Bicycle Therapeutics Investor Presentation

- April 30th, 2026

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Forward-looking statements

This presentation may contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as “aims,” “anticipates,” “believes,” “could,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will,” and variations of these words or similar expressions that are intended to identify forward-looking statements. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements regarding: our future financial or business performance, conditions, plans, prospects, or strategies and other financial and business matters, including expected financial runway; our current and prospective product candidates, planned regulatory interactions and submissions, the progress of and data from clinical trials and preclinical activities, current and prospective collaborations; the timing and success of our development of our current and prospective product candidates; the safety and efficacy profiles of our product candidates; the ability of our platform to identify and pursue novel targets and the timing of data related thereto, including imaging data; our ability to create the world’s first end-to-end ^{212}Pb radiopharmaceutical ecosystem from discovery through development to commercial supply; and our ability to leverage related collaborations and partnerships in furtherance of this and other efforts; and the size and composition of the potential markets for any of our product candidates, if approved.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results, our plans to initiate clinical trials and the designs of the planned trials and other future conditions, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of our product candidates will not be successfully developed or commercialized, the risk of cessation or delay of any ongoing or planned clinical trials or preclinical activities, the risk that we may not realize the intended benefits of our technology, including that we may not identify and develop additional product candidates for our pipeline, the risk that we may not maintain our current partnerships or enter into new partnerships in the future, or that we may not realize the intended benefits of these partnerships, the risk that our product candidates or procedures in connection with the administration thereof will not have the safety and efficacy profiles that we anticipate, the risk that prior results will not be replicated or will not continue in ongoing or future studies or trials, the risk that we will be unable to obtain and maintain regulatory approval for our product candidates, the risk that the size and potential of the markets for our product candidates will not materialize as expected, risks associated with our dependence on third-parties, risks regarding the accuracy of our estimates of expenses and financial runway, risks relating to our capital requirements and needs for additional financing, and risks relating to our ability to obtain and maintain intellectual property protection for our product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled “Risk Factors” in our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission (the “SEC”) on April 30, 2026, as well as in other filings we may make with the SEC in the future, as well as discussions of potential risks, uncertainties and other important factors in our subsequent filings with the SEC. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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Bicycle Therapeutics: Pioneering a new, differentiated class of innovative medicines

Unique Platform

Developing Bicycle® molecules – a novel synthetic peptide modality that can potentially deliver any payload to any target

Technology based on Nobel Prize-winning science

Strong intellectual property portfolio

Internal Programs

Focused on oncology, with multiple clinical molecules

Nuzefatide pevedotin (formerly BT5528) targeting historically undruggable target with ADCs, progressing into Phase 2 in PDAC

Radioligand pipeline addressing novel cancer targets MT1-MMP and EphA2

Zelenectide pevedotin demonstrating differentiated safety profile and strong antitumor activity in mUC

Validating Partnerships

Extending use of platform into diverse range of therapeutic areas such as radioligands and non-core areas such as neurology

Bayer

IONIS

dkfz.

Universitätsmedizin Essen
Universitätsklinikum

NDA

NATIONAL NUCLEAR LABORATORY

Ambitious Company

Deeply experienced team

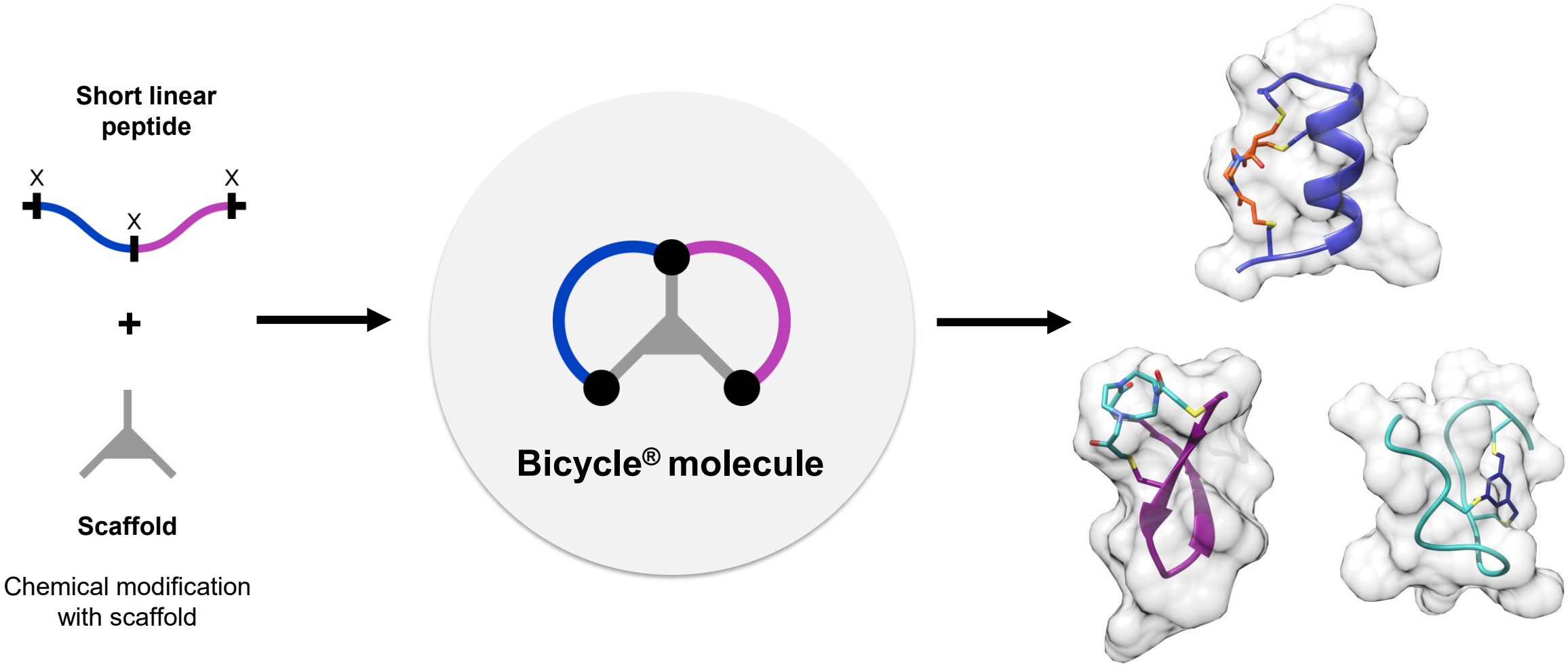
Located in Cambridge, UK, and Lexington, MA

NASDAQ: BCYC

Cash and cash equivalents of $559.5 million as of March 31, 2026, with expected financial runway into 2030

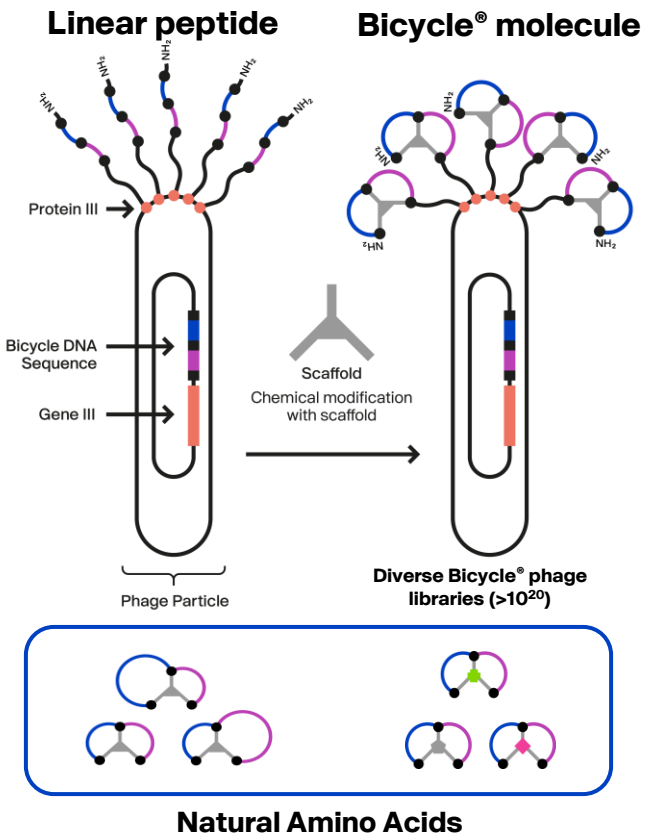
EphA2: Ephrin A2; MT1-MMP: Membrane type 1 matrix metalloproteinase; mUC: metastatic urothelial cancer; PDAC: pancreatic ductal adenocarcinoma; ADC: Antibody Drug Conjugate

Bicycle® molecules are short peptides chemically constrained with a central scaffold that can induce diverse structures



Bicycle® platform delivers a toolkit of modular building blocks to create novel precision-guided medicines

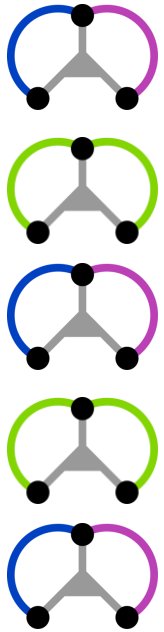
Bicycle® Phage Display Discovery



Peptide & Medicinal Chemistry

Optimize Bicycle® monomers

Non-natural Amino Acids

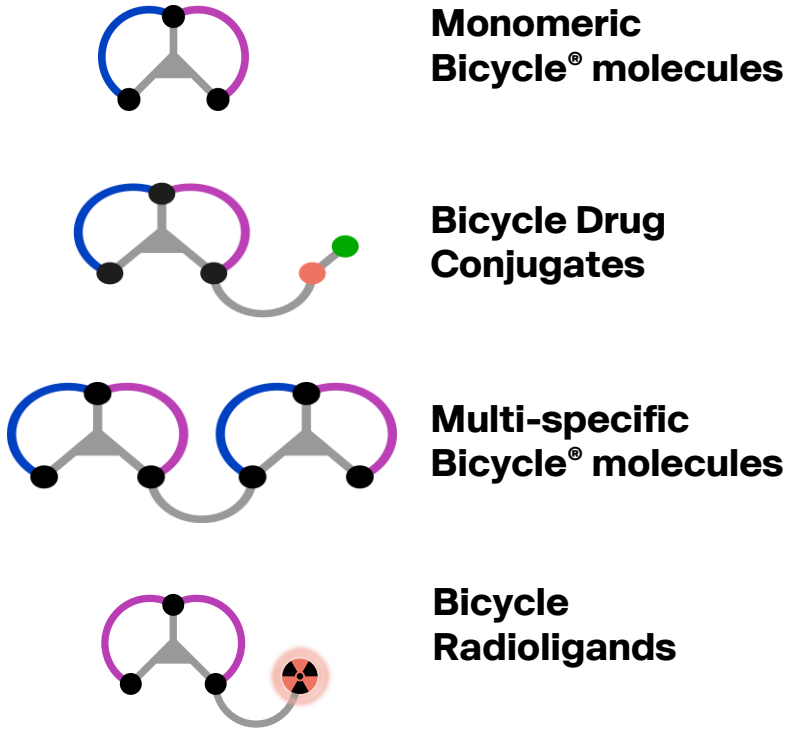


Targeting and Effector Bicycle® molecules

Build and Optimize Therapeutic Bicycle® molecules

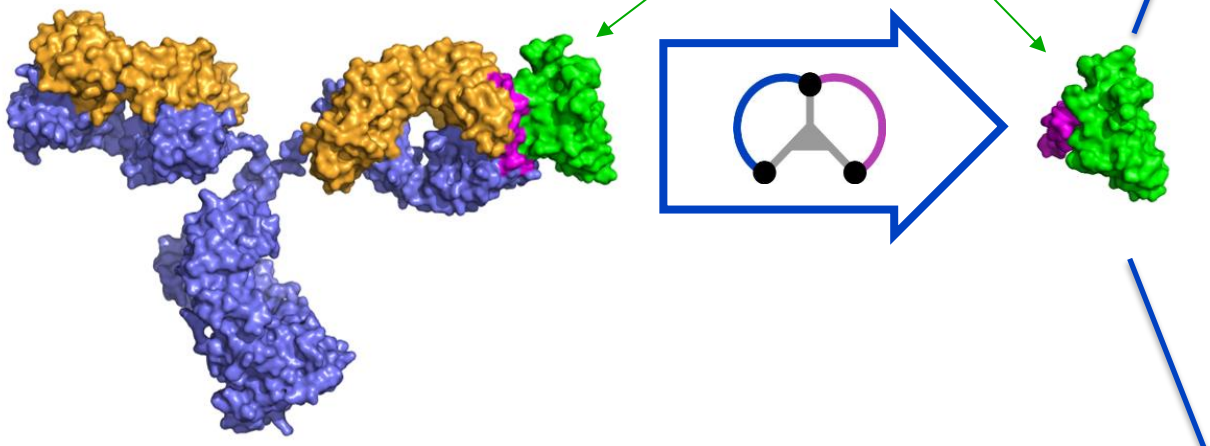
Easy conjugation of Linkers and Payloads

Potential Bicycle® Medicines



Bicycle® molecules have optimal properties for precision guided therapeutics due to their unique design

Bicycle® molecules are designed to mimic an antibody's paratope



Tumor antigen

Antibody

Bicycle® molecule

The Bicycle® Advantage: Optimal properties for precision guided therapeutics

- Small size for rapid tissue penetration
- Tunable PK for optimized target vs. systemic exposure
- High affinity and selectivity for precision targeting and tumor retention

PK: pharmacokinetics.

