innate pharma

Nectin-4 ADC Update

New York, NY

Jonathan Dickinson | CEO, Innate Pharma

February 5th, 2025

EURONEXT: IPH.PA NASDAQ: IPHA

Disclaimer on Forward-Looking Information and Risk Factors

This document has been prepared by Innate Pharma S.A. (the “Company”) solely for the purposes of a presentation to investors concerning the Company. This document is not to be reproduced by any person, nor to be distributed.

This document contains forward-looking statements. The use of certain words, including “believe,” “potential,” “expect” and “will” and similar expressions, is intended to identify forward-looking statements. Although the Company believes its expectations are based on reasonable assumptions, these forward-looking statements are subject to various risks and uncertainties, which could cause the Company’s actual results or financial condition to differ materially from those anticipated. These risks and uncertainties include, among other things, the uncertainties inherent in research and development, including related to safety, progression of and results from its ongoing and planned clinical trials and preclinical studies, review and approvals by regulatory authorities of its product candidates, the Company’s commercialization efforts and the Company’s continued ability to raise capital to fund its development. For an additional discussion of risks and uncertainties which could cause the Company's actual results, financial condition, performance or achievements to differ from those contained in the forward-looking statements, please refer to the Risk Factors (“Facteurs de Risque”) section of the Universal Registration Document filed with the Autorité des Marchés Financiers (“AMF”), available on the AMF website (www.amf-france.org) or on the Company’s website (www.innate-pharma.com), and public filings and reports filed with the U.S. Securities and Exchange Commission (“SEC”), including the Company’s Annual Report on Form 20F for the year ended December 31, 2023, and subsequent filings and reports filed with the AMF or SEC, or otherwise made public, by the Company. Such documents may not be necessarily up to date.

This document contains data pertaining to the Company's potential markets and the industry and environment in which it operates. Some of this data comes from external sources that are recognized in the field or from Company’s estimates based on such sources.

This presentation discusses product candidates that are under clinical development, and which have not yet been approved for marketing by the U.S. Food and Drug Administration or the European Medicines Agency. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

The information contained herein has not been independently verified. No representation, warranty or undertaking, express or implied, is made as to, and no reliance should be placed on, the fairness, accuracy, completeness or correctness of the information or opinions contained herein. The Company is under no obligation to keep current the information contained in this presentation and any opinion expressed is subject to change without notice.

The Company shall not bear any liability whatsoever for any loss arising from any use of this document or its contents or otherwise arising in connection therewith.

This document and the information contained herein do not constitute an offer to sell or a solicitation of an offer to buy or subscribe to shares of the Company in any country.

Agenda

1. Introduction

Jonathan Dickinson | Chief Executive Officer, Innate Pharma

2. Current Nectin-4 landscape

Yohann Loriot | Deputy Chair of the Department of Early Drug Development, Gustave Roussy, Université Paris-Saclay

3. IPH4502 Preclinical data

Yannis Morel | EVP, Chief Operating Officer, Innate Pharma

4. IPH4502 Clinical development plan

Sonia Quaratino | EVP, Chief Medical Officer, Innate Pharma

innate pharma

2025: Focus on 3 Strategic Growth Pillars

NK-cell engagers

- **IPH6501** (CD20) ANKET® Phase 1
- **IPH6101** (CD123) ANKET® Phase 2 trial underway | Phase 1 data presented (Sanofi) |1L study underway| Fast Track Designation for the treatment of acute myeloid leukemia
- **IPH6401** (BCMA) ANKET® Phase 1 (Sanofi)

Antibody Drug Conjugates

- **IPH4502** (Nectin-4) IND cleared, Phase 1 start Jan 2025
  - Differentiated topo-1 ADC targeting varying levels of expression of nectin-4 across tumor types
- **IPH43** (MICA/B) in research

Current Late-Stage Assets

- **Lacutamab** positive Phase 2 data, FDA feedback on next steps, Partnership discussions underway
- **Monalizumab** PACIFIC-9 Phase 3 underway (AstraZeneca)

innate pharma

Key Takeaways

Innate has a solid strategy to deliver long term growth with proprietary and partnered assets and we have 8 key programs in clinical stages of development

- **DRIVING FORWARD OUR ANKET® CLINICAL PORTFOLIO**
  - Phase 1/2 clinical trial underway with IPH6501 in B-cell NHL, agreement with IFLI to include Follicular Lymphoma
  - IPH6101/SAR'579 progressed to Phase 2 by Sanofi, Front line combination with venetoclax study initiated
- **PURSUING DIFFERENTIATED ADCs**
  - IPH4502, anti nectin-4 Antibody Drug Conjugate Phase 1 in Jan 2025
- **LACUTAMAB**
  - Encouraging FDA feedback on regulatory pathway, Phase 3 planning underway
  - Partnership discussions underway
- **MONALIZUMAB**
  - PACIFIC-9 milestone in 2026

Cash position of €96.4m as of September 30, 2024

innate pharma

A Robust Pipeline of Innovative, Differentiated Proprietary & Partnered Assets

Pre-Clinical	Phase 1	Phase 2	Phase 3
IPH67 *Undisclosed, solid tumors*	**IPH6501** *(CD20-IL2v)* B-NHL	**IPH6101/SAR'579** *(CD123)* Blood cancers (Phase 1/2)	**Monalizumab** *(NKG2A)* Unresectable Stg III NSCLC
IPH81 *Undisclosed Target*	**IPH6401/SAR'514** *(BCMA)* Multiple Myeloma	**Lacutamab** *(KIR3DL2)* CTCL	
Others *Undisclosed Targets*	**IPH4502** *(Nectin-4)* Solid tumors	**Lacutamab** *(KIR3DL2)* PTCL	
IPH62 *B7-H3*	**IPH5301** *(CD73)* Solid tumors	**Monalizumab** *(NKG2A)* Neoadjuvant NSCLC	
IPH43 *MICA/B*		**IPH5201** *(CD39)* Neoadjuvant NSCLC	
Others *Undisclosed Targets*			

Monoclonal antibody (mAb)

Antibody Drug Conjugate (ADC)

Antibody-based NK cell engager Therapeutics ANKET

B-NHL: B Cell Non-Hodgkin Lymphoma ; NSCLC = Non-Small Cell Lung Cancer ; CTCL = Cutaneous T Cell Lymphoma ; PTCL = Peripheral T Cell Lymphoma

innate pharma

Nectin-4 landscape

innate pharma

Pr Yohan Loriot, MD, PhD

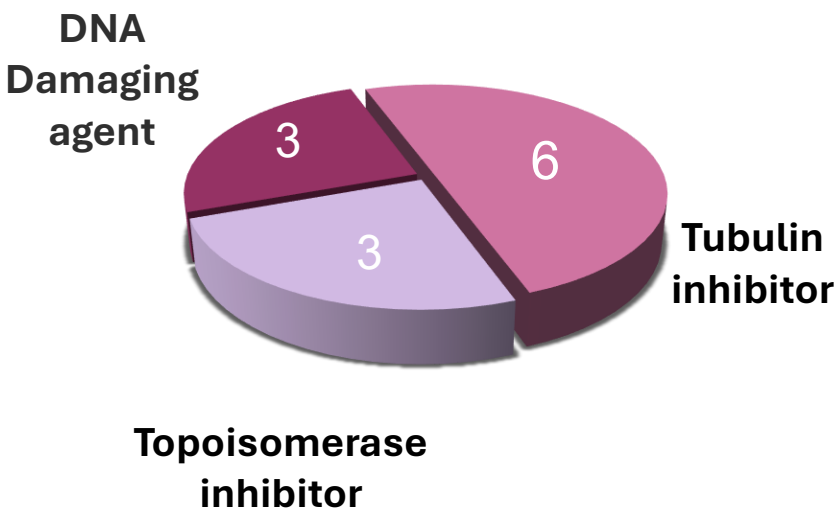
Professor of Medicine at Paris-Saclay University and
Deputy Chair of the Department of Early Drug Development at Gustave Roussy, Villejuif, France

- Medical oncologist specialized in genitourinary cancers*
- Research focuses on drug development, particularly in connection with biomarker discovery, targeted therapies, and immunotherapies
- Leads phase I-III trials in urothelial and prostate cancers
- Member of the steering committees for multiple international clinical trials which have led to drug approvals (erdafitinib, enzalutamide, abiraterone, atezolizumab, sacituzumab, enfortumab)
- >300 peer-reviewed papers (NEJM, Lancet Oncology, JCO, Cancer Discovery, etc.)

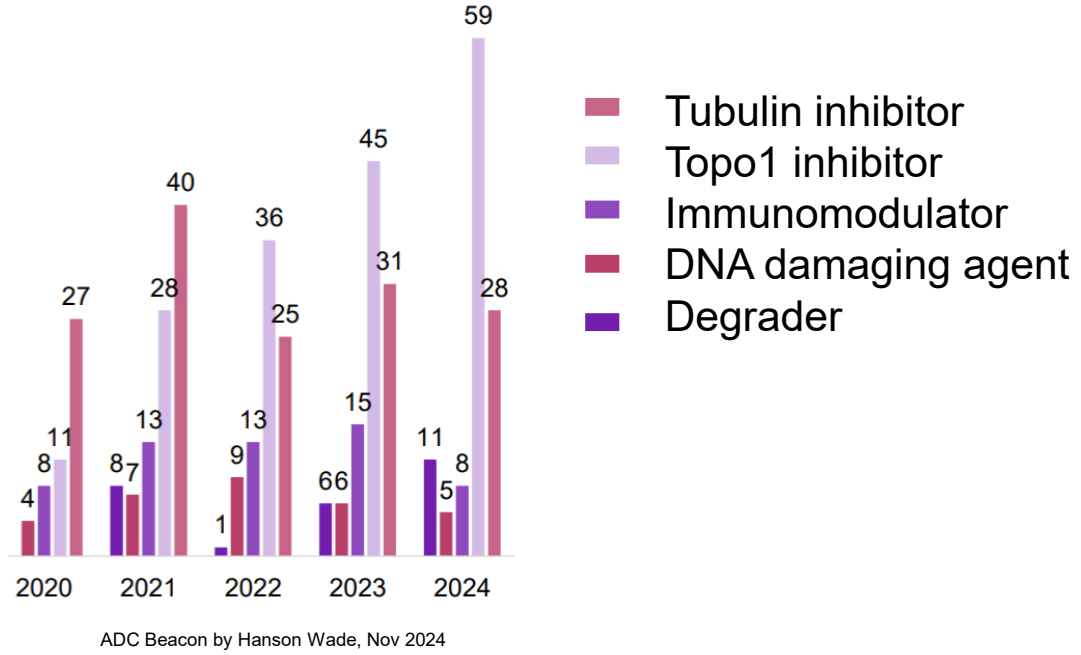
*urothelial, prostate, and testicular cancers

Shifting ADC Landscape: Growth of Topoisomerase Inhibitors based ADCs

ADC approved by payload



255 ADCs (Clinical)



ADC Beacon by Hanson Wade, Nov 2024

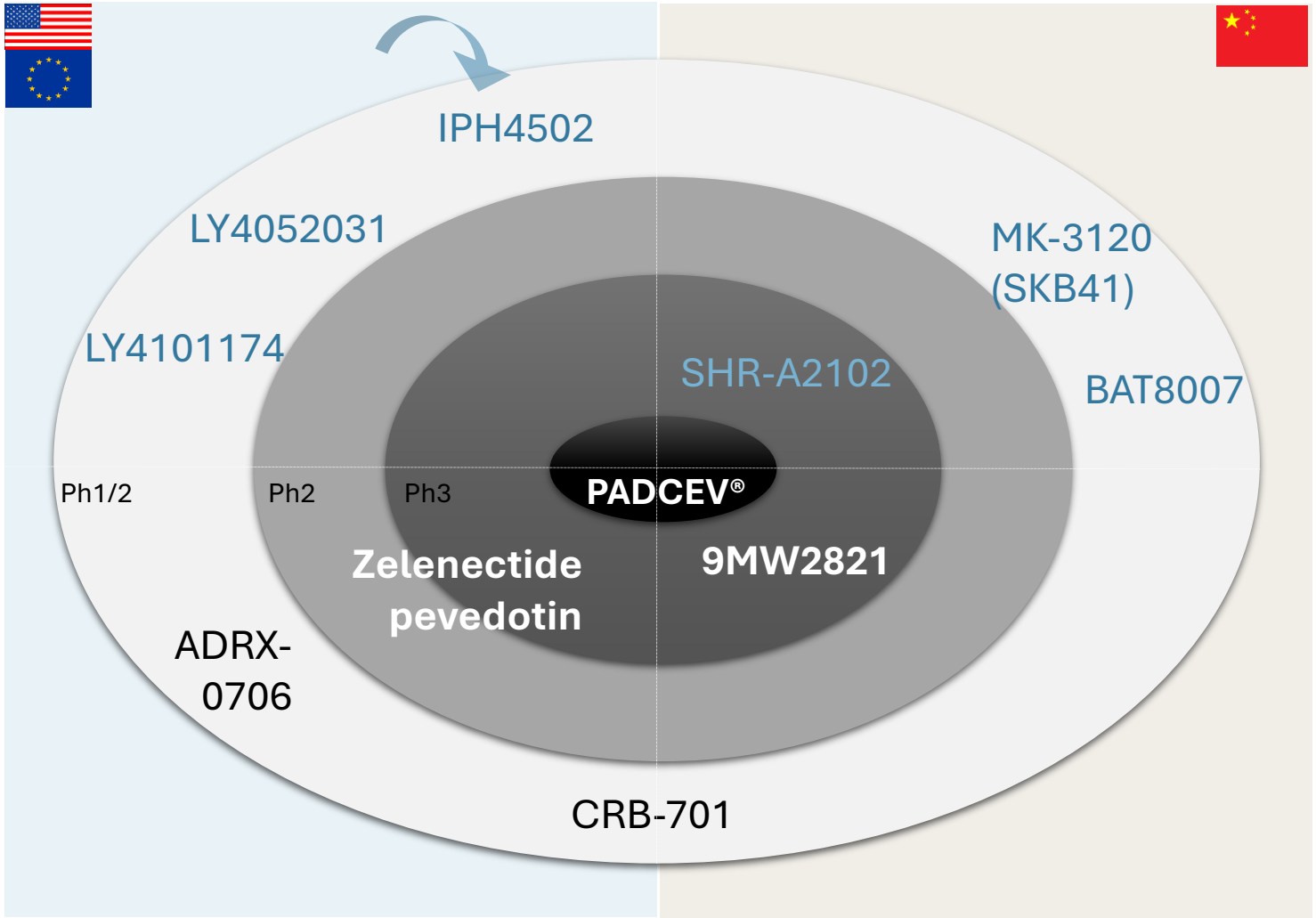
Since 2022, the number of **Topoisomerase inhibitor based ADCs** in the clinic per year is superior to Tubulin inhibitor; with a growing number Exatecan-based ADC (two candidates in Ph3 studies)

innate pharma

Nectin-4 ADC Landscape: MMAE-based ADC Approved; Next Generation Includes Tubulin and Topoisomerase Inhibitor-based ADCs

