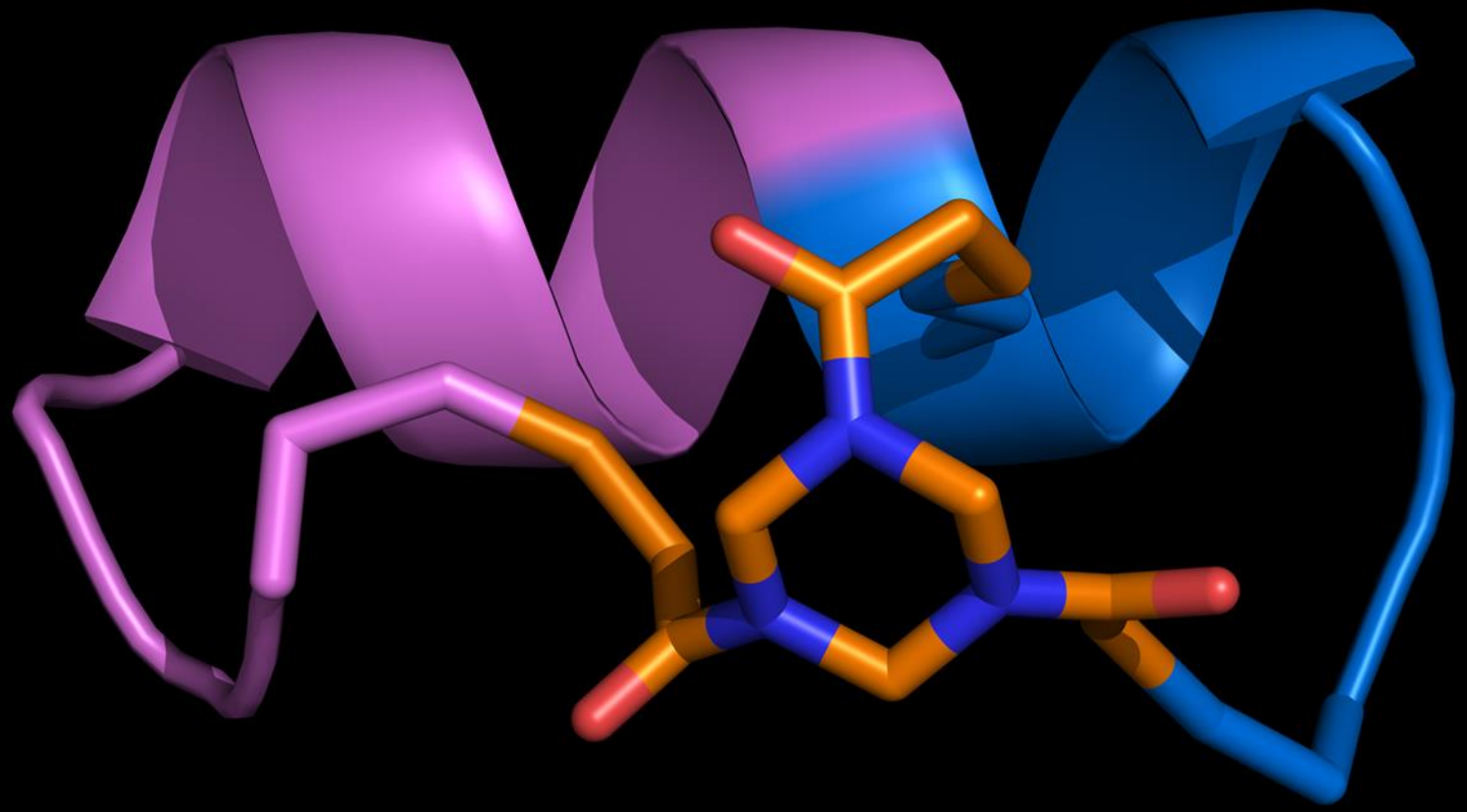
Zelenectide Pevedotin Program Update



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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, trends or strategies and other financial and business matters, including expected financial runway; our current and prospective product candidates, planned clinical trials and preclinical activities, and current and prospective collaborations; the timing of announcement of data and other updates for our clinical programs; the safety and efficacy profile of our product candidates and the success of our development of our current and prospective product candidates; and the size and composition of the potential market 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, the potential impact of our product candidates, if approved, on patients 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 or efficacy profile 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 market for our product candidates, if approved, 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 October 31, 2024, 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.

This presentation does not constitute an offer to sell or a solicitation of an offer to buy securities, nor shall there be any sale of any securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

Today’s speakers

Kevin Lee, Ph.D., MBA

Chief Executive Officer

Alethia Young

Chief Financial Officer

Santiago Arroyo, M.D., Ph.D.

Chief Development Officer

Jennifer Perry, Pharm.D.

Chief Strategy Officer and Head of Commercial

Niklas Klümper, M.D.

University Hospital Bonn

Sherene Loi, M.D., Ph.D.

Peter MacCallum Cancer Centre

Agenda

- Welcome
- Zelenectide pevedotin + pembrolizumab in 1L mUC
- NECTIN4 gene amplification overview
- Zelenectide pevedotin in breast cancer patients with NECTIN4 gene amplification
- Bicycle's NECTIN4 gene amplification development strategy
- Q&A

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

Unique Platform

Developing Bicycle® molecules – a novel synthetic peptide modality that enables the drugging of complex targets

Technology based on Nobel Prize-winning science

Strong intellectual property portfolio

Internal Programs

Focused on oncology, with multiple clinical molecules

Expedited development and regulatory path for zelenectide pevedotin (formerly BT8009) in mUC

Using NECTIN4 gene amplification to expedite development of zelenectide in TNBC, NSCLC and other cancers

First human imaging data validates potential of MT1-MMP as a novel radiopharmaceuticals target

Validating Partnerships

Extending use of platform into diverse range of therapeutic areas like radiopharmaceuticals and neurology

Genentech – A Member of the Roche Group
NOVARTIS
Bayer
IONIS
CANCER RESEARCH UK
Innovate UK
dkfz.

Ambitious Company

Deeply experienced team

Located in Cambridge, UK, and Cambridge, MA

NASDAQ: BCYC

Cash and cash equivalents of $890.9M as of Sept. 30, 2024, with expected financial runway into 2H 2027