We believe The Bicycle® Advantage will lead to enhanced patient benefits

Precision Guided Therapeutics

- Rapid tumor penetration
- Minimized systemic exposure
- Minimal off-target activity
- Tumor retention

Greater Tolerability

- Improved adherence to optimized dosage regimen
- Better combinability

Enhanced Patient Benefit

- Longer responses
- Deeper/broader responses

Our goal: Help patients live longer and live well

We are building a robust pipeline of Bicycle therapeutics

Target	Molecule	Study	Indication	Preclinical	IND enabling/ human imaging	Early-Stage Development	Late-Stage Development
Internal oncology programs							
EphA2	**nuzefatide pevedotin (BDC® molecule)**	Ph2 open label	PDAC				
		Ph1/2 combo with nivolumab	2L+ mUC				
	^{68}Ga BIA molecule	Utility study	All comers				
	EphA2 BRC® molecule	Preclinical					
MT1-MMP	**^{68}Ga BIA molecule**	Utility study	All comers				
	BT1702 (BRC® molecule, ^{212}Pb)	IND enabling	All comers				
Nectin-4	**zelenectide pevedotin (BDC® molecule)**	**Duravelo-2** Ph2 combo with pembrolizumab	1L mUC				
			2L+ mUC				
	BT7480 (Bicycle TICA®)	Ph1/2 combo with nivolumab	All comers				
Additional targets	**Undisclosed**	Preclinical					
Partnered programs							
PLN	**ION826/AZD4063**	Phase 1	Cardiometabolic disease				

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1L: 1st line; 2L+: 2nd line or later; IND: Investigational New Drug; mUC: metastatic urothelial cancer; PDAC: pancreatic ductal adenocarcinoma; BIA: Bicycle® Imaging Agent; BDC®: Bicycle® Drug Conjugate: BRC®: Bicycle® Radioconjugate; TICA® : Bicycle tumor-targeted immune cell agonist®; PLN: phospholamban gene

Nuzefatide pevedotin (formerly BT5528), a potential first-in-class EphA2 targeting BDC® molecule

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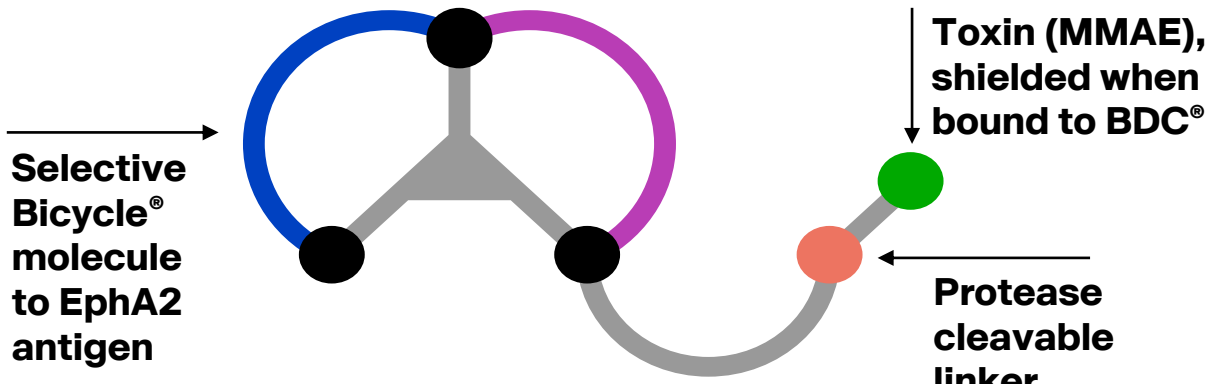
Nuzefatide pevedotin (BT5528): a potential EphA2 targeted therapy



~4 kDa versus ~150+ kDa for ADCs

Lead tumor being studied (Ph2):
Pancreatic

Additional tumors of interest:

Head and neck, Urothelial

Nuzefatide pevedotin

- Novel, potent and selective small peptide
- Targets EphA2 without treatment limiting toxicity seen with other modalities
- Differentiated pharmacology to deliver validated payload
- Generally well-tolerated at clinically active doses in Phase 1/2 trial
- Potential for combinability and long mDOR

Nuzefatide is a differentiated candidate targeting the 'undruggable'

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BDC: Bicycle drug conjugate; EphA2: ephrin type-A receptor 2; mDOR: median duration of response; MMAE: monomethyl auristatin E; Ph2: Phase 2

Multiple antibody-based approaches to target EphA2 have been unsuccessful due to toxicity or lack of efficacy

Molecule	MEDI-547 (Medimmune)	ATRC-301 (Atreca)	MM-310 (Merrimack)	DS-8895a (Daiichi Sankyo)
Format	Antibody drug conjugate	Antibody drug conjugate	scFv antibody fragments conjugated to docetaxel-based liposomes	Afucosylated antibody
Development status	Discontinued during phase 1	Discontinued preclinically	Discontinued during phase 1	Discontinued after phase 1
	"The study was stopped before cohort 2 enrollment due to **treatment-related bleeding and coagulation events**"[1]	Non-human primate toxicology study "revealed **safety signals**, including **bleeding**"[2]	"Phase 1 study unable to reach optimal therapeutic index" due to "**cumulative peripheral neuropathy**"[3]	"**Limited therapeutic efficacy** at doses evaluated and ^{89}Zr-DS-8895a demonstrated low tumour uptake."[4,5]

Successfully targeting EphA2 could provide new ways to address unmet need across tumor types

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[1]Annunziata *et al*, Invest New Drugs. 2013, 31(1): 77-84; [2]Atreca Inc., press release Nov 10, 2022; [3]Merrimack Pharmaceuticals Inc., press release April 4, 2019; [4]Gan *et al*, Invest New Drugs. 2022, 40(4): 747-755; [5]Shitara *et al*, Journal for ImmunoTherapy of Cancer. 2019, 7(1): 219-230. EphA2: ephrin type-A receptor

Patient demographics and clinical characteristics for nuzefatide pevedotin in key dose range finding cohorts

Patient characteristic	All patients (N=161)	Nuzefa 6.5 mg/m² Q2W (n=74)	Nuzefa 8.0 mg/m² Q2W (n=12)	Nuzefa 6.5 mg/m² Q2W + nivo 480 mg Q4W (n=14)
Age, median years (range)	63 (33–83)	63 (33-78)	61 (48-74)	69 (56–83)
Sex, n (%)				
Male	71 (44)	34 (46)	7 (58)	11 (79)
Female	90 (56)	40 (54)	5 (42)	3 (21)
Race, n (%)				
White	129 (80)	55 (74)	12 (100)	13 (93)
Black or African American	5 (3)	0	0	0
Other	27 (17)	19 (26)	0	1 (7)
Baseline ECOG PS, n (%)				
0	66 (41)	30 (40)	5 (42)	8 (57)
1	95 (59)	44 (60)	7 (58)	6 (43)
Tumor type, n (%)				
Urothelial	51 (32)	20 (27)	3 (25)	14 (100)
Non-small cell lung	14 (9)	9 (12)	0	0
Head and neck	17 (11)	8 (11)	9 (75)	0
Pancreas	9 (6)	1 (1)	0	0
Prior lines of therapy in the locally advanced/metastatic setting, median (range)	3 (1–13)	3 (1–13)	2 (1–5)	2 (1–6)
Prior therapy, n (%)				
Checkpoint inhibitor	95 (59)	44 (60)	11 (92)	14 (100)
Platinum	146 (91)	66 (89)	11 (92)	13 (93)
Antimetabolite	115 (71)	53 (72)	8 (67)	12 (86)
Antibody-drug conjugate	36 (22)	16 (22)	2 (17)	11 (79)
Taxane	100 (62)	50 (68)	8 (67)	1 (7)
Antineoplastic	49 (30)	23 (31)	3 (25)	2 (14)
FGFR inhibitor	6 (4)	2 (3)	0	2 (14)

Data as of 09Feb2026. ECOG PS: Eastern Cooperative Oncology Group performance status; FGFR: fibroblast growth factor receptor; nivo: nivolumab; nuzefa: nuzefatide pevedotin; Q2W: once every two weeks; Q4W: once every 4 weeks

Nuzefatide pevedotin is generally well tolerated at clinically active doses both as a monotherapy and in combination with nivolumab

Category, n (%)	All patients (N=161)	Nuzefa 6.5 mg/m² Q2W (n=74)	Nuzefa 8 mg/m² Q2W (n=12)	Nuzefa 6.5 mg/m² Q2W + nivo 480 mg Q4W (n=14)	
TEAEs Grade ≥3	157 (98) 87 (54)	70 (95) 35 (47)	12 (100) 7 (58)	14 (100) 11 (79)	
TESAEs Grade ≥3	52 (32) 47 (29)	17 (23) 16 (22)	3 (25) 3 (25)	8 (57) 8 (57)	
				Nuzefa-related	**Nivo-related**
TRAEs Grade ≥3	143 (89) 42 (26)	68 (92) 16 (22)	12 (100) 3 (25)	12 (86) 4 (29)	10 (71) 3 (21)
TRSAEs Grade ≥3	14 (9) 12 (8)	6 (8) 5 (7)	0 0	1 (7) 1 (7)	2 (14) 2 (14)
Dose modifications				**Nuzefa**	**Nivo**
TEAEs leading to dose reduction TEAEs leading to drug interruption TEAEs leading to drug withdrawn	18 (11) 68 (42) 4 (3)	2 (3) 18 (24) 2 (3)	3 (25) 5 (42) 0	2 (14) 10 (71) 0	0 6 (43) 2 (14)

Very few adverse events led to the withdrawal of nuzefatide across the dose range finding cohorts

Data as of 09Feb2026. Nivo: nivolumab; nuzefa: nuzefatide pevedotin; Q2W: once every 2 weeks; Q4W: once every 4 weeks; TEAE: treatment-emergent adverse event; TESAE: treatment-emergent serious adverse event; TRAE: treatment-related adverse event; TRSAE: treatment-related serious adverse event.

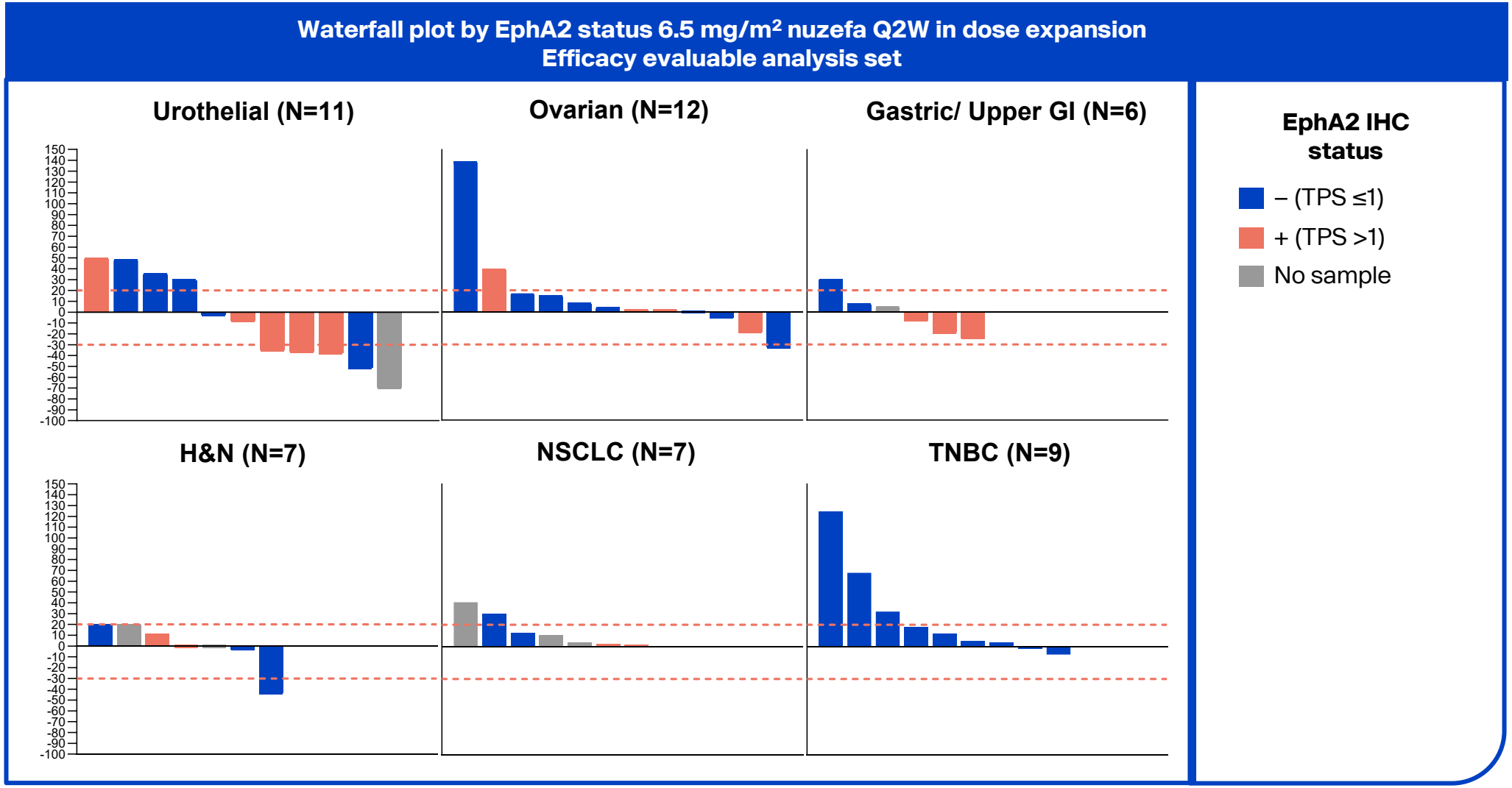
Nuzefatide pevedotin shows a differentiated safety profile with no bleeding to date and few Grade 3 toxicities associated with ADCs

TRAEs of clinical interest[a,b], n (%)	All Patients (N=161)		Nuzefa 6.5 mg/m² Q2W (n=74)		Nuzefa 8.0 mg/m² Q2W (n=12)		Nuzefa 6.5 mg/m² Q2W + nivo 480 mg Q4W (n=14)	
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Peripheral neuropathy[c]	31 (19)	0	13 (18)	0	2 (17)	0	2 (14)	0
Skin reactions[d]	23 (14)	0	11 (15)	0	2 (17)	0	5 (36)	0
Neutropenia[e]	13 (8)	5 (3)	6 (8)	2 (3)	1 (8)	0	0	0
Eye disorders[f]	5 (3)	0	2 (3)	0	0	0	1 (7)	0
Hemorrhage[g]	0	0	0	0	0	0	0	0

EphA2 targeted ADCs have been plagued with severe bleeding, while MMAE bearing ADCs have been limited by Grade 3 peripheral neuropathy and skin reactions

Data as of 09Feb2026. [a]Includes AEs related to nuzefa; [b]Patients can have multiple PT within a category; [c]Based on MedDRA SMQ [Broad] for peripheral neuropathy; [d]Includes the MedDRA SMQ [broad] for Severe Cutaneous Adverse Reactions (SCAR) and MedDRA SOC of Skin and Subcutaneous Tissue disorders, excluding alopecia; [e]Preferred term; [f]SOC of Eye disorders; [g]Hemorrhage (excluding laboratory terms) [narrow] SMQ. ADC: antibody drug conjugate; EphA2: ephrin type-A receptor 2; MedDRA: Medical Dictionary for Regulatory Activities; nivo: nivolumab; nuzefa: nuzefatide pevedotin; PT: Preferred Term; Q2W: once every 2 weeks; Q4W: once every 4 weeks; SCAR: Severe Cutaneous Adverse Reactions; SMQ: Standardized MedDRA Queries; SOC: system organ class; TRAE: treatment-related adverse event.