Topo I ADCs

Tubulin inhibitor ADCs



- EV is the only anti-Nectin-4 ADC approved (UC)
- Most advanced new aNectin-4 ADCs have tubulin inhibitors
- Next generation of Nectin-4 ADCs Topo I are in Phase 1/2, except SHR-A202 entering Ph3 in China

innate pharma

Enfortumab Vedotin is approved in LA/mUC* in monotherapy (3L) and PD-1 combination (1L). Relapses create a growing medical need in post-EV setting

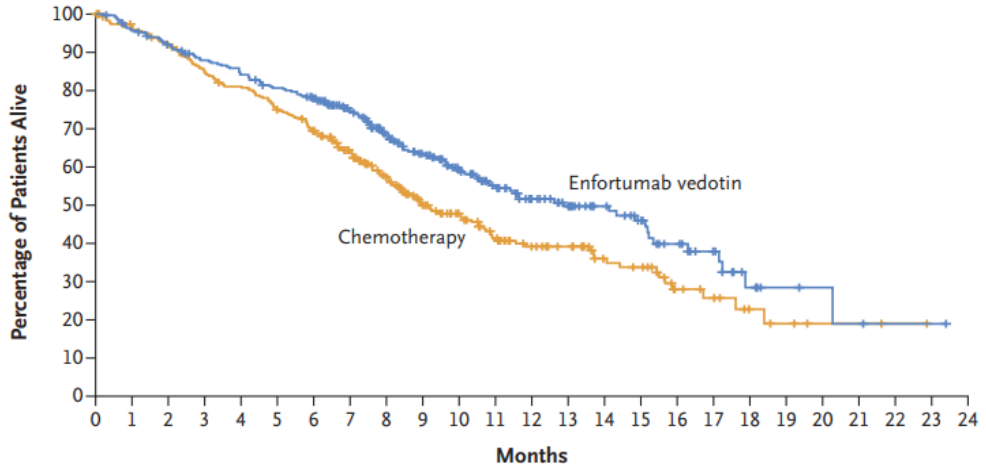
3L LA/mUC

Phase 3 EV-301

EV vs chemotherapy

1.25 mg/kg IV D1+D8+D15 of 28D cycle

ORR	**40.6%** vs. 17.9%
Median PFS	**5.55 mo** vs. 3.71 mo
Median OS	**12.91 mo** vs. 8.94 mo



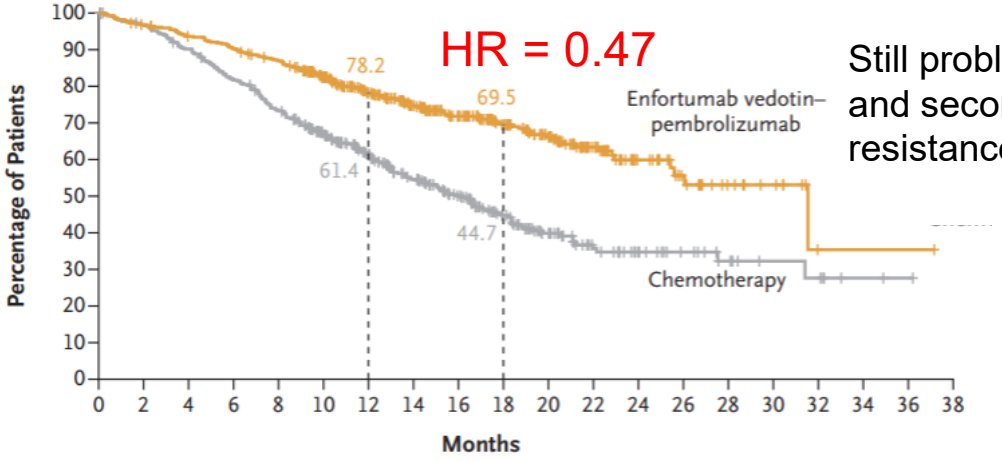
1L LA/mUC

Phase 3 EV-302/ KEYNOTE-A39

EV + pembro vs chemotherapy

1.25 mg/kg IV EV D1+D8 of 21D cycle

ORR	**67.7%** vs 44.4%
Median PFS	**12.5 mo** vs. 6.3 mo
Median OS	**31.5 mo** vs. 16.1 mo



Still problem of primary and secondary resistances

*Locally advanced or metastatic urothelial cancer (LA/mUC)

Rosenberg 2023 (EV-301 long term outcomes)– Powels 2024 (EV-302)

innate pharma

Enfortumab Vedotin treatment related adverse events

TRAE		Phase 3 EV-301 3L+ la/mUC	Phase 3 EV-302/KEYNOTE-A39 1L la/mUC
Serious adverse reactions		22.6% (vs 23.4%) (incl. Urinary tract infection, Acute kidney injury, Pneumonia)	27.7% (incl. Rash, Acute kidney injury, Pneumonitis/ILD)
Peripheral Neuropathy	All grades	48.0%	63.2%
	≥ Gr3	7.4%	6.8%
Skin Reaction	All grades	47.3%	66.8%
	≥ Gr3	14.9%	15.5%
TRAE resulting in	EV Dose Interruption	51 %*	60.5 %
	EV Dose Discontinuation	15.2 %	29,5 %
Fatal adverse reactions		2.4%	0.9%

Most common TRAE leading to discontinuation **Peripheral neuropathy**

Clinical research priority: how to de-escalate therapy (risk of neuropathy) or to develop new agent without risk of neuropathy

*Powels 2021 (EV-301). All other data : Rosenberg 2023 (EV-301 long term outcomes)– Powels 2024 (EV-302)

innate pharma

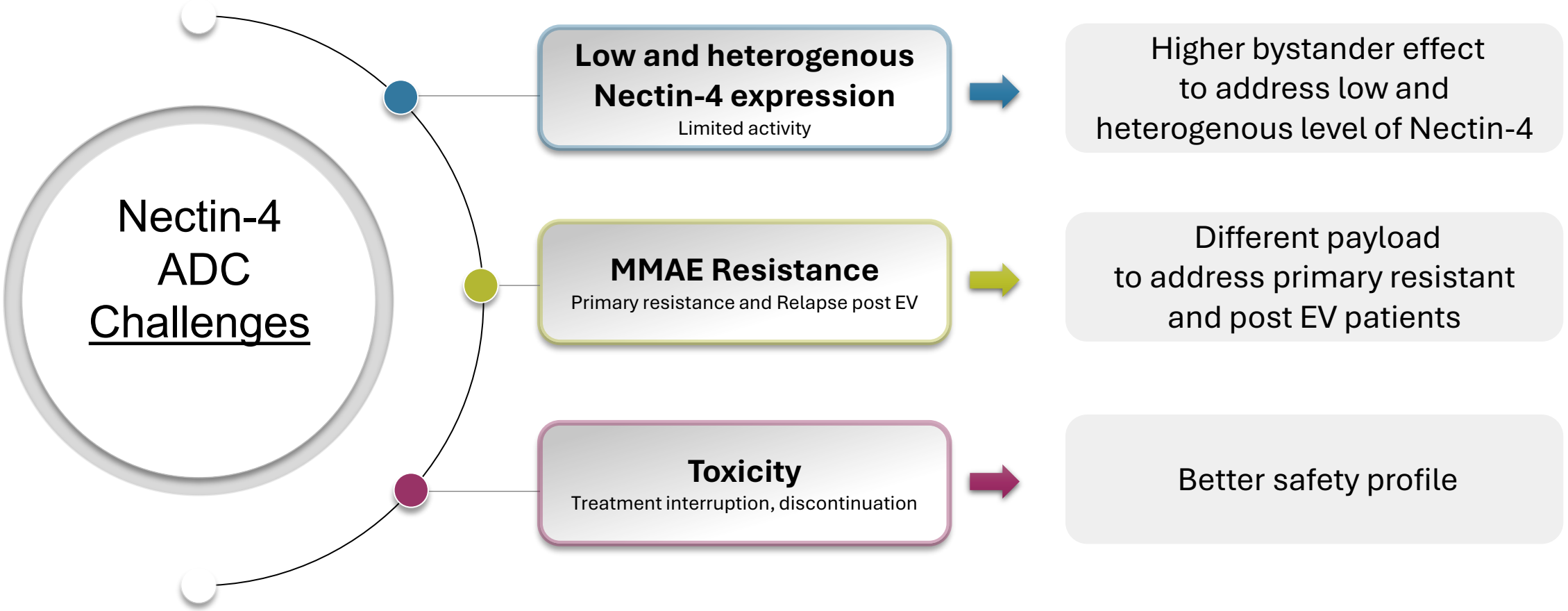
Beyond bladder, not validated signs of activity with Nectin-4-ADCs

Nectin-4 expression

	MMAE-Based Nectin-4 ADC				Topoi ADC
	Enfortumab Vedotin	BT8009 Zelenectide pevedotin	9MW2821	CRB-701	SHR-A2102
Urothelial 2L+	Phase 3 EV-301 ORR **41%**	N=38 EV-naïve ORR **45%** (ESMO24)	n=37, ORR **62.2%** (ASCO24)	N=9, ORR **44%** (ASCO24)	
Esophageal	GEA: n=42 ORR **9.5%** ESCC: n=44 ORR **18.2 %** (ASCO24)		N=39, ORR **15.4%** (ASCO24)		
TNBC	n=42, ORR **19%** (ASCO24)	n=30, ORR **13%** (PR Dec24)	n=20, ORR **45%** (ASCO24)		
Cervical			N=53, ORR **30.2%** (ASCO24) **Phase 3 ongoing**	N=7, ORR **43%** (ASCO24)	
NSCLC	Sq: n=23, ORR **4.3%** Nsq: n=43, ORR **14.0%** (ASCO24)	n=34, ORR **8.8%** (PR Dec24)			Sq: n=16, ORR **18.8%** Nsq: n=30, ORR **36.7%** (ESMO24)
HNSCC	n=46, ORR **23.9%** (ASCO23)				
Ovarian		n=10, ORR **20%** (R&D day Dec23)			

(c)ORR : (confirmed) overall response rate (= partial + complete responses) ; TNBC : triple negative breast cancer ; GEA : Gastroesophageal adenocarcinoma ; ESCC : Esophageal squamous cell carcinoma ; sq : squamous ; nsq : non-squamous

Next generation of Nectin-4 ADCs to overcome challenges associated with approved therapy



innate pharma

IPH4502 – Preclinical data

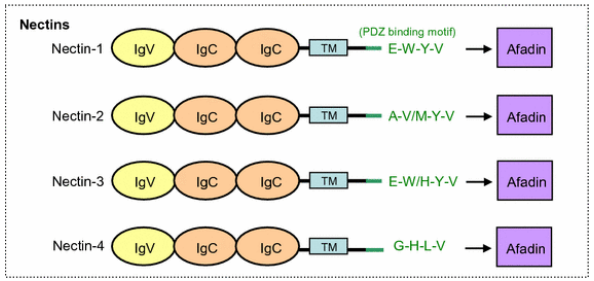
innate pharma

Introduction to Nectin-4

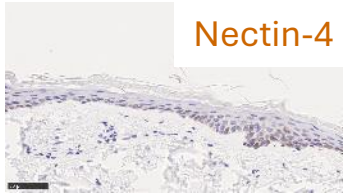
Nectin-4 is a type I transmembrane adhesion molecule with **limited expression in healthy adult tissues**

Overexpressed in multiple **cancers**, making it a relevant tumor target

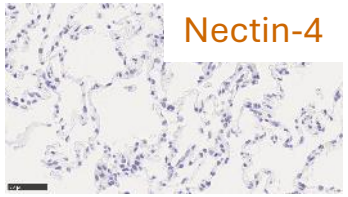
Expression associated with tumor proliferation, metastasis, and **with poor prognosis**



