Bicycle Therapeutics Investor Presentation

- July 30th, 2026

Bicycle®

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 an end-to-end radioisotope and radiopharmaceutical supply chain; 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 July 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 targeting historically undruggable target with ADCs, in a Phase 2 PDAC trial

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

IONIS™

dkfz.

Universitätsmedizin Essen
Universitätsklinikum

NDA

NATIONAL NUCLEAR LABORATORY

Ambitious Company

Deeply experienced team

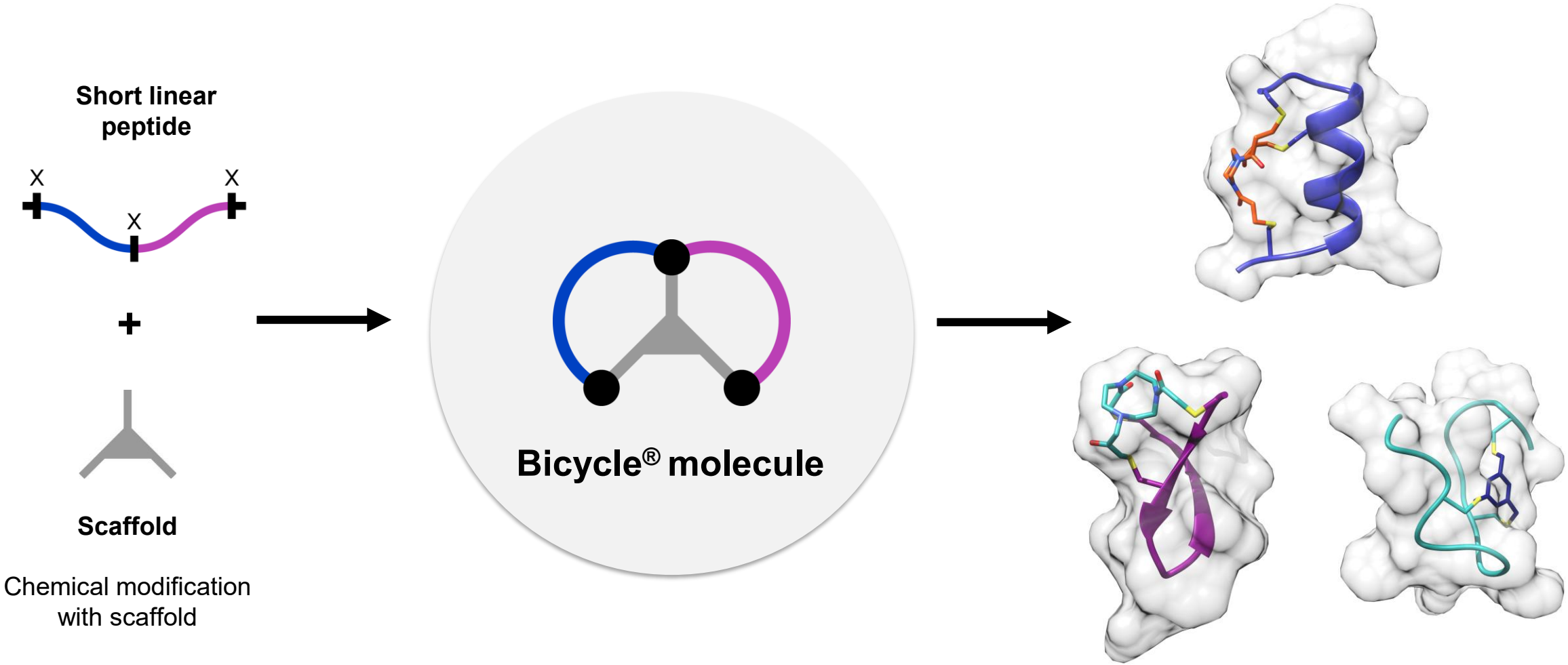
Located in Cambridge, UK, and Lexington, MA

NASDAQ: BCYC

Cash and cash equivalents of $510.1 million as of June 30, 2026, with expected financial runway into 2030

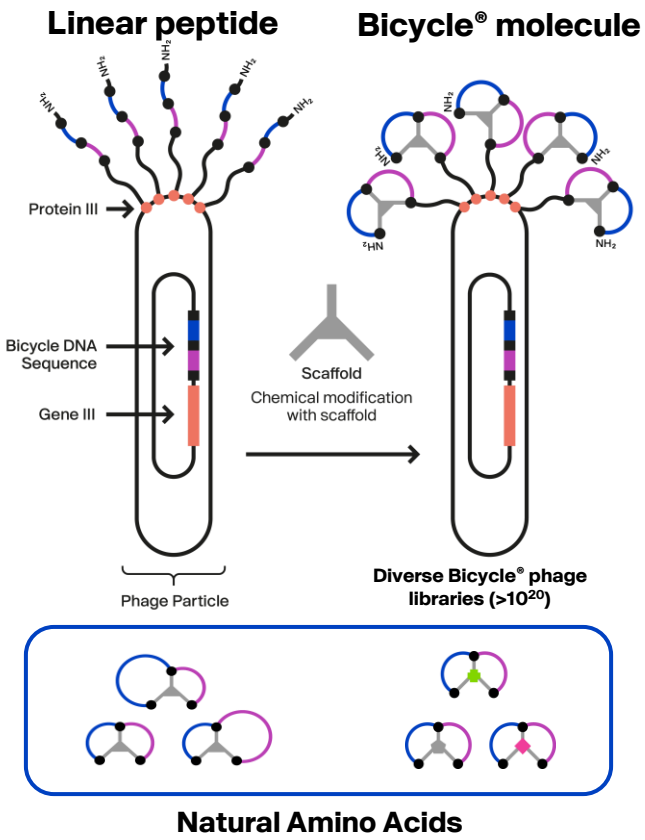
EphA2: Ephrin A2; MT1-MMP: Membrane type 1 matrix metalloproteinase; mUC: metastatic urothelial cancer; PDAC: pancreatic ductal adenocarcinoma; ADC: Antibody Drug Conjugate

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

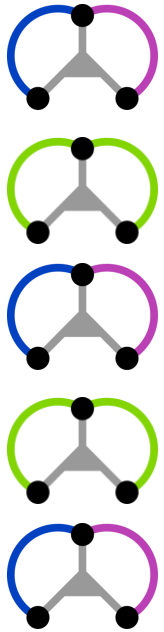
Bicycle® Phage Display Discovery



Peptide & Medicinal Chemistry

Optimize Bicycle® monomers

Non-natural Amino Acids

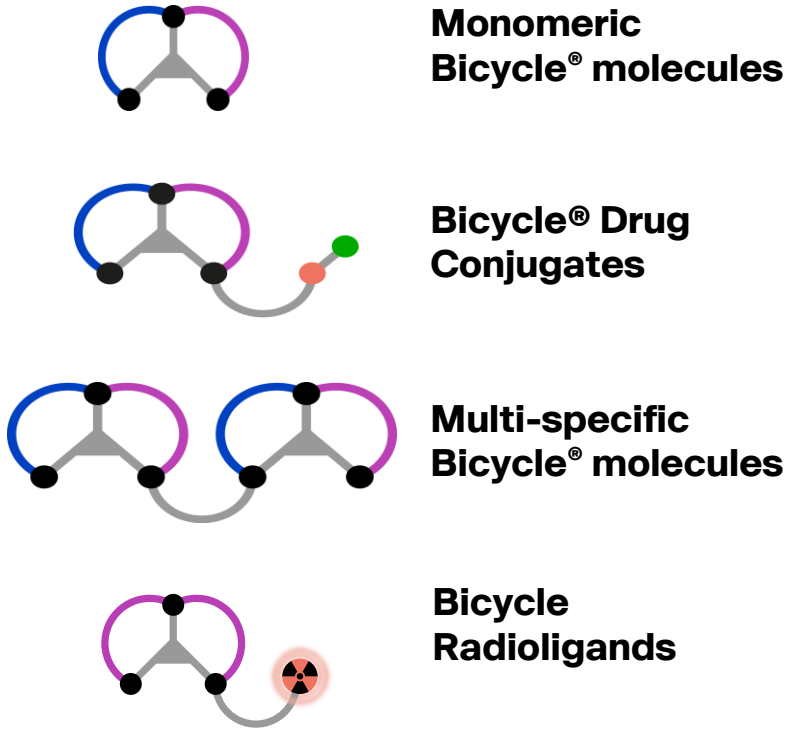


Targeting and Effector Bicycle® molecules

Build and Optimize Therapeutic Bicycle® molecules

Easy conjugation of Linkers and Payloads

Potential Bicycle® Medicines



Monomeric Bicycle® molecules

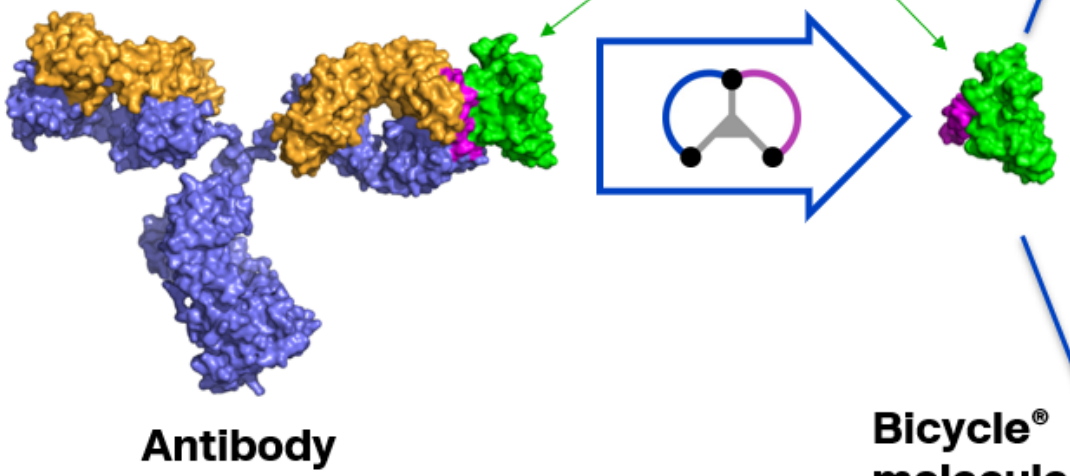
Bicycle® Drug Conjugates

Multi-specific Bicycle® molecules

Bicycle Radioligands

Bicycle® molecules have optimal properties for precision-guided therapeutics

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



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

POTENTIAL: Better targeting ▶ Better tolerability ▶ Better combinability ▶ Better outcomes

PK: pharmacokinetics.

We are building a robust pipeline of Bicycle therapeutics

Target	Program	Study	Indication	Pre-clinical	IND enabling/ human imaging	Clinical
Internal oncology programs						
EphA2	nuzefatide pevedotin (BDC® molecule)	Ph2 open label	PDAC			
	^{68}Ga BIA molecule	Utility study	Solid tumors			
	EphA2 BRC® molecule	Pre-clinical	Solid tumors			
MT1-MMP	^{68}Ga BIA molecule	Utility study	Solid tumors			
	BT1702 (BRC® molecule, ^{212}Pb)	IND enabling	Solid tumors			
Nectin-4	zelenectide pevedotin (BDC® molecule)	Duravelo-2 Ph2 combo with pembrolizumab	1L mUC			
			2L mUC			
Additional targets	Undisclosed	Pre-clinical	Solid tumors			
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; Bicycle TICA® : Bicycle tumor-targeted immune cell agonist®; PLN: phospholamban gene

Nuzefatide pevedotin, a potential first-in-class EphA2 targeting BDC® molecule

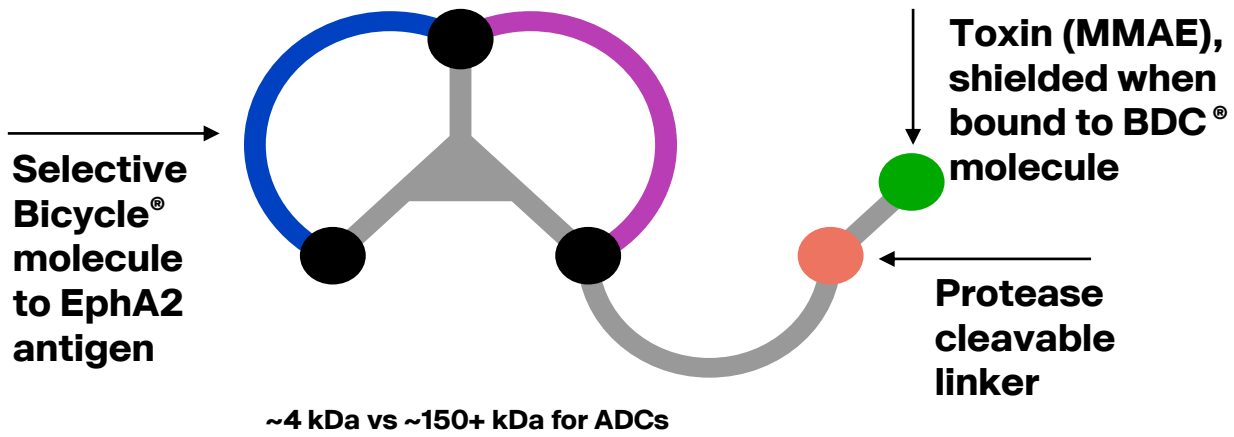
Bicycle®

Nuzefatide pevedotin is a Bicycle® drug conjugate (BDC®) that targets EphA2, a target so far undruggable with ADCs due to severe toxicities

