competent IgG1, with the ability to mediate ADCC and CDC



## Payload

### Exatecan, a Topoisomerase I inhibitor

- Active in EV/MMAE-resistant models
- **Bystander Effect**, higher activity than EV in Nectin-4 low/heterogenous expression
- **DAR = 8**
- **Optimal therapeutic index expected**

## Linker

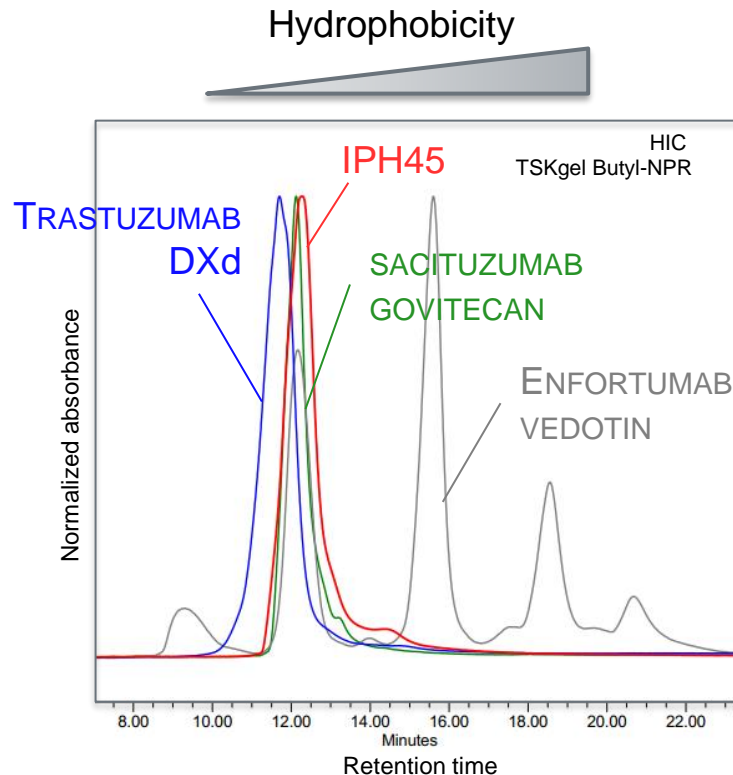
### Cleavable

- **Hydrophilic** → improved half life, low clearance
- **Stable** → improved safety with low release of free drug
- **Excellent conjugability** → high yield manufacturing process

# GMP grade IPH45 is produced at high yield and is preclinically well tolerated

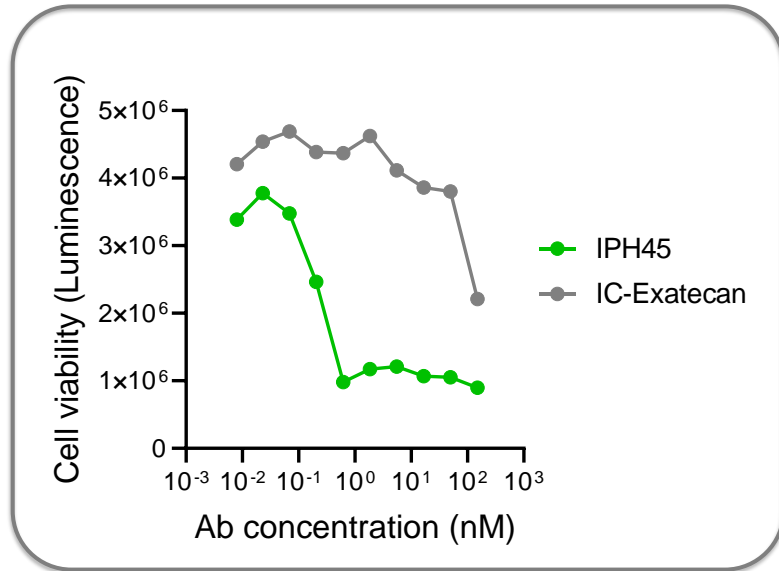
- CMC
  - High yield GMP process: 7.22 g/L; >85% DSP yield
  - DAR 7.9
  - DS and DP are stable under stress conditions
  - IPH45 is more hydrophilic than enfortumab vedotin
- GLP toxicology studies
  - Ongoing in rats and NHP at 10 and 30mg/kg Q2W
  - No deaths and no clinical pathological relevant observations at 28 days for both species