Healthy tissues

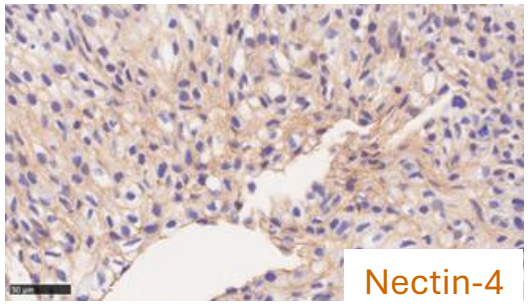


Skin

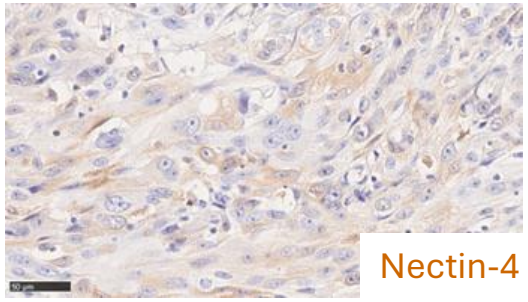


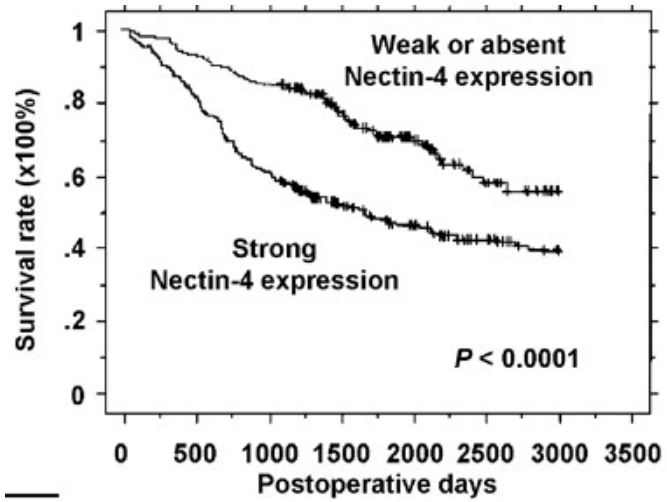
Lung

Urothelial cancer



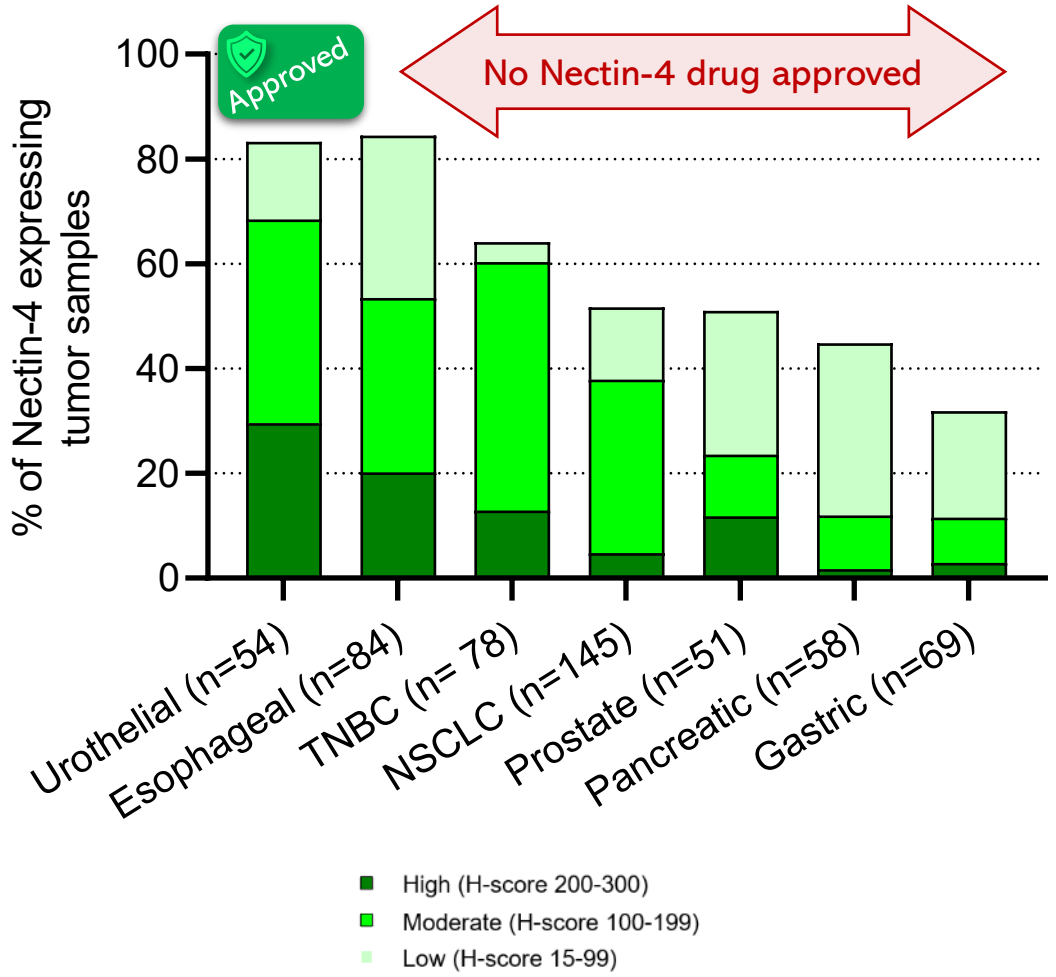
NSCLC





Takano et al., Cancer Res, 2009

IPH4502: A differentiated Nectin-4 targeted ADC with potential to show efficacy in moderate to low Nectin-4 expressing and Padcev resistant tumors



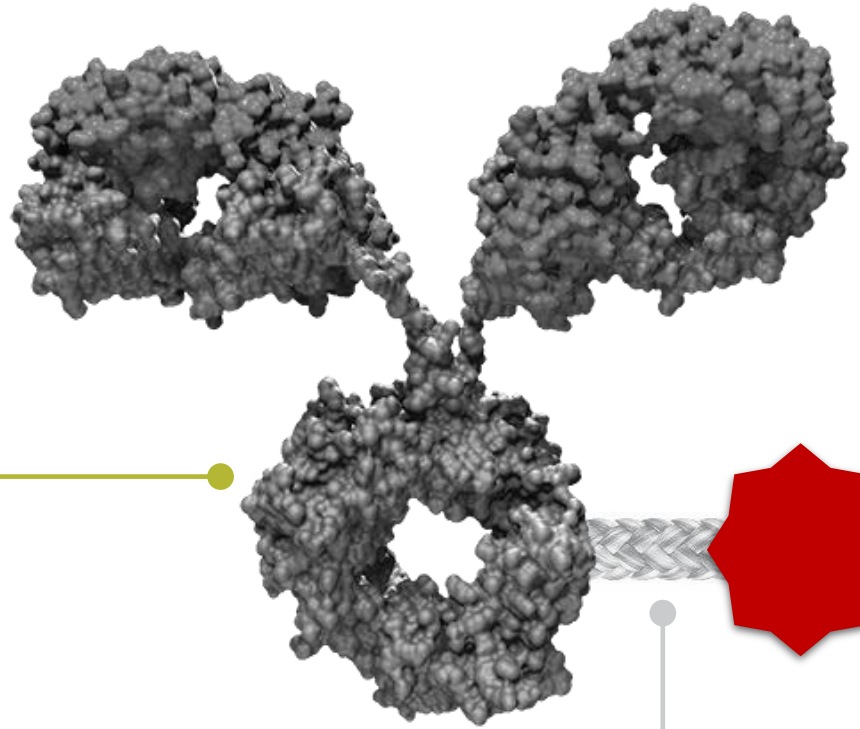
OPPORTUNITIES

- PADCEV (enfortumab vedotin, EV) is approved in bladder cancer where expression of Nectin-4 is the highest
- Relapses are frequently observed creating a growing medical need post-PADCEV
- PADCEV induces toxicity leading to frequent discontinuation
- Limited evidence that PADCEV is active in other indications despite high to moderate expression of Nectin-4

innate pharma

IPH4502: A novel and differentiated Nectin-4 DAR8 exatecan ADC

Phase 1 start in Jan 25



Binder

Proprietary humanized anti-Nectin-4 Antibody

- High affinity
- Non-overlapping epitope with EV*
- Fc-competent IgG1, with the ability to mediate ADCC and CDC

Payload

Exatecan, a Topoisomerase I inhibitor

- Active in **EV/MMAE-resistant** models
- **Higher Bystander Effect than EV, leading to stronger activity in Nectin-4 low tumors**
- **DAR = 8**
- Improved **therapeutic index expected**

Linker

Cleavable

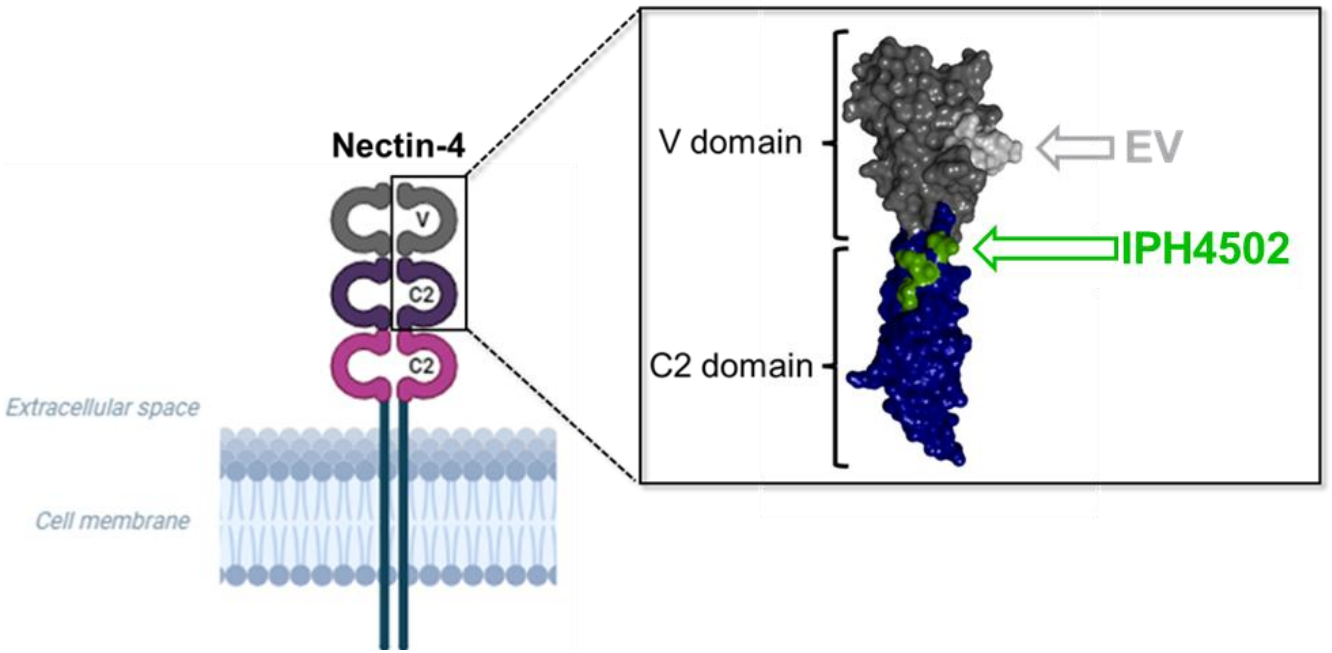
- **Hydrophylic** → improved half-life, low clearance
- **Stable** → improved safety with low release of free drug
- **Excellent conjugability** → high yield manufacturing process

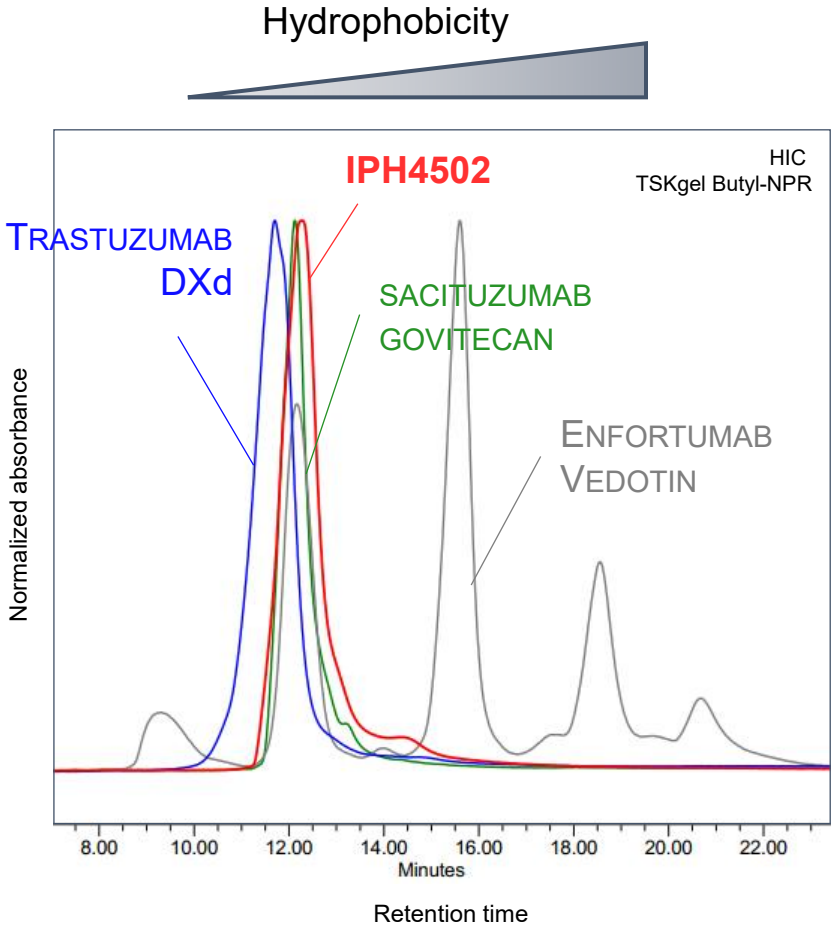
* EV = Enfortumab Vedotin

AACR American Association for Cancer Research ANNUAL MEETING 2024 • SAN DIEGO

innate pharma

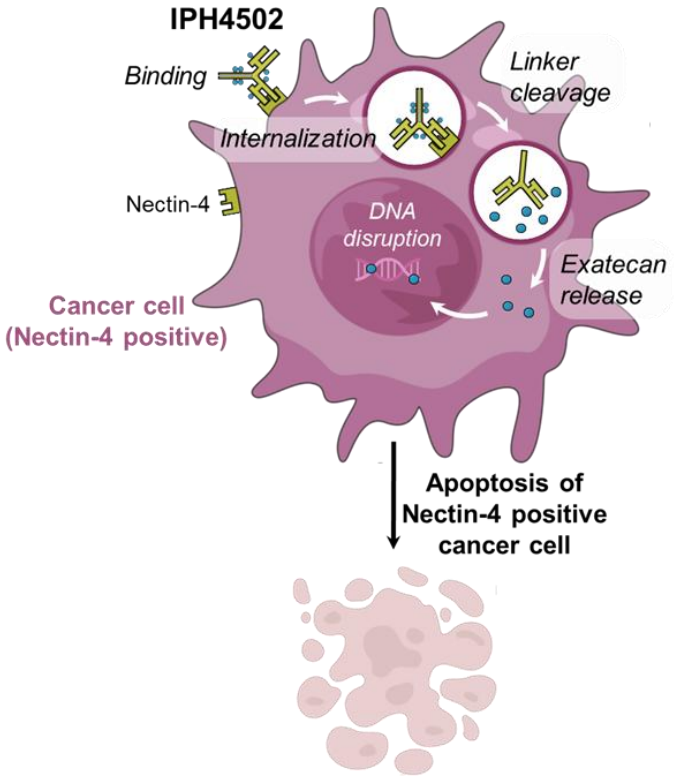
IPH4502 recognizes Nectin-4 on a different epitope and exhibits higher solubility than EV



