First Results from a First-in-Human Phase 1, Open-label, Multi-center Study of the Safety, Tolerability, and Efficacy of IPH4502, an anti-Nectin-4 ADC, as a Single Agent in Advanced Solid Tumors

Abstract number: **PB-089**

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Thomas U. Marron[1], Shiraj Sen[2], Armelle Vinceneux[3], Xin Gao[4], Alex Spira[5], Martin Gutierrez[6], Markus Jensen[7], A.J. Leyco[7], David Magrez[7], Yohann Loriot[8]

[1] Mount Sinai School of Medicine, New York, USA; [2] NEXT Oncology Dallas, Irving, USA; [3] Centre Léon Bérard, Lyon, France; [4] Massachusetts General Hospital, Harvard Medical School, Boston, USA; [5] NEXT Oncology Virginia, Fairfax, USA; [6] Hackensack University Medical Center, Hackensack, USA; [7] Innate Pharma, Marseille, France; [8] Gustave Roussy, Villejuif, France

Background

IPH4502 is a novel Nectin-4-targeted ADC designed with three differentiated components:

- **Exatecan payload (DAR 8):** A potent topoisomerase I inhibitor with low susceptibility to MDR1-mediated efflux, to help overcome MMAE-related resistance associated with enfortumab vedotin (EV).
- **Proprietary stable linker:** Designed to limit premature systemic release of free exatecan and potentially reduce off-target payload exposure
- **Proprietary anti-Nectin-4 antibody:** Targets a non-overlapping epitope relative to EV, with high internalization, potentially enabling activity in tumors with low or heterogeneous Nectin-4 expression
- Here we report preliminary Phase 1 dose-escalation results of IPH4502 in patients with advanced solid tumors (NCT06781983).

Study Design

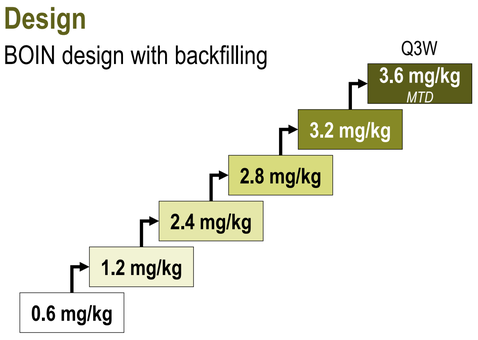
Dose escalation · N=76 | 5 sites in the US and 2 sites in France

Key eligibility

- Unresectable, locally advanced or metastatic solid tumors known to express Nectin-4
- Post prior systemic therapy, no option left with demonstrated clinical benefit
- Measurable disease (RECIST v1.1)
- Prior EV permitted for UC patients

Design

BOIN design with backfilling



Key objectives

Primary
- Safety and tolerability
- Maximum tolerated dose (MTD)

Secondary
- Pharmacokinetics
- Preliminary efficacy (signal seeking)