Nuzefatide pevedotin monotherapy is active across a range of EphA2+ tumor types in the late line setting



Data as of 09Feb2026. EphA2: ephrin type-A receptor 2; GI: gastrointestinal; H&N: head and neck carcinoma; NSCLC: non-small cell lung cancer; nuzefa: nuzefatide pevedotin; Q2W: once every 2 weeks; TNBC: triple-negative breast cancer; TPS: Tumor Proportion Score

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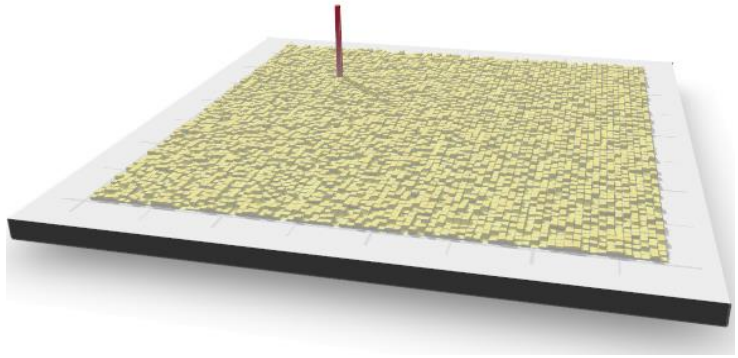
Nuzefatide pevedotin binds only to EphA2, and clinically shows rapid delivery and tumor retention with limited systemic exposure

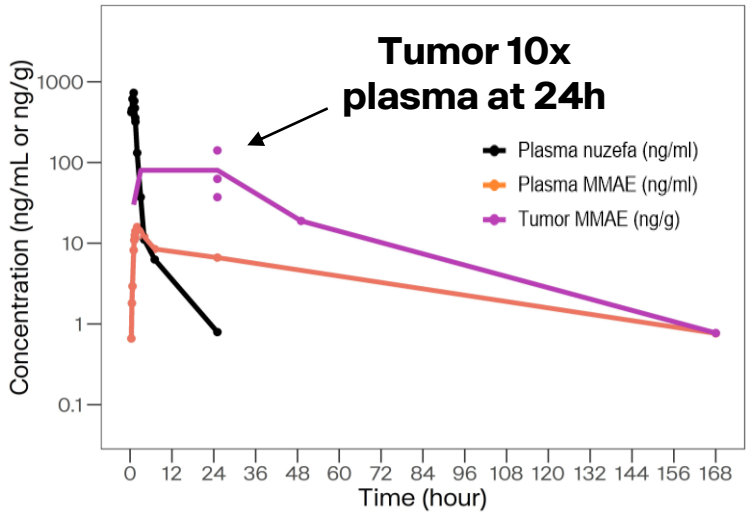
Ligand-binding domain	Binding affinity (SPR K_D nM)
EphA2	1.2
EphA1	>5000
EphA3	>5000
EphA4	>5000
EphA5	>5000
EphA6	>5000
EphA7	>5000
EphB4	>5000

Nuzefatide has exquisite selectivity for EphA2 over other Eph family members

Nuzefatide only binds EphA2



Membrane protein array: no binding of nuzefatide @1µM to 5,527 other proteins, including Fc receptors



Human PK following treatment with nuzefatide at 5 mg/kg, the estimated minimum efficacious dose (MED)

Nuzefatide human PK shows delivery & retention of payload in tumor, with rapid clearance from circulation

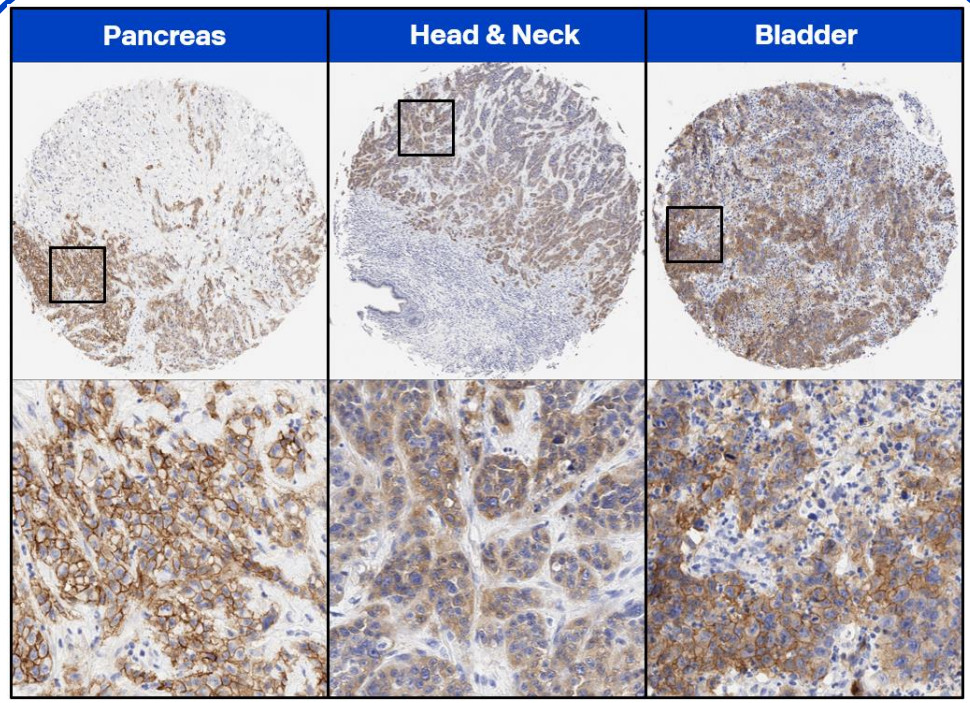
Nuzefatide has a differentiated profile from ADCs that often bind to additional Fc receptors and proteins

ADC: antibody drug conjugate; EphA2: ephrin type-A receptor 2; Fc receptor: fragment crystallizable receptor; PK: pharmacokinetics

EphA2 is a widely expressed tumor antigen with highest expression in pancreatic cancer

Indication	% TPS ≥1	Mean H-score
Pancreas	**63.4%** (59/93)	74.7
HNSCC	**61.4%** (43/70)	19.9
Bladder	**50.0%** (28/56)	34.8
Rectal adeno	**47.3%** (43/91)	44.7
Esophagus	**37.1%** (26/70)	38.8
Melanoma	**36.7%** (29/79)	88.8
GEJ	**28.0%** (23/82)	12.6
CRC	**25.2%** (35/139)	35.3

Data generated internally using commercial TMA samples and CST mAb (clone D4A2), detecting the intracellular domain of EphA2[1]



All data shown uses EphA2 CST 6997 mAb (Cell Signaling Technology) to detect the intracellular domain of EphA2 using commercially available tissue microarray (TissueArray) and whole slides (Discovery Life Science). TPS ≥ 1 (membrane and/or cytoplasmic) was used to determine positivity

EphA2 is expressed in a range of high value tumors including pancreas, HNSCC and urothelial

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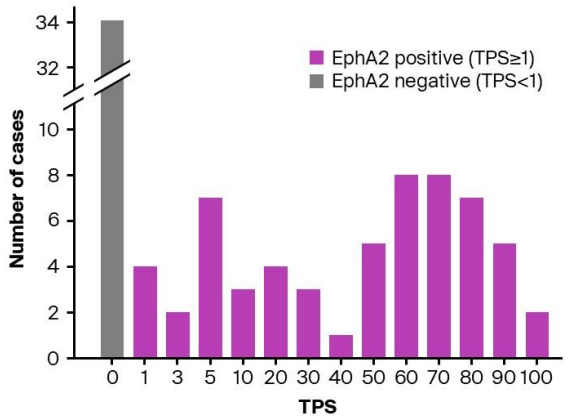
[1]Bicycle Therapeutics unpublished data. CRC: colorectal cancer; CST: Cell Signaling Technology; EphA2: ephrin type-A receptor 2; GEJ; gastroesophageal; HNSCC: head and neck squamous cell carcinoma; mAb; monoclonal antibody; TMA; tumor tissue microarray; TPS: Tumor Proportion Score

EphA2 is a clinically validated target, and the Bicycle advantage can potentially apply in pancreatic cancer

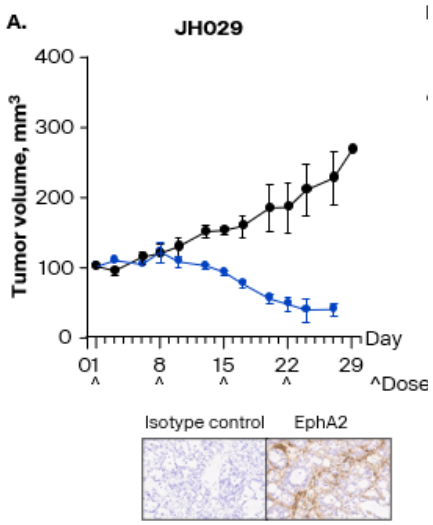
EphA2 PDAC expression

Highly expressed in PDAC TPS>1 (>60% of PDAC)



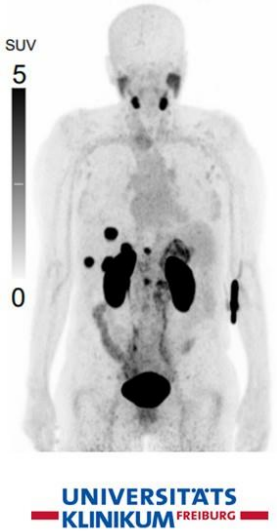
PDAC sensitivity to MMAE

PDAC PDX models responsive to MMAE



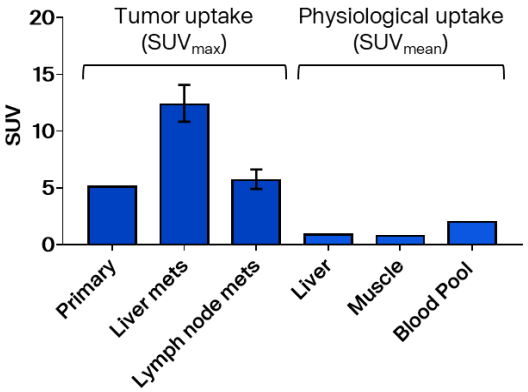
Patient identification strategy

^{68}Ga BIA5501 >80%[1] EphA2 +ve in human imaging



Bicycle advantage in PDAC

Bicycle approach overcomes high intra-tumoral pressure & dense stroma



SUV values showing tracer uptake in patient with lymphonodal and hepatic metastasized pancreatic ductal adenocarcinoma

[1]15 out of 18 patients; ^{68}Ga: Gallium-68 radioactive positron-emitting radioisotope; EphA2: ephrin type-A receptor 2; PDAC: pancreatic ductal adenocarcinoma; PDX: patient-derived xenograft; TPS: Tumor Proportion Score

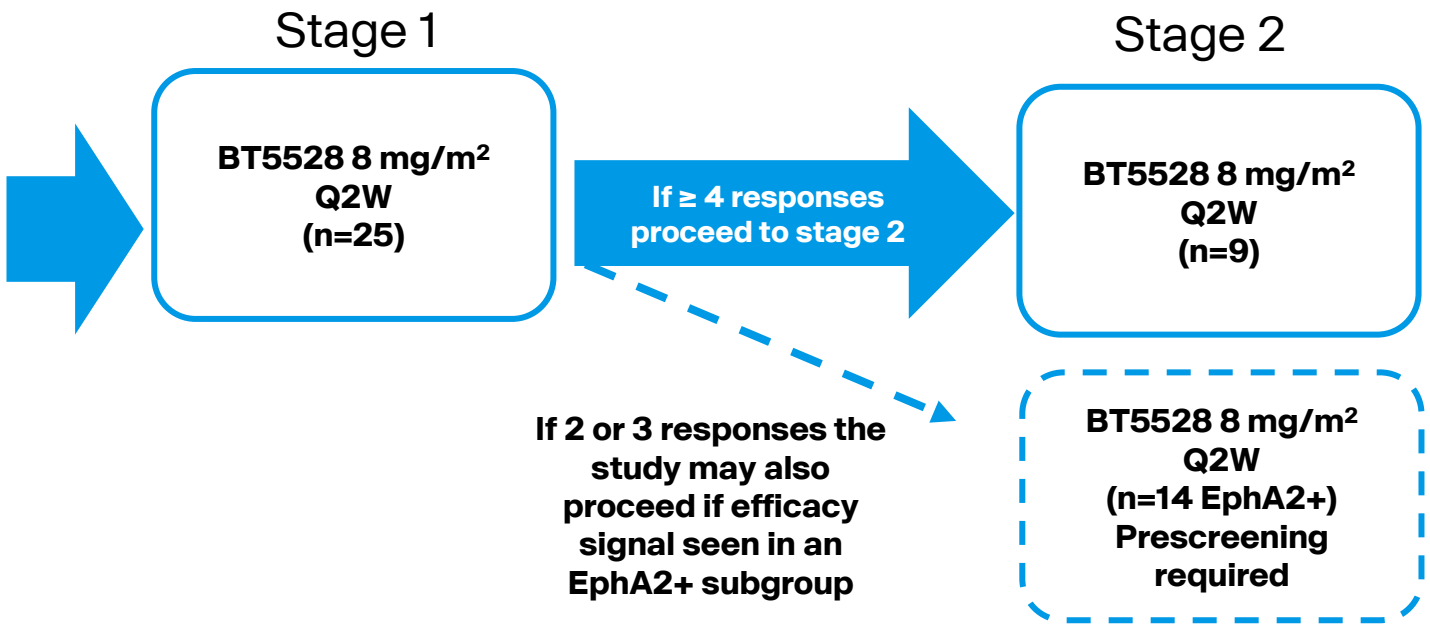
We are exploring nuzefatide pevedotin in a Phase 2 2L+ pancreatic cancer study

BT5528-201 Schema

Eligibility

- Metastatic recurrent PDAC*
- Failed one current line of therapy
- Measurable disease on RECIST v1.1
- ECOG PS 0 or 1
- Taxane naïve
- Evaluable archival or fresh tumor biopsy

*Metastatic recurrent PDAC 2L+ to include any KRASi in either 1L or 2L



Primary Endpoint

- ORR by investigator using RECIST v1.1

8 mg/m² Q2W selected as preferred monotherapy dose based on acceptable safety profile and enhanced ability to deliver payload to tumor[1]

[1]Bicycle Therapeutics unpublished data. 2L: second-line; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EphA2: ephrin type-A receptor 2; ORR: objective response rate; PDAC: pancreatic ductal adenocarcinoma; Q2W: once every 2 weeks; RECIST: Response Evaluation Criteria in Solid Tumors.

Pancreatic cancer could provide an important opportunity for nuzefatide pevedotin to bring a first-in-class treatment to patients

Annual Incidence (Stages 0-IV)[1,2,3]

510,992 Worldwide
65,176 United States

Rank among all cancers (Incidence)

12 Worldwide
11 United States

Patients diagnosed at advanced stage

80%

5-year Survival

11% / 3%
Stages 0-IV Stage IV

Pancreatic cancer

- Considered a silent killer due to the asymptomatic nature of the disease
- Position of the pancreas limits clinical symptoms until tumors reach more advanced stages
- **Poor prognosis due to lack of early diagnosis, quick dissemination to distant sites, and high resistance to current systemic therapies[4,5]**

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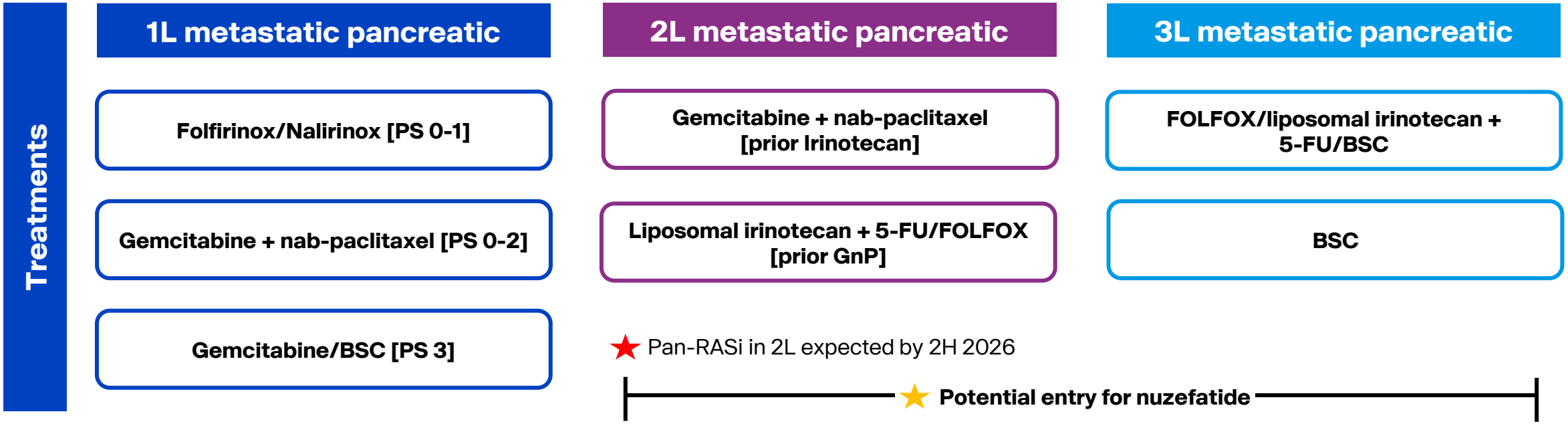
[1]Oracle Life Sciences CancerMPact, Treatment Architecture US Pancreatic Cancer, Sep 2025. Sources: Based on CancerMPact® Patient Metrics U.S., accessed Feb 2025. Ranking is based on relative incidence of 32 tumors in the US; [2]World Health Organization, International Agency for Research on Cancer: Cancer Fact Sheet, Pancreas (gco.iarc.who.it) [3]Li, Lancet, 2004 [4]NCCN Guidelines Pancreatic Adenocarcinoma, Version 2, 2025; [5]Zhou, Int J Cancer, 2017.