Packages IND ready in 2024

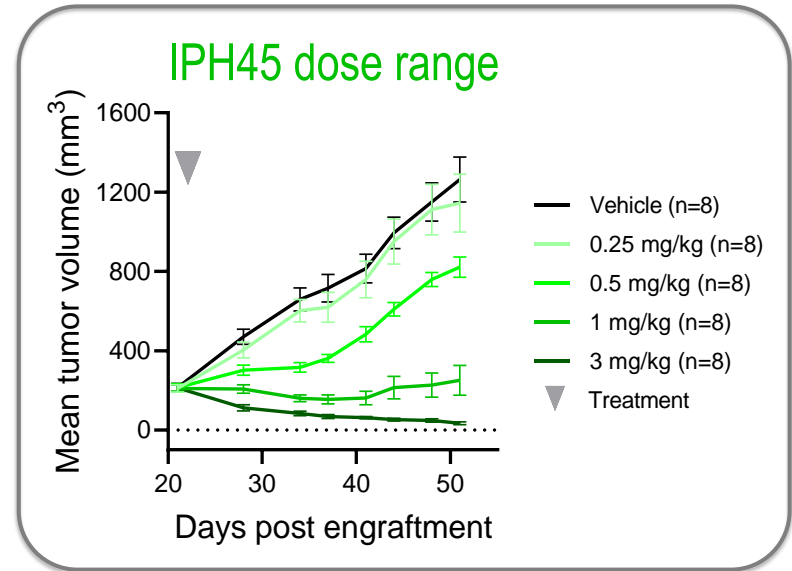


# IPH45 is a potent Nectin-4 ADC *in vitro* and *in vivo*

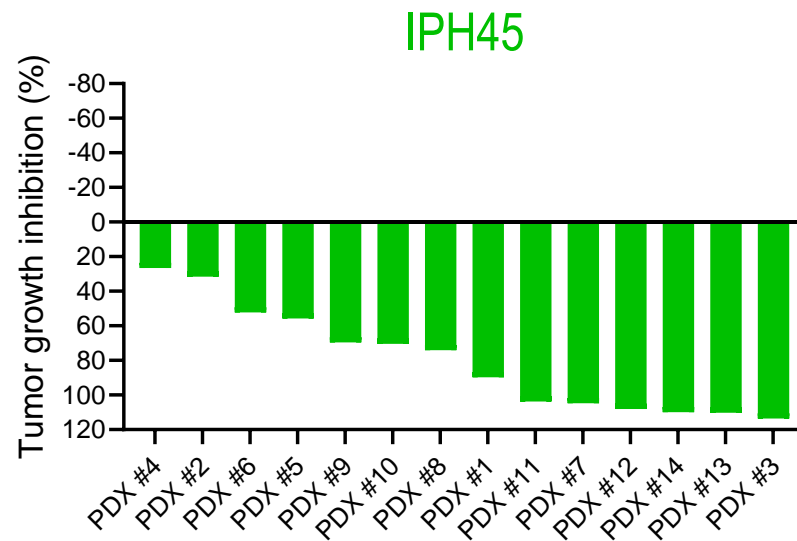
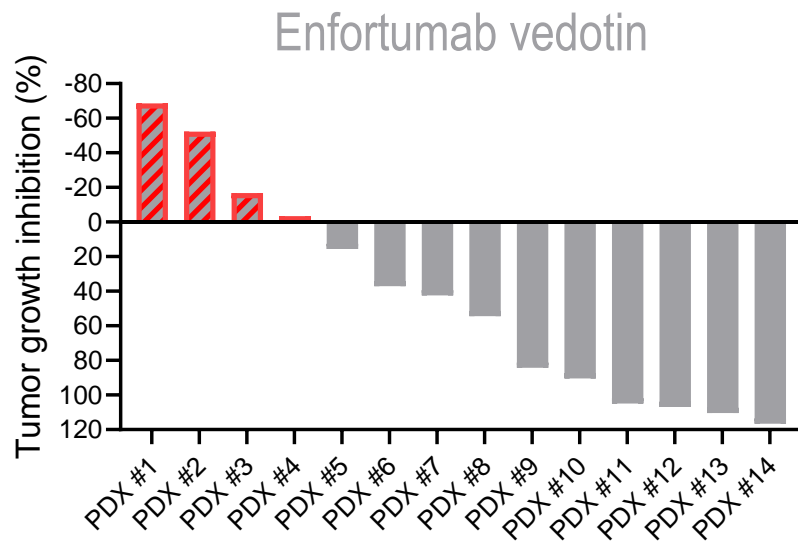
## IPH45 induces Nectin-4<sup>+</sup> cell killing *in vitro*