Zelenectide pevedotin, a Nectin-4 targeting Bicycle® Toxin Conjugate

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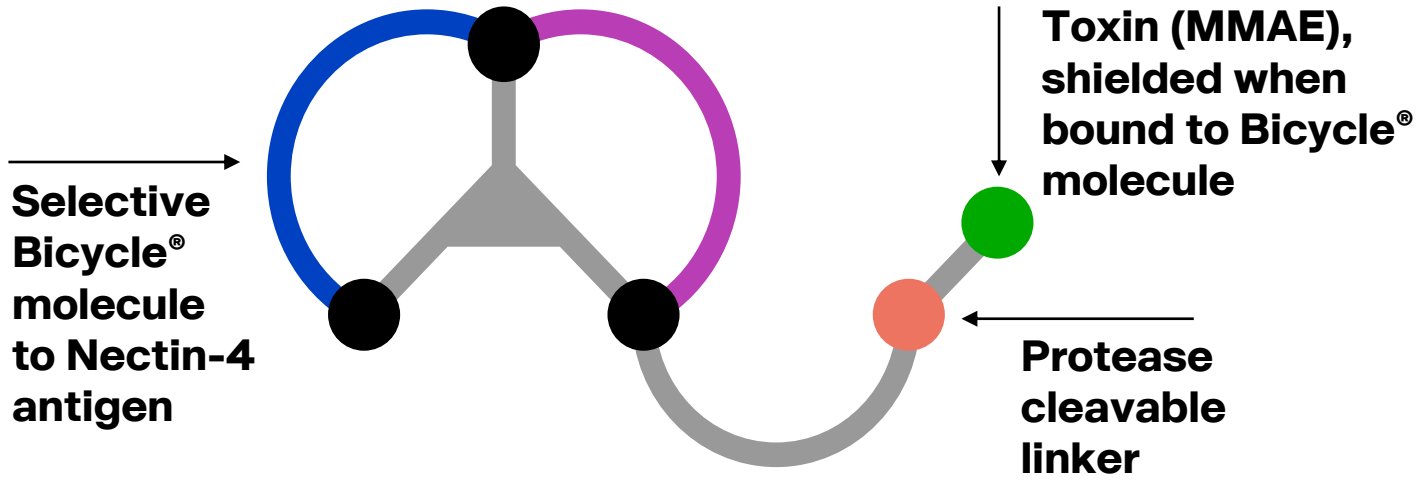
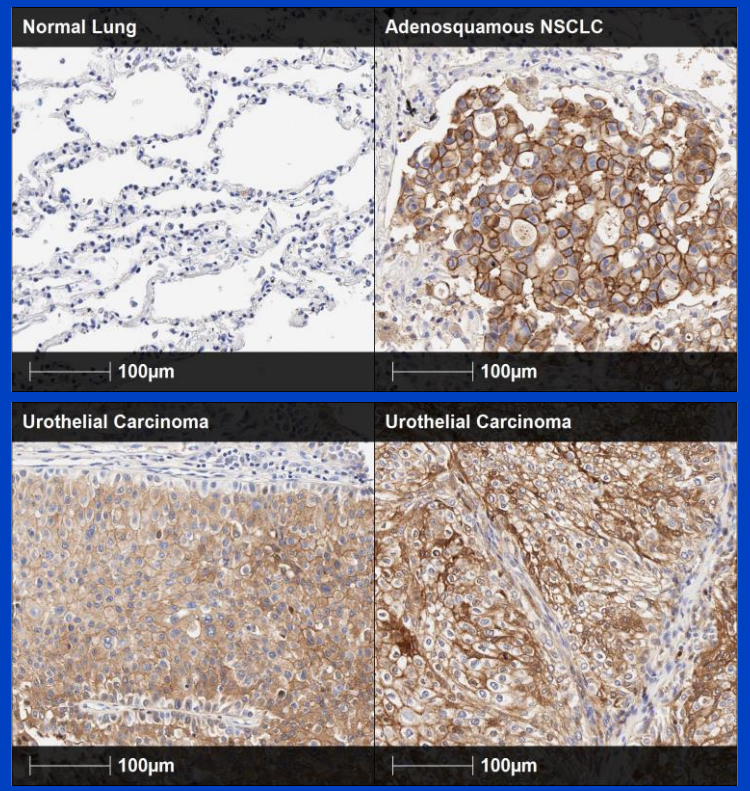
Zelenectide pevedotin targets Nectin-4, a high value target expressed in many tumors



Highly differentiated preclinical performance:

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



MMAE-sensitive tumor types include **bladder, NSCLC, TNBC** and others

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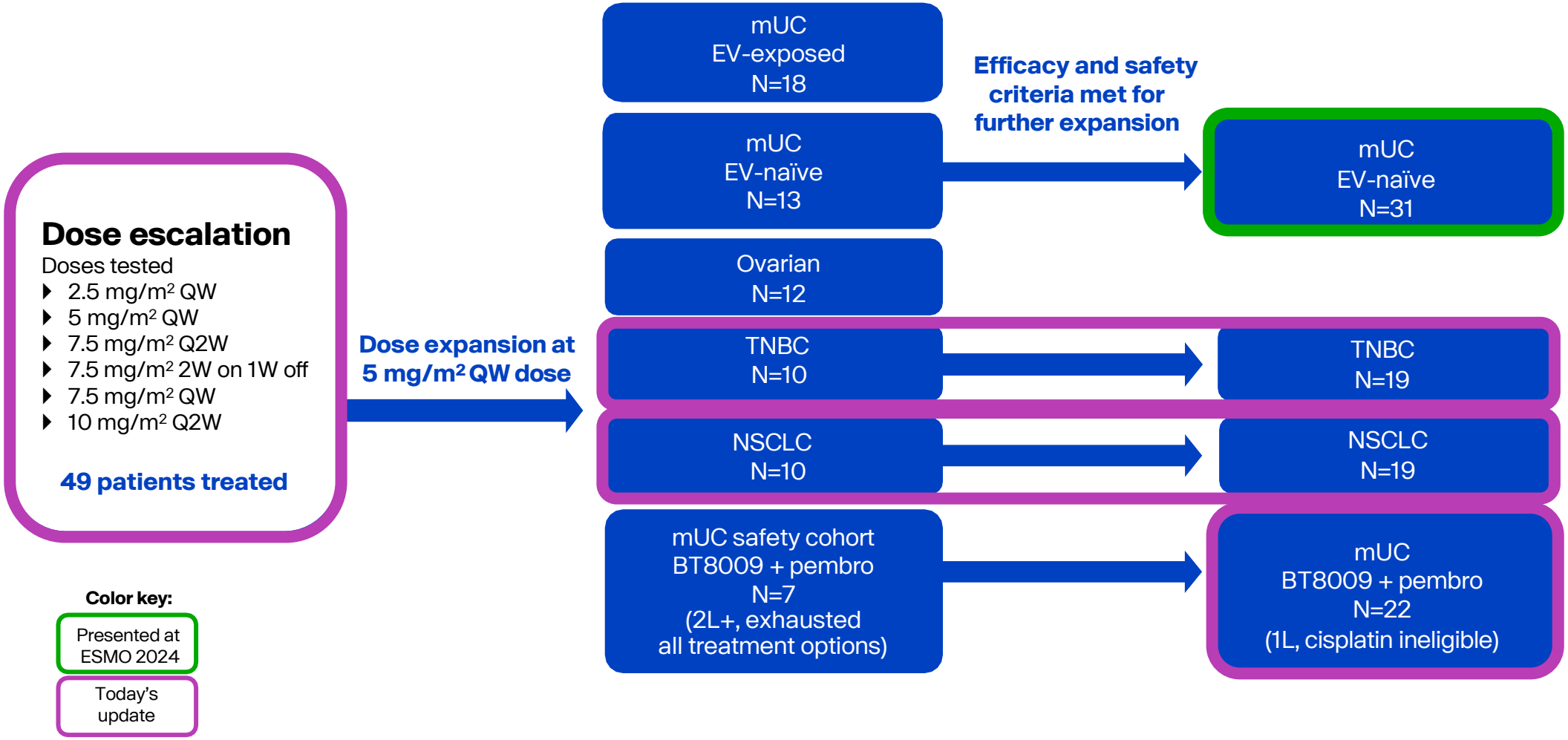
1. Challita-Eid PM et al. 2016. *Cancer Res,* 76(10):3003-3013. 2. Campbell CT et al. 2020. *Cancer Res*, 80(16 Suppl):5300. 3. Cohen H et al. 2021. *J Immunother Cancer*, 9(Suppl 2):A2. 4. Rigby M et al. 2022. Mol Cancer Ther, 21(12):1747-1756. 5. Mudd GE et al. 2022. J Med Chem, 65(21):14337-14347. 6. Kristensson J et al. EORTC-NCI-AACR Symposium 2024.
MMAE: monomethyl auristatin E; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer.

Duravelo-1: Phase 1/2 study of zelenectide pevedotin



1L: 1st line; 2L+: 2nd line or later; ESMO: European Society of Medical Oncology; EV: enfortumab vedotin; mUC: metastatic urothelial cancer; NSCLC: non-small cell lung cancer; QW: weekly; Q2W: every other week; TNBC: triple-negative breast cancer.