The pancreatic treatment landscape is shifting rapidly, but nuzefatide pevedotin may uniquely provide benefit for patients



Potential benefits of nuzefatide pevedotin in 2L+ setting include:

- **Use in patients that develop RASi resistance as treatment landscape evolves**
- **Given rechallenge is seen to have limited benefit[1], targeted delivery of MMAE offers distinct payload**
- **Differentiated safety profile allows opportunity for patients exposed to 1-2 lines of prior treatment**

[1]Putnam key opinion leader insight market research conducted December 2025.
1L: first-line; 2L: second-line; 3L: third-line; 5-FU: fluorouracil; BSC: best supportive care; FOLFIRINOX: folinic acid (leucovorin), 5-FU, irinotecan, and oxaliplatin; FOLFOX: leucovorin, 5-FU and oxaliplatin; GnP: gemcitabine/nab-paclitaxel; NALFIRINOX: liposomal irinotecan (Onivyde), 5-FU, leucovorin, and oxaliplatin; PS: Performance Status; RASi: pan-RAS (rat sarcoma) inhibitor

Bicycle® radioligand pipeline

Bicycle®

Our strategy in radiopharmaceuticals is to be a next-generation player with sustainable access to all isotopes

Partner with leaders in the field

- Build our understanding through strategic partnerships

  Bayer

- Partner with academia to deepen our knowledgebase
- Build unique internal portfolio guided by KOLs

  dkfz. Universitätsmedizin Essen Universitätsklinikum

Pursue novel targets with first-in-class potential

- Platform proven to identify novel peptide ligands
- Use early imaging data to direct indication selection for BRC® and BDC® molecules and build programs in a data-driven manner
- Enable optimal clinical and commercial positioning of BRC® molecules

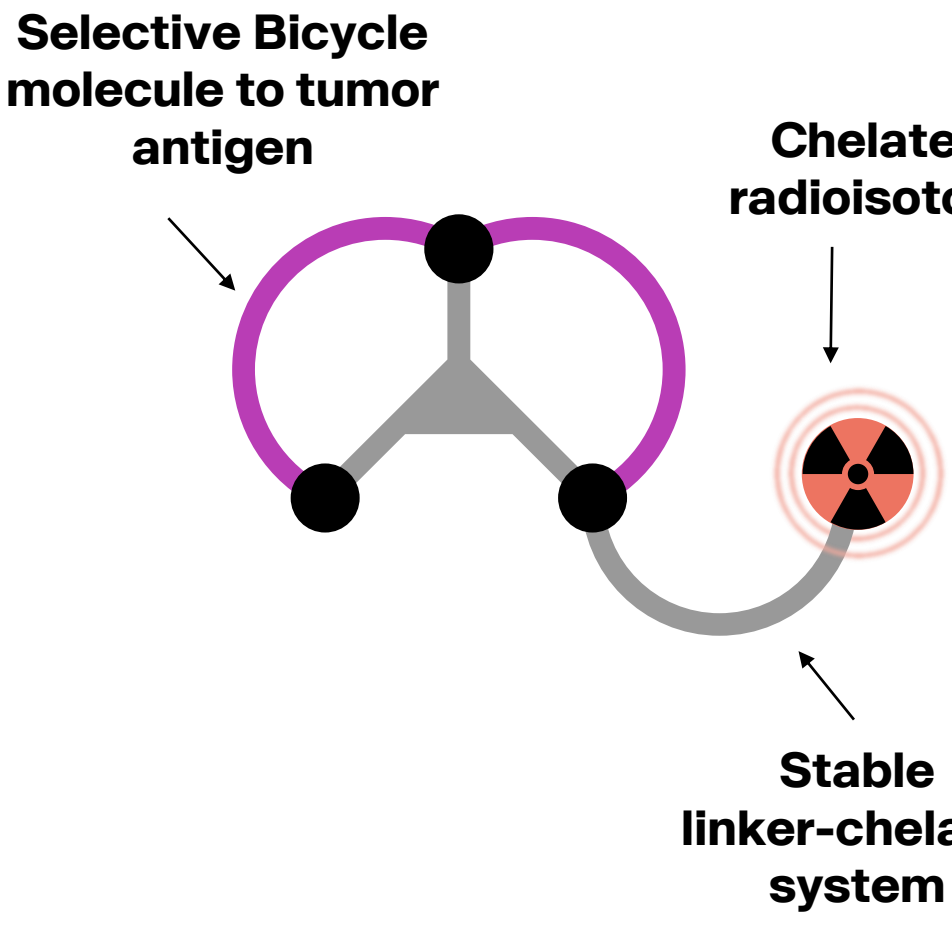
Use the isotope best suited for the target

- Test BRC® molecules with a range of isotope payloads and select the best
- Establish arrangements with leading isotope suppliers & manufacturers

  Eckert & Ziegler SpectronRx NDA NATIONAL NUCLEAR LABORATORY

- Scale to support broad portfolio of clinical applications

Bicycle® molecule advantages for delivering cytotoxic payloads are also advantages for delivering radioisotopes

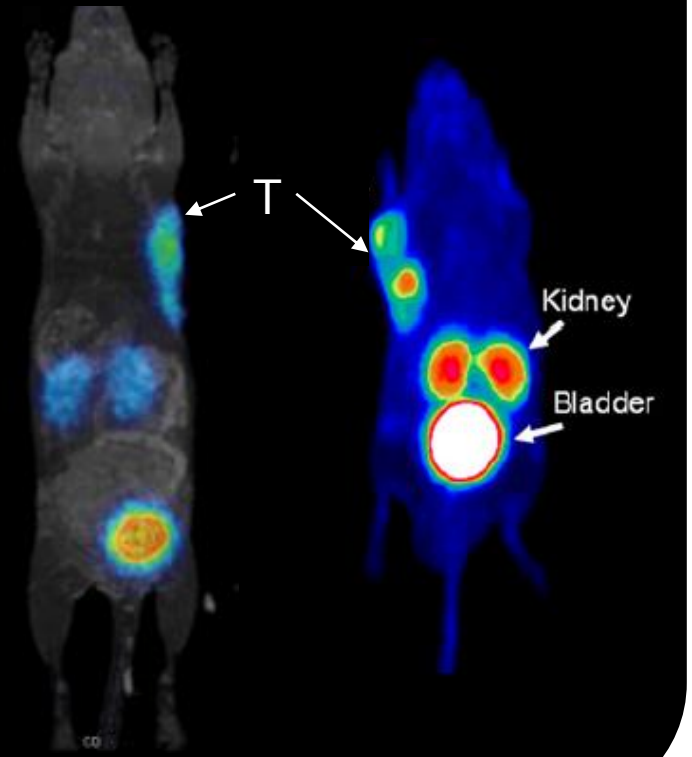


- Highly selective and tumor penetrant
- Pipeline of Bicycle molecules to novel tumor antigens
- Minimal systemic exposure

Bicycle® radioligands show selective tumor uptake and ideal PK across a range of targets and tumor models

MT1-MMP

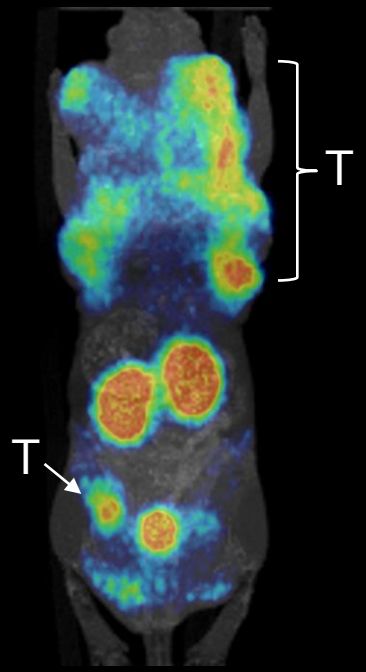
Fibrosarcoma



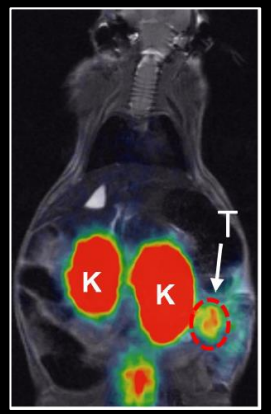
Left: HT1080 tumor model, 2h P.I. (DKFZ unpublished data)
Right: HT1080 tumor model, 40 to 60 min P.I. Eder M et al. 2019. *Cancer Res.* 79(4):841-852

EphA2

Breast



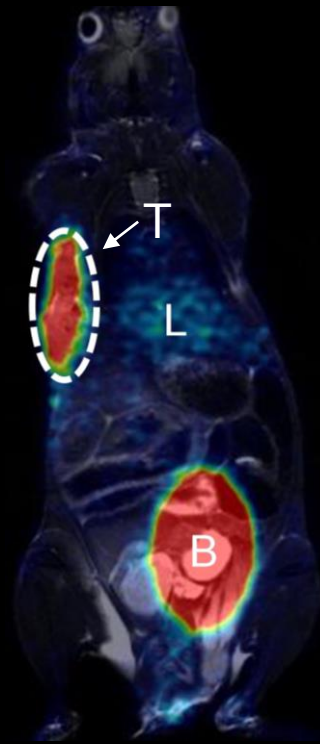
Pancreatic

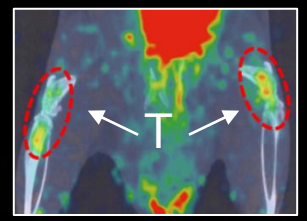


Left: MMTV-PyMT transgenic mouse model, 2h P.I.
Right: Panc-1 orthotopic tumor model 1h P.I.
Sharma AK et al. 2023. *Cancer Res,* 83(7 Suppl):2768

CD38

Multiple myeloma





Left: MOLP8 tumor xenograft, 90 min P.I.
Right: MOLP8 disseminated tumor model (Sharma AK et al. BioRxiv)

Bicycle® dkfz.

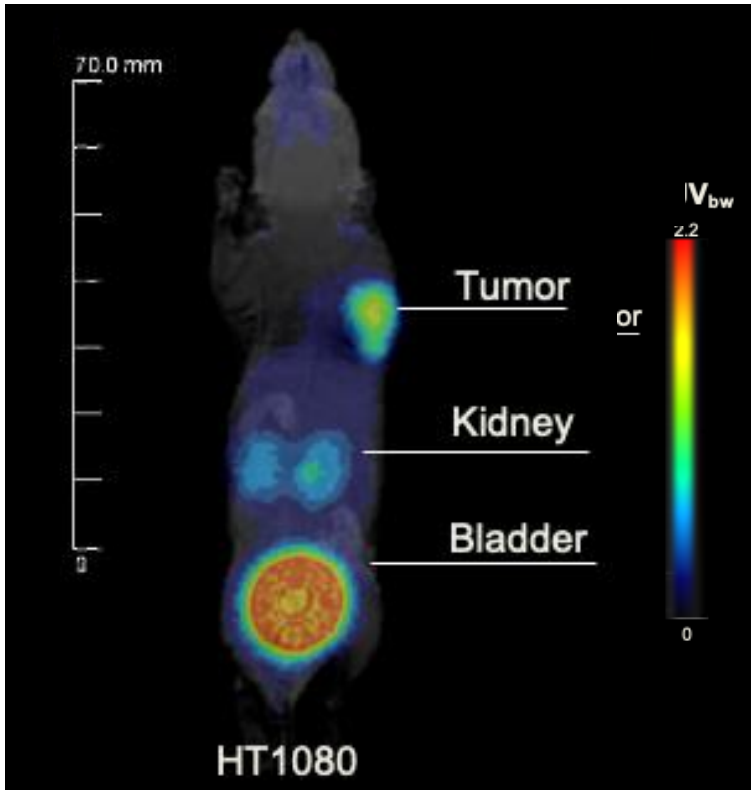
MT1-MMP is a novel target in the treatment of cancer

- Membrane type 1 matrix metalloproteinase (MT1-MMP)
- Overexpressed in variety of cancers and associated with poor prognosis
- Potential first-in-class opportunity

Tumor Type	Number of cases tested	MT1-MMP positive
Lung squamous	76	**59%**
Bladder	96	**56%**
Esophageal	66	**55%**
Triple negative breast cancer	81	**43%**
Ovarian cancer	82	**11%**
Lung adenocarcinoma	69	**9%**

MT1-MMP expression was determined using IHC performed with in house validated antibody, positive cases were defined as H-score ≥ 50 in tumor cell membrane.

Early MT1-MMP-targeting BIA molecules show high tumor enrichment in PET imaging studies



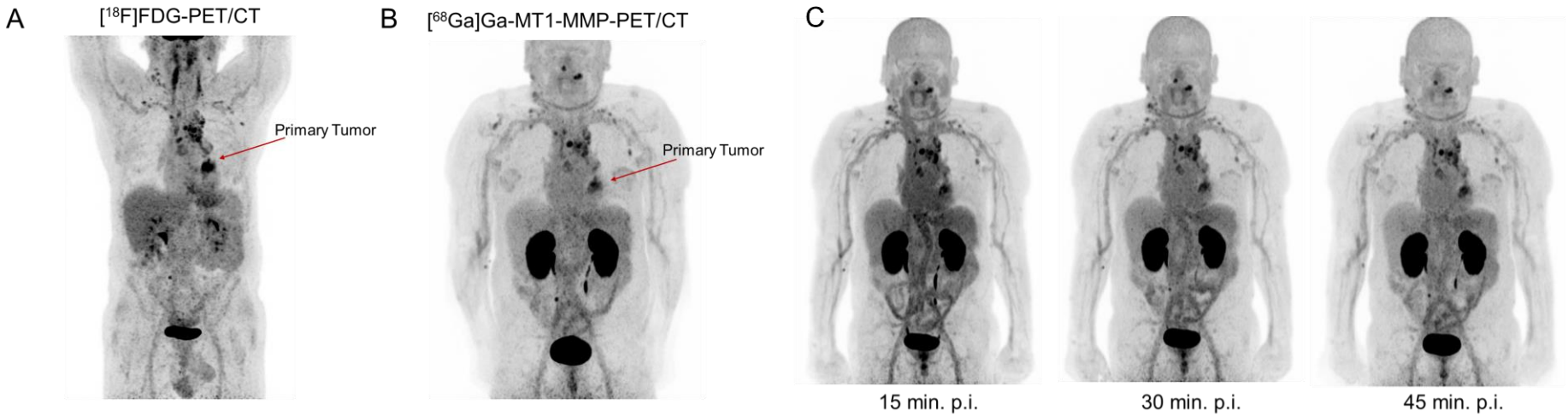
Whole-body maximum intensity projection of ^{68}Ga-labeled BIA molecule targeting MT1-MMP 60 min. p.i. obtained from PET/MR imaging

Bicycle®

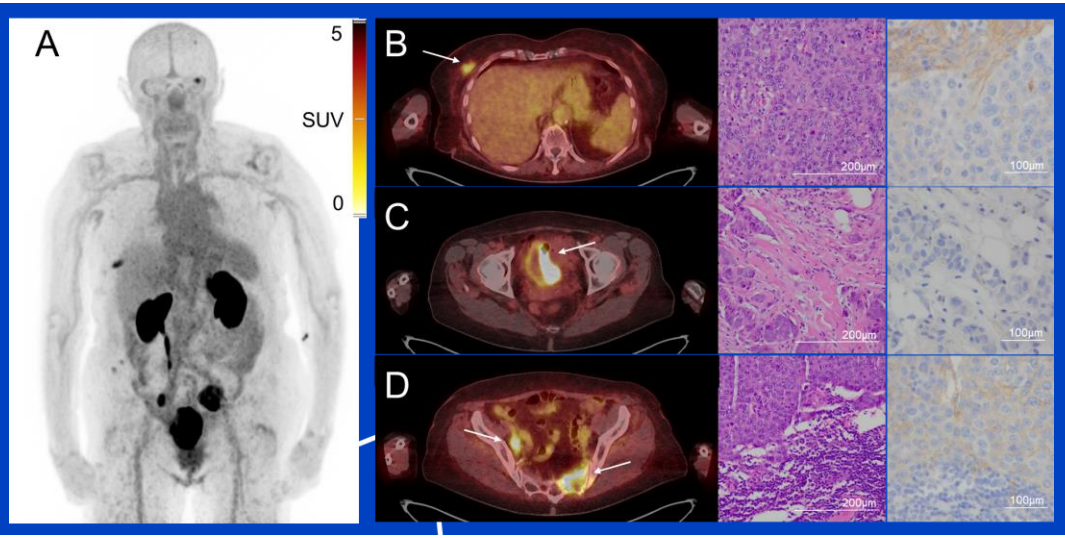
1. Gelb T et al. 2019. *Mol Cancer Ther*, 18(12_Suppl):A047. 2. Eder M et al. 2019. *Cancer Res*. 79(4):841-852.