EphA2 background

- Highly expressed in many tumor types
  - Pancreas, head and neck, bladder
- All antibody-based approaches have failed due to severe toxicity or lack of efficacy
- There are currently no approved drug conjugates targeting EphA2

Nuzefatide pevedotin



Highly differentiated preclinical and clinical performance:

- Novel, potent and selective small peptide
- Targets EphA2 without treatment-limiting toxicity seen with ADCs
- Differentiated pharmacology to deliver validated payload

ADC: antibody drug conjugate; EphA2: ephrin type-A receptor 2; kDa: kilodalton; MMAE: monomethyl auristatin E

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 tumor uptake."[4,5]

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

[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 from Study BT5528-100. 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 from Study BT5528-100. 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 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 (%)	Nuzefatide Exposed Patients (N=161)					
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Peripheral neuropathy[c]	31 (19.3)	20 (12.4)	11 (6.8)	0	0	0
Skin reactions[d]	23 (14.3)	20 (12.4)	3 (1.9)	0	0	0
Neutropenia[e]	13 (8.1)	0	8 (5.0)	0	5 (3.1)	0
Eye disorders[f]	5 (3.1)	4 (2.5)	1 (0.6)	0	0	0
Hemorrhage[g]	0	0	0	0	0	0

Conclusion

- **Nuzefatide demonstrated an acceptable safety profile across dose levels as a monotherapy and in combination with nivolumab**

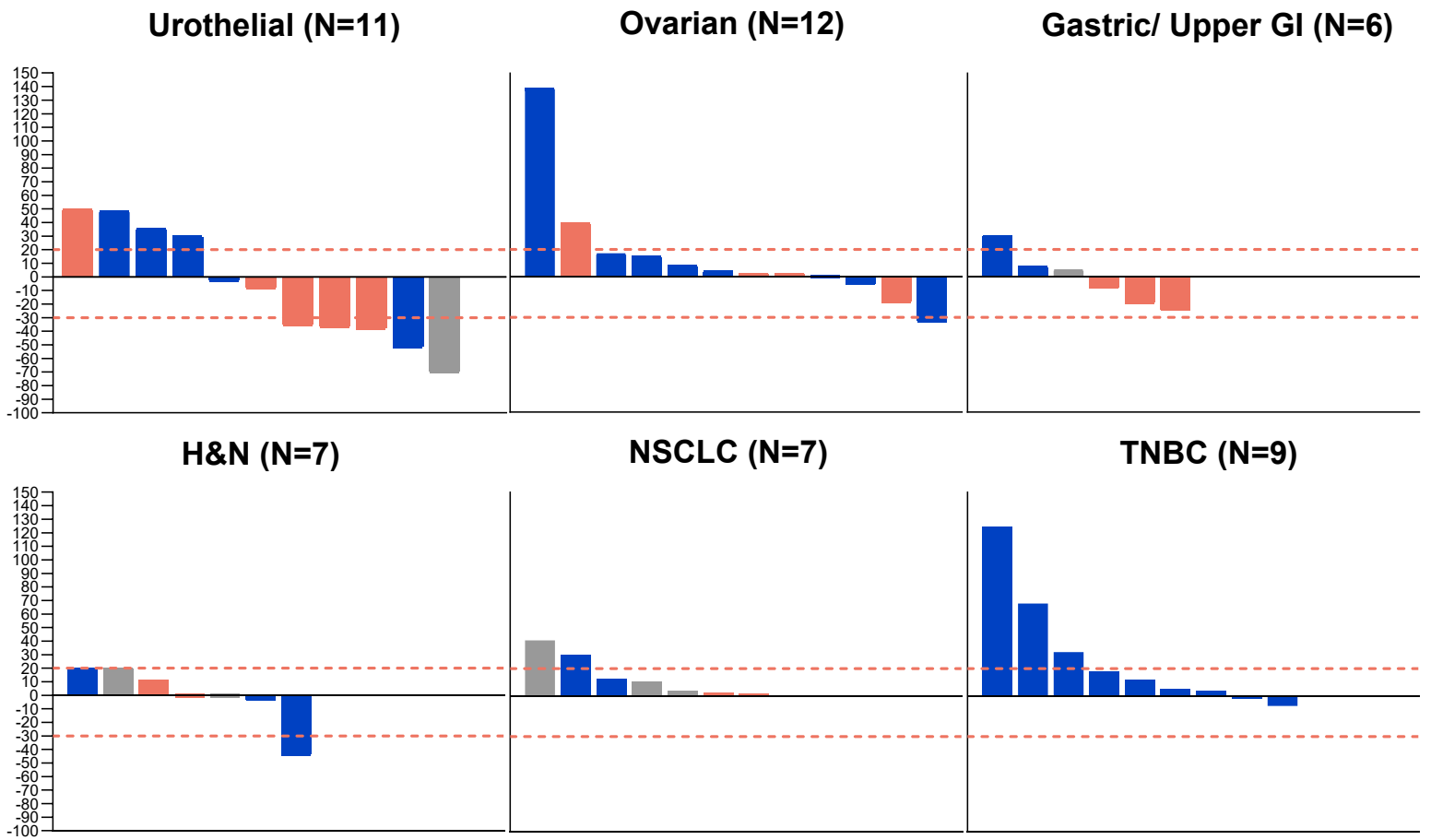
Next steps

- **Explore potential in 2L+ PDAC**

Data as of 09Feb2026 from Study BT5528-100. [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 neutropenia; [f]SOC of Eye disorders; [g]Hemorrhage (excluding laboratory terms) [narrow] SMQ. 2L+: second line and beyond; ADC: antibody drug conjugate; MedDRA: Medical Dictionary for Regulatory Activities; PDAC: pancreatic ductal adenocarcinoma; PT: Preferred Term; 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

Waterfall plot by EphA2 status 6.5 mg/m² nuzefa Q2W in dose expansion
Efficacy evaluable analysis set



EphA2 IHC status

- – (TPS ≤1)
- + (TPS >1)
- No sample

Data as of 09Feb2026 from Study BT5528-100. 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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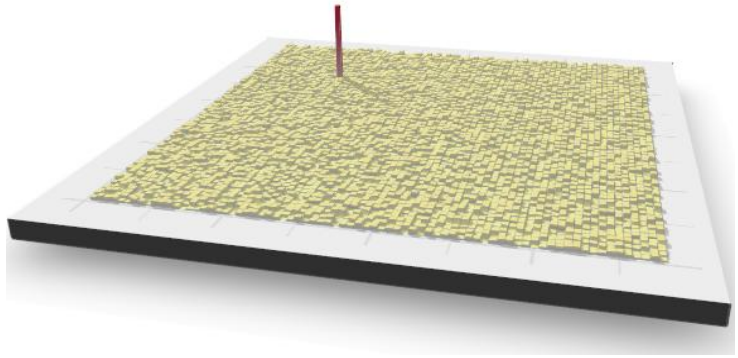
Nuzefatide pevedotin binds only to EphA2, and clinically shows rapid delivery and tumor retention with limited systemic exposure

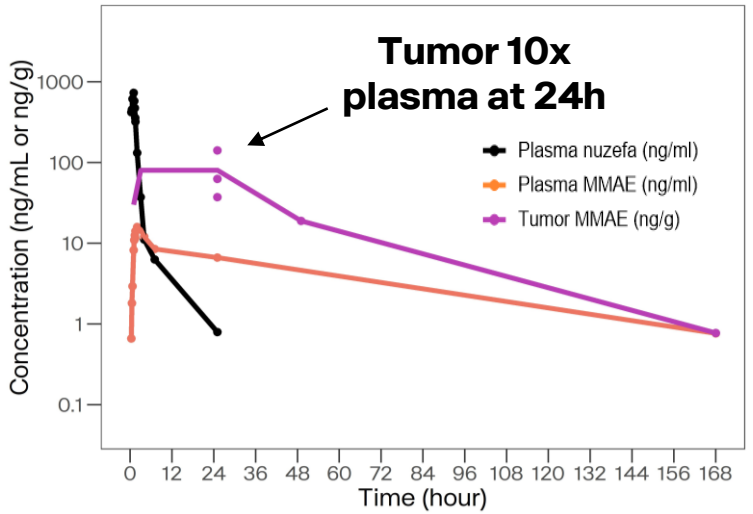
Ligand-binding domain	Binding affinity (SPR K_D nM)
EphA2	1.2
EphA1	>5000
EphA3	>5000
EphA4	>5000
EphA5	>5000
EphA6	>5000
EphA7	>5000
EphB4	>5000

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

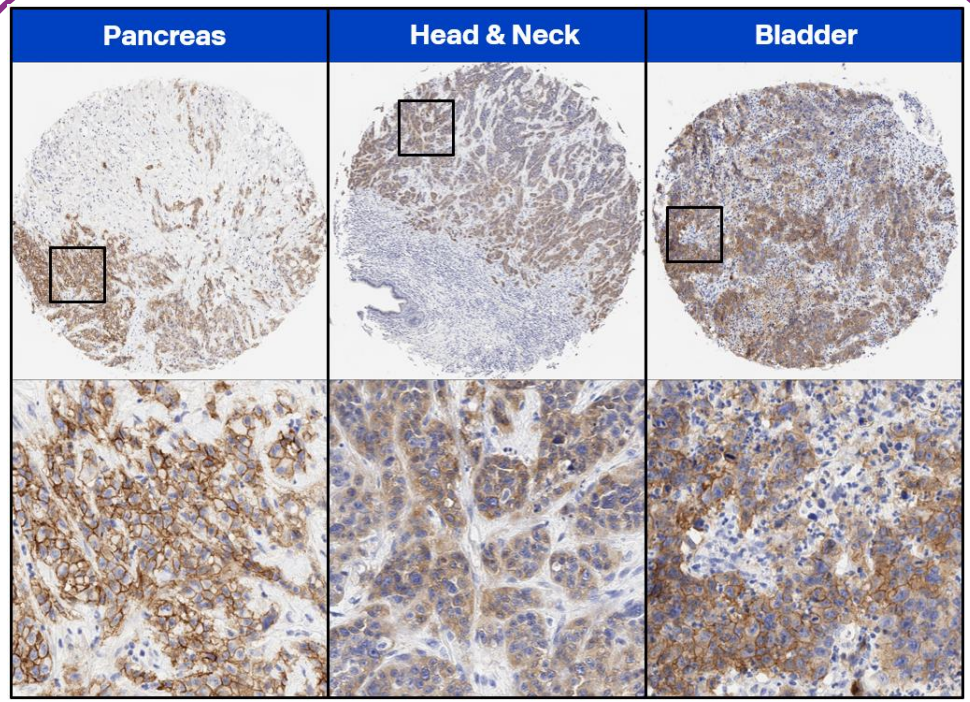
Nuzefatide has a differentiated profile from ADCs that often bind to additional Fc receptors and proteins

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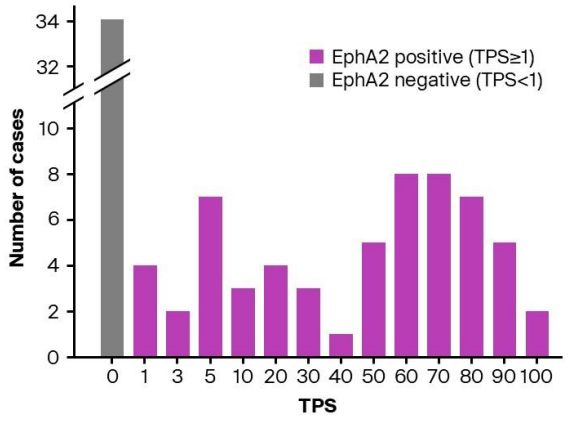
[1]Bicycle Therapeutics unpublished data. CRC: colorectal cancer; CST: Cell Signaling Technology; EphA2: ephrin type-A receptor 2; GEJ; gastroesophageal; HNSCC: head and neck squamous cell carcinoma; mAb; monoclonal antibody; TMA; tumor tissue microarray; TPS: Tumor Proportion Score