Zelenectide pevedotin + pembrolizumab showed a promising response and differentiated safety profile in 1L mUC

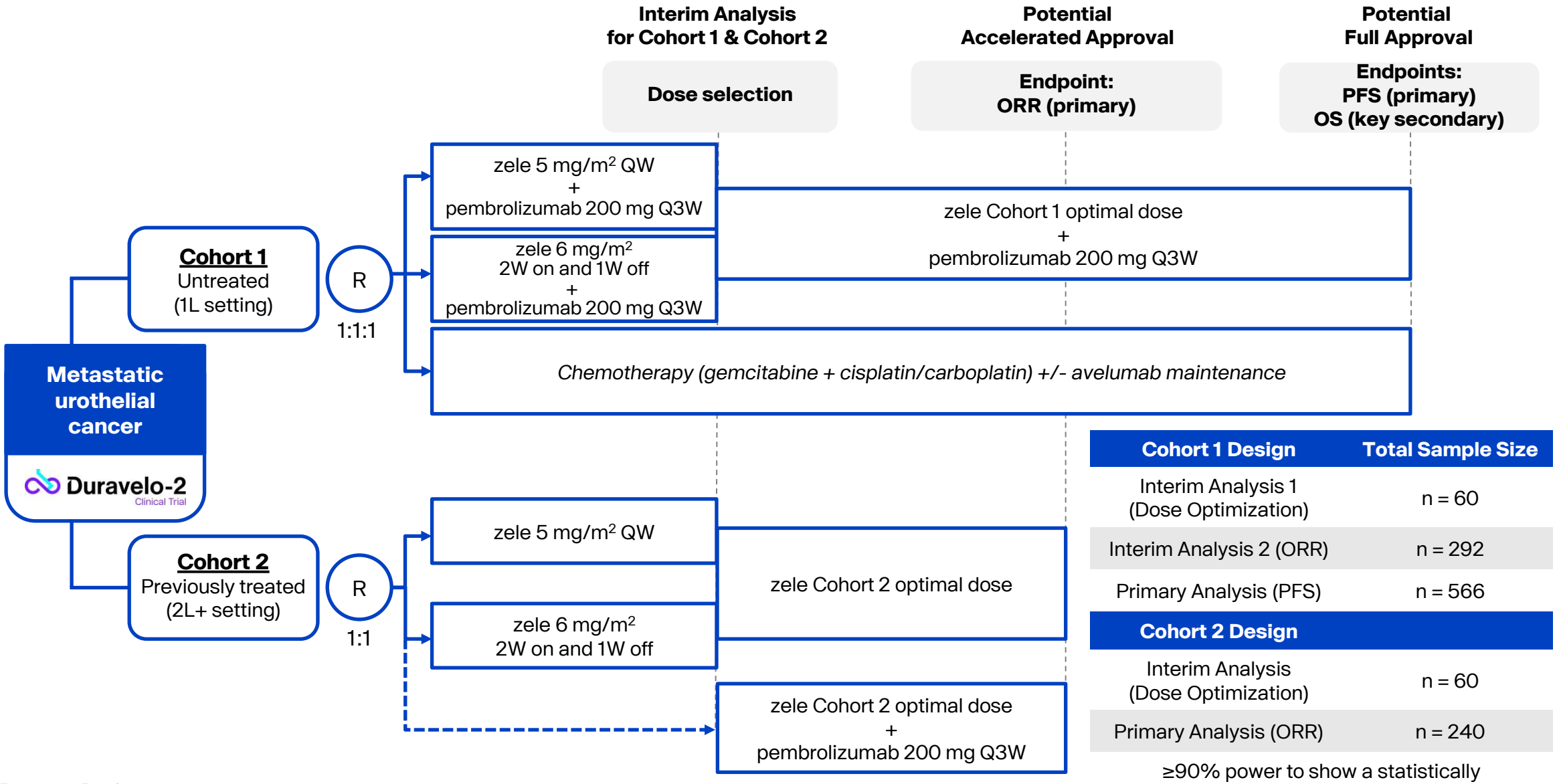
- 22 previously untreated (1L) mUC cisplatin-ineligible patients were enrolled and treated with zelenectide + pembrolizumab
  - Median age was 77 years old
  - 68% (15/22) of enrolled patients were male
  - 50% (11/22) of enrolled patients had an ECOG performance score of 2
- 20/22 patients were efficacy evaluable[a]
  - **ORR = 60% (12/20)[b]**
- Safety and tolerability profile broadly consistent with Duravelo-1 2L+ monotherapy and combination cohorts

TRAEs of Clinical Interest, n (%)	Zelenectide pevedotin 5 mg/m² QW + 200 mg pembrolizumab Q3W N=22 zelenectide and/or pembro-related	
	Any grade	Grade ≥3
Peripheral Neuropathy[c]	**6 (27)**	**1 (5)**
Sensory events*	6 (27)	1 (5)
Motor events	0	0
Skin Reactions[d]	**13 (59)**	**1 (5)**
Rash	7 (32)	1 (5)
Erythema	1 (4.5)	0
Pruritus	5 (23)	0
Rash erythematous	2 (9)	0
Dry Skin	1 (5)	0
Eye Disorders	**2 (9)**	**0**
Hyperglycemia[e]	2 (9)	0

More detailed information will be presented at a future medical meeting

Data as of 13Sep24.
SOC Preferred Terms MedDRA: v27.0. Treatment-related adverse events (TRAE) were counted once per maximum reported common terminology criteria for AEs (CTCAE), version 5.0.
[a]Efficacy evaluable defined as patients who have received at least 1 dose of zelenectide or pembrolizumab and had a post-baseline scan. [b]ORR includes partial responses and complete responses. Of the responses, 5 were confirmed and 7 were unconfirmed. 15 patients remain on treatment at time of data cut. [c]Peripheral Neuropathy Standardised MedDRA Queries (SMQ) [broad]. *Sensory events include PTs of peripheral neuropathy and polyneuropathy. [d]Severe Cutaneous Standardised MedDRA Queries (SMQs) [broad] and preferred terms are defined in: Skin and Subcutaneous Tissue System Organ Class (SOC), where Alopecia is excluded. [e]Preferred term.
1L: 1st line; 2L+: 2nd line or later; ECOG: Eastern Cooperative Oncology Group; mUC: metastatic urothelial cancer; ORR: overall response rate; QW: weekly; Q3W: once every three weeks.

Phase 2/3 Duravelo-2 registrational trial in mUC



Cohort 1 Design	Total Sample Size
Interim Analysis 1 (Dose Optimization)	n = 60
Interim Analysis 2 (ORR)	n = 292
Primary Analysis (PFS)	n = 566
Cohort 2 Design	
Interim Analysis (Dose Optimization)	n = 60
Primary Analysis (ORR)	n = 240

≥90% power to show a statistically significant benefit in ORR, PFS and OS

1L: 1st line; 2L+: 2nd line or later; PFS: progression-free survival; ORR: objective response rate; OS: overall survival; mUC: metastatic urothelial cancer; QW: weekly; Q2W: every other week; Q3W: once every 3 weeks.