BIA: Bicycle® Imaging Agent

First human MT1-MMP imaging representative of data seen so far in 12 patients with various solid tumors



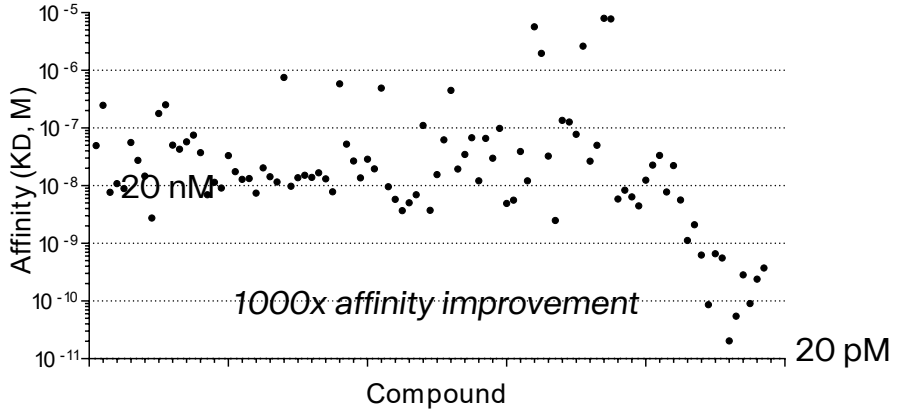
MT1-MMP-PET/CT imaging in advanced pulmonary adenocarcinoma.
Maximum intensity projections of [^{18}F]FDG-PET/CT (A) and [^{68}Ga]Ga-BCY25286 PET/CT at 60 mins (B) and at early time points (C) post injection.



MT1-MMP-PET/CT imaging in breast and urothelial cancer.
Maximum intensity projection of [^{68}Ga]Ga-BCY25286 PET imaging (A) with representative axial PET/CT fusion slices (B-D) and corresponding immunohistochemistry staining (H&E, MT1-MMP-specific) showing the primary breast cancer (B) and bladder cancer (C) with both lymph node and bone metastases in the left sacral bone (D; white arrows). Immunohistochemistry confirmed membranous or stromal MT1-MMP expression in the primary breast cancer, bladder cancer and lymph node metastasis.

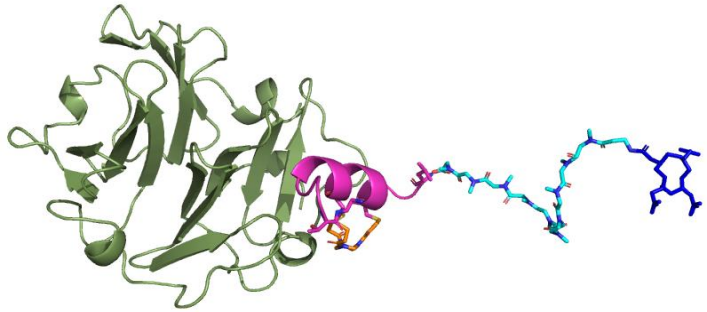
Generation of an MT1-MMP BRC® molecule with potential theranostic applications

Binding properties



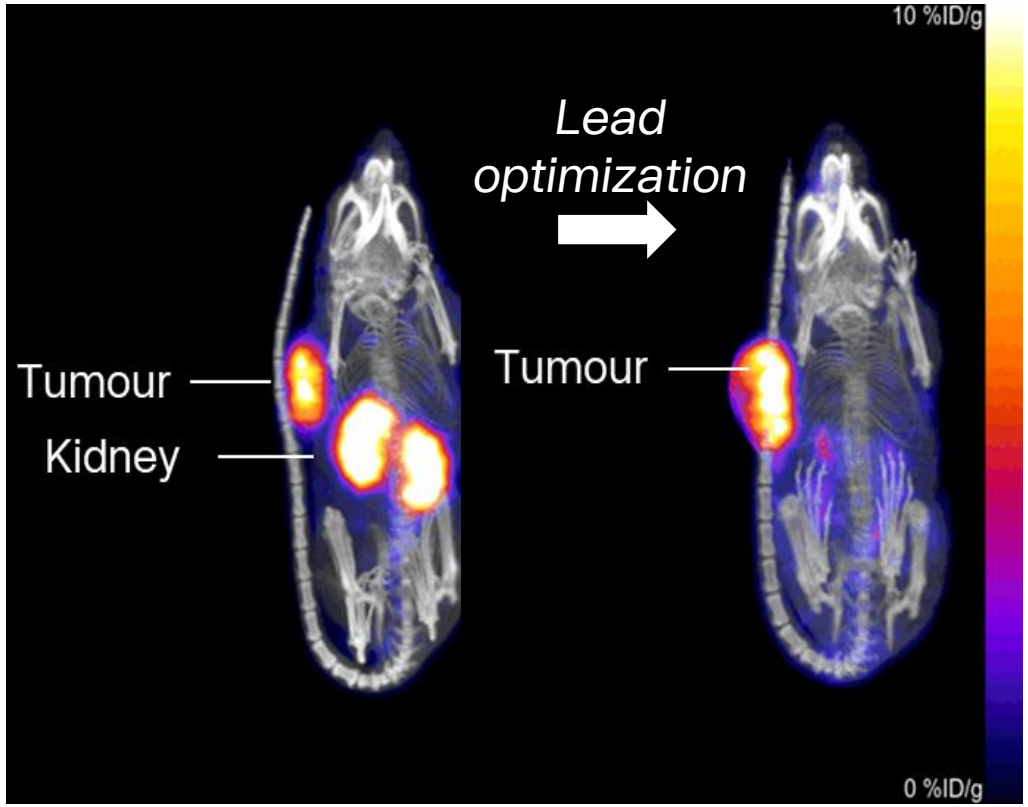
Binding affinities of compounds synthesized during lead optimization, as determined by surface plasmon resonance.

Structurally enabled



A co-crystal structure of MT1-MMP protein and bicyclic peptide was obtained and used to study molecular interactions and guide chemical optimisation

Kidney uptake / retention



^{111}In SPECT images of early (left) versus optimized (right) BRC® molecules 24 hours post injection. Optimized BRC® molecule shows reduced payload levels in the kidneys and maintains high payload levels in the tumor.

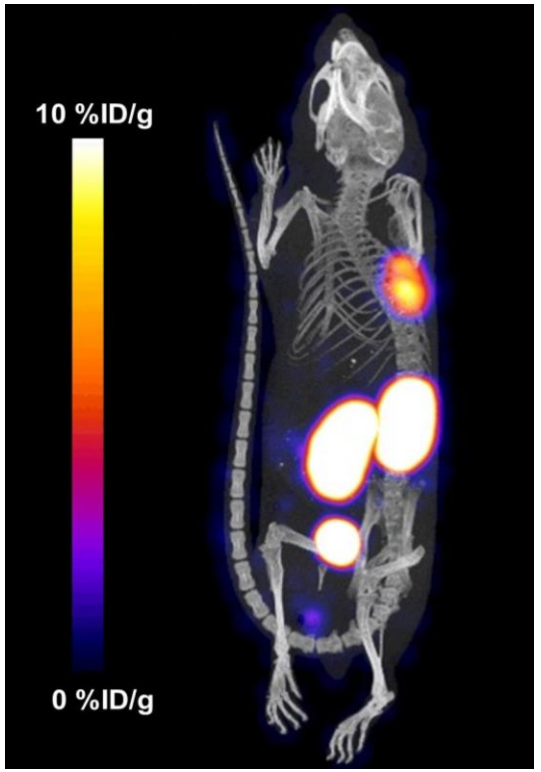
Our next radioligand target: EphA2, a first-in-class opportunity

- EphA2 overexpression associated with higher grade and/or stage in a variety of cancers[1,2]
- Moved into human imaging in 2025

Tumor Type	Number of cases tested	EphA2 positive
Pancreatic	80	**60%**
Bladder	139	**58%**
Head and Neck	61	**46%**
Lung squamous	88	**30%**
Stomach	57	**30%**
Ovarian	73	**29%**

EphA2 expression was determined using IHC with pAb (RnD AF3035) on tissue microarrays. Positive cases were defined as TPS score >1 in tumor membrane or cytoplasm. For lung cancer, only samples annotated for adenocarcinoma or squamous subtype were included. TMAs included: Pancreatic - PA2081b, Bladder - BL2082a, Head and Neck - HN803f, Lung squamous – LC1921b and ATGC1118, Stomach - ST1001a, Ovarian - BC11115c, Esophageal - ES2081, TNBC - BR1301, Lung adenocarcinoma – LC706b, LC1921b, and ATGC1118. Cores with ambiguous results were removed. Top 6 indications were listed.

High tumor uptake and low uptake in non-tumor tissues

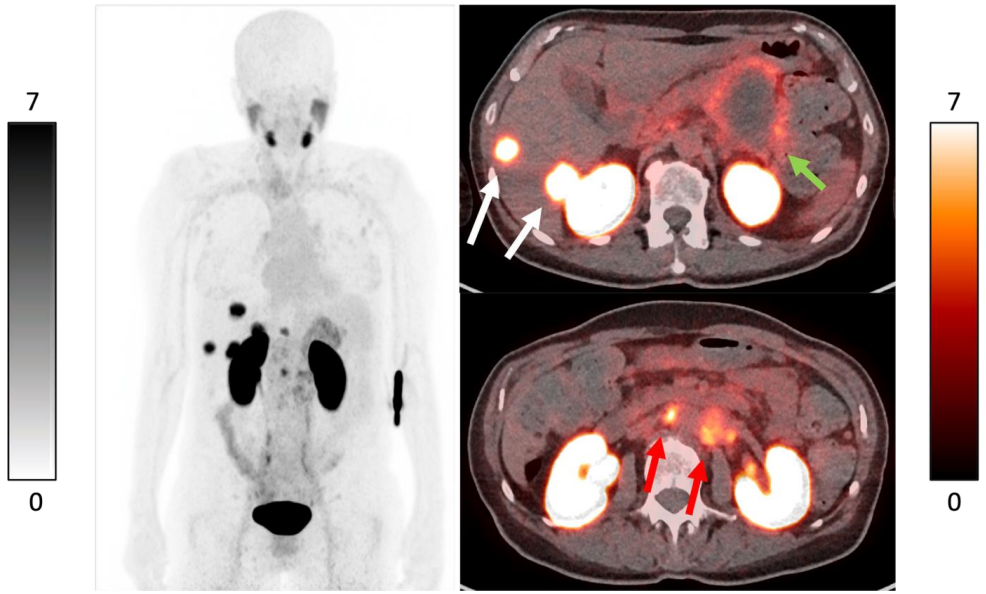


Example SPECT/CT Maximum Intensity Projection (MIP) 60 min. p.i. of 230 pmol of [111In]In labeled BRC® molecule

1. Zhou L et al. 2021. *Int J Clin Exp Pathol*, 14(4):484-49. 2. Cioce M and Fazio VM. 2021. *Cancers (Basel)*, 13(4):700.

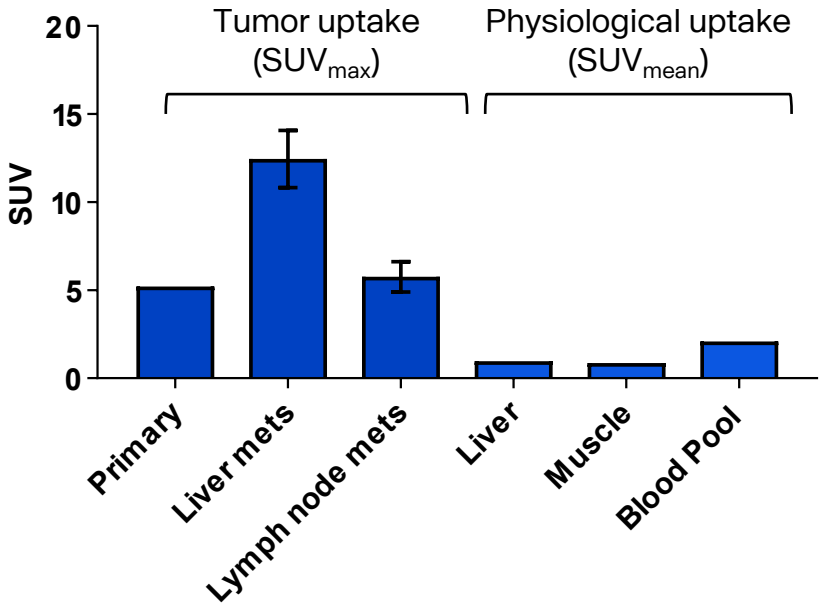
^{68}Ga-labelled EphA2 targeted bicycle imaging agent demonstrates target expression and availability for Bicycle engagement

Patient with lymphonodal and hepatic metastasized pancreatic ductal adenocarcinoma imaged with ^{68}Ga-labelled EphA2 targeted bicycle peptide



Maximum intensity projection (left) acquired 45 minutes p.i.. Fused axial PET/CT images (right) 45 minutes p.i. showing pancreatic tumor mass (green arrow), hepatic metastases (white arrows) and lymphonodal metastases (red arrows).