Data cutoff (DCO) date of August 17, 2026

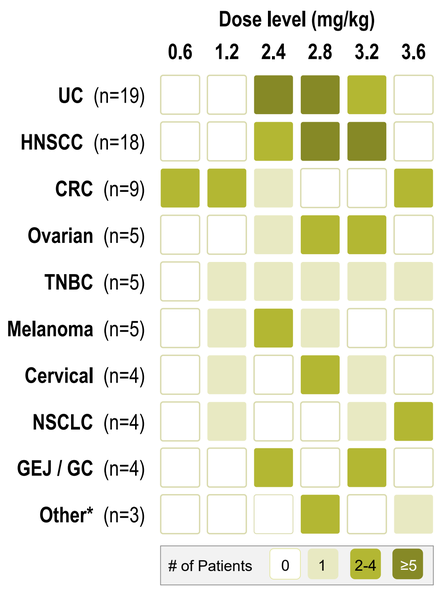
1. Patient Characteristics

Patient demographics and baseline characteristics

Characteristic	All participants (N=76)	UC patients (n=19)
Age, median (range), years	63 (30–78)	64 (40–77)
Sex, female / male, n (%)	23 (30.3) / 53 (69.7)	3 (15.8) / 16 (84.2)
ECOG PS 0 / 1, n (%)	25 (32.9) / 51 (67.1)	3 (15.8) / 16 (84.2)
Prior lines of systemic therapy, n (%)	**median 3.5**	**median 3**
1	6 (7.9)	1 (5.3)
2	9 (11.8)	3 (15.8)
3	23 (30.3)	10 (52.6)
≥4	38 (50.0)	5 (26.3)
Prior therapy, n (%)		
Platinum chemotherapy	63 (82.9)	18 (94.7)
PD-1 / PD-L1	61 (80.3)	19 (100.0)
Topo I ADC	8 (10.5)	1 (5.3)
Enfortumab vedotin	19 (25.0)	19 (100.0)
Nectin-4 H-score[1], n (%)[2]		
Negative (0–14)	20 (30.8)	3 (17.6)
Low (15–99)	17 (26.2)	2 (11.8)
Moderate (100–199)	8 (12.3)	3 (17.6)
High (200–300)	20 (30.8)	9 (52.9)

[1] Nectin-4 expression categorized by H-score: negative (0–14), low (15–99), moderate (100–199), high (200–300), as described in Challita-Eid et al., Cancer Res. 2016. [2] Percentages calculated among patients with available H-score data (n=65 for all participants, and n=17 for UC patients). Immunohistochemistry was performed using the anti-Nectin-4 antibody clone EPR21192-113.

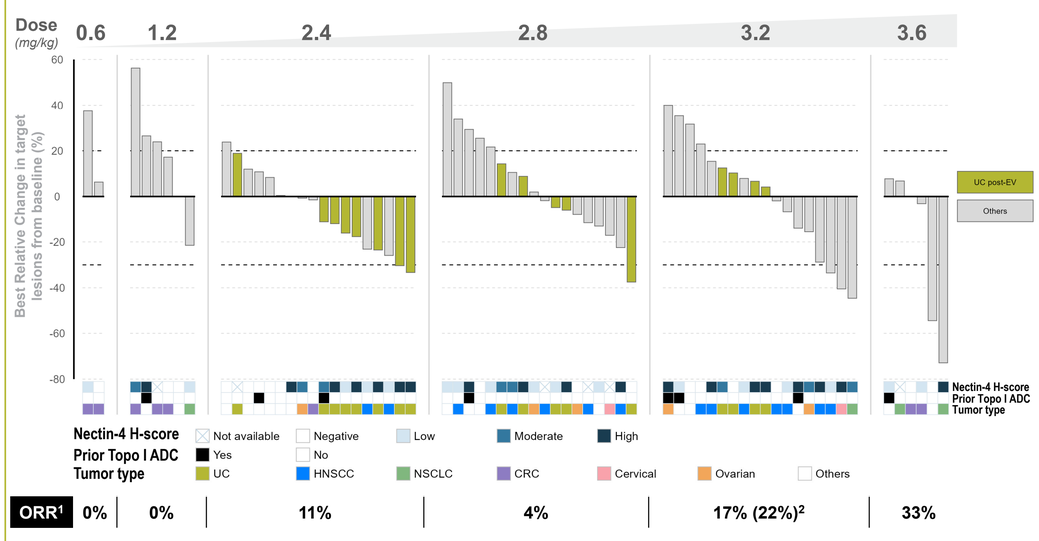
Tumor types and patient distribution across dose levels



*Other: cholangiocarcinoma, prostate and cervical cancer of neuroendocrine type.

2. Antitumor Activity

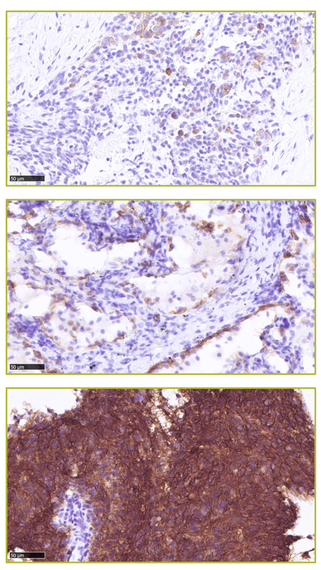
Preliminary antitumor activity observed across multiple dose levels and tumor types



[1] ORR includes participants with complete and partial responses (confirmed and unconfirmed), based on data from DCO August 17, 2026. [2] Includes one additional response reported after the DCO; source data verification is ongoing and data displayed may be subject of change.