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

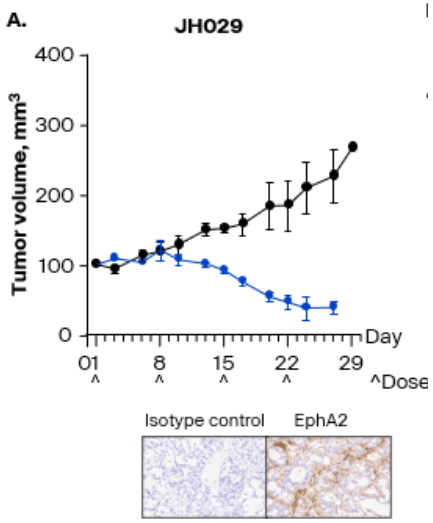
EphA2 PDAC expression

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



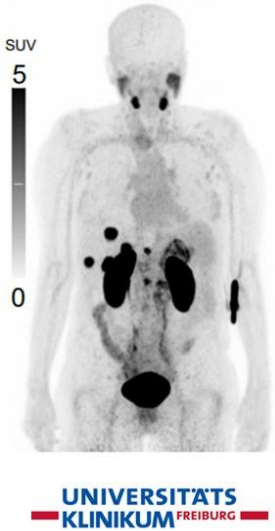
PDAC sensitivity to MMAE

PDAC PDX models responsive to MMAE



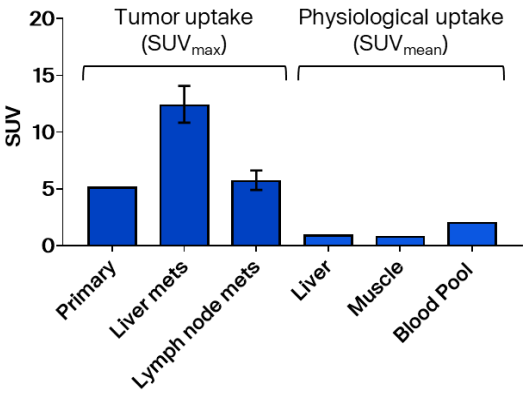
Patient identification strategy

^{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

Bicycle®

[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

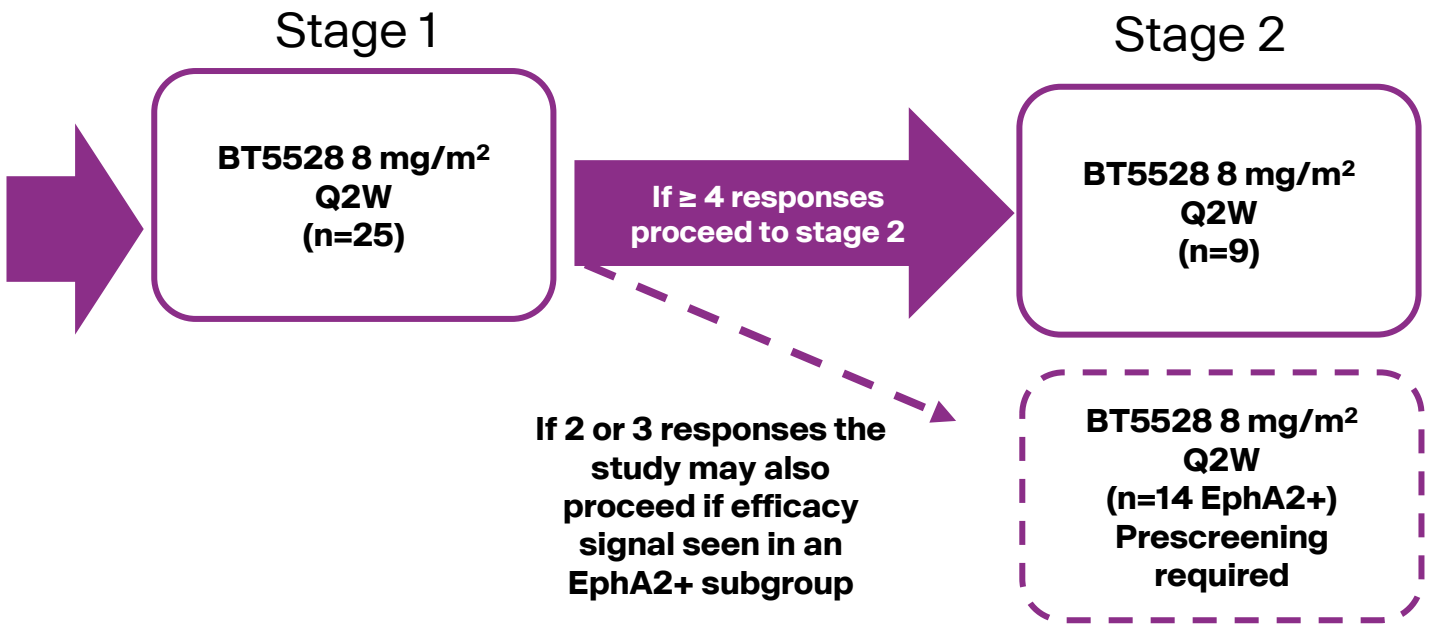
We are exploring nuzefatide pevedotin in a Phase 2 2L+ pancreatic cancer study

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

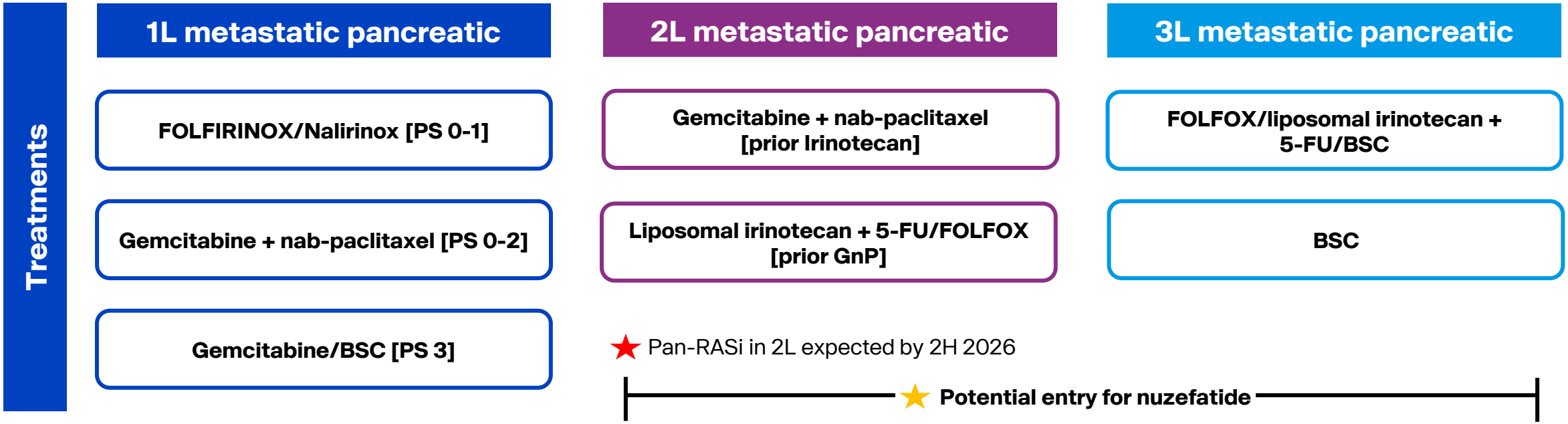
11% / 3%
Stages 0-IV Stage IV

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]**

[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
- 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

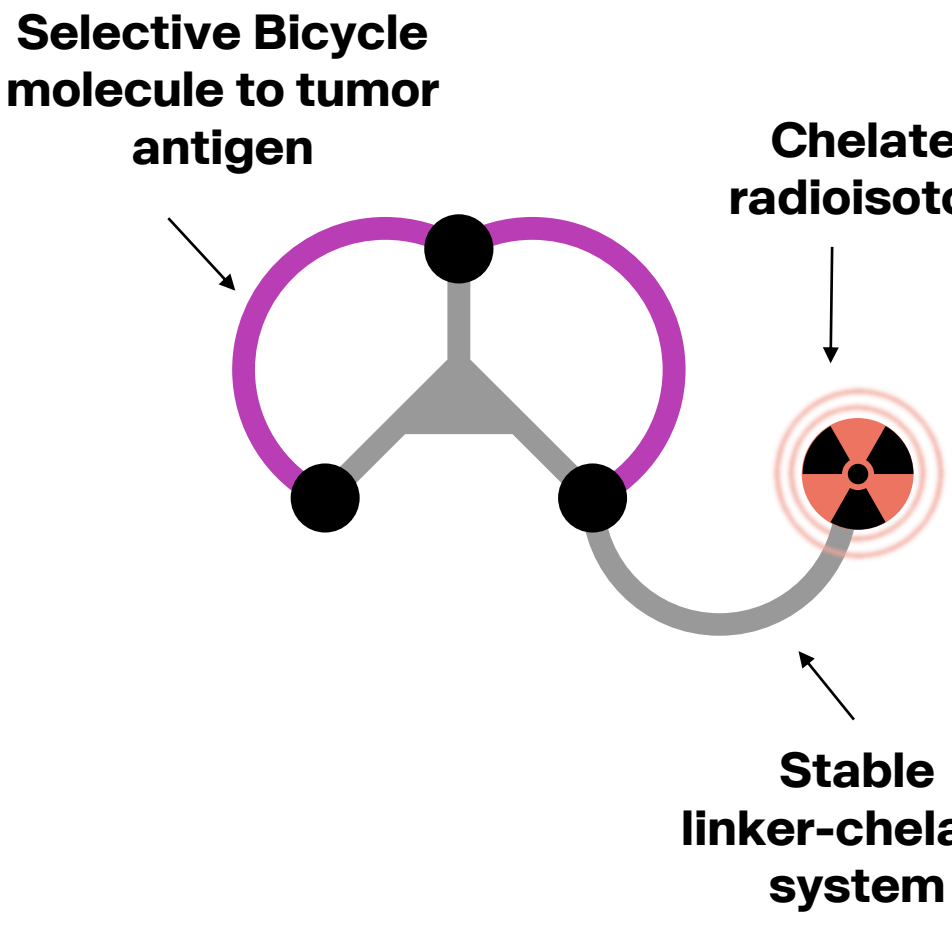
Use the isotope best suited for the target

- 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

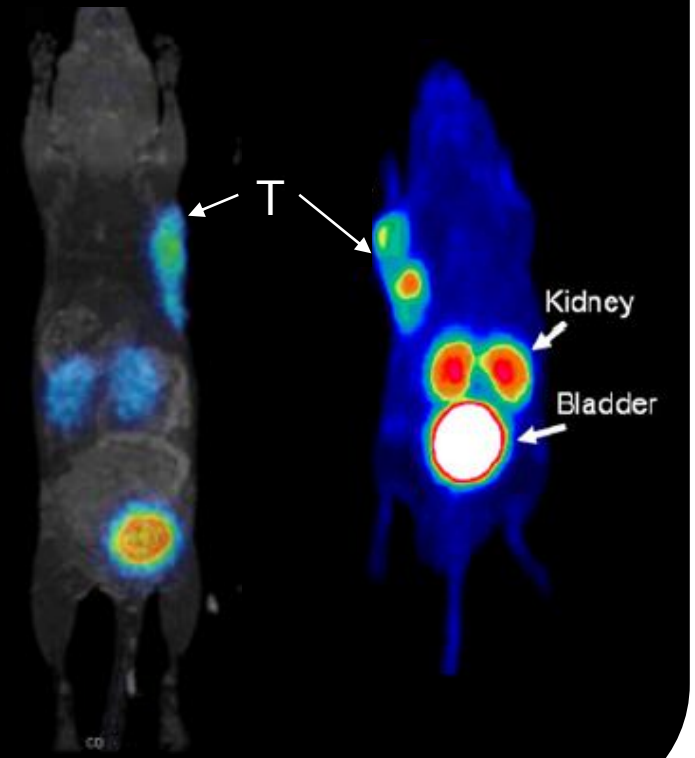


- Highly selective and tumor penetrant
- Pipeline of Bicycle molecules to novel tumor antigens
- Minimal systemic exposure

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

MT1-MMP

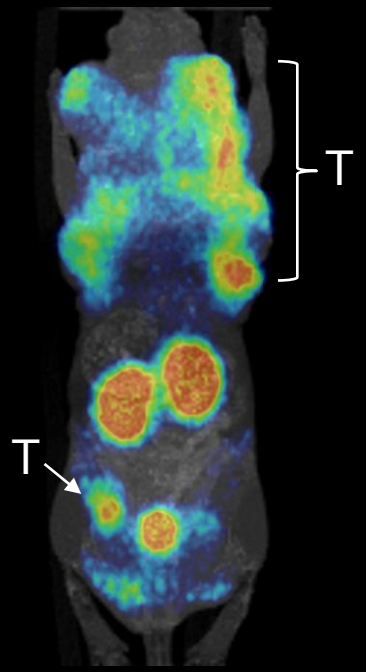
Fibrosarcoma



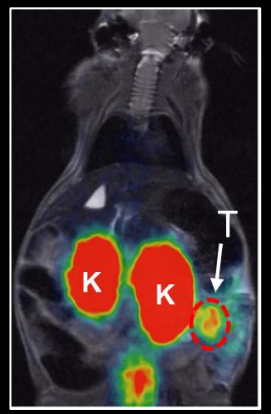
Left: HT1080 tumor model, 2h P.I. (DKFZ unpublished data)
Right: HT1080 tumor model, 40 to 60 min P.I. Eder M et al. 2019. *Cancer Res.* 79(4):841-852

EphA2

Breast



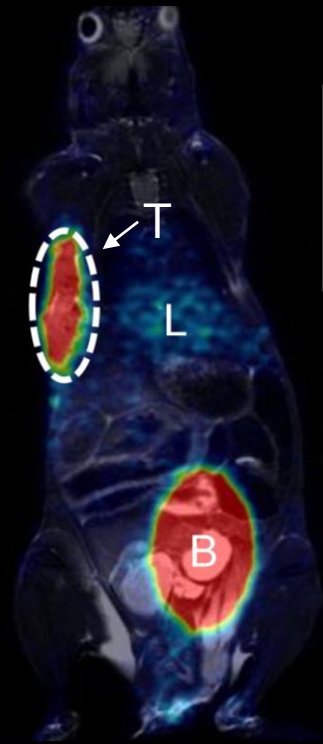
Pancreatic

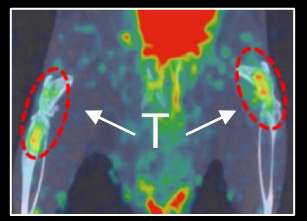


Left: MMTV-PyMT transgenic mouse model, 2h P.I.
Right: Panc-1 orthotopic tumor model 1h P.I.
Sharma AK et al. 2023. *Cancer Res,* 83(7 Suppl):2768

CD38

Multiple myeloma





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

Bicycle® dkfz.