NECTIN4 gene amplification overview

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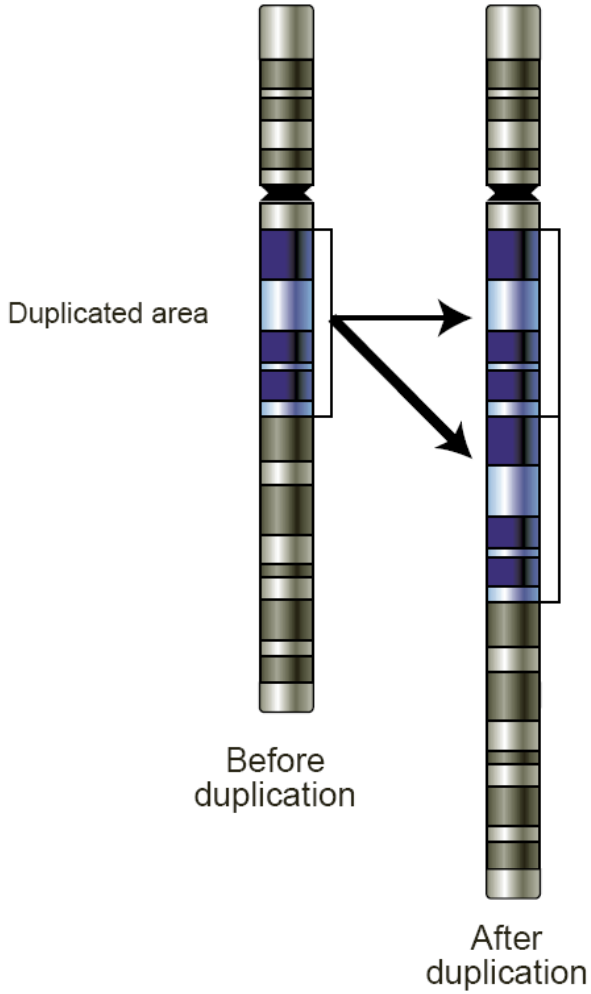
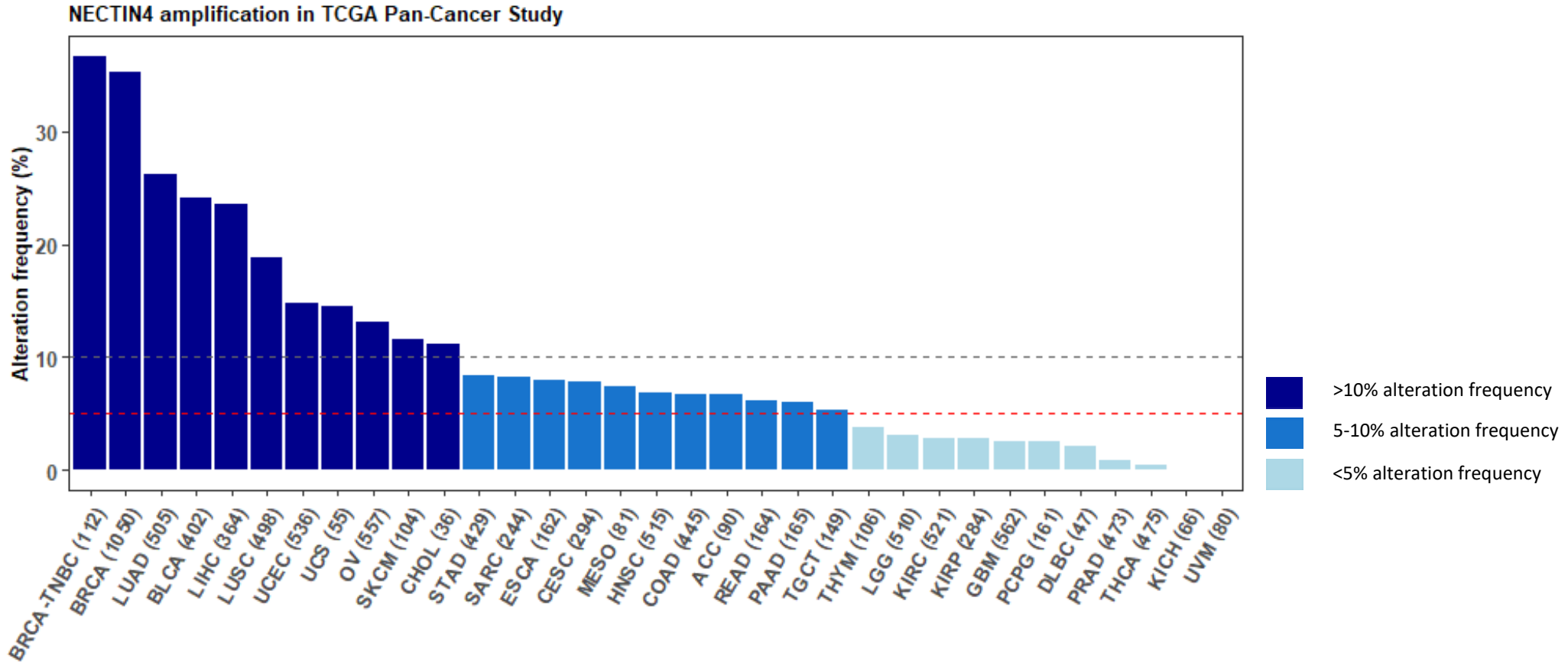
Background to NECTIN4 gene amplification

- Gene amplification is a common mechanism by which cancer cells gain function
- More copies of a gene often translates to more protein expressed
- **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**
- NECTIN4 gene amplification was identified as a predictive biomarker for EV response in mUC[2]
- Since zelenectide pevedotin binds to Nectin-4, it was hypothesized that NECTIN4 gene amplification may predict response and could serve as a biomarker for therapy stratification



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. EV: enfortumab vedotin; mUC: metastatic urothelial cancer.

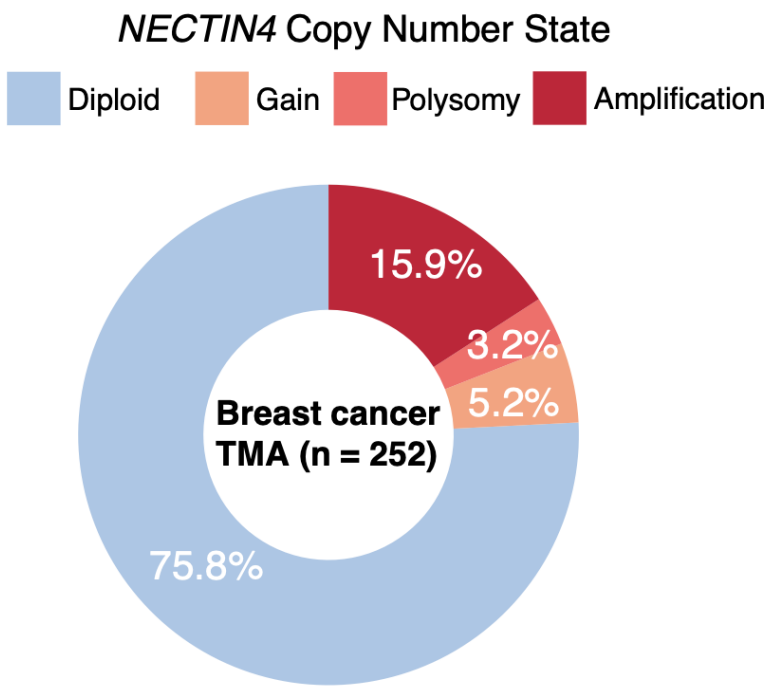
The NECTIN4 gene is frequently amplified in cancer