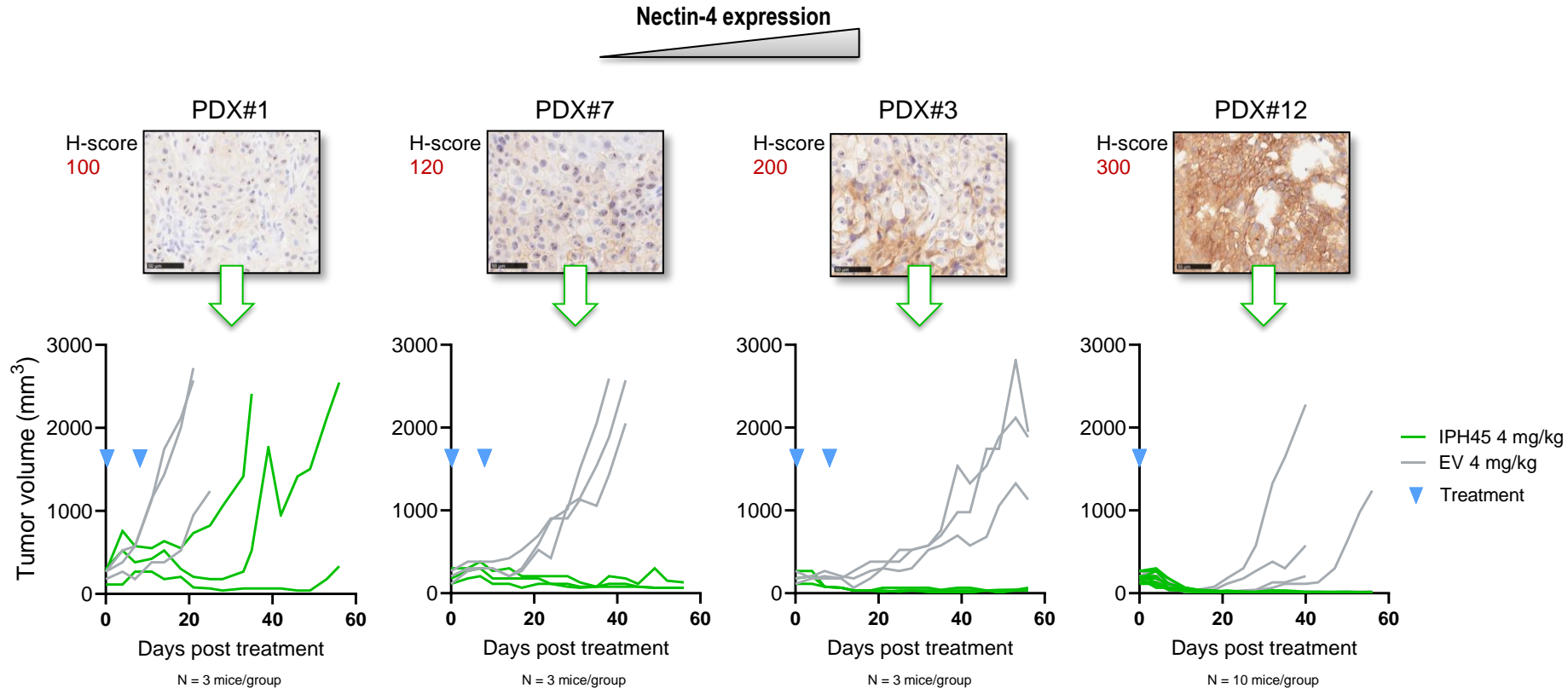
## IPH45 demonstrates robust efficacy in xenograft model