3. Antitumor Activity Across Nectin-4 Levels

Clinical activity in low-to-high Nectin-4 tumors



Nectin-4 Low
H-score = 60
HNSCC, male patient, 78 years
Target lesions −33.5%[1]

Nectin-4 Moderate
H-score = 190
NSCLC, male patient, 72 years
Target lesions −44.7%[1]

Nectin-4 High
H-score = 300
Cervical cancer, female patient, 63 years
Target lesions −40.5%[1]

[1] Sum of longest diameters (RECIST 1.1) of target lesions, change from baseline

4. Safety Profile

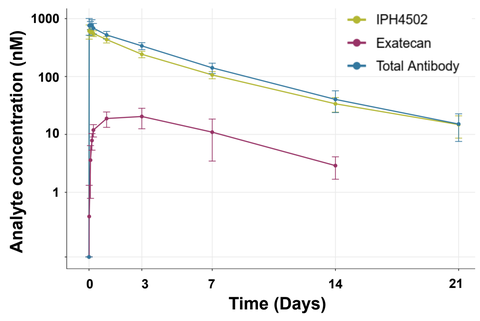
Treatment-emergent adverse events ≥10% (all participants)

	Overall (N=76); n (%)		0.6 mg/kg (N=3); n (%)		1.2 mg/kg (N=7); n (%)		2.4 mg/kg (N=18); n (%)		2.8 mg/kg (N=24); n (%)		3.2 mg/kg (N=18); n (%)		3.6 mg/kg (N=6); n (%)	
	All grade	≥ G3	All grade	≥G3	All grade	≥G3	All grade	≥G3	All grade	≥G3	All grade	≥G3	All grade	≥G3
Patients with any TEAE	**73 (96.1)**	**33 (43.4)**	3 (100)	3 (100)	6 (85.7)	2 (28.6)	17 (94.4)	7 (38.9)	23 (95.8)	10 (41.7)	18 (100)	8 (44.4)	6 (100)	3 (50.0)
Fatigue	**37 (48.7)**	**1 (1.3)**	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)	9 (50.0)	1 (5.6)	13 (54.2)	0 (0.0)	10 (55.6)	0 (0.0)	3 (50.0)	0 (0.0)
Nausea	**34 (44.7)**	**0 (0.0)**	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	9 (50.0)	0 (0.0)	12 (50.0)	0 (0.0)	11 (61.1)	0 (0.0)	1 (16.7)	0 (0.0)
Anemia	**24 (31.6)**	**9 (11.8)**	0 (0.0)	0 (0.0)	1 (14.3)	1 (14.3)	4 (22.2)	2 (11.1)	10 (41.7)	4 (16.7)	7 (38.9)	2 (11.1)	2 (33.3)	0 (0.0)
Stomatitis	**21 (27.6)**	**3 (3.9)**	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (16.7)	0 (0.0)	9 (37.5)	1 (4.2)	4 (22.2)	0 (0.0)	5 (83.3)	2 (33.3)
Diarrhea	**16 (21.1)**	**0 (0.0)**	1 (33.3)	0 (0.0)	3 (42.9)	0 (0.0)	4 (22.2)	0 (0.0)	2 (8.3)	0 (0.0)	5 (27.8)	0 (0.0)	1 (16.7)	0 (0.0)
Vomiting	**13 (17.1)**	**0 (0.0)**	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (33.3)	0 (0.0)	2 (8.3)	0 (0.0)	4 (22.2)	0 (0.0)	1 (16.7)	0 (0.0)
Dysgeusia	**13 (17.1)**	**0 (0.0)**	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (22.2)	0 (0.0)	3 (12.5)	0 (0.0)	6 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
Decreased appetite	**11 (14.5)**	**1 (1.3)**	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	4 (22.2)	0 (0.0)	4 (16.7)	1 (4.2)	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)
Constipation	**8 (10.5)**	**0 (0.0)**	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (16.7)	0 (0.0)	4 (16.7)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)	0 (0.0)
Dose interruption/delay	**13 (17.1)**		0 (0.0)		0 (0.0)		4 (22.2)		5 (20.8)		4 (22.2)		0 (0.0)	
Dose reduction	**6 (7.9)**		0 (0.0)		0 (0.0)		1 (5.6)		1 (4.2)		3 (16.7)		1 (16.7)	
IPH4502 discontinuation	**4 (5.3)**		0 (0.0)		0 (0.0)		0 (0.0)		2 (8.3)		0 (0.0)		2 (33.3)	