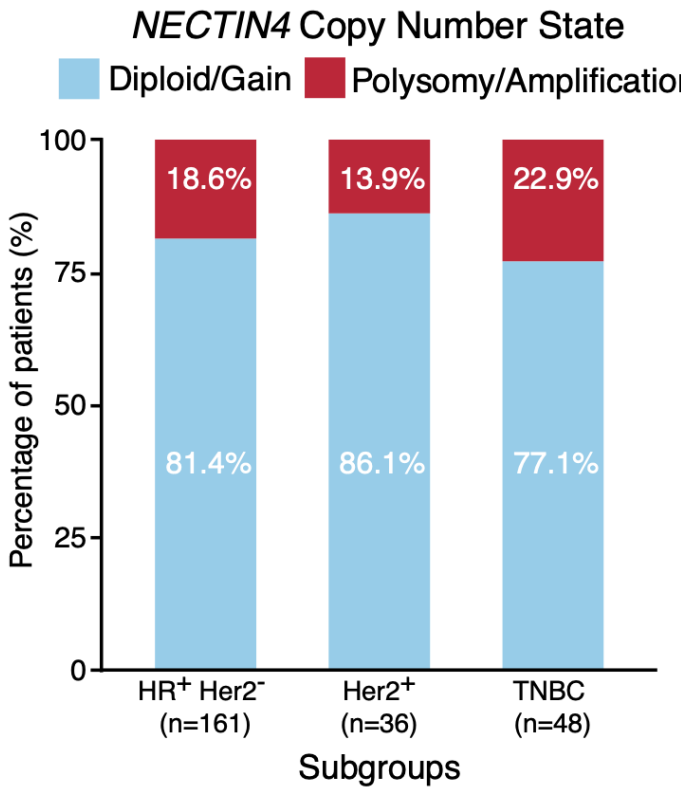


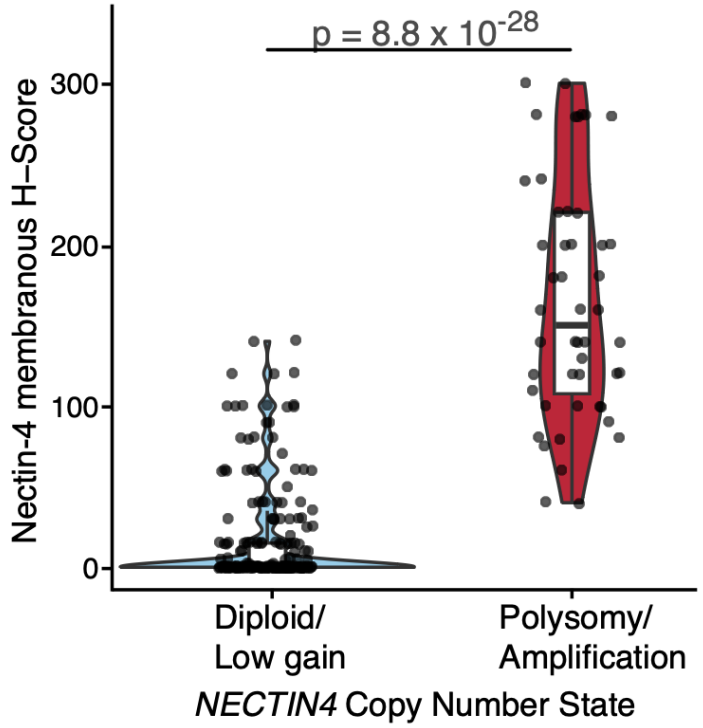
- Gene level copy number data (Affymetrix single nucleotide polymorphism [SNP] 6.0 array) from Absolute pipeline was downloaded from GDC. SNP array and alternative technologies (eg FISH, NGS) are likely to identify distinct & overlapping cases of *NECTIN4* gene amplification, potentially yielding different alteration frequencies.
- Frequency of NECTIN4 gene amplification was determined by NECTIN4 copy number divided by mode of all genes' copy number around the chromosome 1 centromere (p21.1 to q21.3)>=2 or *NECTIN4* copy number >=6.
- TCGA study abbreviations: Triple Negative Breast Cancer (TNBC) was selected by filtering Breast Cancer (BRCA) patients with ER, PR and HER2 status based on PMID23000897. Red dash line: 5%; grey dash line: 10% alteration frequency.

Unpublished data by Bicycle Therapeutics. FISH: fluorescence in situ hybridization; NGS: next-generation sequencing; GDC: Genomic Data Commons; TCGA: The Cancer Genome Atlas Program.

The NECTIN4 gene is frequently amplified in breast cancer and is associated with enhanced expression of Nectin-4 on the membrane



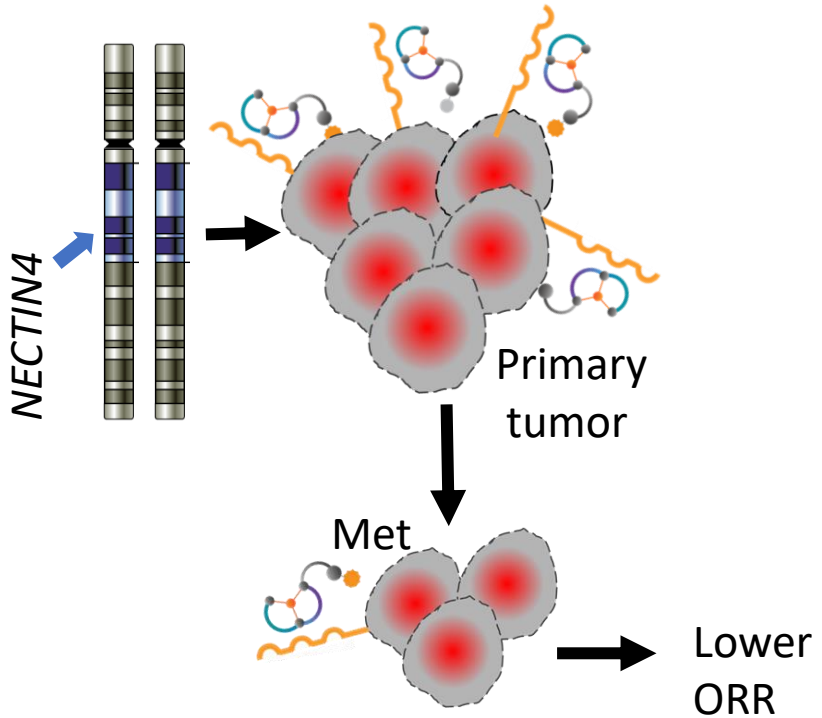




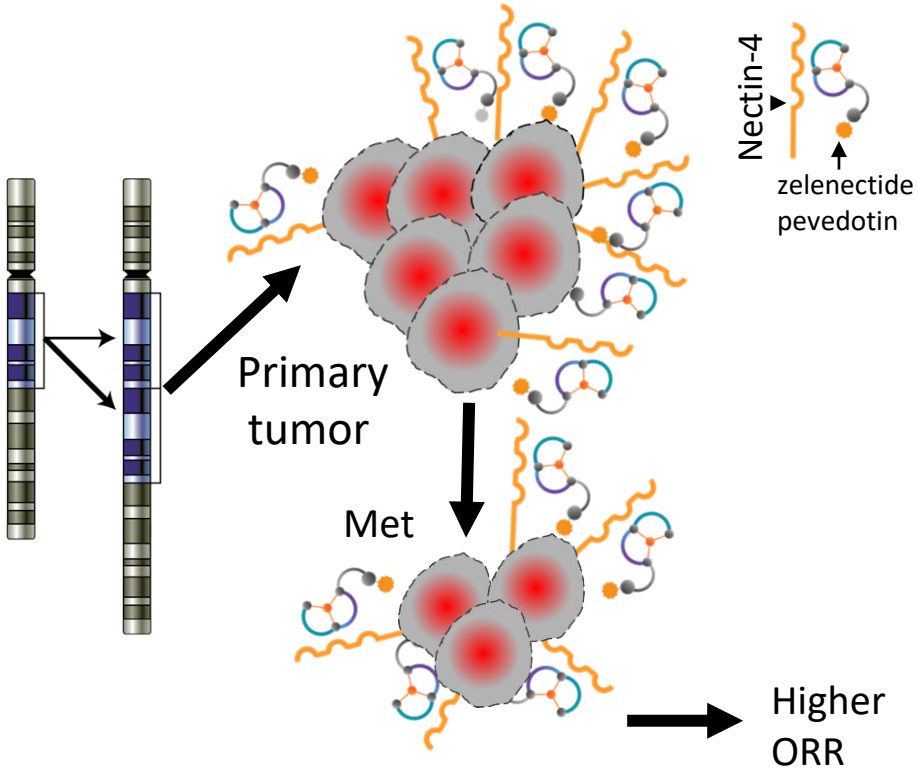
Unpublished data by Klümper N, Brägelmann J & Eckstein M.

Working hypothesis: NECTIN4 gene amplification leads to stable Nectin-4 expression, more drug binding sites and higher response rates

Without NECTIN4 gene amplification



With NECTIN4 gene amplification



1. Klümper N, et al. *Clin Cancer Res.* 2023;29(8):1496–1505. 2. Klümper N, et al. *J Clin Oncol.* 2024;42(20):2446–2455. Met: metastases; ORR: overall response rate.