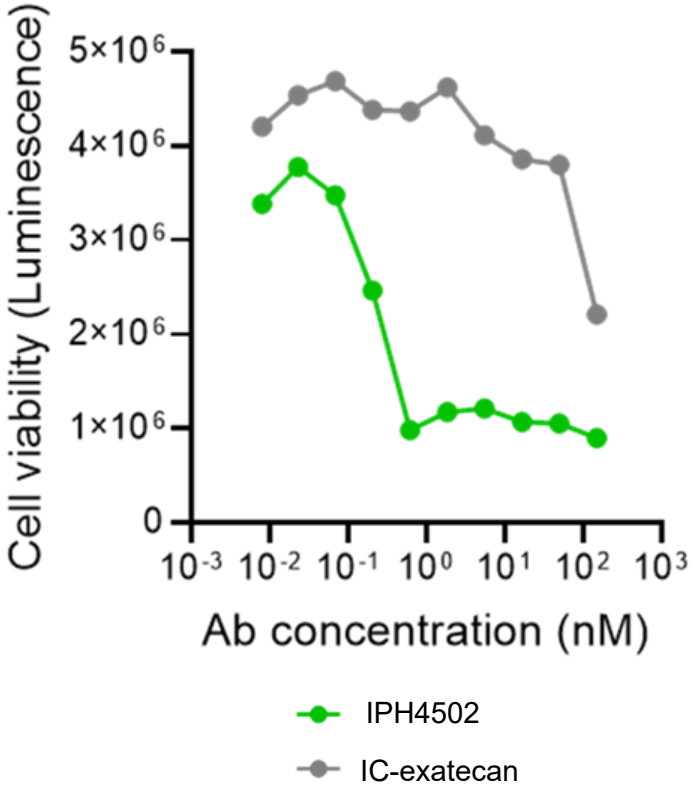


innate pharma

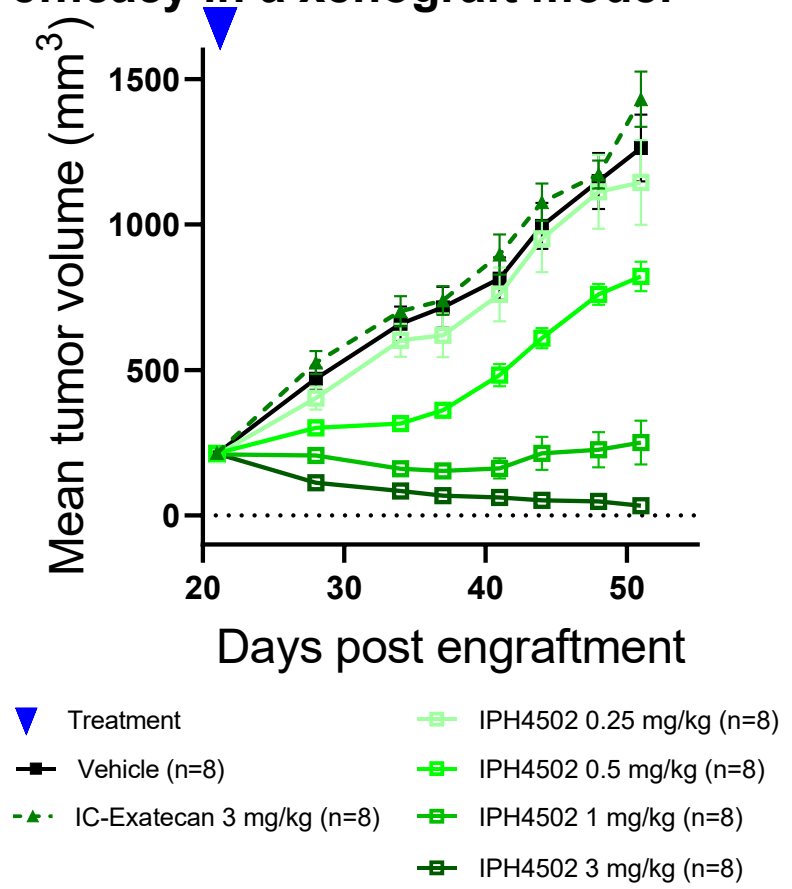
IPH4502 is a potent Nectin-4 ADC in vitro and in vivo



IPH4502 induces Nectin-4⁺ cell killing *in vitro*



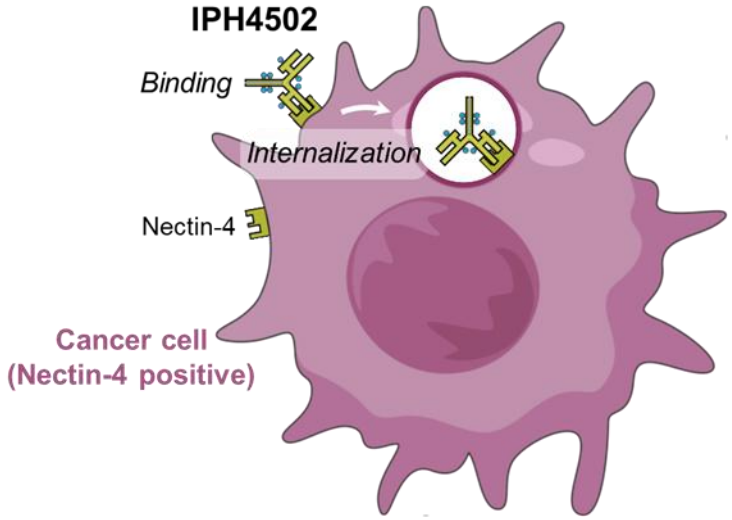
IPH4502 demonstrates robust efficacy in a xenograft model

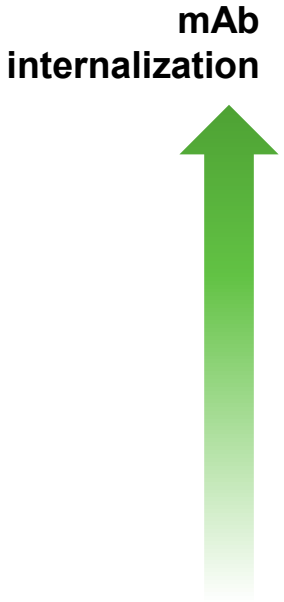


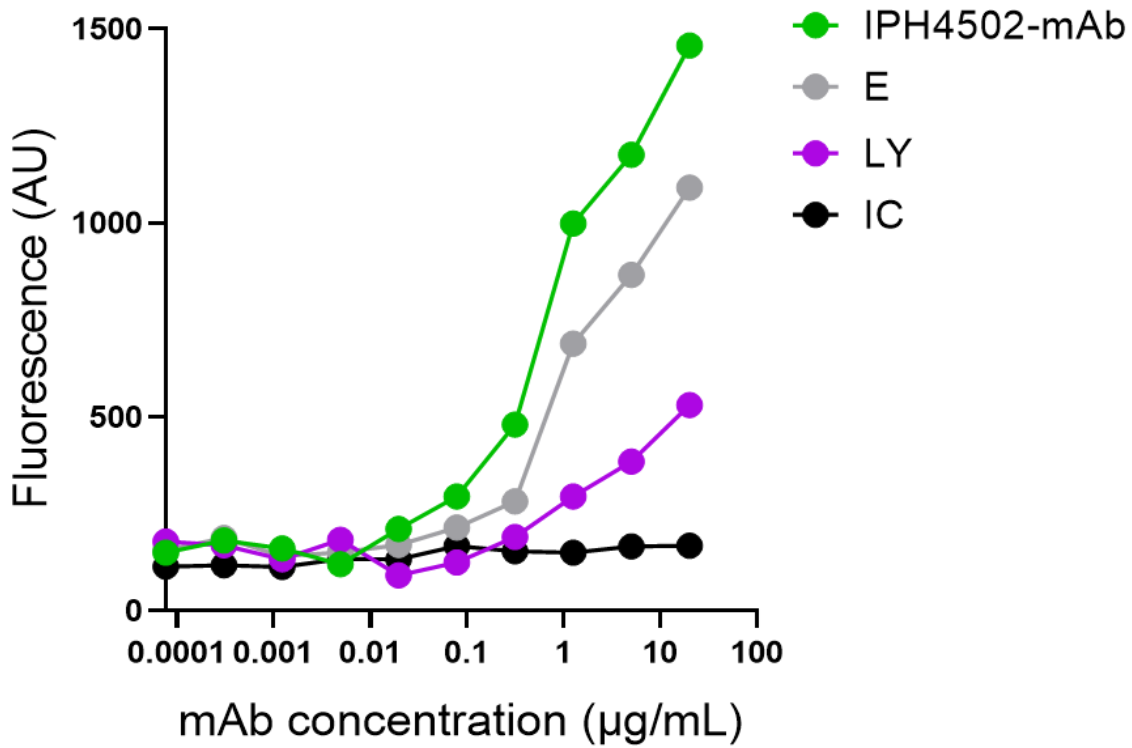
SUM190-PT model (human breast cancer cell line)

innate pharma

IPH4502 demonstrates more efficient internalization than other Nectin-4 ADC





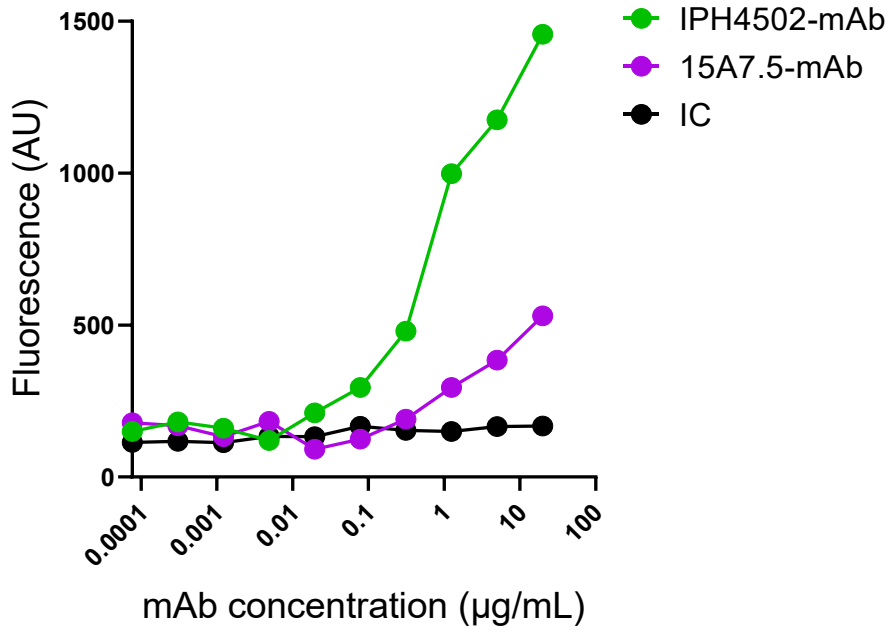


Internalization of naked antibodies coupled to pHAb amine in Nectin-4 expressing SUM190 PT cells was monitored at 24h
E = mAb having the amino acid sequence of Enfortumab; LY = humanized 15A7.5 mAb from patent EP4086284A1 (ETX-22 / LY4101174-mAb Lopez et al., 2024)
pHAb = pH sensitive dye that increases fluorescence upon internalization

innate pharma

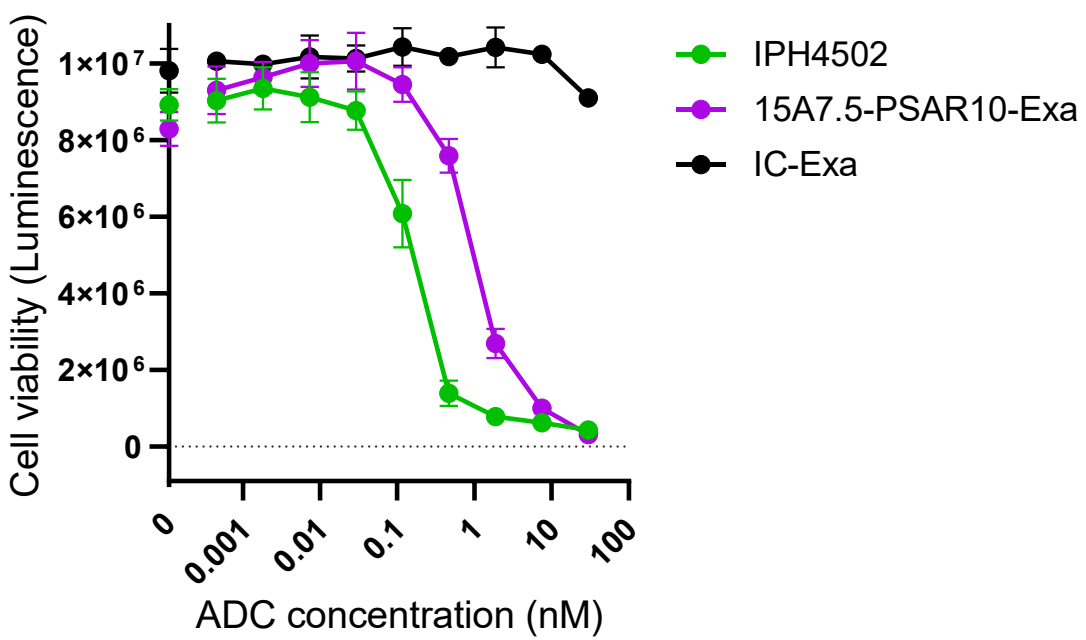
IPH4502 demonstrates higher internalization and cytotoxicity than 15A7.5-PSAR10-exatecan