- **MTD at 3.6 mg/kg with stomatitis as the only DLT.** In addition to stomatitis, one case of Grade 3 esophagitis was documented at 3.6 mg/kg (same pathophysiology as stomatitis)
- **Low hematologic toxicity profile:** No febrile neutropenia or dose-limiting hematologic toxicity
- **Low skin toxicity:** Macular and maculopapular rash each affected 2.6% of patients, including one Grade 3 maculopapular rash
- **Other findings:** No peripheral neuropathy | Ocular AEs limited to Grade 1–2 | One Grade 2 pneumonitis event led to dose reduction, with treatment continuing

5. Pharmacokinetics

Plasma concentration, Cycle 1 (3.6 mg/kg, N=6)



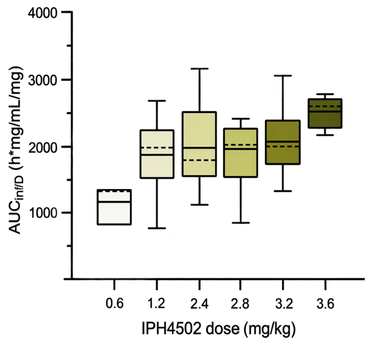
- **Low systemic free-exatecan levels**
- **Slow payload release**

Free exatecan C_{max} at Days 2–3

Low free exatecan levels are consistent with low hematologic toxicity and support linker stability

Data are presented as mean ± standard deviation. Mean exatecan concentration at Day 21 could not be calculated because concentrations were below the limit of quantification in 5 of 6 patients.

IPH4502 area under the curve (AUC) dose normalized (AUC/D)



- **Higher exposure at 3.6 mg/kg**
  The increase in dose-normalized IPH4502 AUC at 3.6 mg/kg versus 3.2 mg/kg likely suggests Nectin-4 saturation
- **Split-dose exploration**
  These pharmacokinetic findings support exploring split dosing

Conclusions & Takeaways

Population

- **76 heavily pretreated patients across >10 tumor types** (median 3.5 prior lines), with no Nectin-4 preselection. All UC patients (n=19) were previously treated with EV
- 6 dose levels evaluated (0.6–3.6 mg/kg Q3W)

Safety

- **MTD = 3.6 mg/kg Q3W** (BOIN); Stomatitis was the only DLT
- **Well tolerated** with low hematologic toxicity (no febrile neutropenia), low skin toxicity, and no signal of peripheral neuropathy
- **Low free exatecan levels** supporting **linker stability** and consistent with low hematologic toxicity

Activity

- **Antitumor activity across multiple dose levels**, with an **ORR up to 33%** (2/6) at 3.6 mg/kg
- Objective responses in **UC post-EV**, and in **NSCLC, HNSCC, ovarian cancer, cervical cancer and cervical cancer of neuroendocrine type**
- Responses observed **across** low, moderate and high **Nectin-4 expression levels**

Abbreviations

ADC, antibody-drug conjugate; **AE**, adverse event; **AUC**, area under the curve; **AUC/D**, dose-normalized AUC; **BOIN**, Bayesian optimal interval; **C_{max}**, maximum observed concentration; **CRC**, colorectal cancer; **DAR**, drug-to-antibody ratio; **DCO**, data cutoff; **DLT**, dose-limiting toxicity; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **EV**, enfortumab vedotin; **G3**, grade 3; **GEJ/GC**, gastroesophageal junction/gastric cancer; **HNSCC**, head and neck squamous cell carcinoma; **MDR1**, multidrug resistance protein 1; **MMAE**, monomethyl auristatin E; **MTD**, maximum tolerated dose; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **PD-1**, programmed cell death protein 1; **PD-L1**, programmed death-ligand 1; **Q3W**, every 3 weeks; **RECIST**, Response Evaluation Criteria in Solid Tumors; **TEAE**, treatment-emergent adverse event; **TNBC**, triple-negative breast cancer; **Topo I**, topoisomerase I; **UC**, urothelial cancer

Preclinical Outlook

Preclinical data:
Poster PB-080

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