Zelenectide pevedotin in breast cancer patients with NECTIN4 gene amplification

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Breast cancer patient demographics and clinical characteristics

- 38 heavily pretreated patients with breast cancer were enrolled and treated with zelenectide pevedotin
- 32 patients were confirmed to have TNBC and 6 patients had non-TNBC
- Dosing in TNBC patients:
  - 31 patients received zelenectide pevedotin 5 mg/m^2 QW
  - 1 patient received zelenectide pevedotin 7.5 mg/m^2 on Day 1 and Day 8 of a 21-day cycle

Patient characteristic, n (%)	Patients with BC (N=38)	Patients with TNBC (N=32)
Median age, years (range)	52.5 (30-83)	52.0 (30-76)
Sex, n (%)		
Female	38 (100.0)	32 (100.0)
Race,[a] n (%)		
White	14 (36.8)	11 (34.4)
Asian	2 (5.3)	2 (6.3)
Black or African American	1 (2.6)	0
Other	20 (52.6)	18 (56.3)
ECOG PS, n (%)		
0	18 (47.4)	16 (50.0)
1	20 (52.6)	16 (50.0)
Median prior lines of therapies (range)	**6 (1-15)**	**6 (2-13)**
Prior therapy, n (%)		
Taxane-based	35 (92.1)	30 (93.8)
ADC (any)	**27 (71.1)**	**27 (84.4)**
Sacituzumab govitecan	**26 (68.4)**	**26 (81.3)**
T-DXd	**5 (13.2)**	**5 (15.6)**
Platinum-based	18 (47.4)	15 (46.9)
Checkpoint inhibitor	17 (44.7)	16 (50.0)
Endocrine therapy	14 (36.8)	9 (28.1)
HER2-targeted therapy	7 (18.4)	6 (18.8)
CDK4/6 inhibitor	7 (18.4)	2 (6.3)

Data as of 13Sep2024.
[a]Information for one patient was missing
ADC: antibody-drug conjugate; BC: breast cancer; CDK 4/6: cyclin-dependent kinase 4/6; ECOG PS: Eastern Cooperative Oncology Group performance status; HER2: human epidermal growth factor receptor; QW: weekly; TNBC: triple negative breast cancer; T-DXd: trastuzumab deruxtecan.

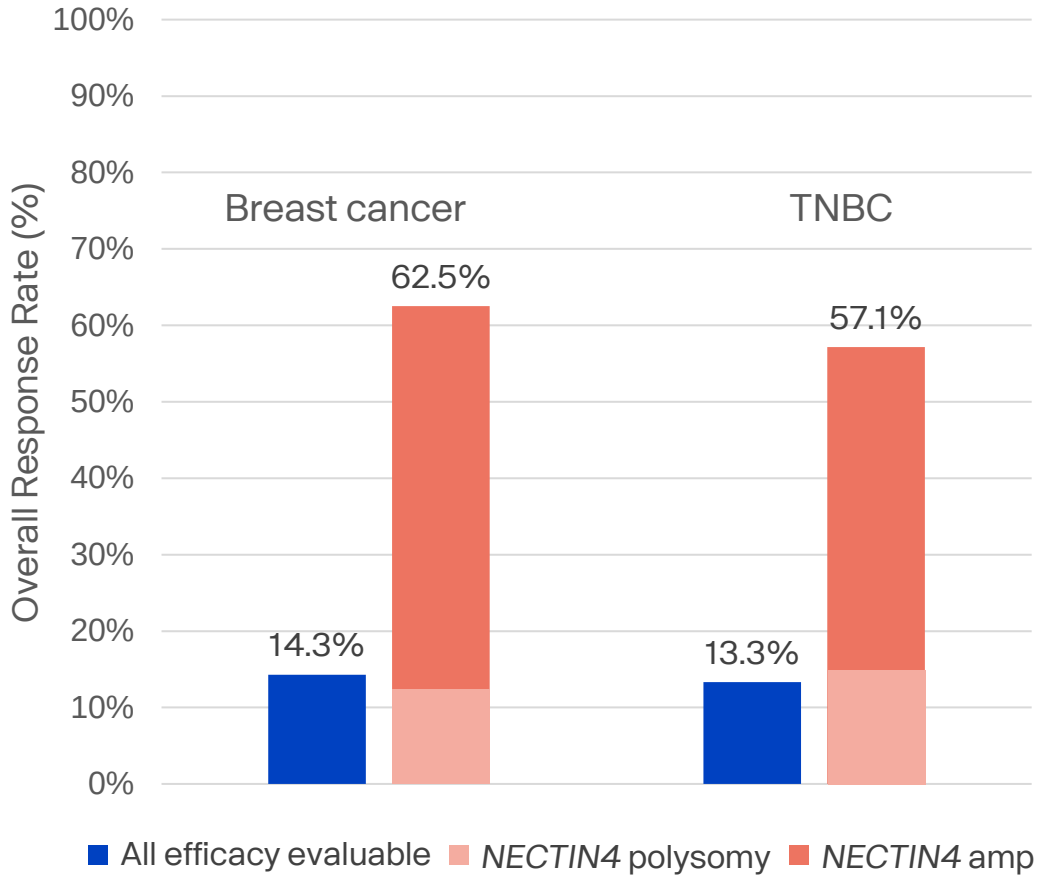
Breast cancer patients with NECTIN4 gene amplification or polysomy experienced a significantly higher response to zelenectide pevedotin

Breast Cancer

- 35/38 patients enrolled were efficacy evaluable,[a] with the majority receiving zelenectide pevedotin 5 mg/m^2 QW
  - **ORR = 14.3% (5/35)[b]**
- 8/23 samples that were available for NECTIN4 FISH testing and passed QC demonstrated NECTIN4 gene amplification or polysomy[c]
  - **ORR in NECTIN4 gene amplification or polysomy = 62.5% (5/8)[b,c]**
- No responses in non-amplified or non-polysomy patients

TNBC

- 30/32 patients enrolled were efficacy evaluable,[a] with the majority receiving zelenectide pevedotin 5 mg/m^2 QW
  - **ORR = 13.3% (4/30)[b,c]**
- 7/19 samples that were available for NECTIN4 FISH testing and passed QC demonstrated NECTIN4 gene amplification or polysomy
  - **ORR in NECTIN4 gene amplification or polysomy = 57.1% (4/7)[b,c]**
  - All 3 TNBC patients with NECTIN4 gene amplification who responded to zelenectide had prior treatment with sacituzumab govitecan
- No responses in non-amplified or non-polysomy patients



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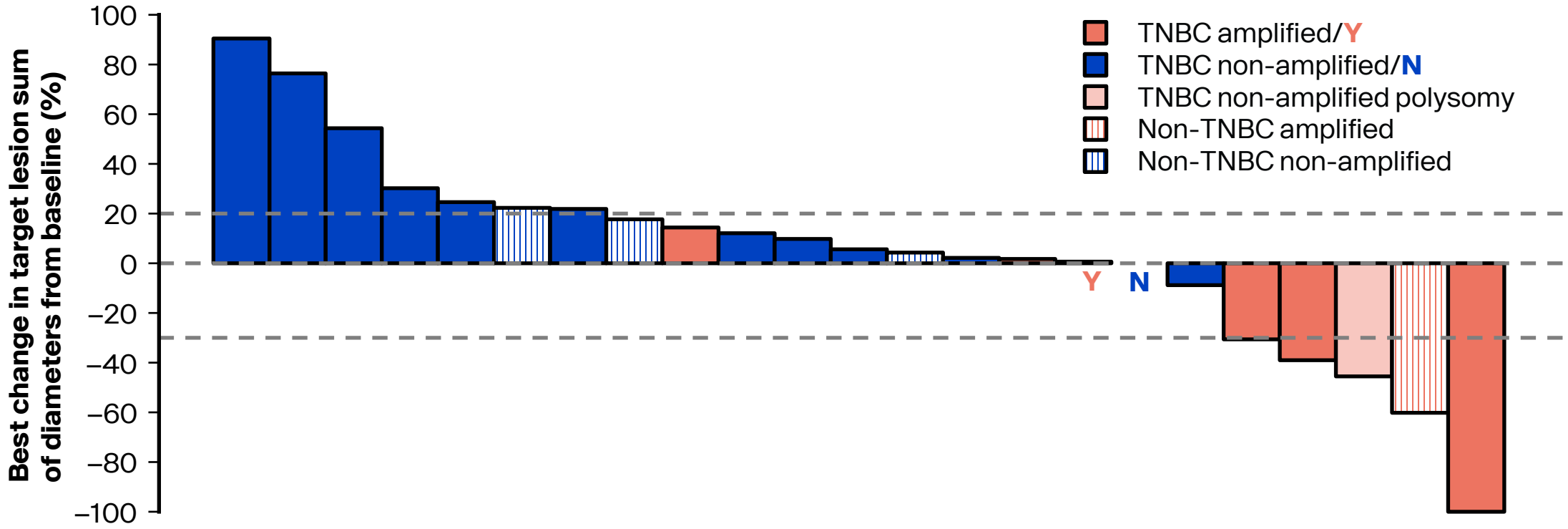
Data as of 13Sep2024.
[a]Efficacy evaluable patients had at least one postbaseline scan available for RECIST v1.1 review. One patient's postbaseline scan was not evaluable per RECIST v1.1.
[b]ORR comprised of partial responses, including 1 unconfirmed response. [c]One patient harbored a NECTIN4 polysomy.
FISH: fluorescence in situ hybridization; ORR: overall response rate; QC: quality control; QW: weekly; TNBC: triple-negative breast cancer.