Internalization



Internalization of naked mAbs coupled to pHAb amine in Nectin-4 expressing SUM190 PT cells was monitored at 24h
15A7.5 = humanized mAb from patent EP4086284A1 (ETX-22 / LY4101174-mAb)
pHAb = pH sensitive dye that increases fluorescence upon internalization

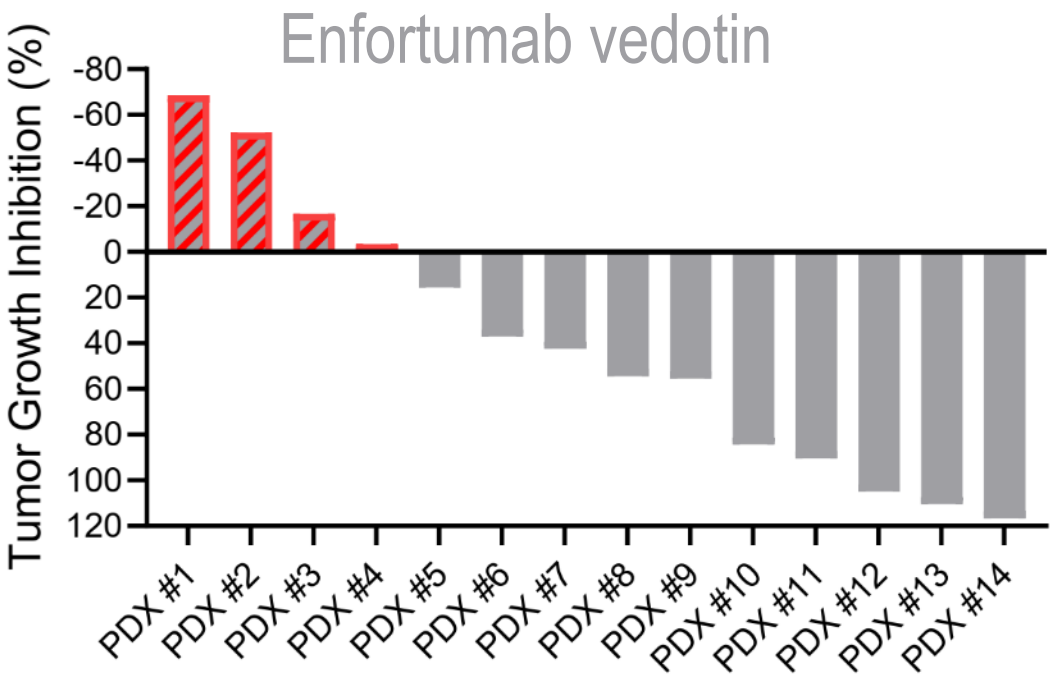
Cytotoxicity

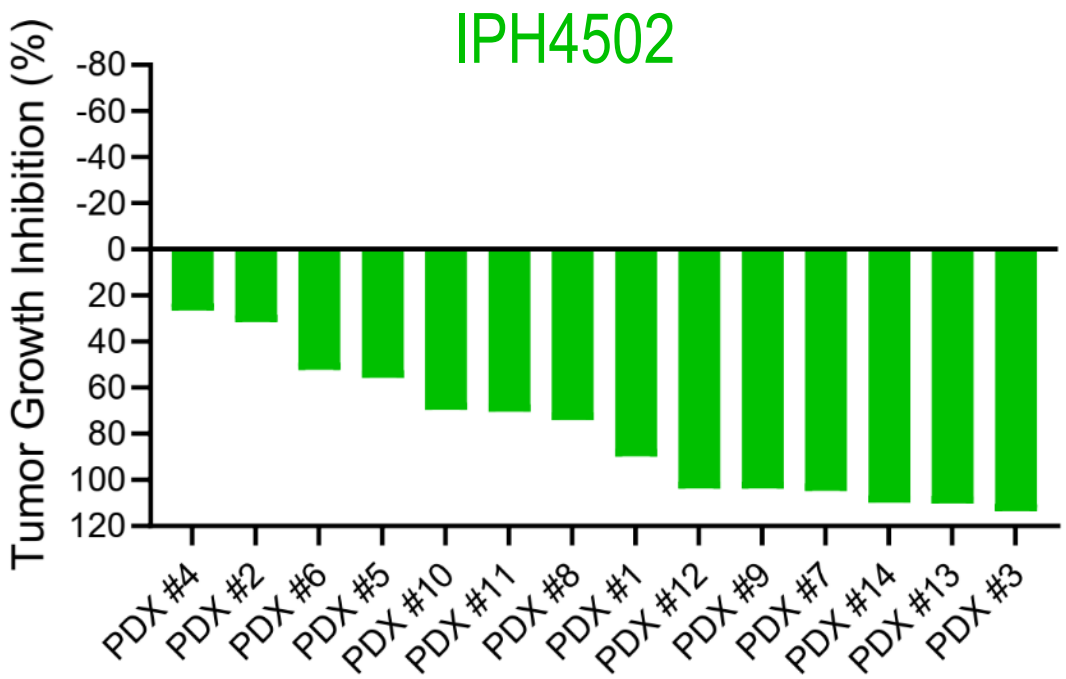


ADCs were incubated for 10 days with SUM190 PT cells and cell viability was evaluated with CellTiter-Glo® assay.
15A7.5-PSAR10-Exa = humanized 15A7.5 coupled to exatecan at DAR 8 with PSAR10 linker (Lopez et al., 2024; ETX-22 / LY4101174)

innate pharma

IPH4502 shows stronger anti-tumor activity than EV in multiple PDX models from UC patients



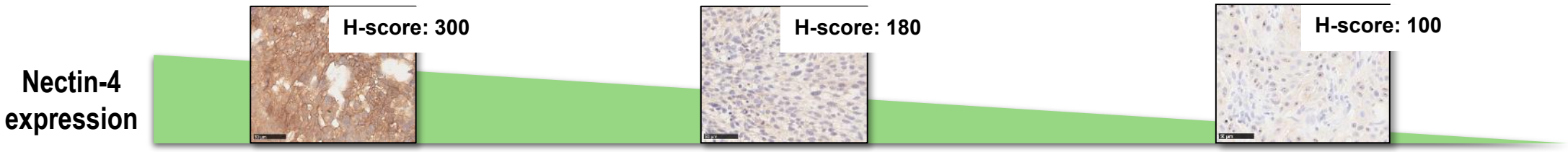


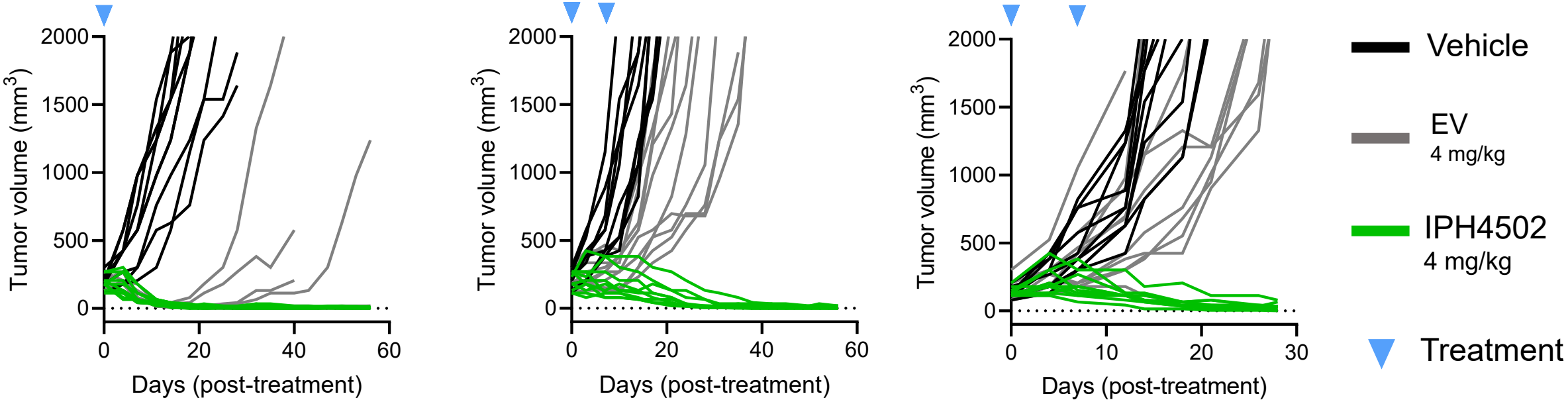
Mice were treated with the same dose (4mg/kg) for both ADCs at day 0 (randomization) and day 7

Tumor Growth Inhibition (TGI) = relative change in tumor volume compared to the initial mean tumor volume for the treated group (EV or IPH4502) and the control group (IC-Exatecan) on the last day when all mice from IC-Exa group still alive (n=3 mice per group)

innate pharma

IPH4502: Shows efficacy across various Nectin-4 expression levels and demonstrates superior activity to EV in bladder PDX models



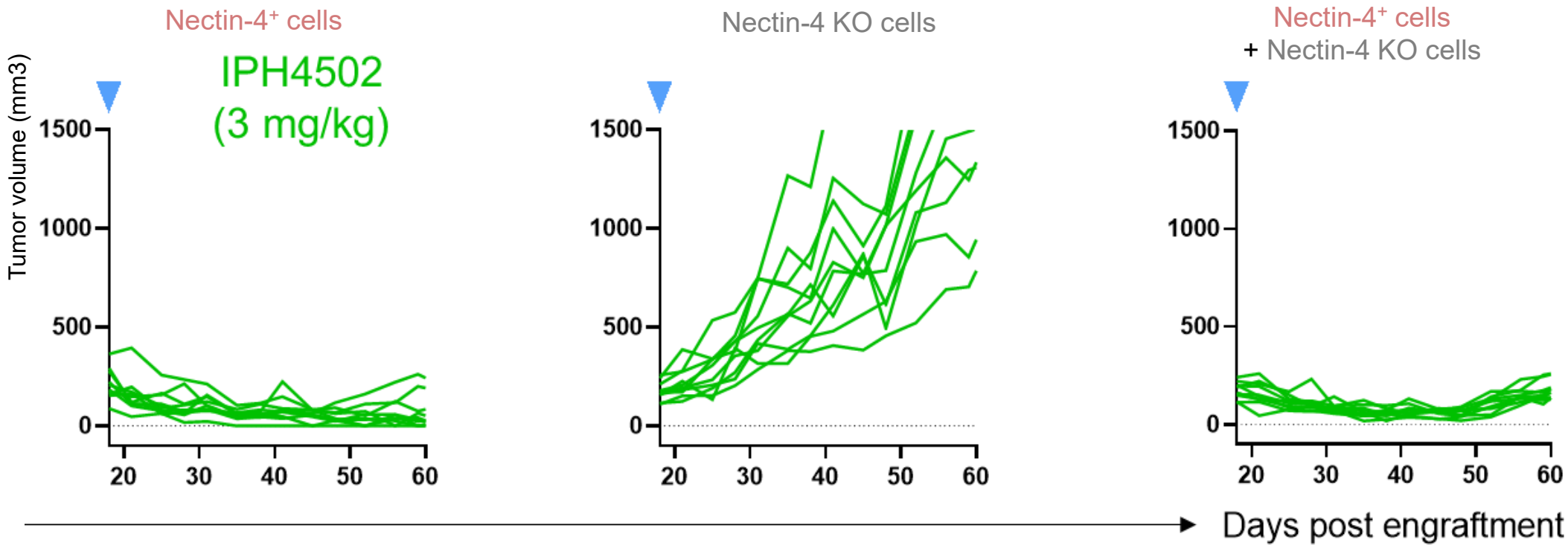


n=10 mice/group
EV (enfortumab vedotin, PADCEV) MMAE-ADC

AACR ANNUAL MEETING 2024 • SAN DIEGO
SITC 2024

innate pharma

IPH4502: Demonstrates in vivo potential for efficacy in heterogenous Nectin-4 expressing tumors via target-dependent bystander effect



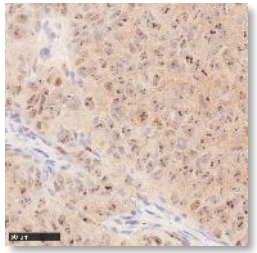
In vivo bystander killing ⇨ **Address heterogeneous Nectin-4 expression**