# IPH45 shows broader and stronger efficacy than EV in multiple PDX models from UC patients

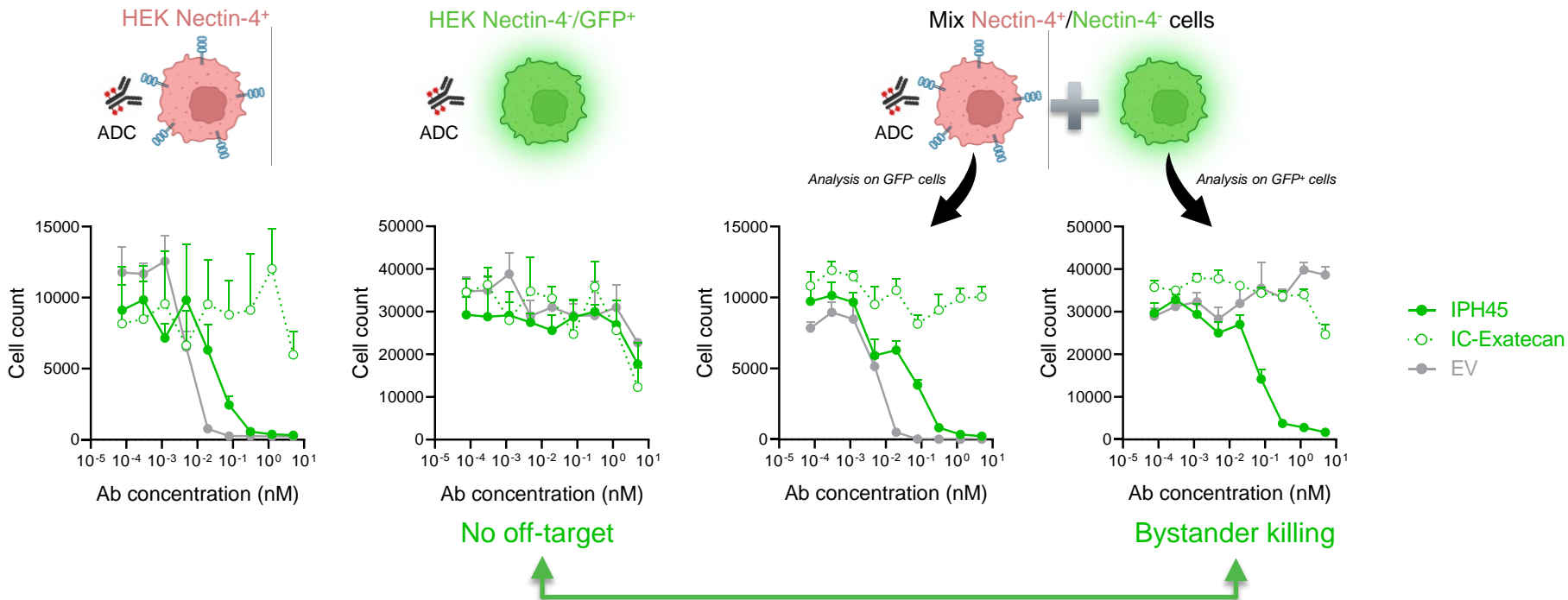


# IPH45 shows efficacy across all tested levels of Nectin-4 expression, and demonstrates superior activity to EV

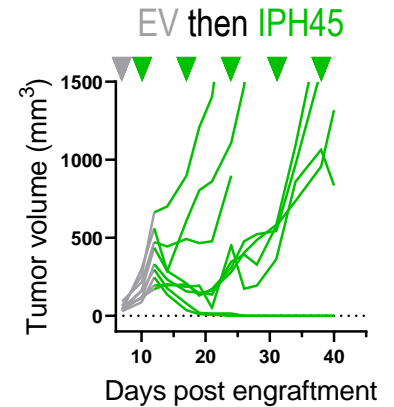
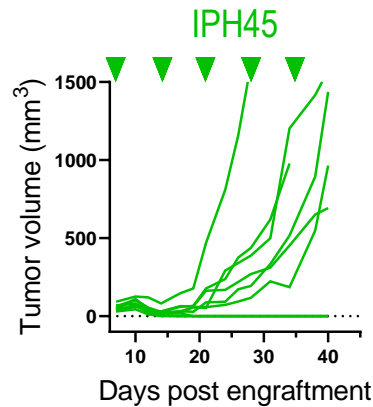
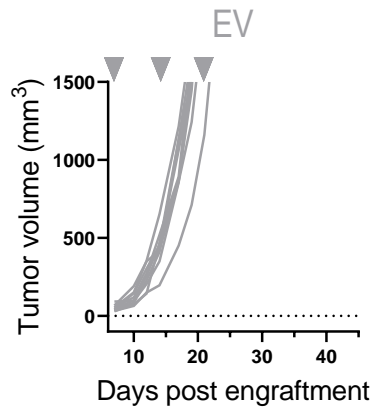
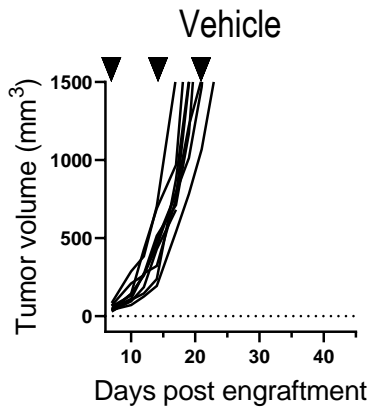
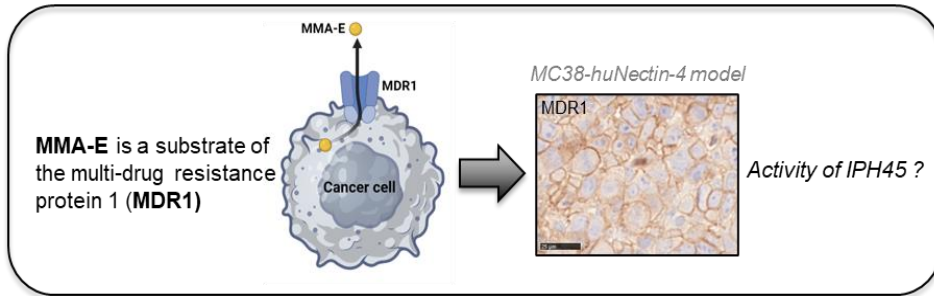