Of the patients with breast cancer who experienced a clinical response, 100% had NECTIN4 gene amplification or polysomy



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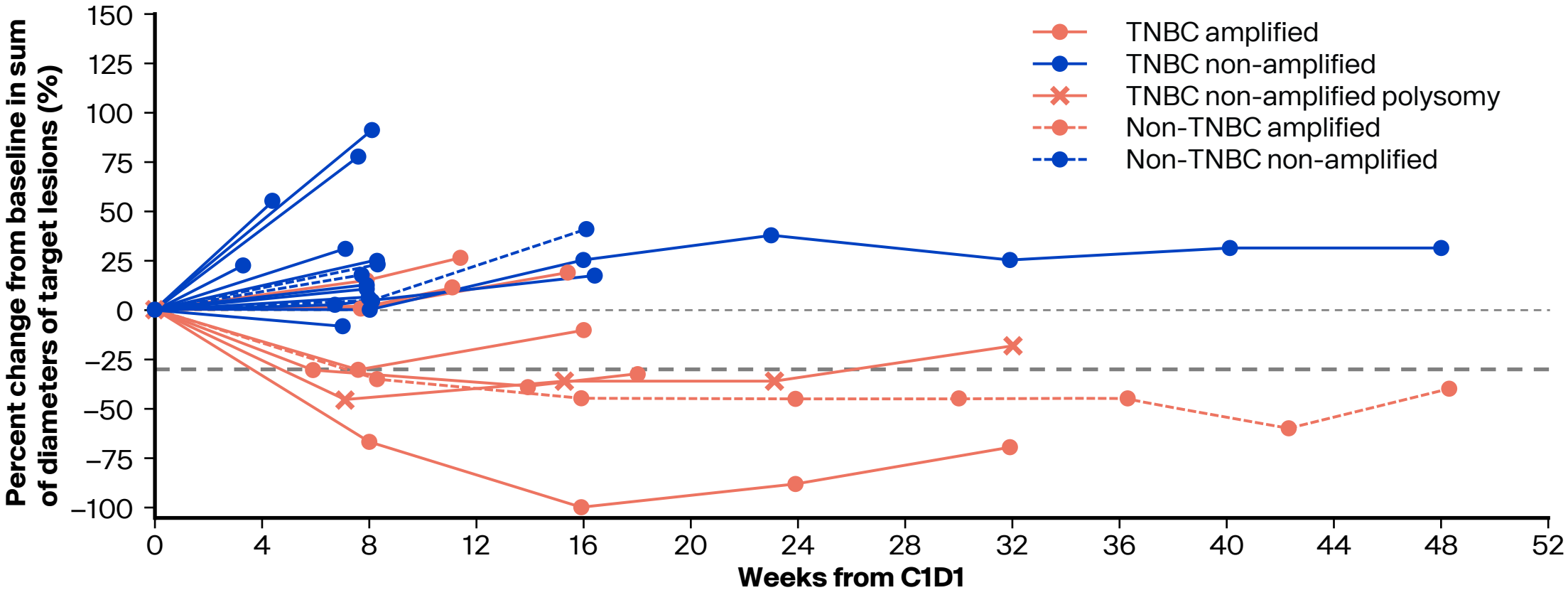
Data as of 13Sep2024. N=23.
TNBC: triple-negative breast cancer.

Breast cancer patients with NECTIN4 gene amplification or polysomy were more likely to experience a long duration of response



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Data as of 13Sep2024. N=23.
C1D1: cycle 1, day 1; TNBC: triple-negative breast cancer.

Safety and tolerability profile of zelenectide pevedotin in breast cancer was consistent with data from other Duravelo-1 cohorts

Category, n (%)	Patients with Breast Cancer (N=38)			
TEAEs	38 (100.0)			
Grade ≥3	20 (52.6)			
TRAEs	35 (92.1)			
Grade ≥3	13 (34.2)			
TESAEs	12 (31.6)			
TRSAEs	6 (15.8)			
TRSAEs Grade ≥3	4 (10.5)			
TRAEs (≥15%)[a]	All Grades	Grade 1	Grade 2	Grade ≥3
Pyrexia	15 (39.5)	15 (39.5)	0	0
Nausea[b]	14 (36.8)	10 (26.3)	3 (7.9)	1 (2.6)
Diarrhea	13 (34.2)	12 (31.6)	1 (2.6)	0
Asthenia	9 (23.7)	5 (13.2)	3 (7.9)	1 (2.6)
Fatigue	9 (23.7)	4 (10.5)	4 (10.5)	1 (2.6)
Alopecia	7 (18.4)	4 (10.5)	3 (7.9)	0
Decreased appetite	7 (18.4)	3 (7.9)	2 (5.3)	2 (5.3)
Neutropenia	7 (18.4)	0	2 (5.3)	5 (13.2)
Abdominal pain	6 (15.8)	4 (10.5)	2 (5.3)	0
Anemia	6 (15.8)	1 (2.6)	5 (13.2)	0
Dose modifications[c]	21 (55.3)			
Dose interruptions	18 (47.4)			
Dose reductions	8 (21.1)			
Dose discontinuation	0			

Data as of 13Sep2024.
[a]SOC Preferred Terms MedDRA: v27.0. [b]Prophylactic antiemetics are prohibited during Cycle 1 of dose escalation, and use of anti-emetics associated with QT prolongation is prohibited during the study. [c]Dose modifications included 5 patients treated at doses higher than RP2D 5 mg/m^2 QW. Interruptions were common, usually for low grade toxicity, and usually lasted 1 week with resumption at interrupted dose.
TEAE: treatment emergent adverse event, TESAE: treatment emergent serious adverse event, TRSAE: treatment-related serious adverse events, TRAE: treatment-related adverse event.

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Adverse events of clinical interest with zelenectide pevedotin in breast cancer were broadly consistent with data from other Duravelo-1 cohorts

TRAEs of Clinical Interest, n (%)	Patients with Breast Cancer (N=38)			
	All Grades	Grade 1	Grade 2	Grade ≥3
Peripheral neuropathy[a]	12 (31.6)	4 (10.5)	7 (18.4)	1 (2.6)
Neuropathy peripheral	5 (13.2)	3 (7.9)	2 (5.3)	0
Peripheral sensory neuropathy	5 (13.2)	2 (5.3)	3 (7.9)	0
Neuralgia	4 (10.5)	0	3 (7.9)	1 (2.6)
Dysesthesia	1 (2.6)	1 (2.6)	0	0
Paresthesia	1 (2.6)	1 (2.6)	0	0
Skin reactions[b]	6 (15.8)	6 (15.8)	0	0
Erythema	2 (5.3)	2 (5.3)	0	0
Stomatitis	2 (5.3)	2 (5.3)	0	0
Dermatitis acneiform	1 (2.6)	1 (2.6)	0	0
Dry skin	1 (2.6)	1 (2.6)	0	0
Eczema	1 (2.6)	1 (2.6)	0	0
Erythema multiforme	1 (2.6)	1 (2.6)	0	0
Hyperhidrosis	1 (2.6)	1 (2.6)	0	0
Hyperglycemia[c]	3 (7.9)	1 (2.6)	2 (5.3)	0
Eye disorders[d]	2 (5.3)	0	2 (5.3)	0

Data as of 13Sep2024.
[a]Peripheral neuropathy Standardised MedDRA Queries (SMQ) [broad]. [b]Includes the MedDRA term of Severe Cutaneous Adverse Reactions (SCAR) SMQ [broad] and events that fell into the MedDRA SOC of Skin and Subcutaneous Tissue disorders, excluding alopecia. [c]Preferred term. [d]SOC of eye disorders.
TRAE: treatment-related adverse event.