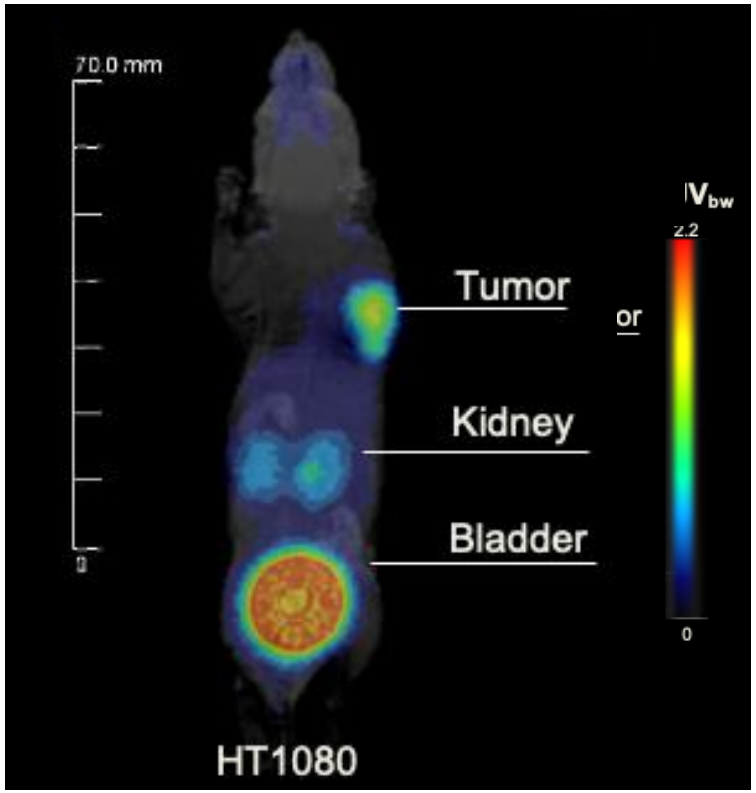
MT1-MMP is a novel target in the treatment of cancer

- 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



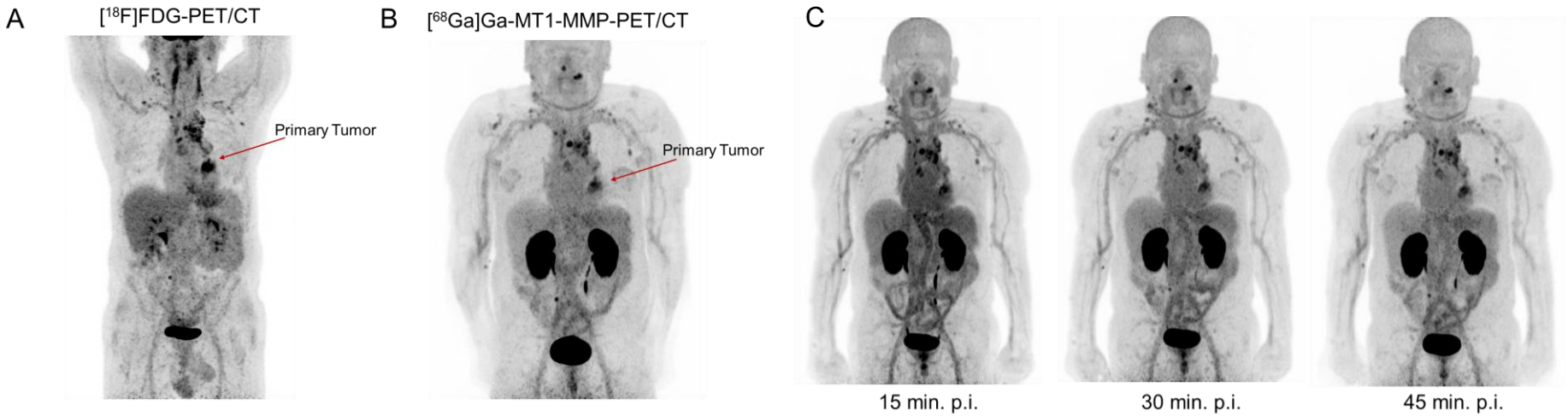
Whole-body maximum intensity projection of ^{68}Ga-labeled BIA molecule targeting MT1-MMP 60 min. p.i. obtained from PET/MR imaging

Bicycle®

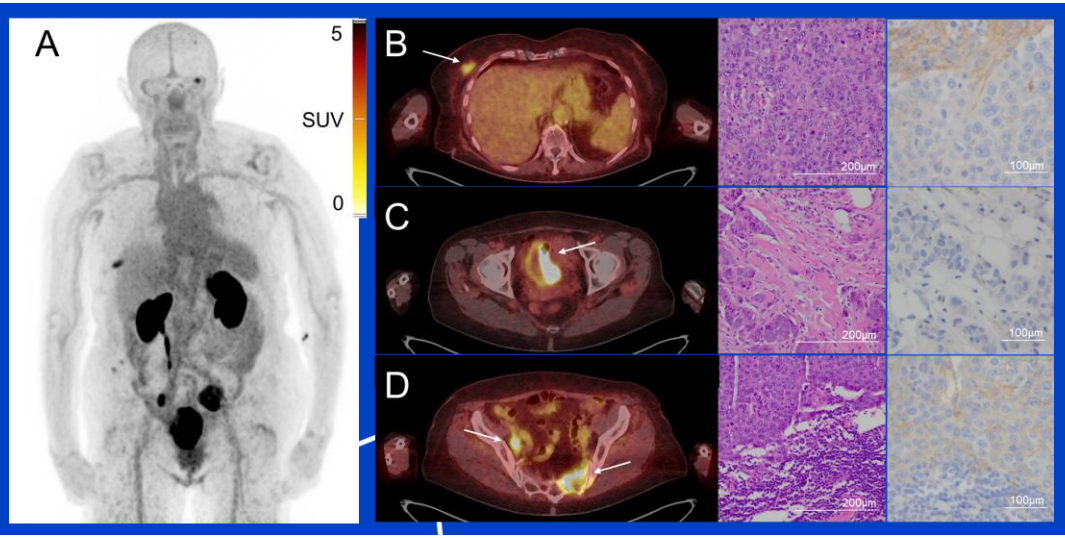
1. Gelb T et al. 2019. *Mol Cancer Ther*, 18(12_Suppl):A047. 2. Eder M et al. 2019. *Cancer Res*. 79(4):841-852.

BIA: Bicycle® Imaging Agent

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



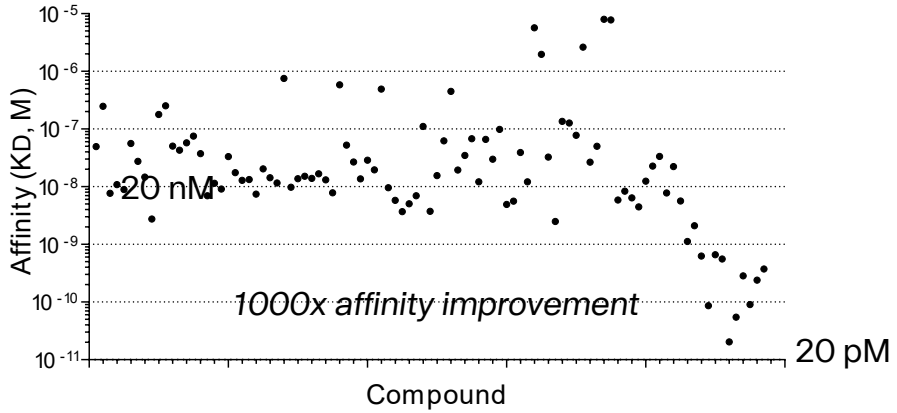
MT1-MMP-PET/CT imaging in advanced pulmonary adenocarcinoma.
Maximum intensity projections of [^{18}F]FDG-PET/CT (A) and [^{68}Ga]Ga-BCY25286 PET/CT at 60 mins (B) and at early time points (C) post injection.



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

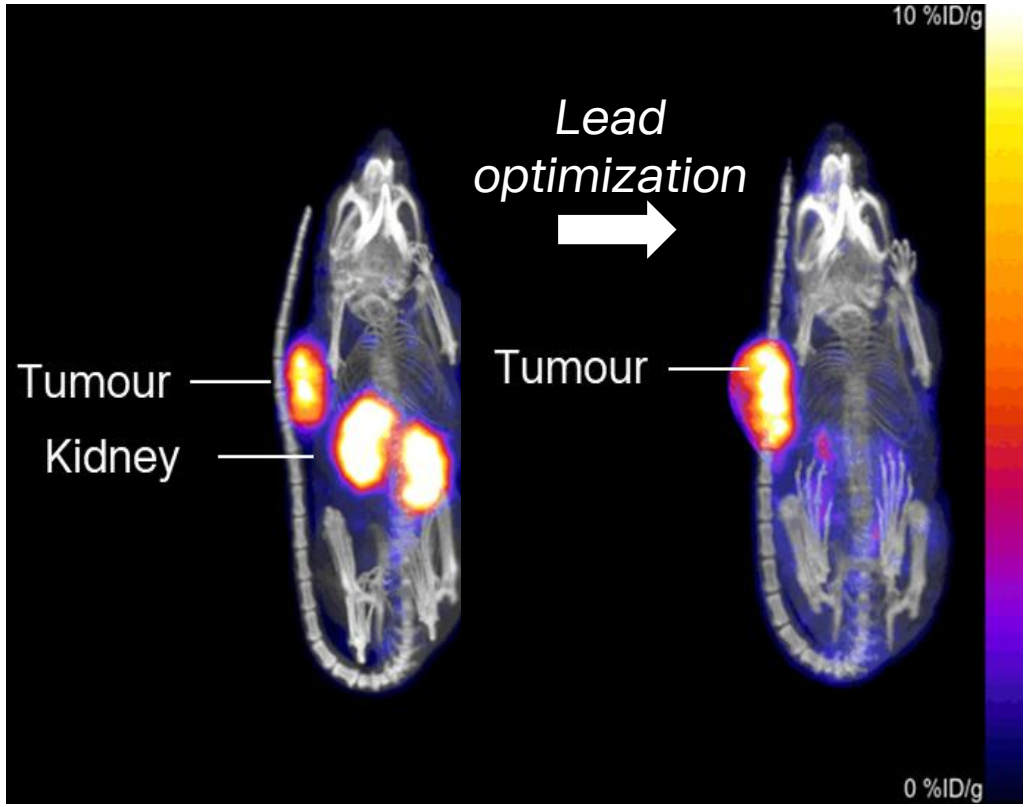


Binding affinities of compounds synthesized during lead optimization, as determined by surface plasmon resonance.

Structurally enabled

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

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.