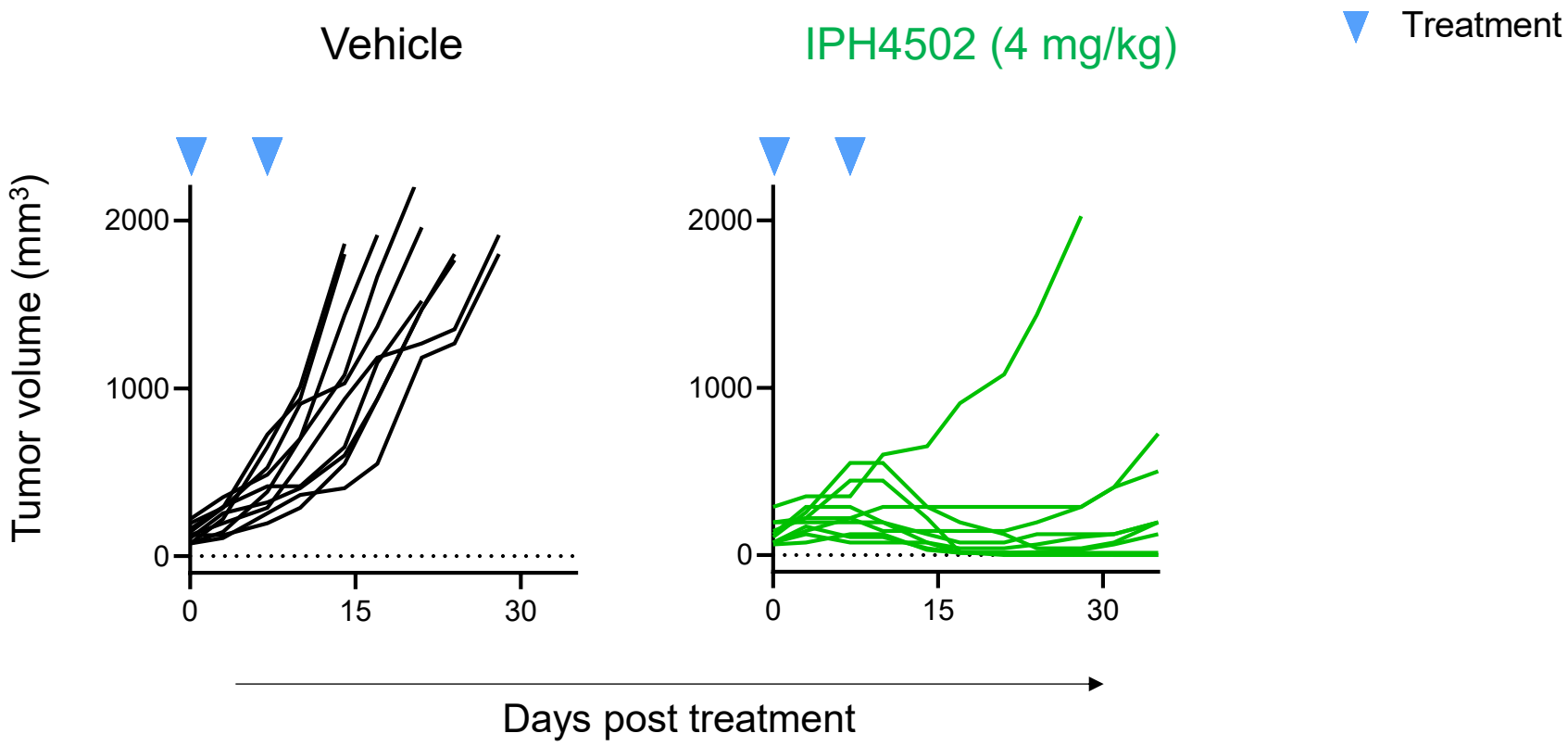
innate pharma

IPH4502 shows anti-tumor efficacy in a PDX model from Nectin-4+ cancer indication beyond bladder

PDX model of TNBC

TNBC
Nectin-4
H-score: 200

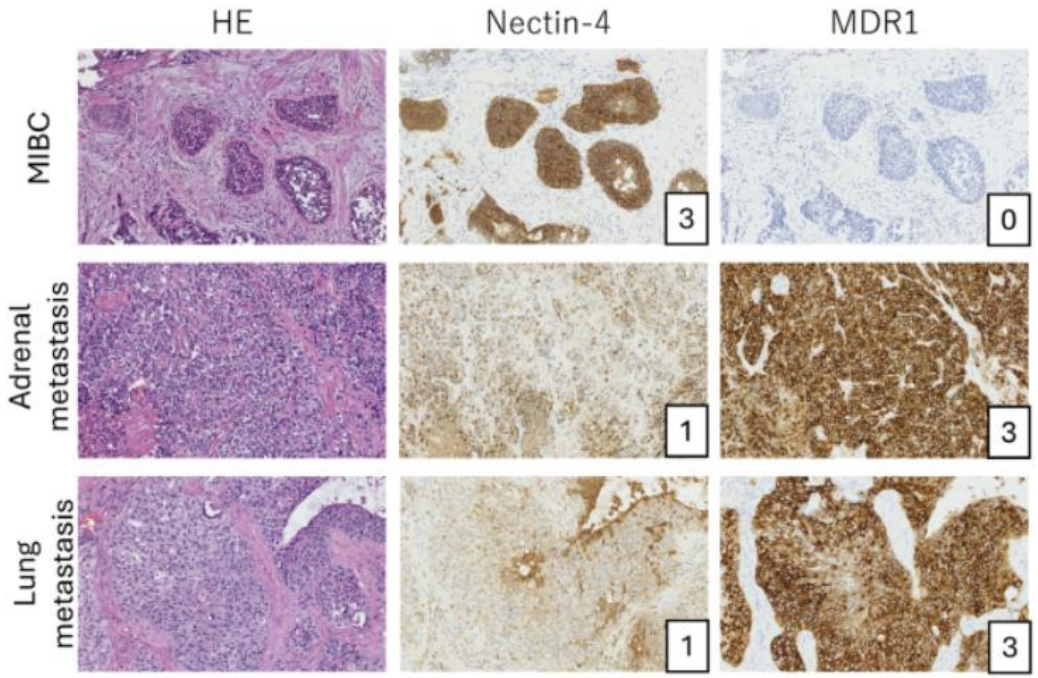




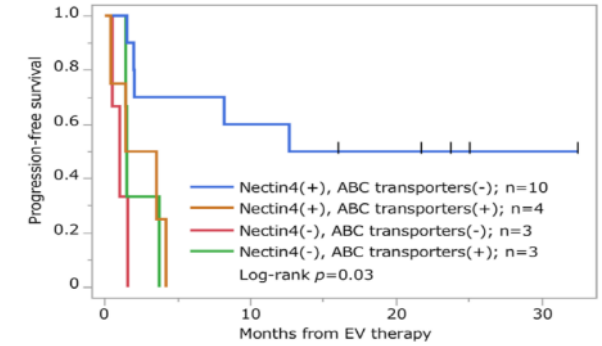
n=10 mice/group

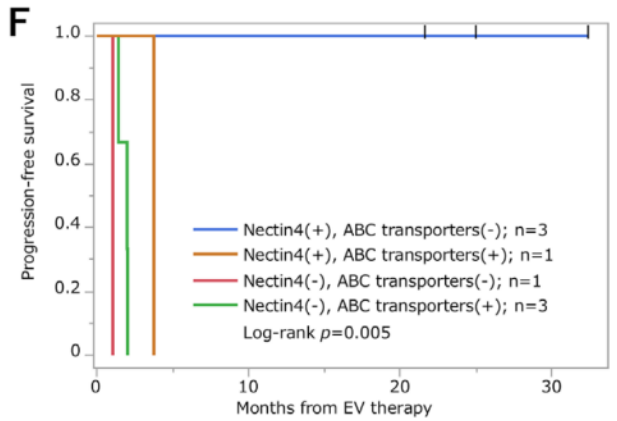
ABC transporters expression correlates with resistance to enfortumab vedotin in urothelial carcinoma

In metastatic lesions, Nectin-4 is lower and ABC transporter expression is increased



ABC transporter expression in primary tumor or metastasis correlates with resistance



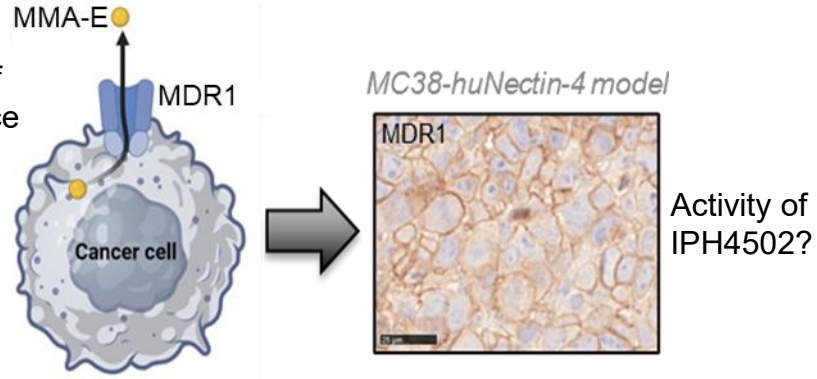


Kijima 2024 - Predictive role of ABC transporters in the efficacy of enfortumab vedotin for urothelial carcinoma

innate pharma

IPH4502 demonstrates efficacy in EV-primary refractory model

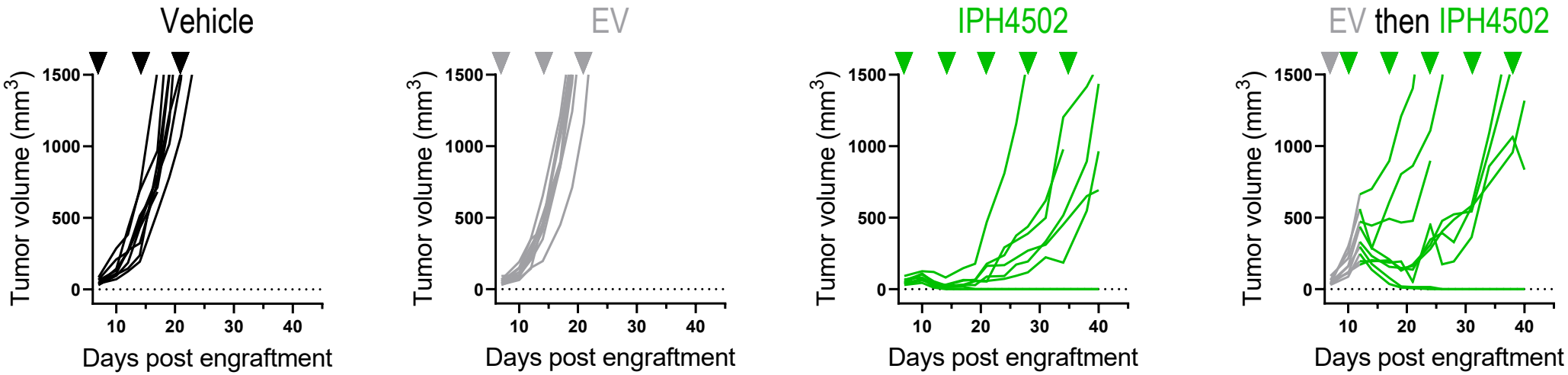
MMAE is a substrate of the multi-drug resistance protein 1 (**MDR1**)



MC38-huNectin-4 model

Activity of IPH4502?

▼ Treatment



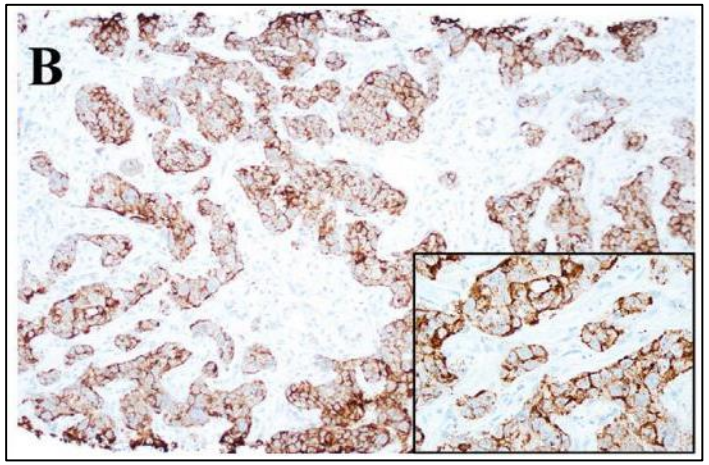
9 mice/group; MC38 human Nectin-4; All treatments at 10 mg/kg; ABC Nectin-4 ~200 000
***EV** (enfortumab vedotin, PADCEV) MMAE-ADC*

innate pharma

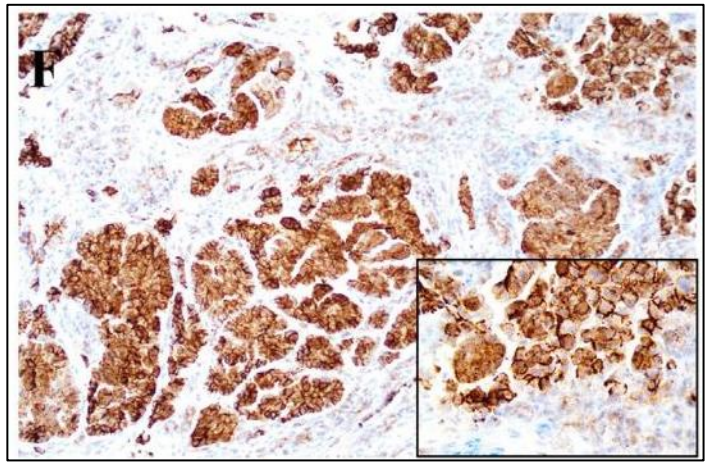
Nectin-4 remains highly expressed in EV-relapsed cancer patients

Nectin-4 expression was assessed by IHC in fresh biopsies from sites of tumor progression following EV from 3 patients