Standardized uptake values in primary tumor, metastases and physiologic uptake



SUV values showing tracer uptake in patient with lymphonodal and hepatic metastasized pancreatic ductal adenocarcinoma

- Demonstrates feasibility of payload delivery to primary and metastatic lesions in patients with PDAC through EphA2 targeting
- Rapid visualisation of primary tumor/metastases within 15 minutes of tracer injection
- Potential diagnostic tool for EphA2-positive malignancies, facilitating personalized treatment strategies

Bicycle®

^{68}Ga: Gallium-68 radioactive positron-emitting radioisotope; CT: computed tomography; EphA2: ephrin type-A receptor 2; PDAC: pancreatic ductal adenocarcinoma; PET: positron emission tomography; SUV: standardized uptake values

Radioisotope supply chain is core to our next-generation radio-oncology ambition, enabled by our strategic partners

- Access to broad range of **next-generation radioisotope** payloads to maintain leadership opportunity
- Potential world-leading **radioisotope supply chain**
- Bespoke **^{212}Pb generators** being developed exclusively for Bicycle Therapeutics by SpectronRx, with initial quantities of ^{212}Pb successfully produced

Eckert & Ziegler SpectronRx NDA NATIONAL NUCLEAR LABORATORY

We are building a pipeline of next-generation radioligands to address currently intractable targets

Target	Molecule	Preclinical	Human Imaging / IND enabling	Next Milestone
MT1-MMP	^{68}Ga BIA molecule			
	BT1702 (BRC®, ^{212}Pb)			FTIH 2027
EphA2	^{68}Ga BIA molecule			1H 2026
	BRC® molecule			FTIH 2028
Additional Targets	BIA molecule			
	BRC® molecule			

Bicycle®

FTIH: first time in humans; IND: Investigational New Drug Application; BIA: Bicycle® Imaging Agent; BRC®: Bicycle® Radioconjugate

We believe Bicycle® radioligands are well-positioned to deliver novel radiopharmaceuticals

SUMMARY

- Our technology platform is well-suited to develop radiopharmaceutical medicines, enabling us to pursue novel targets and remain isotope agnostic
- First human imaging data 1) validates the potential of MT1-MMP as a novel target and first-in-class opportunity and 2) helps us understand how BRC® molecules are being distributed throughout the human body
- Our next target will be EphA2, another potential first-in-class opportunity

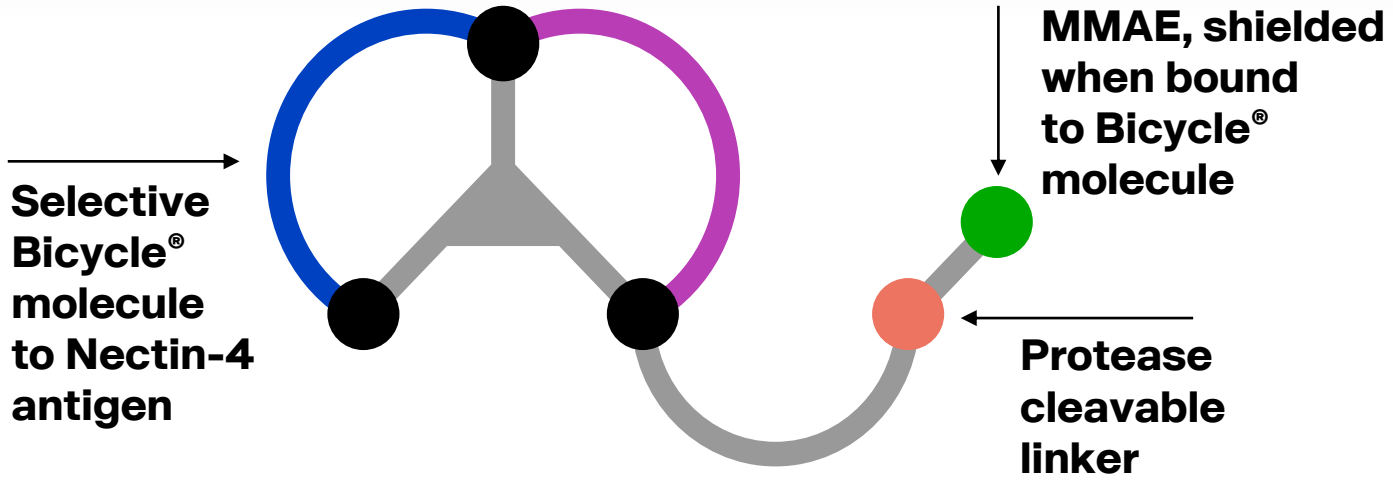
NEXT STEPS

- ✓ **1H 2026: Additional EphA2 human imaging data**
- ▶ **2027: Initiation of the first company-sponsored BRC® clinical trial (BT1702, an MT1-MMP targeting BRC® carrying a ^{212}Pb radioisotope payload for theranostic use)**

Zelenectide pevedotin, a Nectin-4 targeting Bicycle® Drug Conjugate (BDC®)

Bicycle®

Zelenectide targets Nectin-4, a high value target expressed in many tumors



Highly differentiated preclinical performance:

- Superior selectivity
- Excellent activity in multiple tumor models
- Reduced skin/eye toxicity

- Rapidly and extensively binds to Nectin-4 tumors
- Being studied as a potential treatment for multiple solid tumors including **mUC**

MMAE: monomethyl auristatin E; mUC: metastatic urothelial cancer; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer.

In the Ph1/2 Duravelo-1 study, zelenectide has shown a promising response and differentiated safety profile in 2L+ EV-naïve mUC

Patient characteristics

- 45 previously treated patients with mUC were enrolled and treated with zelenectide
  - Median age: 67 years old
  - 93% (42/45) had previously received CPI and platinum-based therapy

Efficacy data

- 38/45 patients were efficacy evaluable[a]
  - **ORR = 45% (17/38)[b]**
- mDOT: 16.1 weeks (range 1-101.4)
- **mDOR: 11.1 months (95% CI [3.9, NR])**
- Median duration of follow-up: 4.2 months (range 0.5-28.6)

TRAEs of Clinical Interest, n (%)	Zelenectide 5 mg/m² QW in 2L+ EV-naïve mUC[c] N=45			
	Grade 1	Grade 2	≥Grade 3	Total
Peripheral neuropathy[d]	9 (20)	7 (16)	0	16 (36)
Peripheral sensory neuropathy[e]	6 (13)	0	0	6 (13)
Skin reactions[f]	6 (13)	2 (4)	0	8 (18)
Hyperglycemia[e]	2 (4)	0	1 (2)	3 (7)
Neutropenia[e]	2 (4)	2 (4)	2 (4)	6 (13)
Eye disorders[g]	2 (4)	1 (2)	0	3 (7)

Data as of 22Mar24.
[a]Number of efficacy-evaluable patients with at least one adequate postbaseline response assessment. One patient had progressive disease because of a new lesion, but did not have an adequate postbaseline target lesion assessment. [b]Responses under response evaluation criteria in solid tumor (RECIST) v1.1. [c]Includes data from dose escalation and dose expansion. [d]Standardized Medical Dictionary for Regulatory Activities (MedDRA) Queries (SMQ) [broad]. [e]Preferred term. [f]Includes the MedDRA SMQ of Severe Cutaneous Adverse Reactions (SCAR) and preferred terms under the MedDRA system organ class (SOC) of Skin and Subcutaneous Tissue disorders, excluding alopecia. [g]SOC of eye disorders.
2L+: 2nd line or later; CPI: checkpoint inhibitor; EV: enfortumab vedotin; mDOR: median duration of response; mDOT: median duration of treatment; mUC: metastatic urothelial cancer; NR: not reached; ORR: overall response rate; QW: weekly; TRAE: treatment-related adverse event.

In the Ph1/2 Duravelo-1 study, zelenectide + pembrolizumab has shown a generally well-tolerated safety profile in 1L cisplatin-ineligible mUC

Patient characteristics

- 22 previously untreated, cisplatin-ineligible mUC patients were enrolled and treated with zelenectide + pembrolizumab
  - Median age: 77 years old
  - **46% (10/22) had an ECOG performance score of 2**

Safety summary

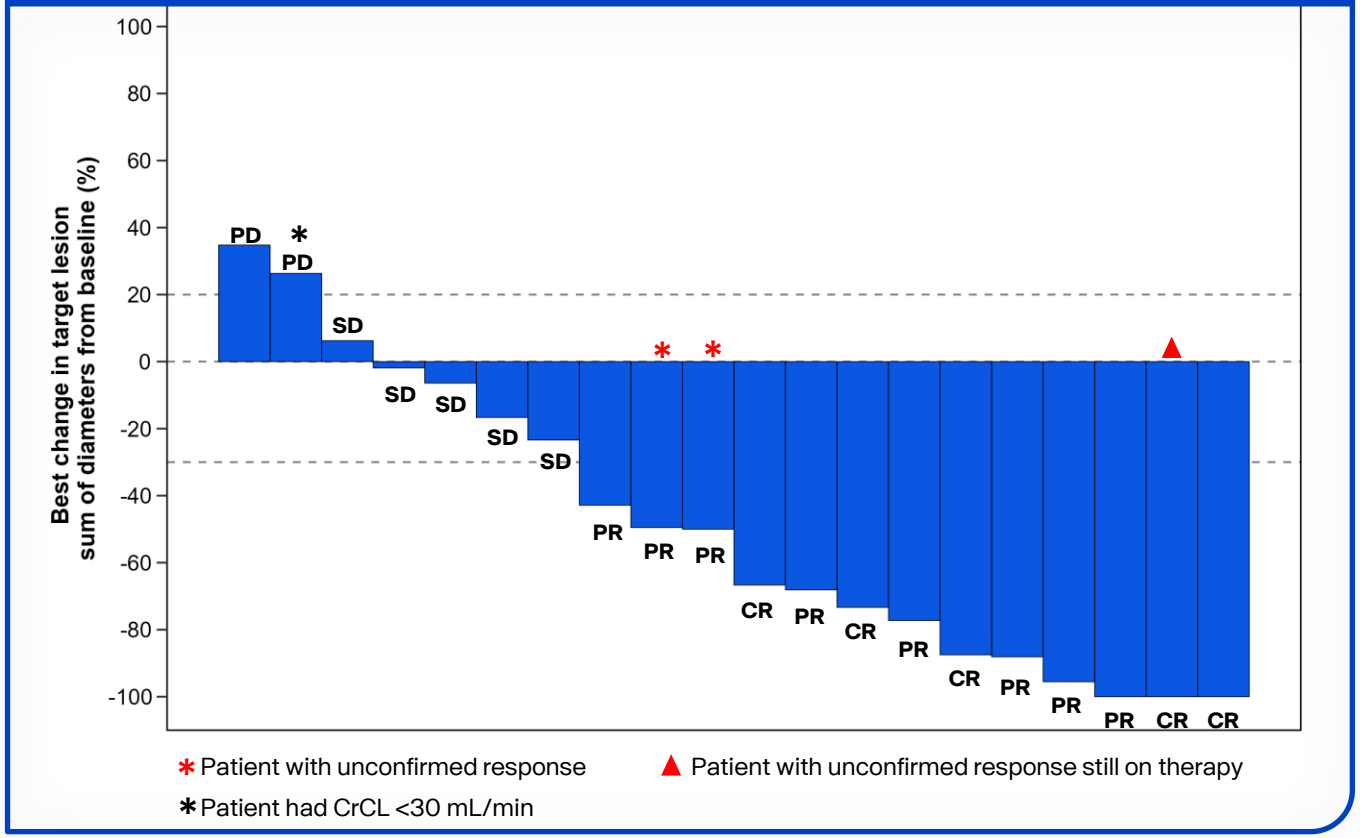
- All cases of Grade 3 TRAEs of clinical interest were reversible
- No Grade 4/5 TRAEs of clinical interest and no treatment-related deaths

TRAEs of Clinical Interest, n (%)	Zelenectide 5 mg/m^2 QW + 200 mg pembrolizumab Q3W N=22 Zelenectide or zelenectide + pembrolizumab-related			
	Any grade	Grade 1	Grade 2	Grade 3
Peripheral Neuropathy[a]	**11 (50)**	**6 (27)**	**3 (14)**	**2 (9)**
Sensory Events[b]	7 (32)	3 (14)	3 (14)	1 (5)
Motor Events[c]	1 (5)	1 (5)	0	0
Skin Reactions[d]	**11 (50)**	**8 (36)**	**2 (9)**	**1 (5)**
Rash	7 (32)	5 (23)	1 (5)	1 (5)
Pruritus	5 (23)	4 (18)	1 (5)	0
Rash Erythematous	1 (5)	0	1 (5)	0
Erythema	1 (5)	1 (5)	0	0
Dry Skin	1 (5)	1 (5)	0	0
Hyperglycemia[e]	**5 (23)**	**4 (18)**	**1 (5)**	**0**
Eye Disorders[f]	**4 (18)**	**3 (14)**	**1 (5)**	**0**

Data as of 03Jan25.
[a]MedDRA SMQ [Broad] for peripheral neuropathy used. [b]Includes Preferred Terms of peripheral sensory neuropathy, neuropathy peripheral and polyneuropathy. [c]Includes Preferred Term of Peripheral Motor Neuropathy. [d]Includes MedDRA SMQ [broad] for Severe Cutaneous Adverse Reactions (SCAR) and Skin and Subcutaneous Tissue disorders SOC, excluding alopecia. [e]Preferred term. [f]Eye Disorders SOC.
1L: 1st line; ECOG: Eastern Cooperative Oncology Group; mUC: metastatic urothelial cancer; QW: weekly; Q3W: once every three weeks; TRAE: treatment-related adverse event.

In the Ph1/2 Duravelo-1 study, zelenectide + pembrolizumab has shown an encouraging response in 1L cisplatin-ineligible mUC

Waterfall plot across 1L cisplatin-ineligible la/mUC patients[a, b]
N=20
(efficacy evaluable patients only; includes 3 unconfirmed responses)



Best Overall Response[a,b], n (%)	Zelenectide 5 mg/m² QW + 200 mg pembrolizumab Q3W N=20 All	Confirmed
Complete Response (CR)	5 (25)	4 (20)
Partial Response (PR)	8 (40)	6 (30)
Stable Disease (SD)	5 (25)	
Progressive Disease (PD)	2 (10)	
ORR (CR+PR)	13 (65) 95% CI (41, 85)	10 (50) 95% CI (27, 73)
CBR (CR+PR+SD≥16 wks)	16 (80)	
DCR (CR+PR+SD)	18 (90)	

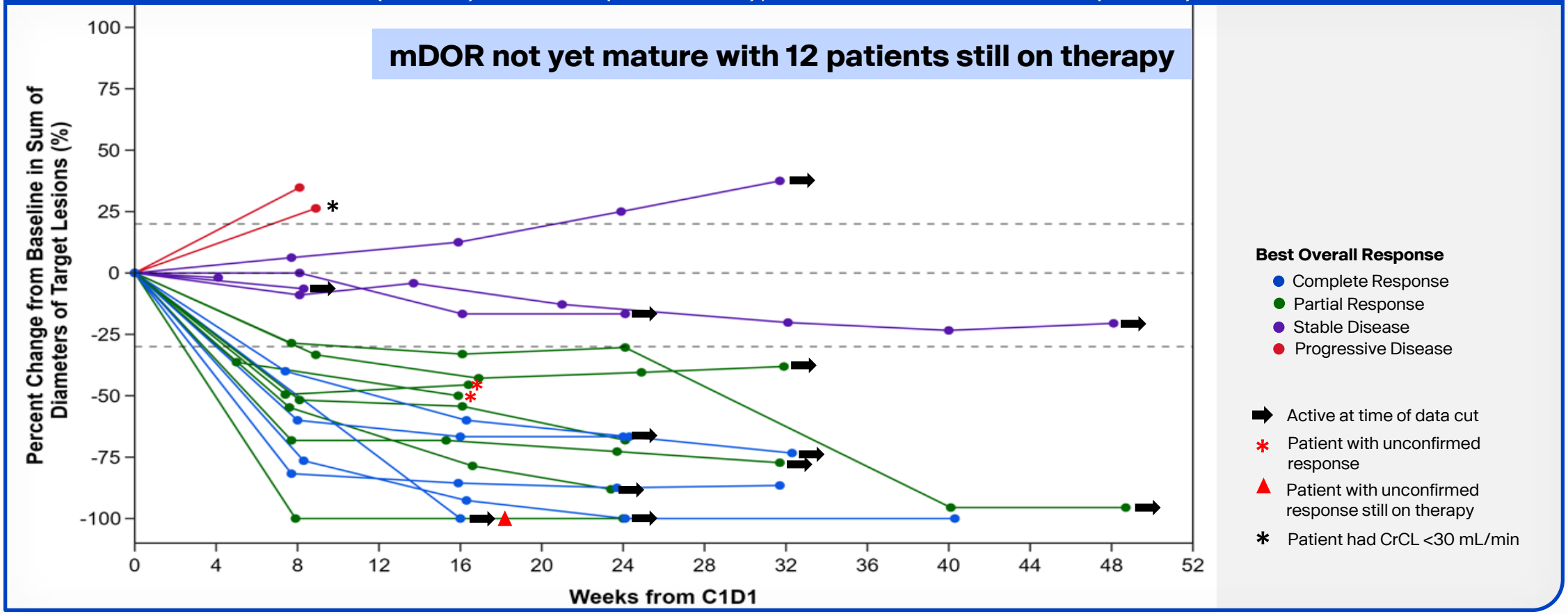
mDOT is currently 23 weeks (range 1-58)

mDOR is not yet mature with 12 patients still on therapy

Data as of 03Jan25.
[a]Efficacy evaluable defined as patients who have received at least 1 dose of zelenectide or pembrolizumab and with measurable disease at baseline and had an adequate post-baseline assessment. [b]Responses under response evaluation criteria in solid tumor (RECIST) v1.1.
1L: 1st line; CBR: clinical benefit rate; CrCL: creatinine clearance; DCR: disease control rate; la/mUC: locally advanced/metastatic urothelial cancer; mDOR: median duration of response; mDOT: median duration of treatment; mL/min: milliliters per minute; ORR: overall response rate; QW: weekly; Q3W: once every three weeks.