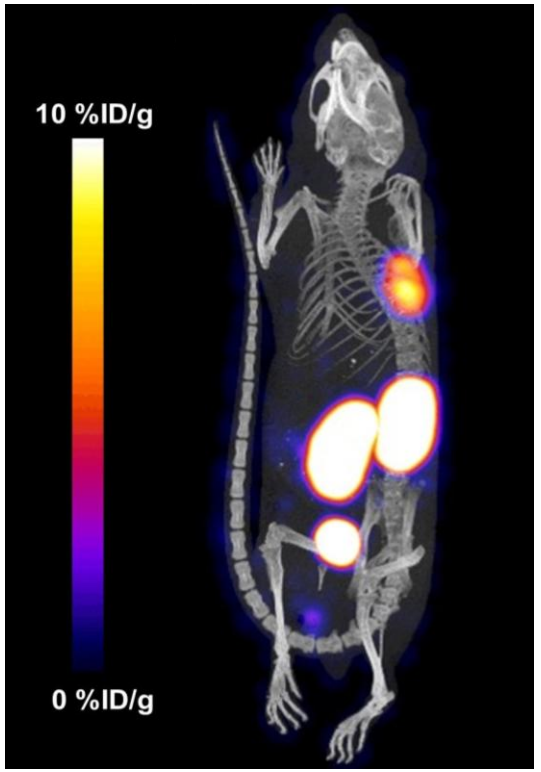
Our next radioligand target: EphA2, a first-in-class opportunity

- 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

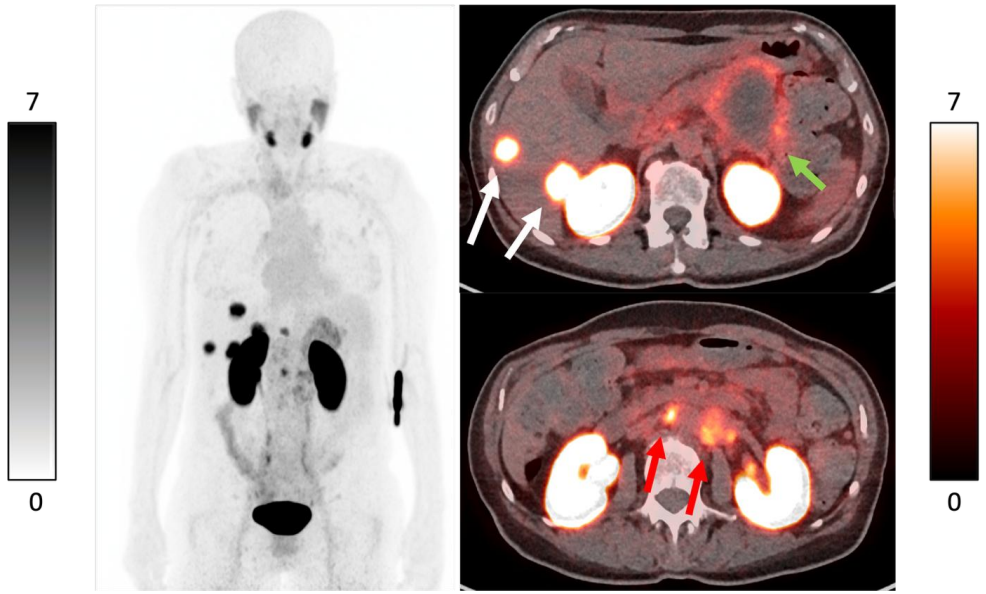


Example SPECT/CT Maximum Intensity Projection (MIP) 60 min. p.i. of 230 pmol of [111In]In labeled BRC® molecule

1. Zhou L et al. 2021. *Int J Clin Exp Pathol*, 14(4):484-492. 2. Cioce M and Fazio VM. 2021. *Cancers (Basel)*, 13(4):700.

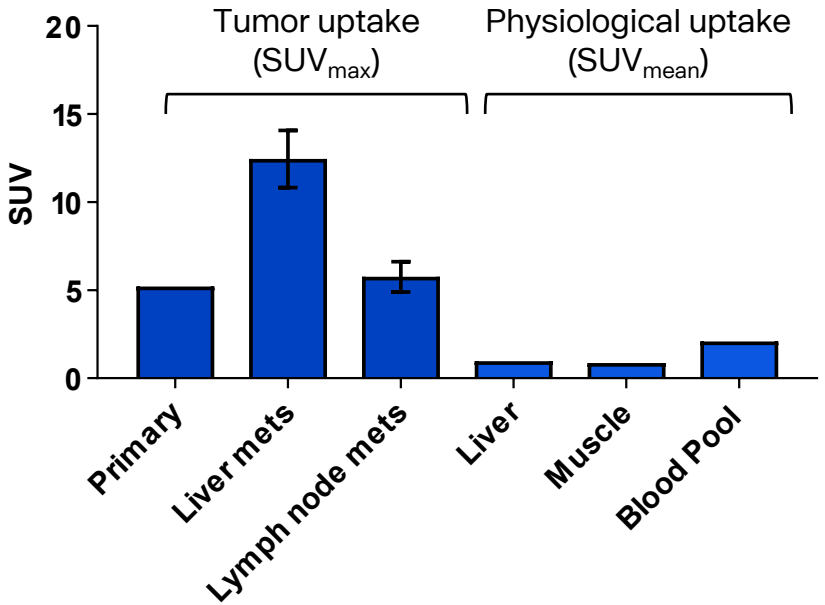
^{68}Ga-labeled EphA2 targeted bicycle imaging agent demonstrates target expression and availability for Bicycle engagement

Patient with lymphonodal and hepatic metastasized pancreatic ductal adenocarcinoma imaged with ^{68}Ga-labeled 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 visualization 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			
	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

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

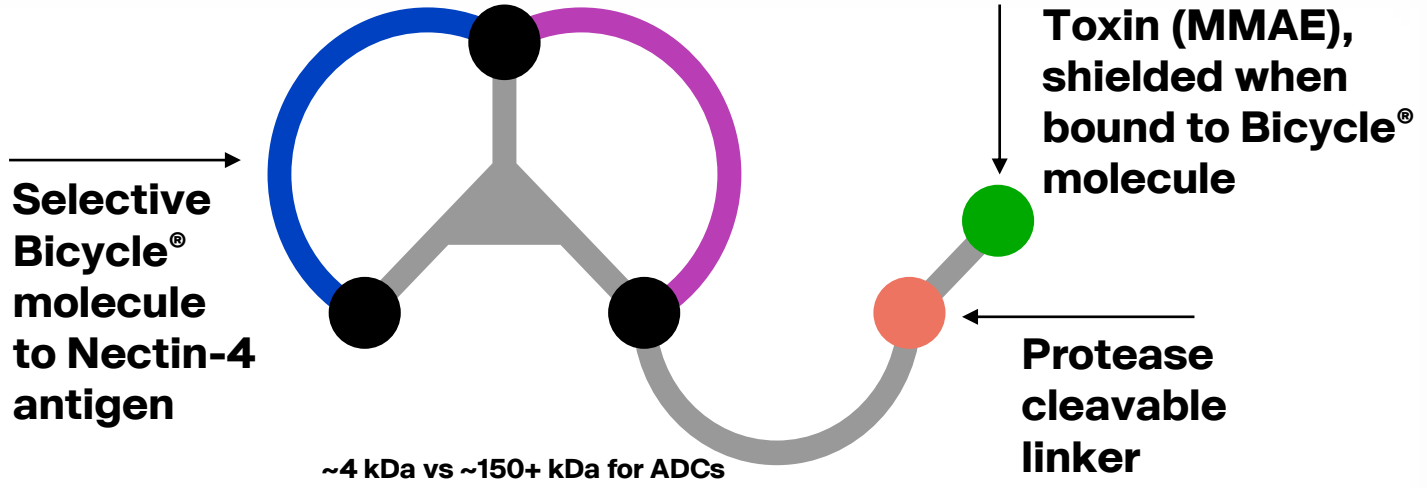
Bicycle®

Zelenectide is designed to provide strong efficacy while reducing the significant toxicity associated with Nectin-4 drug conjugates

Nectin-4 background

- Highly expressed in many tumor types
  - Bladder, lung, breast
- Nectin-4 MMAE ADC combined with IO is considered the SOC in 1L mUC
- Despite strong efficacy with the SOC, high rates and grades of adverse events limit some patients with mUC from receiving or staying on the SOC[1,2,3]

Zelenectide pevedotin



Highly differentiated preclinical and clinical performance:

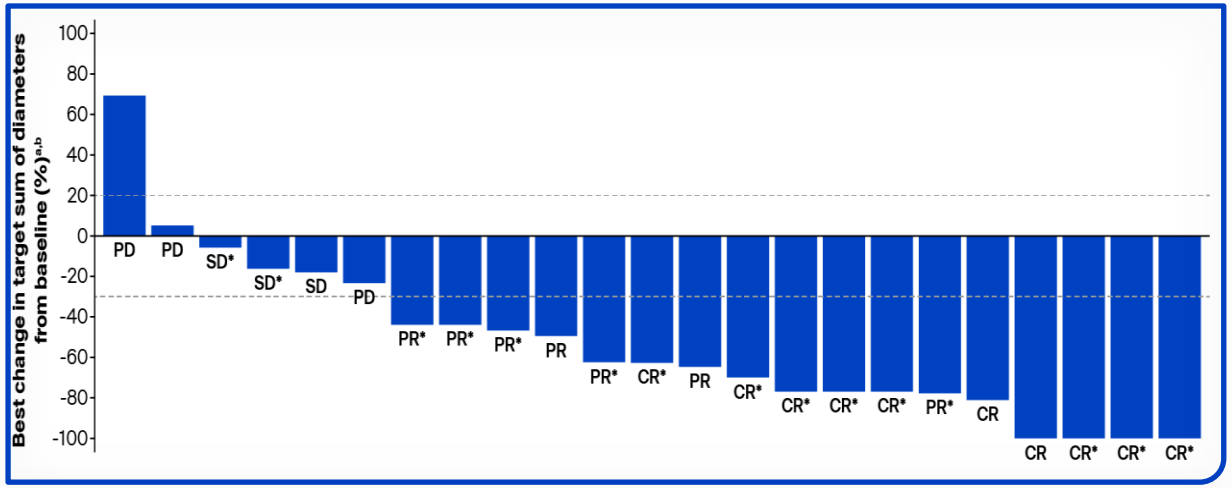
- Superior selectivity
- Excellent activity in multiple tumor models
- Reduced peripheral neuropathy, skin and eye toxicity

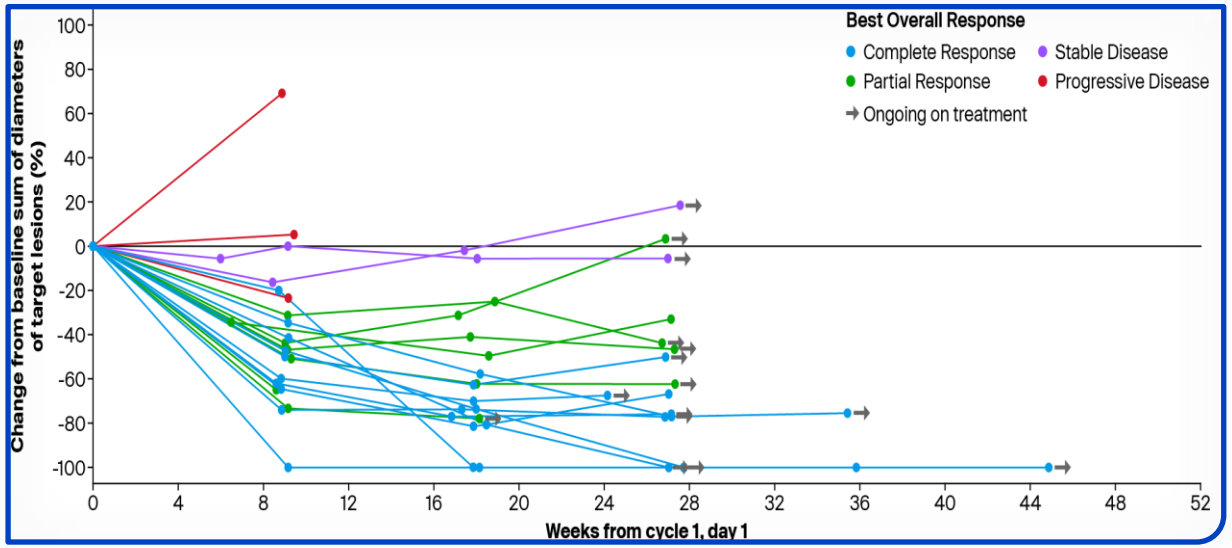
[1]Powles et al. *NEJM* 2024;390(10):875-888. [2]PADCEV label accessed 11May2026. [3]Zelenectide pevedotin Demand Study, The Link Group, Dec 2025
. 1L: first line therapy; ADC: antibody drug conjugate; BDC: Bicycle Drug Conjugate; kDa: kilodalton; MMAE: monomethyl auristatin E; mUC: metastatic urothelial cancer; SJS: Stevens Johnson Syndrome; TENS: toxic epidermal necrolysis; SOC: standard of care; IO: Immuno-oncology agent.