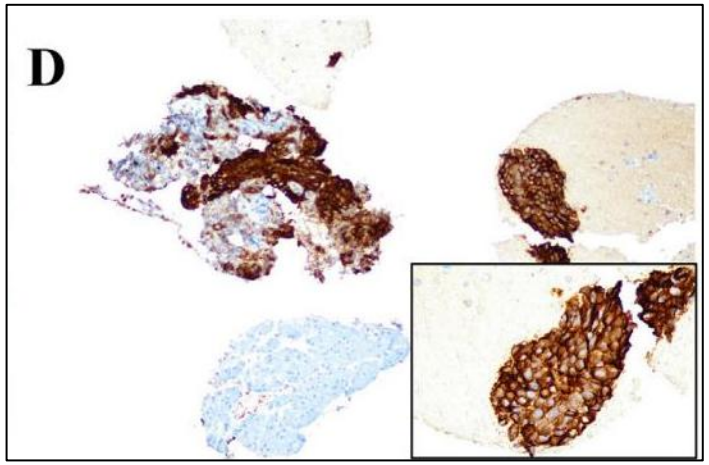
Liver metastasis



Lymph node metastasis



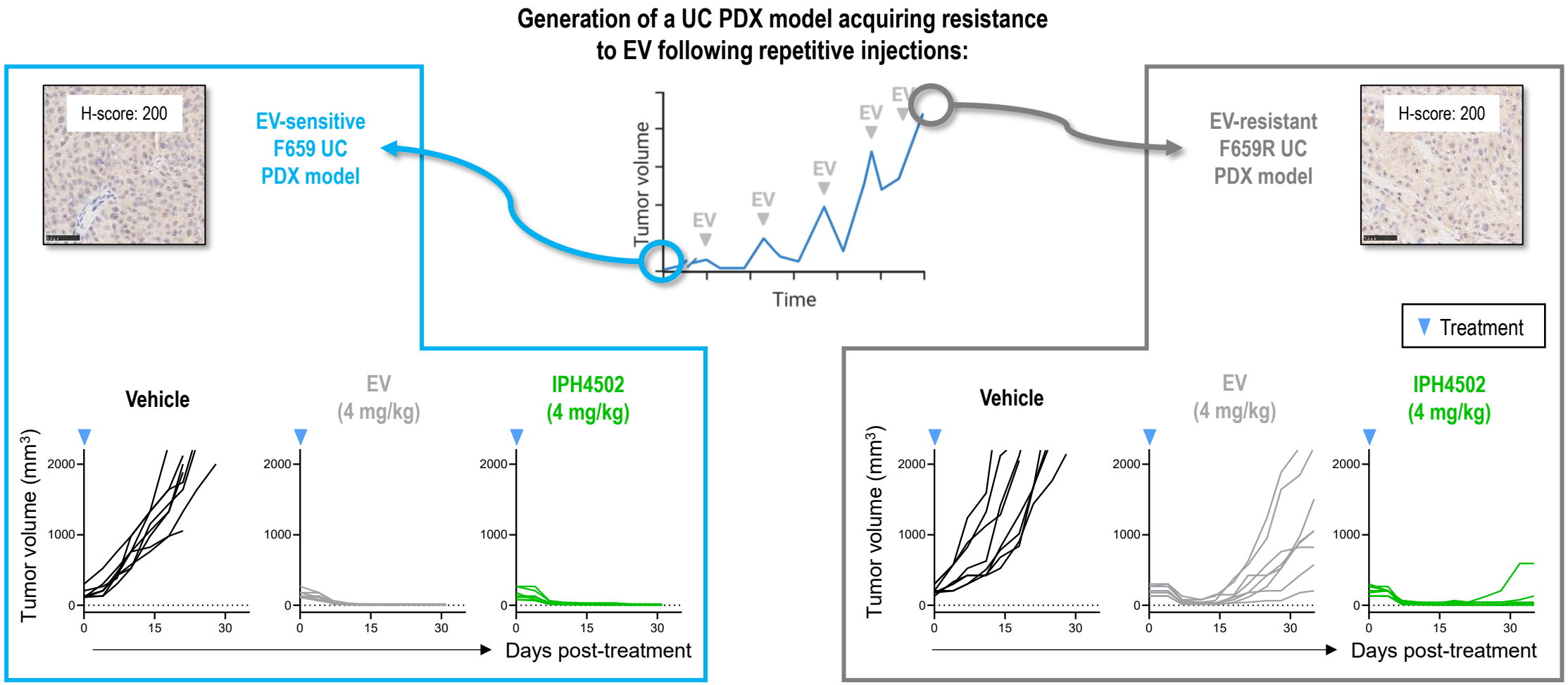
Duodenal metastasis



Nectin-4 expression is conserved in high grade UC patients with disease progression after treatment with EV (between 4-8 cycles)

Adapted from Hoffman-Censits, Urologic Onc. 2022

IPH4502 has anti-tumor activity in a PDX-model of acquired EV-resistance

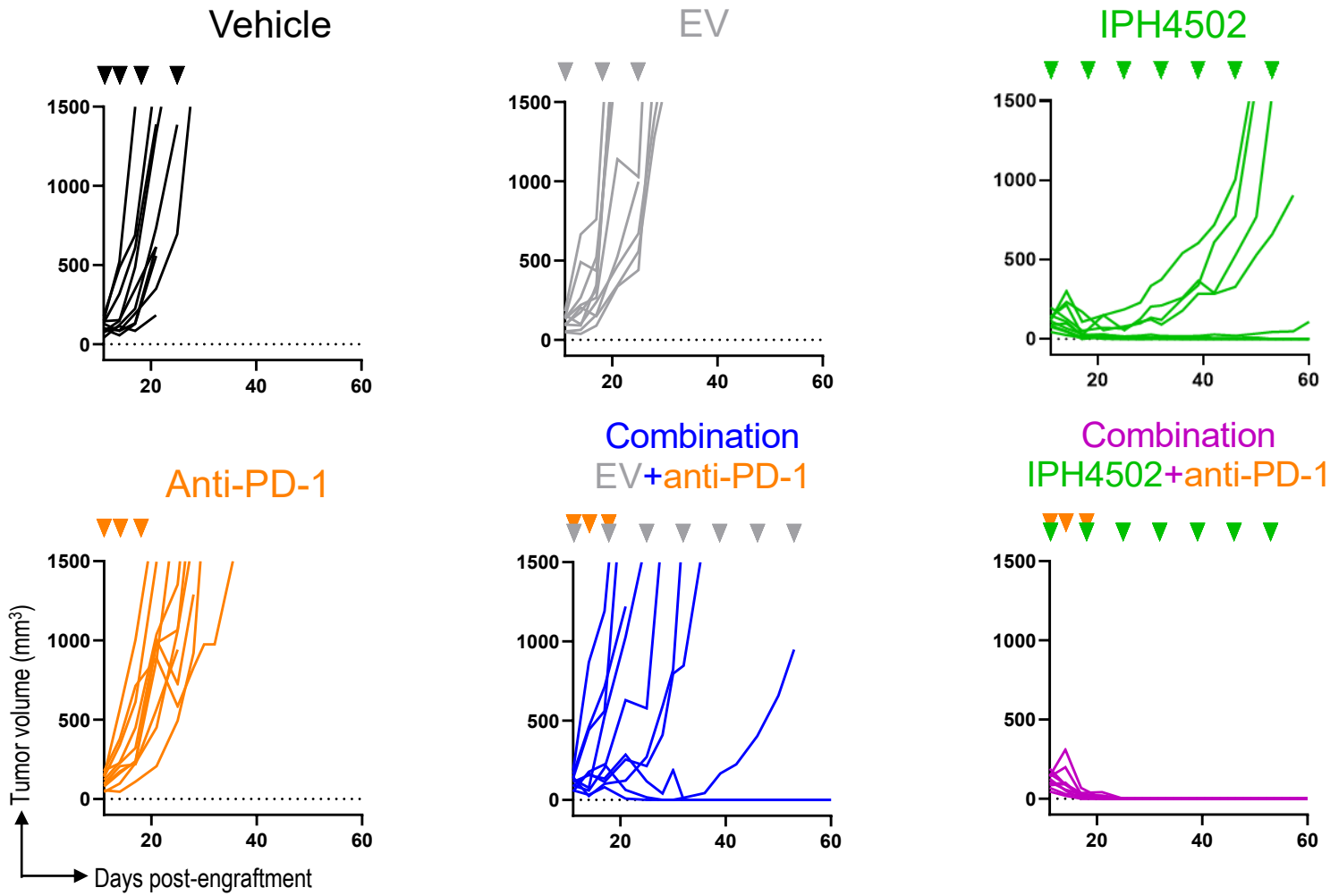


NMRI-Nude mice were subcutaneously implanted with tumor fragments. The F659R PDX model was generated through the repetitive in vivo treatment of the F659 PDX model with EV, which was repeated until the model exhibited resistance to EV. (n=8 mice/group)

innate pharma

IPH4502 shows increased anti-tumor activity in combination with anti-PD-1 in an EV-refractory model

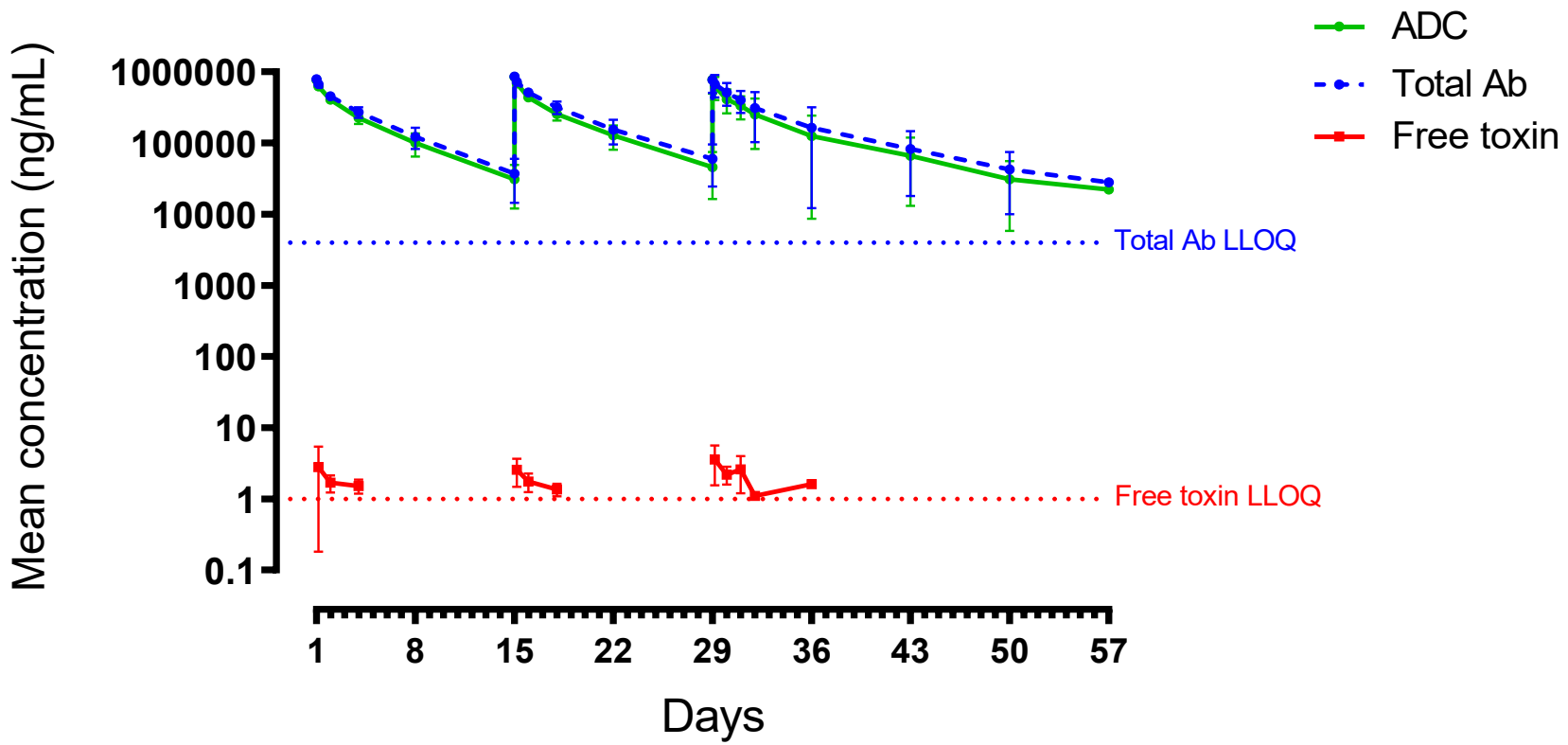
▼ Treatment



MC38-huN4 model in C57BL/6 mice depleted of B cells, all molecules at 10 mg/kg (n=10 mice/group).

innate pharma

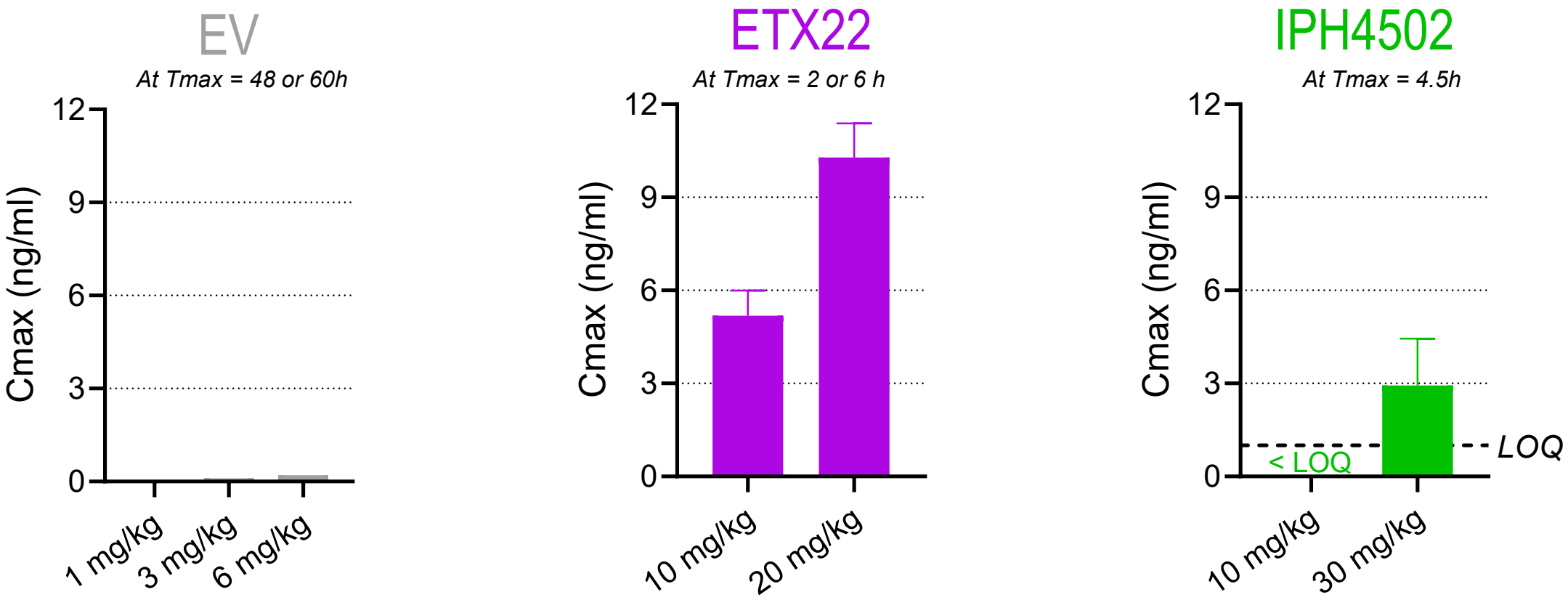
IPH4502 has high ADC exposure and minimal exatecan systemic release in NHP