# By contrast to EV, IPH45 demonstrates a high target-dependent bystander effect in vitro

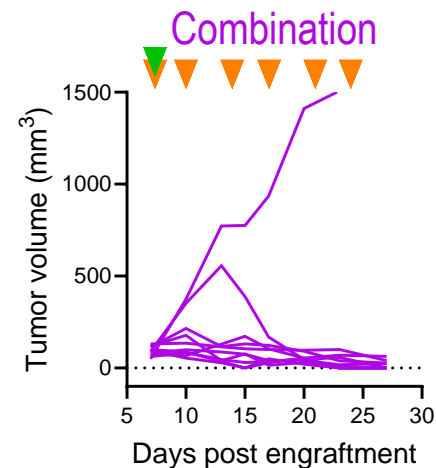
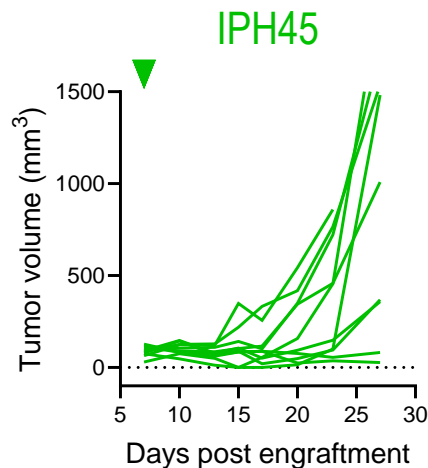
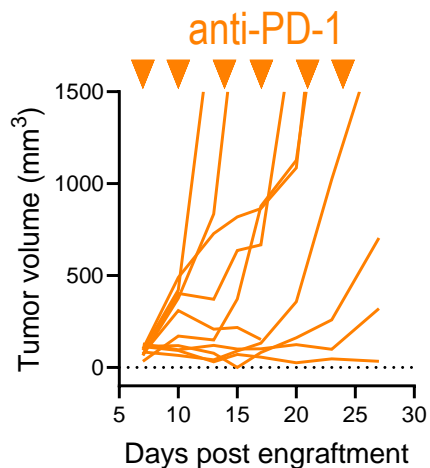
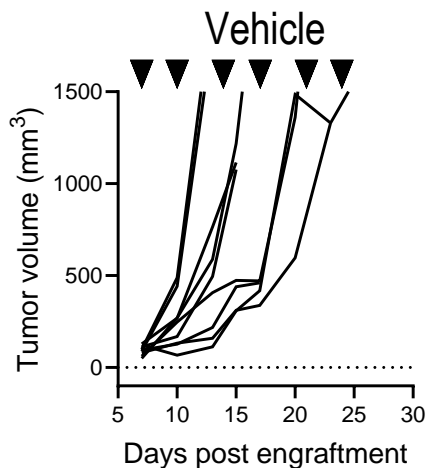


# IPH45 demonstrates efficacy in an EV-refractory model



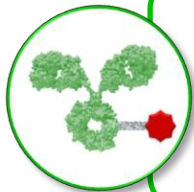
▼ Treatment

# Combination of IPH45 and anti-PD1 demonstrates strong efficacy in a PD-1-resistant model

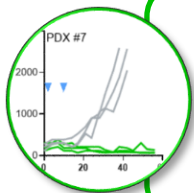


▼ Treatment

## **IPH45** is a differentiated exatecan-based Nectin-4 ADC with potential for improved clinical benefits across multiple tumor types



- Unique epitope, non-overlapping with enfortumab vedotin (EV)
- Cleavable hydrophilic linker
- DAR 8 and Exatecan with bystander effect



- Anti-tumor efficacy across tumor indications & various levels of Nectin-4 expression and in EV-refractory models
- Stronger efficacy than EV in Nectin-4 low PDX models of UC tumors
- Increased anti-tumor activity when combined with anti-PD-1

**IPH45 is progressing towards the clinic. IND targeted in 2024**

# Acknowledgements



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