Zelenectide + pembrolizumab shows an encouraging response in 1L untreated mUC similar to published efficacy for standard of care

Responses in evaluable patients treated with zele 6 mg/m² D1/8 + pembro by BICR (n=23)[a,b]

- 62% cORR subsequent to data cut (n=26)[a, c]
- Median duration of zele treatment at 6 mg/m² was 6.3 months (range, 0.7-10.6)
- 65% (15/23) of patients remained on treatment at time of analysis





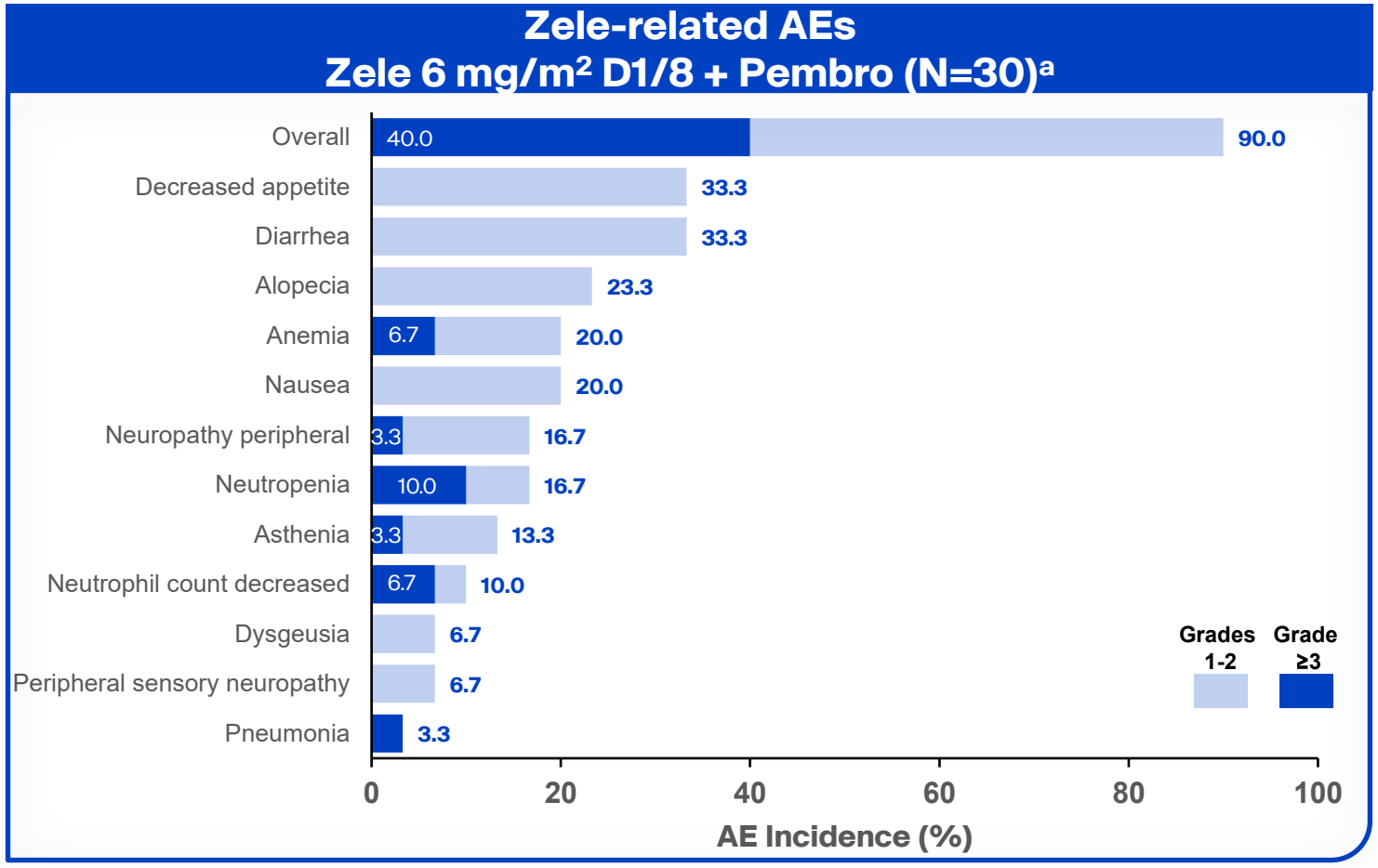
Data as of 23Jul2025 from Study BT8009-230. [a]Four patients had no measurable disease at baseline per BICR and were excluded from the efficacy analysis. [b]Three patients had no post-baseline sum of diameter target lesion measurements. A total of 23 patients are included in the waterfall and spider plots. Asterisks denote ongoing on treatment. [c]Subsequent to the data cut, an additional confirmed response was observed, which would result in 62% overall response rate. The confirmed ORR at time of the data cut was 58% [95% CI 36.9-76.6]. BICR, blinded independent central review; cORR, confirmed objective response rate; CR, complete response; mUC: metastatic urothelial carcinoma; pembro, pembrolizumab; PD, progressive disease; PR, partial response; SD, stable disease; zele, zelenectide pevedotin.

Bicycle®

In the same data set, zelenectide plus pembrolizumab also shows a differentiated safety profile in 1L untreated mUC

Zele + pembro at optimal dose in previously untreated la/mUC

- Median relative dose intensity in patients receiving 6 mg/m^2 was 97.0%
- Zele-related AEs were mostly Grades 1-2
- Only 1 patient discontinued zele due to a zele-related AE
- Median duration of follow-up was 7.0 months (range, 1.2-10.5)



Data as of 23Jul2025 from Study BT8009-230. [a]Includes AEs related to zele or zele + pembro of any grade that occurred in ≥20% of patients or of Grade ≥3 that occurred in ≥5% of patients in the 5 mg/m^2 D1/8/15 or 6 mg/m^2 D1/8 dose optimization arm. Patients with multiple AEs are counted only once by the worst NCI-CTCAE category within a preferred term. AE: adverse event; D: day; la/mUC: locally advanced/metastatic urothelial carcinoma TRAE: treatment-related adverse event; zele: zelenectide pevedotin

Zelenectide + pembrolizumab has a differentiated safety profile with no severe skin toxicity and few Grade 3 toxicities observed

Zele-related AEs of clinical interest, n (%)[a,b]	Zelenectide 6 mg/m^2 D1/8 + Pembrolizumab (N=30)					
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Peripheral neuropathy[c]	11 (36.7)	6 (20.0)	4 (13.3)	1 (3.3)	0	0
Sensory events	10 (33.3)	6 (20.0)	3 (10.0)	1 (3.3)	0	0
Motor events	1 (3.3)	0	1 (3.3)	0	0	0
Skin reactions[d]	5 (16.7)	3 (10.0)	2 (6.7)	0	0	0
Eye disorders[e]	3 (10.0)	3 (10.0)	0	0	0	0
Hyperglycemia[f]	0	0	0	0	0	0

Conclusion

- **Zelenectide + pembrolizumab demonstrates similar clinical efficacy to published data for standard of care in 1L untreated mUC but does not show the same safety risk**

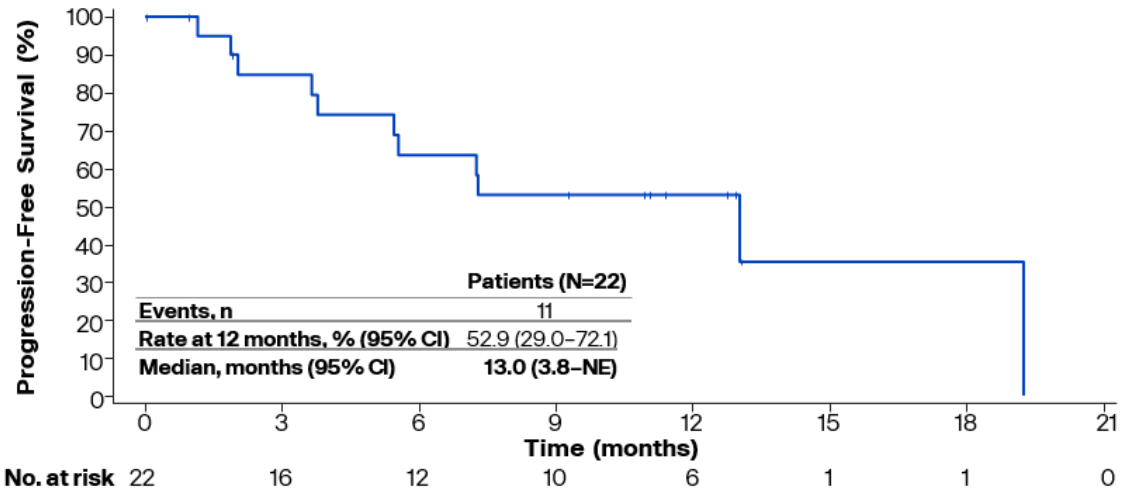
Next steps

- **Randomized Phase 2 data in 2H 2026 will determine most appropriate path for zelenectide**

Data as of 23Jul2025 from Study BT8009-230. [a]Includes AEs related to zele or zele + pembro. [b]Patients can have multiple preferred terms within a category. [c]MedDRA SMQ [Broad] for peripheral neuropathy. [d]MedDRA SMQ [broad] for SCAR and high level terms of 'bullous conditions,' 'dermatitis and eczema,' 'rashes, eruptions and exanthems NEC,' 'erythemas,' and 'dermatitis ascribed to specific agent.' [e]SOC of eye disorders. [f]Preferred Term
D1/8: day 1 and day 8

In a Phase 1 trial, zelenectide + pembrolizumab exhibits similarly encouraging efficacy and safety results in 1L cisplatin-ineligible mUC

Progression free survival for zelenectide 5 mg/m² QW + pembrolizumab in 1L mUC cis-ineligible patients (N=22)[a]



Median progression free survival 13m (95% CI 3.8-NE, N=22)

Treatment-related AECIs in 1L mUC cis-ineligible patients treated with zelenectide 5 mg/m² QW + pembrolizumab

TRAEs of clinical interest, n (%)[b, c]	Patients (N=22)					
	Any Gr	Gr 1	Gr 2	Gr 3	Gr 4	Gr 5
Peripheral neuropathy[d]	14 (63.6)	5 (22.7)	6 (27.3)	3 (13.6)	0	0
Sensory events	13 (59.1)	4 (18.2)	6 (27.3)	3 (13.6)	0	0
Motor events	1 (4.5)	1 (4.5)	0	0	0	0
Skin reactions[e]	11 (50.0)	5 (22.7)	4 (18.2)	2 (9.1)	0	0
Hyperglycemia[f]	5 (22.7)	4 (18.2)	1 (4.5)	0	0	0
Eye disorders[g]	4 (18.2)	3 (13.6)	1 (4.5)	0	0	0

No Grade 4 or Grade 5 TRAE of clinical interest occurred

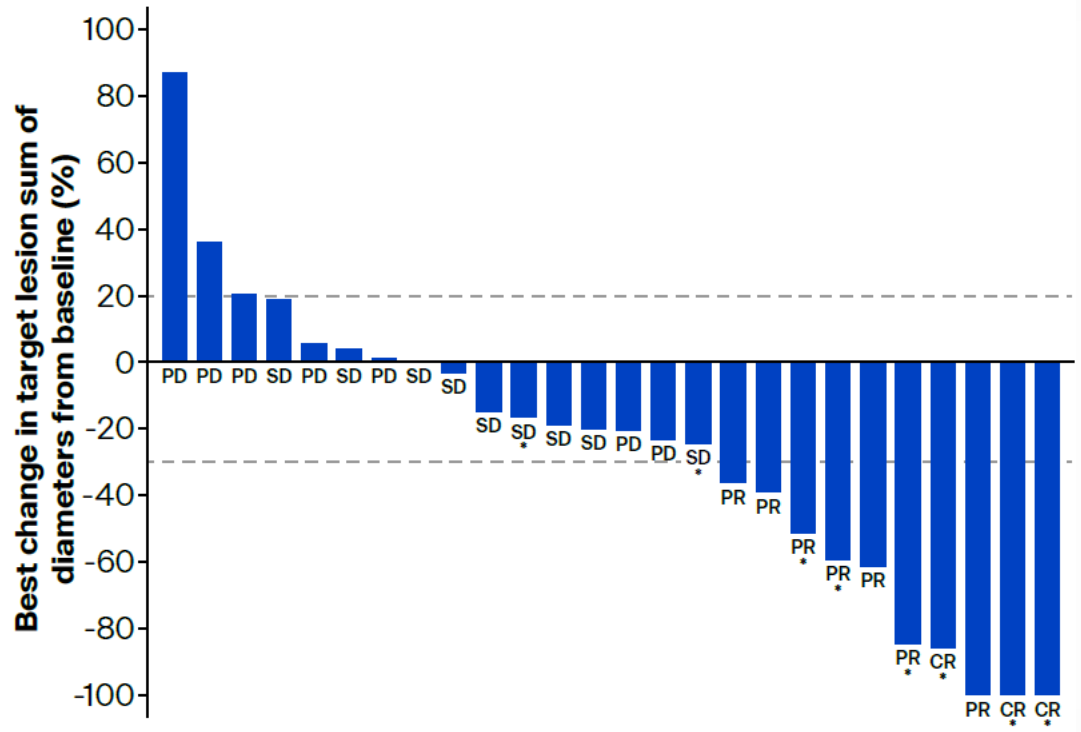
Promising median progression free survival and safety profile seen in a frail population with advanced age, 32% with liver metastases, and 45% of patients characterized as ECOG PS 2