In the Ph1/2 Duravelo-1 study, zelenectide + pembrolizumab has shown a long duration of response in 1L cisplatin-ineligible mUC

Spider plot across 1L cisplatin-ineligible la/mUC patients[a, b]
N=20
(efficacy evaluable patients only; includes 3 unconfirmed responses)



Median duration of follow-up is 7.1 months (range 1.0-13.2)

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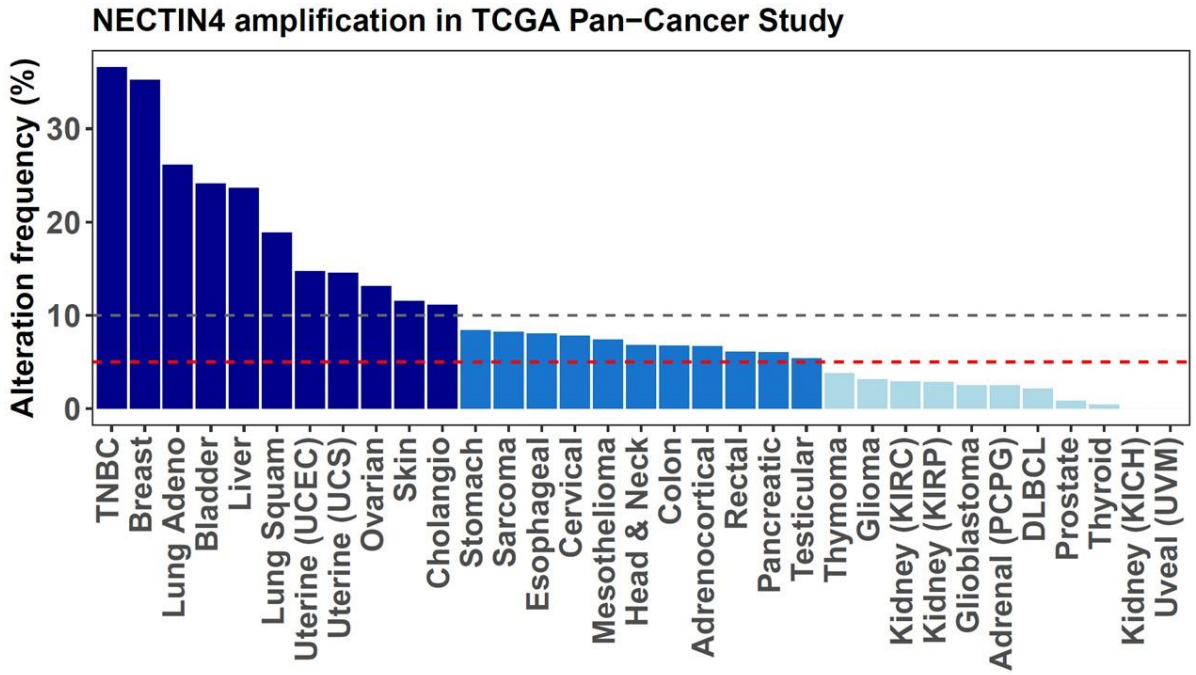
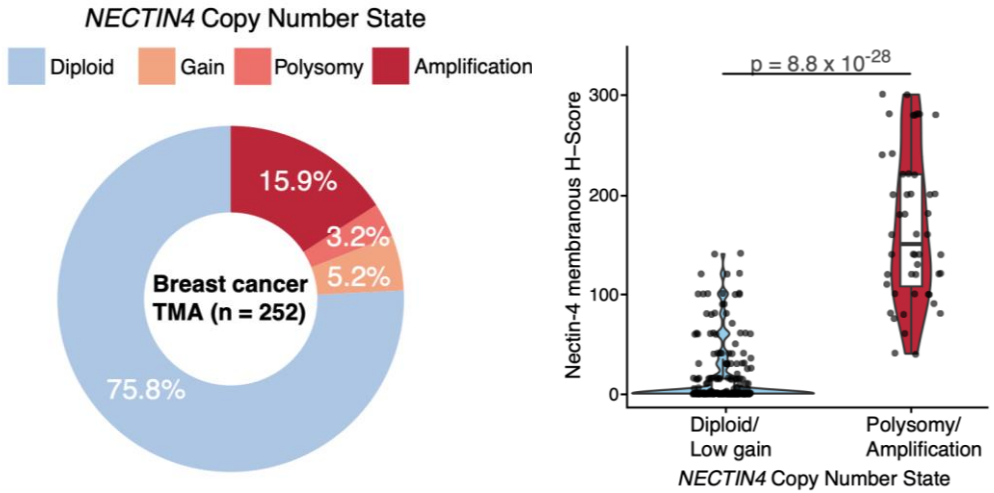
Data as of 03Jan25.
[a]Efficacy evaluable defined as patients who have received at least 1 dose of zelenectide or pembrolizumab and with measurable disease at baseline and had an adequate postbaseline assessment. [b]Responses under response evaluation criteria in solid tumor (RECIST) v1.1.
1L: 1st line; C1D1: Cycle 1 Day 1; CrCL: creatinine clearance; la/mUC: locally advanced/metastatic urothelial cancer; mDOR: median duration of response; mL/min: milliliters per minute.

NECTIN4 gene amplification potentially represents a significant opportunity for targeted treatment beyond bladder cancer



NECTIN4 gene amplification correlates with enhanced membranous Nectin-4 expression in breast cancer



Unpublished data by Klümper N, Brägelmann J & Eckstein M

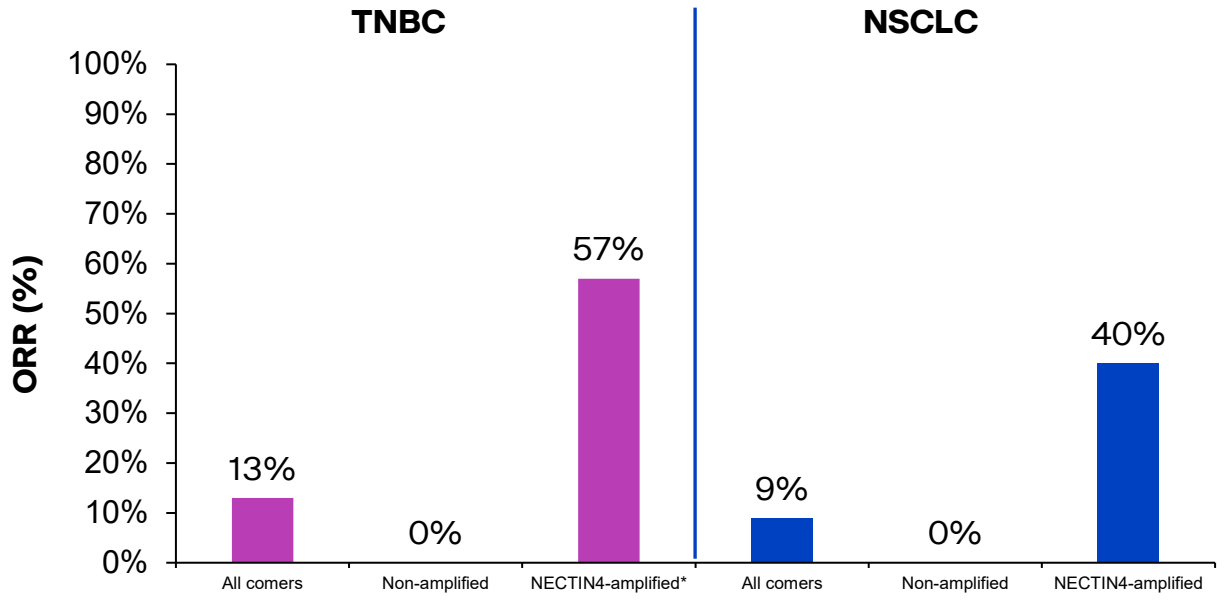
- Bicycle Therapeutics identified that the NECTIN4 gene sits on a commonly amplified chromosomal site in cancer (1q23)[1] and filed multiple patent applications around this observation over the ensuing years
- In 2024, Klümper et al. identified NECTIN4 gene amplification as a predictive biomarker for response to anti-NECTIN4 therapy in mUC[2]

Bicycle®

1. Gelb T, et al. *Cancer Res* 2021;81(13_Suppl):Abstract nr 391. 2. Klümper N, et al. *J Clin Oncol.* 2024;42(20):2446–2455.
mUC: metastatic urothelial cancer; TNBC: triple-negative breast cancer.

Patients with NECTIN4 gene amplification showed an enhanced response to zelenectide in 2L+ TNBC and NSCLC

Zelenectide monotherapy response in 2L+ breast and lung cancer patients



Breast Cancer

- Breast Cancer: 35/38 patients enrolled were efficacy evaluable
  - 63% ORR (5/8) in patients with NECTIN4 gene amplification* vs. 14% ORR (5/35) in efficacy evaluable patients
- TNBC: 30/32 patients enrolled were efficacy evaluable
  - 57% ORR (4/7) in patients with NECTIN4 gene amplification* vs. 13% ORR (4/30) in efficacy-evaluable patients
  - 100% DCR (7/7) in patients with NECTIN4 gene amplification*

NSCLC

- 34/40 patients enrolled were efficacy evaluable
  - 40% ORR (2/5) in patients with NECTIN4 gene amplification vs. 9% ORR (3/34) in efficacy evaluable patients
  - 100% DCR (5/5) in patients with NECTIN4 gene amplification

All Indications

- Safety and tolerability profile in line with other 2L+ monotherapy cohorts

Regulatory

- FDA Fast Track designation in TNBC[1] and NSCLC[2]

Data as of 13Sep2024.
*Includes polysomy. 1. FDA Fast Track designation of zelenectide for the treatment of adults with previously treated NECTIN4 amplified locally advanced (unresectable) or metastatic TNBC.
2. FDA Fast Track designation of zelenectide for the treatment of adult patients with previously treated, NECTIN4 amplified, advanced or metastatic NSCLC.
2L+: 2nd line or later; DCR: disease control rate; FDA: U.S. Food and Drug Administration; NSCLC: non-small cell lung cancer; ORR: objective response rate; TNBC: triple-negative breast cancer.

Bicycle receives regulatory alignment on optimal dose as 6mg/m² zelenectide two weeks on, one week off plus pembrolizumab

- **Optimal dose of 6mg/m² zelenectide two weeks on, one week off plus pembrolizumab demonstrates response rates comparable to published rates for standards of care and differentiated tolerability profile**
  - At this dose only one patient discontinued therapy due to a treatment related adverse event (TRAE) at the 27-week cutoff
  - Physician assessed overall response rate (ORR) of 65%
  - Blinded independent central review (BICR) confirmed ORR of 58% at the 27-week cutoff. Subsequent to the 27-week cutoff, an additional confirmed BICR response was observed, which would result in an ORR of 62%
  - Bicycle Therapeutics expects to present initial dose selection data from the Duravelo-2 trial at a future scientific conference
- **Preliminary regulatory feedback (EMA, FDA, MHRA) indicates multiple potential options for continued development of zelenectide in mUC**
- **Converting Duravelo-2 to a randomized Phase 2 study and pausing development in all indications, while determining the optimal regulatory path for the program**
  - Once available, data from the randomized Phase 2 trial will be shared with the scientific and medical community

ORR: objective response rate; mUC: metastatic urothelial cancer.

Zelenectide, a first-in-class BDC® molecule, has a differentiated safety profile and strong anti-tumor activity

SUMMARY

- Demonstrated potentially differentiated safety and robust efficacy profile as monotherapy and in combination with pembrolizumab in mUC
- FDA Fast Track designation in mUC
- Program is being deprioritized, while evaluating potential regulatory options and next steps

NEXT STEPS

- ✓ **1Q 2026: Discussions with multiple regulatory agencies on dose selection and potential expedited approval pathways**
- ✓ **Q1 2026: Announce dose selection**
- ▶ **Present dose selection data from Ph2/3 Duravelo-2 study in 2026**
- ▶ **Convert Duravelo-2 to a randomized Ph2 study and evaluate next steps**

1L: 1st line; 2L+: 2nd line or later; FDA: U.S. Food and Drug Administration; mUC: metastatic urothelial cancer; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer.

Looking ahead

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2026 strategic priorities and anticipated milestones

Nuzefatide

1H 2026

- ✓ Nuzefatide pevedotin + nivolumab combination data in mUC patients
- ✓ Additional information on PDAC indication at a future scientific conference
- ▸ Progress enrollment in Phase 2 study in PDAC using 8 mg/m2 Q2W dose

Bicycle radioligands

1H 2026

- ✓ Additional EphA2 human imaging data
- ▸ Ongoing IND-enabling activities for BT1702 (BRC®, ^{212}Pb)

Nectin-4

2026

Zelenectide

- ▸ Dose selection data from Ph2/3 Duravelo-2 study
- ▸ Additional Ph 1 DV1 combo data with pembrolizumab in 1L cis-ineligible mUC
- ▸ Longer-term Phase 1 DV1 monotherapy data in 2L+ mUC

BT7480

- ▸ Ph 1 BT7480 combination data with nivolumab

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1L: 1st line; 2L+: 2nd line or later; mUC: metastatic urothelial cancer; pembro: pembrolizumab; PDAC: pancreatic ductal adenocarcinoma

Leveraging The Bicycle® Advantage in our mission to transform the lives of patients