GLP toxicology study: IPH4502 was administered at 30 mg/kg IV with 30 minutes infusion once every two weeks (Q2W) for a total of 3 doses
ADC, total Ab and free toxin mean concentrations (±SD) in plasma were determined using validated LC-MS/MS methods; LLOQ, lower limits of quantification
IPH4502 MW (molecular weight): 163 kDa; IPH4502-mAb (naked antibody) MW: 149 kDa; exatecan MW: 531.6 Da

IPH4502 has minimal exatecan systemic release in NHP

Free-toxin: Cmax



Values reported from ETX-22 = EORTC 2023, mean values from male and female. EV data from Padcev BLA

innate pharma

IPH4502 has broad potential in Nectin-4 expressing solid tumors

- IPH4502 is a next-generation differentiated Nectin-4 exatecan ADC with **high internalization** and **bystander effect**
- Linker's hydrophilicity and stability translate into **high ADC exposure** and **low release of free exatecan** into cynomolgus monkey plasma
- IPH4502 shows **superior efficacy to EV** in bladder cancer models with **low Nectin-4** expression, as well as in models of primary or induced **resistance to EV**
- IPH4502 shows efficacy in **non-bladder tumor types** (e.g. TNBC) and strong **combination potential** with PD-1 targeting agents

innate pharma

IPH4502 – Clinical development plan

IPH4502 Assumptions for IPH4502 Clinical plan

IPH4502 to overcome Nectin-4 ADCs limitations

Broader therapeutic window

Potential beyond Bladder
↑ activity in low and heterogeneous Nectin-4 expressors

Target resistant populations to standard of care EV

Favorable safety profile

- High Bystander effect
- High Internalization
- Non-competitive epitope vs EV
- Superior efficacy to EV in bladder cancer models with low and heterogeneous Nectin-4 expression
- Stable Linker with low release of free exatecan into cynomolgus monkey plasma
- Overcome MDR1-mediated resistance to MMAE
- Activity in secondary resistance to EV models

**Stable N4 expression in refractory tumors from patients treated with EV*

innate pharma

IPH4502 potential in solid tumors: UC and Beyond

IPH4502 potential benefit vs MMAE ADCs

UC

Address growing unmet need of **post-Padcev mUC patients***

Move up to **1L mUC** in combination with PD1 with less toxicity expected than EV

Expand beyond UC

High potential in **several tumor types not responsive nor addressed by MMAE ADCs** with low/med and heterogeneous expression of Nectin-4

**Stable N4 expression in refractory tumors from patients treated with EV*

innate pharma

Large addressable market with significant upside

Indications included in the Phase 1 dose escalation

>200K US/EU patients	**100-200K** US/EU patients	**<100K** US/EU patients
Bladder	HNSCC	Cervical
NSCLC	Ovarian	Esophageal
Breast	GEJ	Melanoma
CRC		
Prostate		

innate pharma

IPH4502 Phase 1 study design

US and EU

DOSE ESCALATION

DOSE OPTIMIZATION

STUDY POPULATION

Solid tumor types known to express Nectin-4*

Bladder, Cervical, Breast, NSCLC, GEJ, Esophageal, HNSCC, Prostate, Melanoma, Ovarian, CRC

DESIGN FEATURES

- Step-wise dose escalation to determine MTD for further dose optimization
- Bayesian optimal interval design (BOIN) to optimize MTD identification
- Backfill (BF) cohorts between dose escalation cohorts to increase # treated patients at active dose

Up to 30 pts in dose escalation
Up to 15 pts in Backfill cohorts

DESIGN FEATURES

- Randomize at least 2 dosing schedules with clinical activity to optimize dose and determine the recommended phase 2 dose (RP2D)
- Explore indications with signs of anti-tumor activity

Up to 30 pts per indication

OBJECTIVES

Primary Objectives:
Safety (DLT, MTD) and tolerability of IPH4502
Determine RP2D

Secondary Objectives:
- PK
- Immunogenicity
- Preliminary efficacy

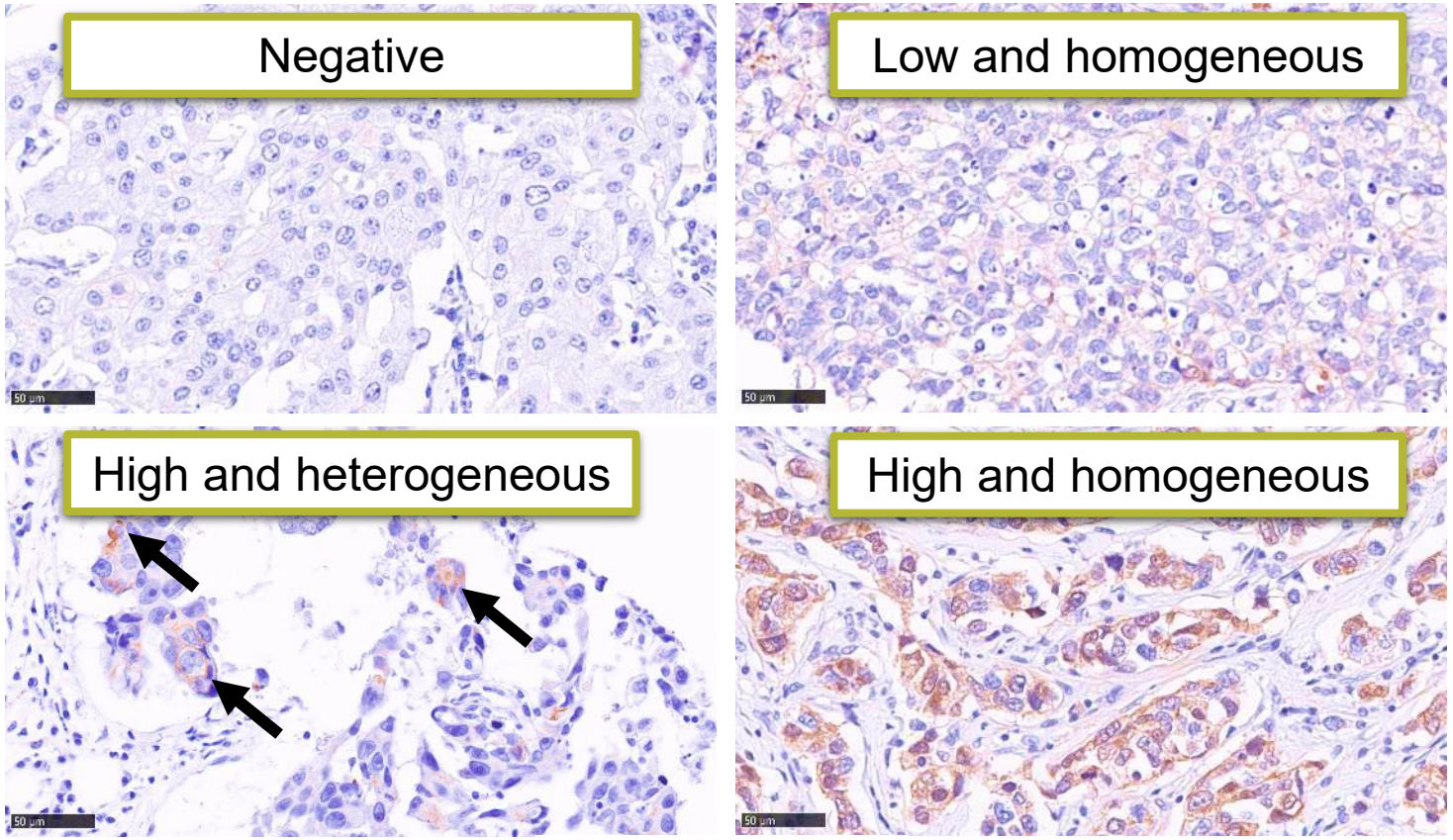
FPI JAN 2025

*Provisional Indications selection

innate pharma

IPH4502 Biomarker plan

Nectin-4 expression



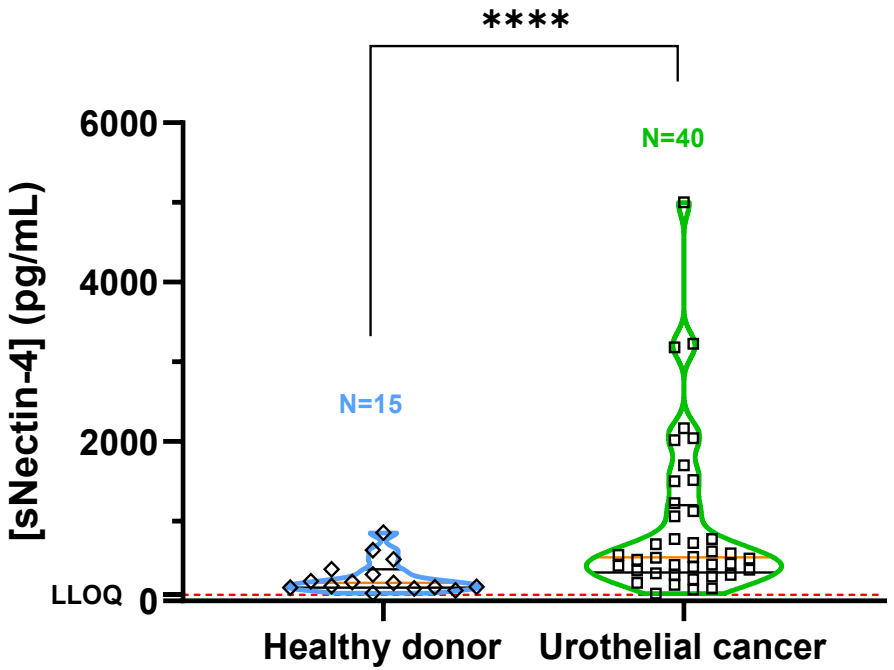
Breast cancer

The clinical program includes a biomarker plan to identify patient populations who most benefit from the IPH4502 treatment

- Analysis of Nectin-4 expression in cancer tissue from study patients
- Soluble biomarkers
- Analysis of clinical features and exposure-response analysis

innate pharma

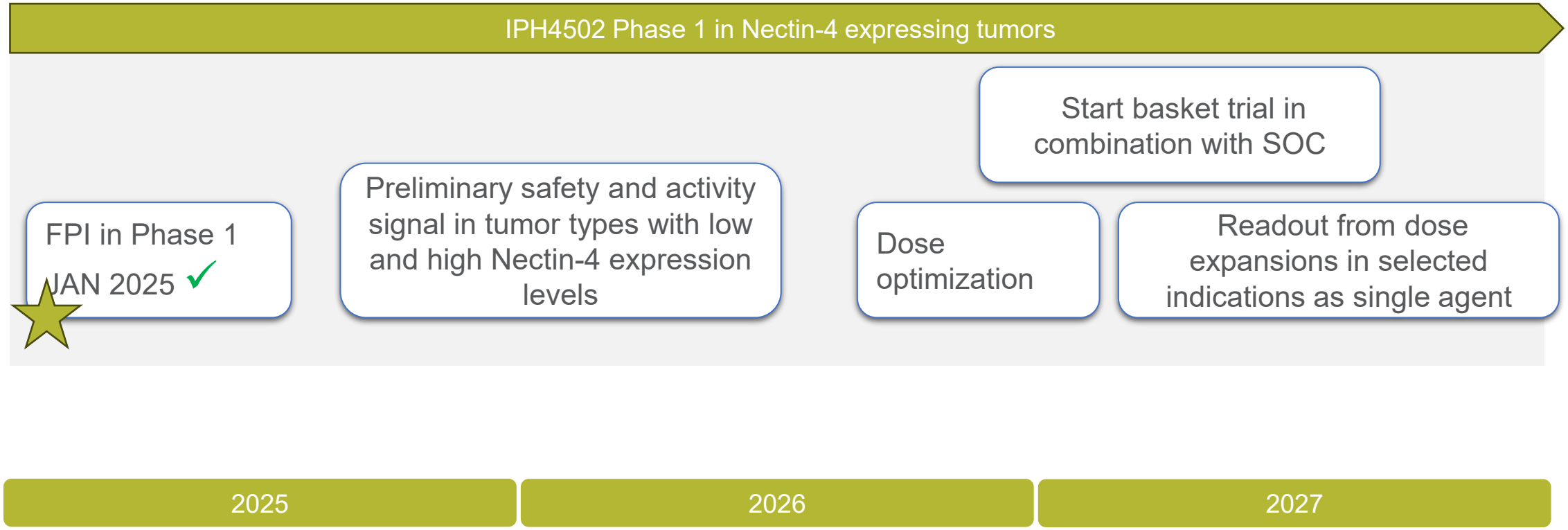
Soluble Nectin-4 is higher in cancer patients than in healthy donors



A soluble form of Nectin-4 (sNectin-4), has been identified in several other tumor types such as ovarian cancer (Derycke et al. 2010), breast cancer (Fabre-Lafay et al. 2007), or NSCLC (Takano et al. 2009).

*. ****, p<0.0001; unpaired t test with Welch's correction. LLOQ, lower limit of quantification; sNectin-4, soluble Nectin-4.*

IPH4502 Multiple Clinical Milestones to be Delivered in Mid-term



Data will inform next steps

innate pharma

Thank you

www.innate-pharma.com
investors@innate-pharma.fr

EURONEXT : IPH.PA NASDAQ : IPHA