Bicycle®

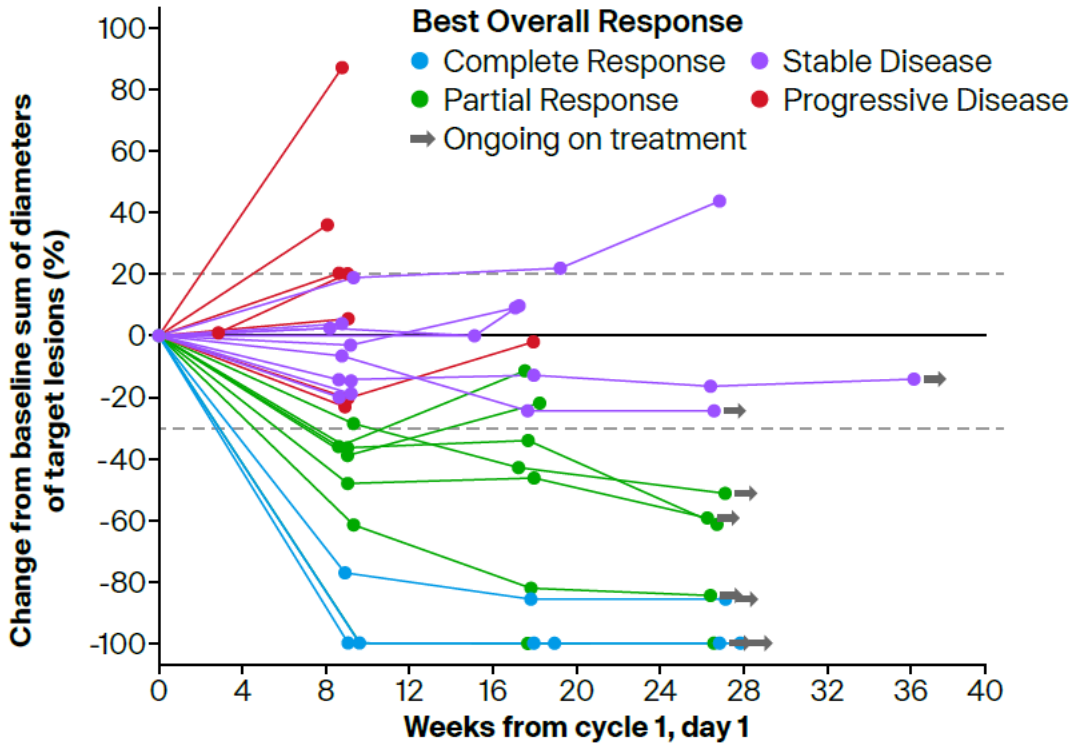
[a]Data as of 01Aug25 from Study BT8009-100. [b]Includes AEs related to zele, pembro, or zele + pembro. [c]Patients can have multiple preferred terms within a category. [d]Includes TEAEs Related to Study Drug of Peripheral Neuropathy [Broad](SMQ). [e]Includes the MedDRA SMQ [broad] for Severe Cutaneous Adverse Reactions (SCAR) and the following high-level terms (HLTs): "bullous conditions", "dermatitis and eczema", "rashes, eruptions and exanthems NEC", "erythemas", and "dermatitis ascribed to specific agent". [f]Preferred term. [g]SOC of eye disorders. 1L: first line; AECI: adverse events of clinical interest; cis-ineligible: cisplatin-ineligible; ECOG PS: Eastern Cooperative Oncology Group performance status; mUC: metastatic urothelial carcinoma; m: months; NE: not estimable; QW: weekly; pembro: pembrolizumab; zele: zelenectide pevedotin

In 2L mUC, zelenectide also shows promising efficacy results as monotherapy

Efficacy-evaluable patients treated with zele 6 mg/m² D1/8 by BICR (n=26)[a]



Efficacy-evaluable patients treated with zele 6 mg/m² D1/8 by BICR (n=26)[a]



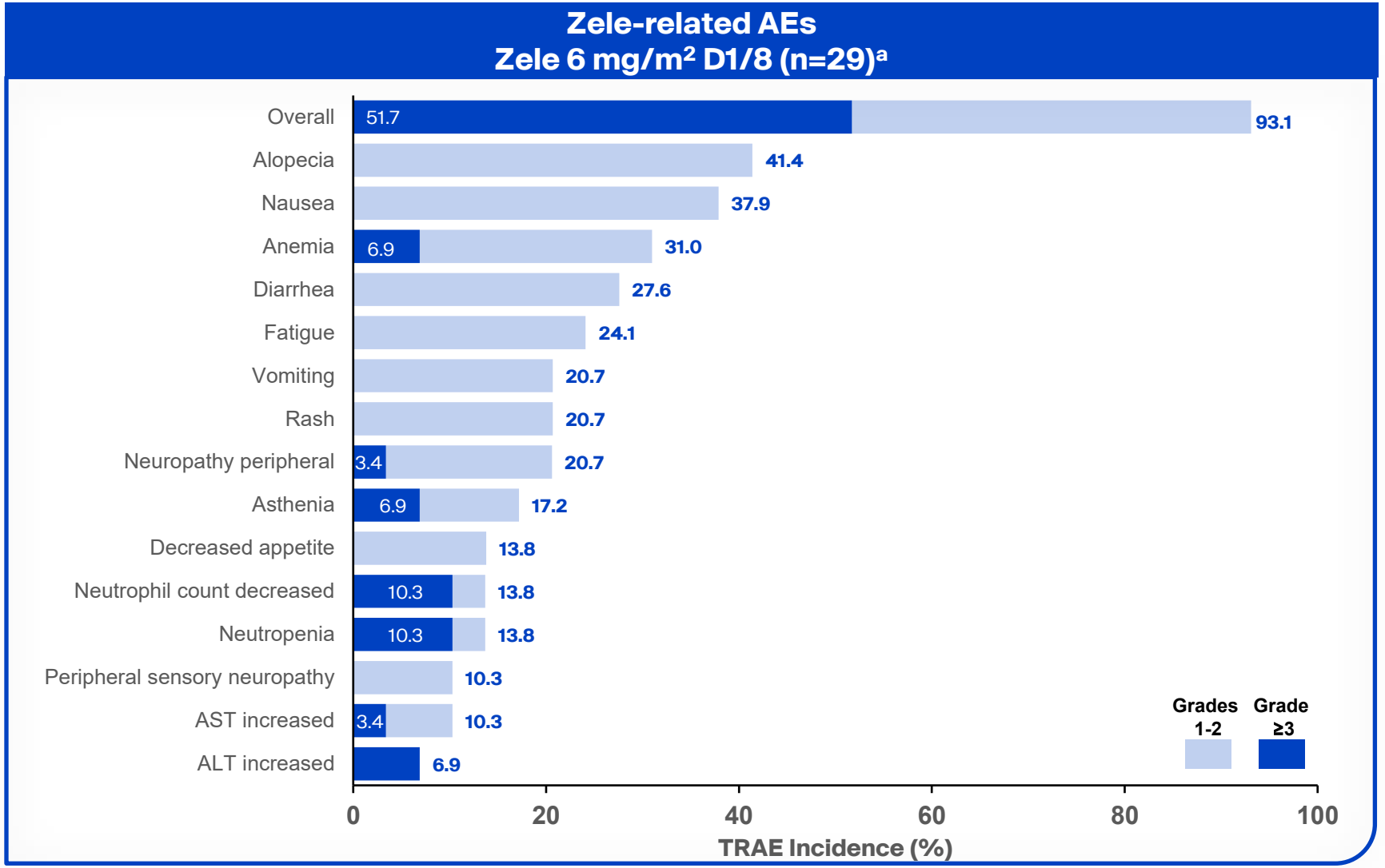
Confirmed ORR at the optimal dose was 30% [95% CI 13.8–50.2], with 8 patients remaining on treatment at time of analysis (n=27)[b]. Two additional patients had unconfirmed responses resulting in a 37% ORR regardless of confirmation.

Data as of 14Jun2025 from Study BT8009-230. [a]Four patients were not included based on no measurable disease at baseline (n=2), not receiving zele (n=1), and a lack of adequate post-baseline target lesions (n=1). *Asterisks and grey arrows indicate patients continuing zele treatment, except patients with PD as their best overall response. [b]ORR with confirmation (%) is defined as the proportion of participants with BOR with confirmation of CR or PR; 95% CI was calculated by using exact Clopper-Pearson method. BICR: blinded independent central review; CR: complete response; D: day; ORR: objective response rate; PD: progressive disease; PR: partial response; SD: stable disease; zele: zelenectide pevedotin.

Zelenectide monotherapy potentially provides a well-tolerated treatment in 2L mUC

Zele monotherapy at optimal dose in previously treated mUC

- Majority of TRAEs were Grade 1-2
- No Grade 4 or 5 TRAEs were reported in patients treated with 6 mg/m^2
- No treatment discontinuations occurred at the optimal dose
- Median duration of follow-up was 6.2 months (range, 0.1-9.9)



Data as of 14Jun2025 from Study BT8009-230. [a]Includes AEs related to zele of any grade that occurred in ≥20% of patients or of Grade ≥3 that occurred in ≥5% of patients in the 5 mg/m^2 D1/8/15 or 6 mg/m^2 D1/8 dose optimization arm. Patients with multiple AEs are counted only once by the worst NCI-CTCAE category within a preferred term. The safety-evaluable population treated with 6 mg / m^2 zele excluded n=1 patient who did not receive zele. AE: adverse event; D: day; mUC: metastatic urothelial carcinoma; TRAE: treatment-related adverse event; zele: zelenectide pevedotin

Treatment-related adverse events of clinical interest were predominantly Grade 1 for zelenectide in 2L mUC

Zele-related AEs of clinical interest, n (%)	Zelenectide 6 mg/m^2 D1/8 (n=29[b])					
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Peripheral neuropathy[c]	11 (37.9)	9 (31.0)	1 (3.4)	1 (3.4)	0	0
Sensory events	11 (37.9)	9 (31.0)	1 (3.4)	1 (3.4)	0	0
Motor events	0	0	0	0	0	0
Skin reactions[d]	8 (27.6)	8 (27.6)	0	0	0	0
Eye disorders[e]	3 (10.3)	3 (10.3)	0	0	0	0
Hyperglycemia[f]	1 (3.4)	0	0	1 (3.4)	0	0

- **Majority of peripheral neuropathy was Grade 1 (82%, 9/11)**
- **No motor events were reported**
- **All skin reactions were Grade 1, and no patients reported severe skin reactions**
- **Eye disorders were Grade 1 and only 1 patient experienced hyperglycemia**

Data as of 14Jun2025 from Study BT8009-230. [a]Patients can have multiple preferred terms within a category. [b]The safety-evaluable population treated with 6 mg /m^2 zele excluded n=1 patient who did not receive zele. [c]MedDRA SMQ [Broad] for peripheral neuropathy [d]MedDRA SMQ [broad] for SCAR and high levels terms of "bullous conditions," "dermatitis and eczema," "rashes, eruptions and exanthems NEC," "erythemas," and "dermatitis ascribed to specific agent." . [e]SOC of eye disorders. [f]Preferred term. AE: adverse event; D: day; zele: zelenectide pevedotin

Patients with mUC still need more treatments that allow them to live longer and live well

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

614,000 Worldwide

85,080 United States

Rank among all cancers (Incidence)

10 Worldwide

6 United States

Patients developing metastatic disease

25%

5-year Survival

64% / 7%

Stages 0-IV Stage IV

- One of the highest lifetime treatment costs per patient of all cancers[3,4]
- High recurrence rate and ongoing invasive monitoring lead to economic and human toll of this disease[3,4]
- **Improved safety profiles are needed to bring the promise of innovative treatment options to mUC[5]**

1. Oracle CancerMPact, Treatment Architecture US Bladder Cancer, Dec 2025. Sources: Based on CancerMPact® Patient Metrics U.S., accessed Feb 2025. Ranking is based on relative incidence of 31 tumors; Risk factors from National Cancer Institute (cancer.gov), NCCN Guidelines *Bladder Cancer* v2.2025, ASCO's patient information website (Cancer.Net), American Cancer Society (cancer.org).
2. World Health Organization, International Agency for Research on Cancer: Cancer Fact Sheet, Bladder (gco.iarc.who.it)
3. Journal of Urology, Adult Urology, Late Recurrences Following Radical Cystectomy Have Distinct Prognostic and Management Considerations, Sep2020.
4. European Urology, The Financial Burden of Localized and Metastatic Bladder Cancer, May2025.
5. Zelenectide pevedotin Demand Study, The Link Group, Dec 2025

mUC: metastatic urothelial cancer.

Despite having an efficacious standard of care in 1L mUC, oncologists still want improved regimens to help more patients

Variety of regimens are still used in 1L mUC instead of SOC

~40% ... of patients receive regimens other than a Nectin-4 ADC[1,2,3]

86% ... of oncologists believe there is still room for improvement in current treatments[1]

Primary reasons for prescribing alternative regimens in 1L mUC

50% concerns about peripheral neuropathy[1]

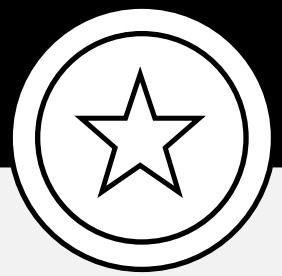
43% concerns about safety profile[1]

40% general tolerability issues[1]

1. Zelenectide pevedotin Demand Study, n = 115 medical oncologists, The Link Group, Dec 2025
2. IQVIA Oncology Real-World Data | Prepared for Bicycle Therapeutics | IQVIA Oncology Analytics Platform, Jan 2026. Unique Total 1L Patients: 14,438; Unique New 1L Patients: 9,063
3. Oracle CancerMPact, Treatment Architecture US Bladder Cancer, Dec 2025.