Near- / mid-term priorities

Progress nuzefatide Phase 2 clinical trial in PDAC

Advance novel drug conjugate and radioligand pipeline

Evaluate potential regulatory options and next steps for zelenectide

Long term goal

Help patients live longer and live well

PDAC: pancreatic ductal adenocarcinoma

Appendix

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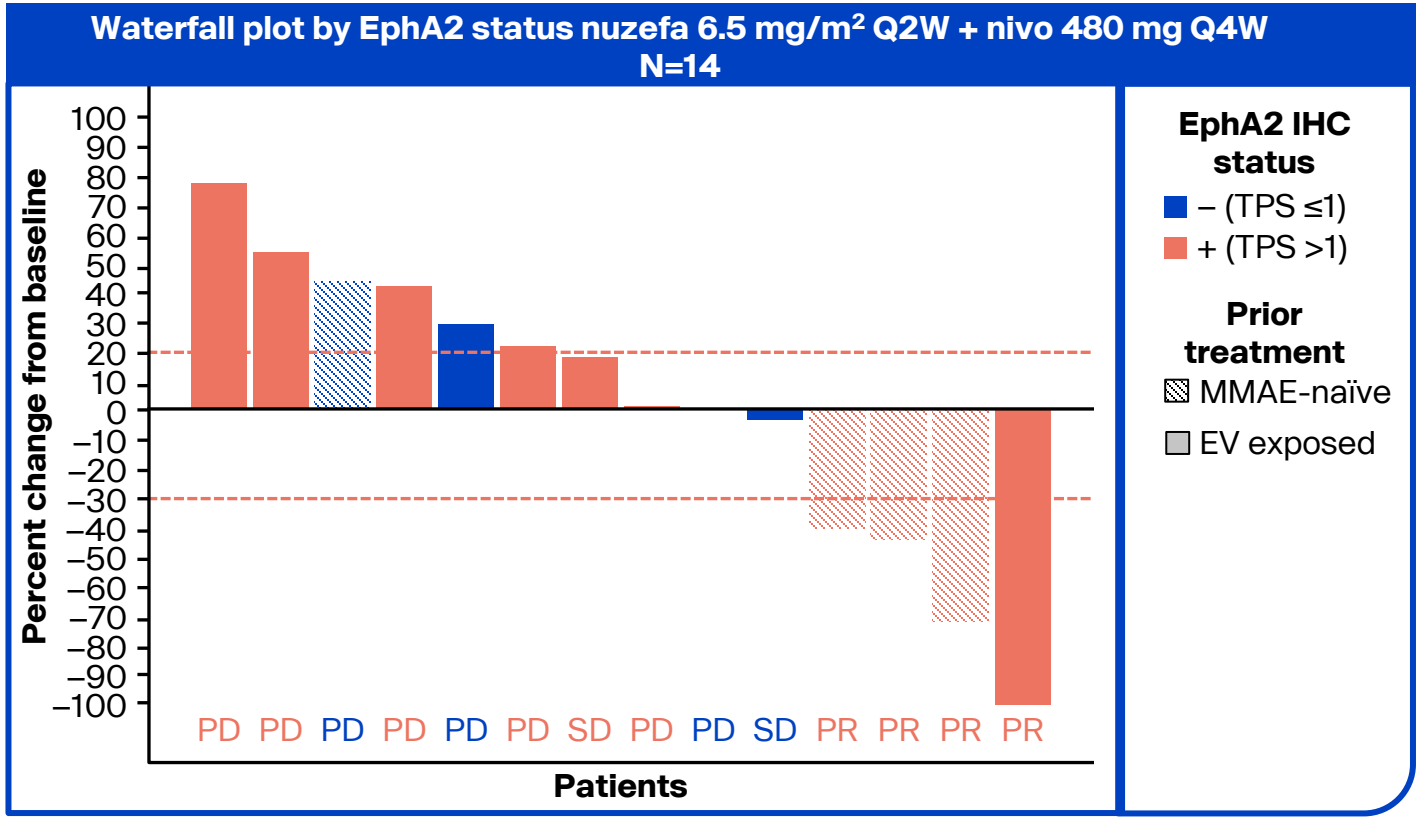
Nuzefatide pevedotin in combination with nivolumab is active in EphA2+, MMAE-naïve late line urothelial patients



- In mUC patients treated with nuzefa 6.5 mg/m² Q2W + nivo, 4/10 (40%) with EphA2+ tumors responded
- In the subset of patients with EphA2+ tumors that were MMAE-naïve, 3/3 achieved a confirmed partial response (ORR 100%)

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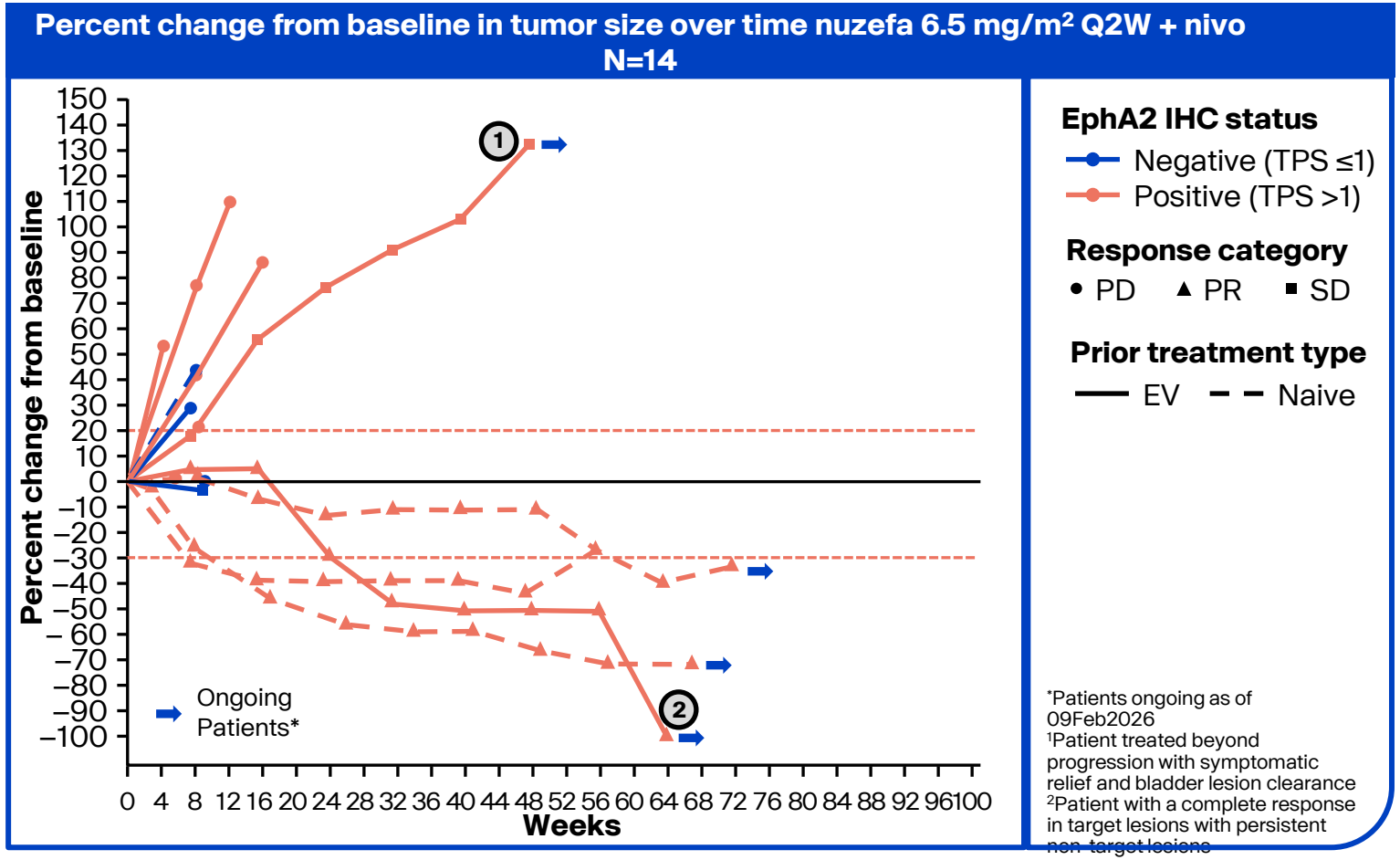
Data as of 09Feb2026. Best post baseline response status from EDC was used for the response category. EDC: electronic data capture; EphA2: ephrin type-A receptor 2; EV: enfortumab vedotin; IHC: immunohistochemistry; MMAE: monomethyl auristatin E; mUC: metastatic urothelial carcinoma; nivo: nivolumab; nuzefa: nuzefatide pevedotin; PD: progressive disease; PR: partial response; Q2W: once every 2 weeks; Q4W: once every 4 weeks; SD: stable disease; TPS: Tumor Proportion Score; ORR: objective response rate.

Nuzefatide pevedotin in combination with nivolumab led to a substantial duration of treatment in EphA2+ MMAE naïve mUC



- **In the subset of late line mUC patients with EphA2+ tumors that were MMAE-naïve, as of 14 Apr ‘26, the minimum DoT was 53.9 weeks (377 days) and longest 83.1 weeks (582 days)**

Clinical proof of concept has been achieved as monotherapy and combination with nivolumab

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Data as of 09Feb2026. Best post baseline response status from EDC was used for the response category. EDC: electronic data capture; EphA2: ephrin type-A receptor 2; EV: enfortumab vedotin; IHC: immunohistochemistry; MMAE: monomethyl auristatin E; mUC: metastatic urothelial carcinoma; nivo: nivolumab; nuzefa: nuzefatide pevedotin; PD: progressive disease; PR: partial response; Q2W: once every 2 weeks; SD: stable disease; TPS: Tumor Proportion Score.

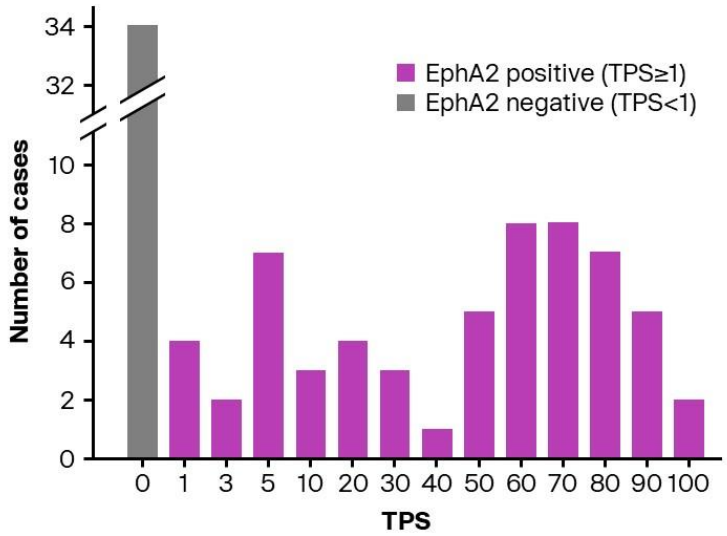
Nuzefatide pevedotin is generally well tolerated at clinically active doses both as a monotherapy and in combination with nivolumab

Nuzefa-related AEs reported in ≥10% of patients[a], n (%)	All Patients (N=161)		Nuzefa 6.5 mg/m² Q2W (n=74)		Nuzefa 8.0 mg/m² Q2W (n=12)		Nuzefa 6.5 mg/m² Q2W + nivo 480 mg Q4W (n=14)	
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Nausea	68 (42)	2 (1)	37 (50)	1 (1)	4 (33)	0	3 (21)	0
Fatigue	57 (35)	9 (6)	28 (38)	3 (4)	6 (50)	1 (8)	4 (29)	2 (14)
Diarrhea	45 (28)	2 (1)	23 (31)	1 (1)	3 (25)	0	4 (29)	0
Anemia	35 (22)	9 (6)	15 (20)	3 (4)	6 (50)	1 (8)	3 (21)	1 (7)
Vomiting	31 (19)	2 (1)	12 (16)	1 (1)	2 (17)	0	2 (14)	0
Alopecia	25 (16)	0	12 (16)	0	3 (25)	0	0	0
Decreased appetite	24 (15)	1 (1)	15 (20)	0	1 (8)	0	1 (7)	0
Aspartate aminotransferase increased	17 (11)	2 (1)	6 (8)	0	4 (33)	1 (8)	1 (7)	1 (7)
Pyrexia	17 (11)	0	13 (18)	0	0	0	0	0
Headache	16 (10)	0	7 (10)	0	1 (8)	0	1 (7)	0

Data as of 09Feb2026. [a]Includes nuzefa-related AEs reported in ≥10% of the All Patients population (N=161). AE: adverse event; nivo: nivolumab; nuzefa: nuzefatide pevedotin; Q2W: once every 2 weeks; Q4W: once every 4 weeks.

Preclinical evaluation of nuzefatide pevedotin suggests robust activity is achievable across a range of PDX PDAC models

Human PDAC TMA show high EphA2 positivity (TPS ≥1)



EphA2, erythropoietin-producing hepatocellular receptor A2; TPS, Tumor Proportion Score.

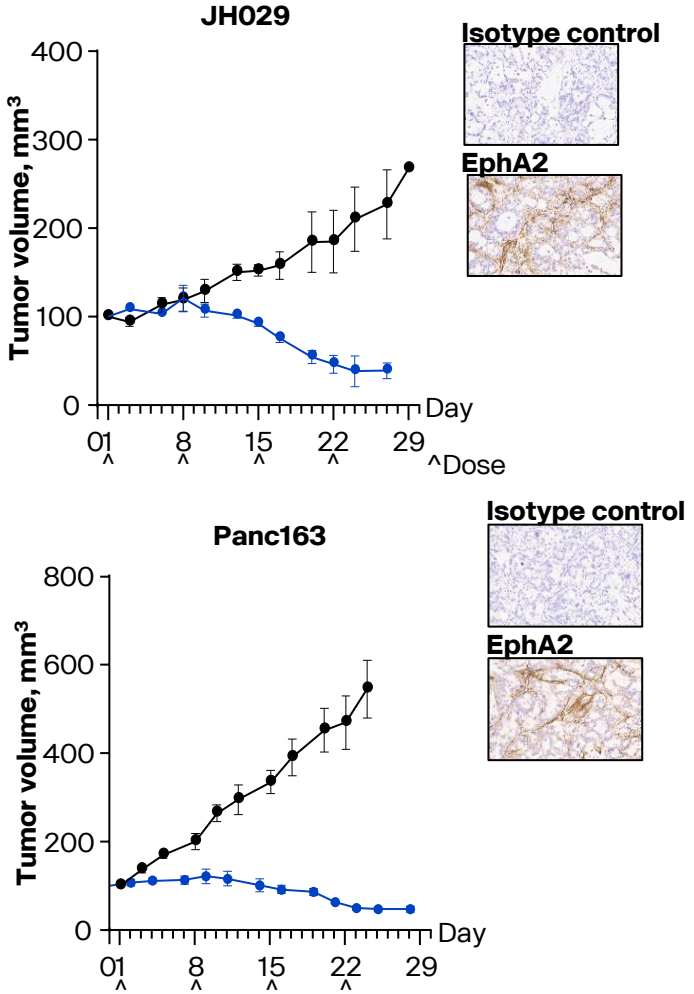
- Most (63%) samples in human pancreatic tumor microarray) EphA2 positive (TPS ≥1)
- PA1921c : 93 cases, 179 cores, in a PDAC microarray

The majority of PDAC PDX models were sensitive to nuzefatide

PDX ID	TPS Score, %	Nuzefa TGI, %	Desmoplasia Grade
JH029	**20**	**157**	**Mature**
Panc163	**30**	**114**	**Intermediate**
Panc286	55	111	Mature
Panc421	**90**	**110**	**Immature**
Panc033	50	103	N/A
Panc030	50	100	Mature
Panc008	67	91	Mature
Panc281	80	75	Intermediate
JH033	18	70	Mature
JH051	1	52	Immature
Panc094	20	50	Immature
Panc287	60	31	Intermediate
JH094	67	22	Immature
Panc028	80	5	Mature

- 6/14 EphA2 positive PDX showed high sensitivity to nuzefatide (TGI ≥100%)

43% of all PDX models were highly sensitive to 3mg/kg QW nuzefatide



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EphA2: ephrin type-A receptor 2; N/A: not applicable; PDX: patient-derived xenograft, PDAC: pancreatic ductal adenocarcinoma; QW: once weekly; TGI: tumor growth inhibition; TMA: Tissue Microarray; TPS: Tumor Proportion Score

Experts support ongoing development of new treatments in metastatic pancreatic cancer due to the high unmet need

KOL views on unmet need[1]

"Forty percent of patients are not eligible for chemotherapy. They just die within a short period of time. So, it would be good if you could ***find a drug which we could use for patients who are not fit enough for chemotherapy."***

"If we continue to give people chemotherapy, ***the neuropathy that they get for the rest of their lives is a major quality of life issue."***

"Once patients are treated, whether it's chemotherapy or it's inhibitors, at some point they become resistant. ***So, overcoming drug resistance is key****."*

~50% of 2L patients succumb to their disease reinforcing the need for more treatments that can help patients live longer and live well

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[1]FirstWord Therapy Trends. KOL Insight: Pancreatic Cancer. March 2026 (www.firstwordreports.com). Report covers insights from 6 KOLs in the US and 6 KOLs from Europe. 2L: second-line; KOL: key opinion leader

Thank you

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