1L: 1st line treatment, mUC: metastatic urothelial cancer, SOC: standard of care, ADC: antibody drug conjugate

Duravelo-2 converted to a Phase 2 trial with results expected in 2H 2026



DOSE SELECTION

- Optimal dose of zelenectide 6 mg/m^2 (D1/8) plus pembro demonstrates **response rates comparable to published data for standard of care and a differentiated safety profile**

REGULATORY ENGAGEMENT

- Preliminary regulatory feedback (EMA, FDA, MHRA) indicates **multiple potential pathways for the continued development and approval of zelenectide in mUC**

DATA AVAILABILITY

- Duravelo-2 study has been converted into a randomized Phase 2 trial and **further results expected in the second half of 2026**

D: day, pembro: pembrolizumab, EMA: European Medicines Agency, FDA: Food and Drug Administration, MHRA: Medicines and Healthcare products Regulatory Agency, mUC: metastatic urothelial cancer

Looking ahead

Bicycle®

Strategic focus enables multiple potential value generating milestones

2025 - Q1 2026 achievements

- ✓ Platform validation with zelenectide data
- ✓ Strategic portfolio reprioritization and focus on nuzefatide & radiotherapeutics
- ✓ Human imaging de-risks novel targets
- ✓ Established multiple strategic partnerships to create end-to-end radiopharmaceutical supply chain
- ✓ Strengthened leadership & Board
- ✓ **Extended expected cash runway into 2030**

Strategic priorities and anticipated milestones 2026 and beyond

Nuzefatide pevedotin

- Progress enrollment in Phase 2 trial in PDAC using 8 mg/m^2 Q2W dose

Bicycle radiotherapeutics

- Ongoing IND-enabling activities for BT1702 (BRC® molecule, ^{212}Pb) and clinical start in 2027
- Progress EphA2 BRC molecule to clinical start in 2028

Zelenectide pevedotin

- Randomized Phase 2 trial data readout in 2H2026 and determine most appropriate path

Novel targets and new payloads

- Strategic focus on novel targets and new payloads

^{212}Pb: Lead-212 radioactive alpha-emitting radioisotope; BRC: Bicycle® radioconjugate; EphA2: ephrin type-A receptor 2; PDAC: pancreatic ductal adenocarcinoma; Q2W: once every 2 weeks.

Our mission:

To help patients live longer and live well

Bicycle®

Appendix

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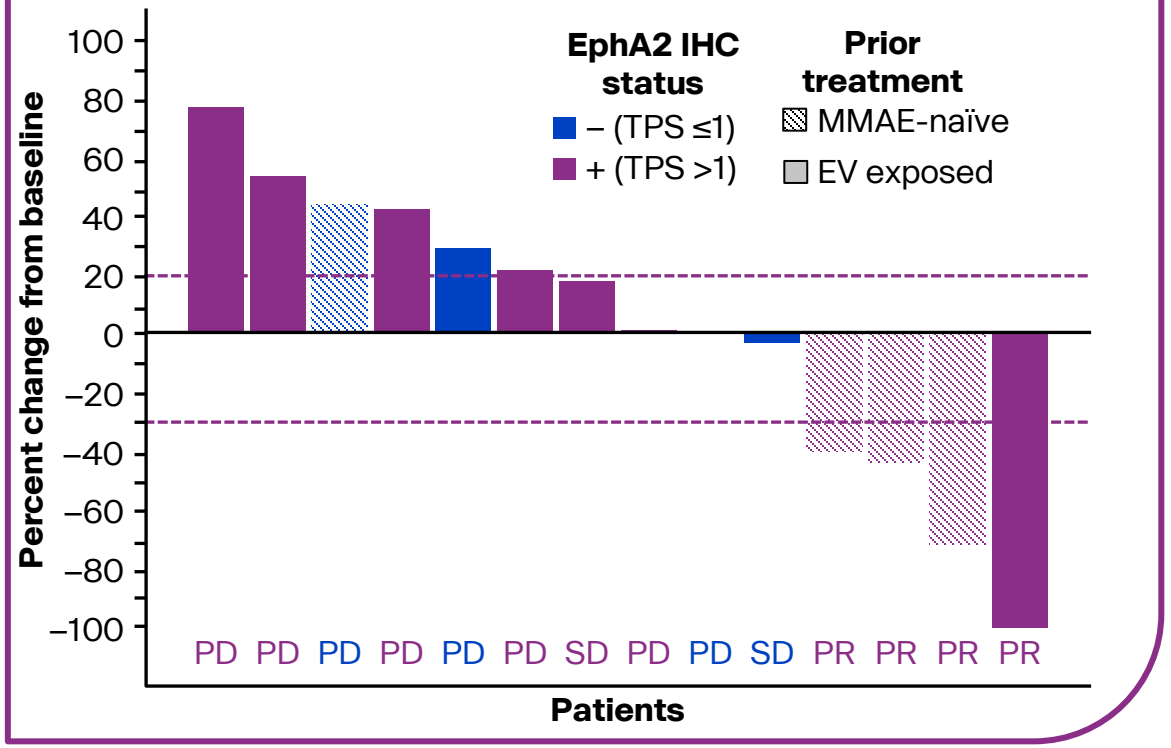
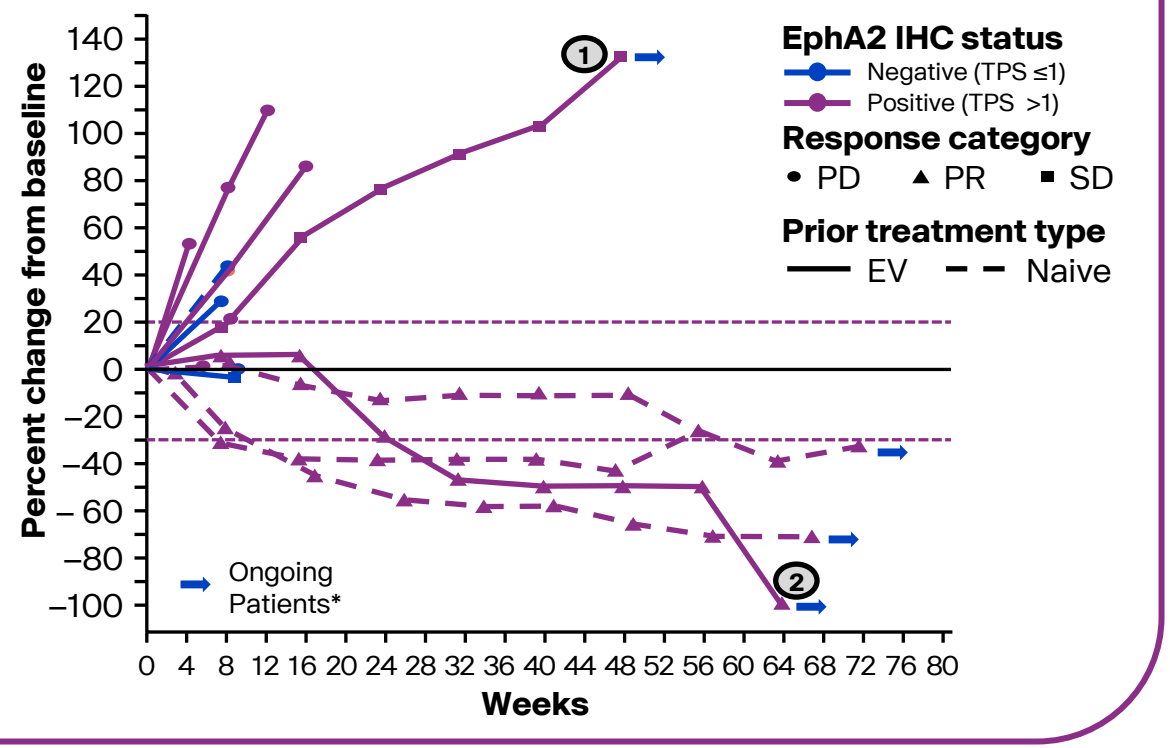
Nuzefatide + nivolumab is active in EphA2+, MMAE-naïve LL mUC patients and exhibits a long duration of action

Waterfall plot for 6.5 mg/m² nuzefatide Q2W + nivolumab in late line mUC (N=14)



Spider plot for 6.5 mg/m² nuzefatide Q2W + nivolumab in late line mUC (N=14)



- In the subset of patients with EphA2+ tumors that were MMAE-naïve, 3/3 achieved a confirmed partial response (ORR 100%)
- In the subset of patients with EphA2+ tumors that were MMAE-naïve, as of 14 April '26, the minimum DoT was 53.9 weeks

Data as of 09Feb2026 from Study BT5528-100. [1]Patient treated beyond progression with symptomatic relief and bladder lesion clearance. [2]Patient with a complete response in target lesions with persistent non-target lesions. DoT: duration of treatment; EV: enfortumab vedotin; LL: late line; MMAE: monomethyl auristatin E; mUC: metastatic urothelial cancer; PD: progressive disease; PR: partial response; Q2W: once every two weeks; SD: stable disease; TPS: Tumor Proportion Score; ORR: overall response rate.

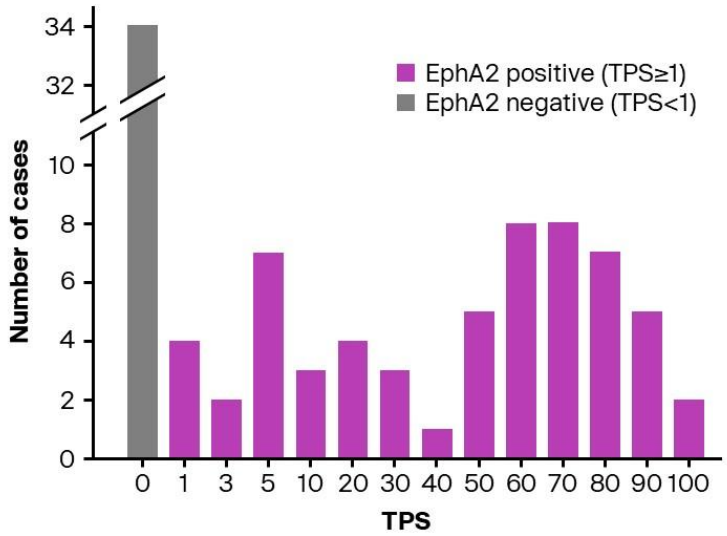
Nuzefatide pevedotin is generally well tolerated at clinically active doses both as a monotherapy and in combination with nivolumab

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 from Study BT5528-100. [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.

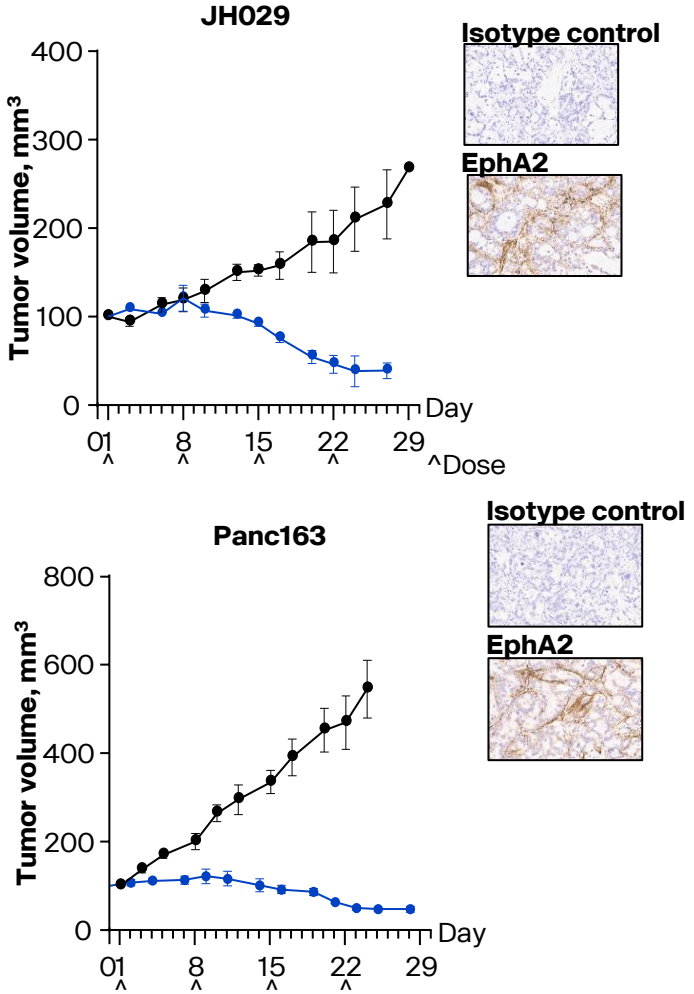
- Most (63%) samples in human pancreatic tumor microarray~~)~~ EphA2 positive (TPS ≥1)
- PA1921c : 93 cases, 179 cores, in a PDAC microarray

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



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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