Conclusions

- NECTIN4 gene amplification appears to be a frequent genomic event in breast cancer
  - 35% (8/23) of tested patients with breast cancer and 37% (7/19) of tested patients with TNBC demonstrated NECTIN4 gene amplification + polysomy
- NECTIN4 gene amplification + polysomy appears to predict response to zelenectide pevedotin in heavily pretreated breast cancer patients, with an ORR of 62.5% (5/8)
  - ORR of 57.1% (4/7) in TNBC patients with NECTIN4 gene amplification + polysomy
- Overall, there were no responses in non-amplified or non-polysomy patients
- In this study, zelenectide pevedotin was generally well-tolerated in breast cancer patients
- Despite the limited sample size, this post-hoc analysis underscores zelenectide pevedotin's promising anti-tumor activity in breast cancer patients with NECTIN4 gene amplification

ORR: objective response rate; TNBC: triple negative breast cancer.

Our NECTIN4 gene amplification development strategy

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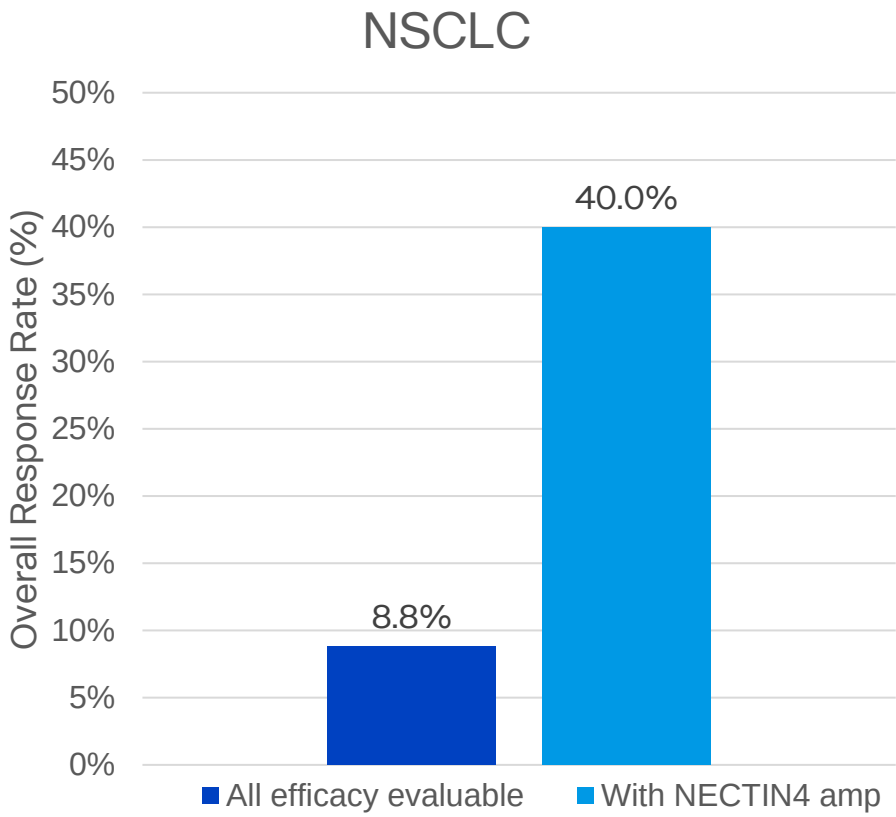
NSCLC patients with NECTIN4 gene amplification showed an enhanced response to zelenectide pevedotin

- 40 previously treated patients with NSCLC were enrolled and treated with zelenectide pevedotin
  - Median age was 63.5 years old
  - Median prior lines of therapy (range): 3 (1-8)
- 34 patients were efficacy evaluable[a]
  - **ORR = 8.8% (3/34)[b]**
- 6/19 samples that were available for NECTIN4 FISH testing and passed QC demonstrated NECTIN4 gene amplification
  - 5/6 patients with NECTIN4 gene amplification were efficacy evaluable[a]
  - **ORR in NECTIN4 gene amplification = 40.0% (2/5)**
- Of the 19 patients tested for NECTIN4 gene amplification, none of the non-amplified patients responded
- Safety and tolerability profile broadly consistent with Duravelo-1 2L+ monotherapy cohorts



More detailed information will be presented at a future medical meeting

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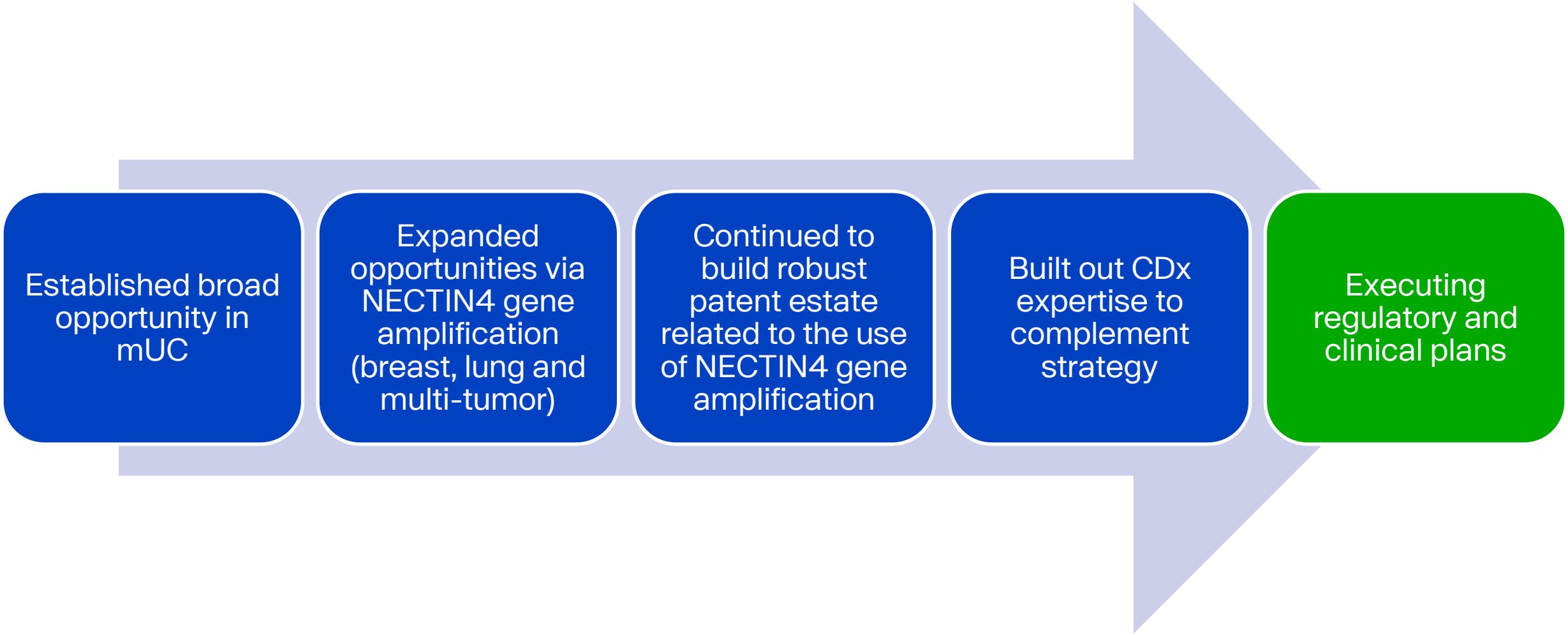
Data as of 13Sep2024.
[a]Efficacy evaluable defined as patients who have received at least 1 dose of zelenectide pevedotin and had a post-baseline scan. [b]ORR comprised of partial responses, including 1 unconfirmed response.
2L+: 2nd line or later; ECOG: Eastern Cooperative Oncology Group performance status; FISH: fluorescence in situ hybridization; ORR: overall response rate; QC: quality control; NSCLC: non-small cell lung cancer.

Over 2024, we laid a robust foundation enabling zelenectide pevedotin to be first-in-class in multiple NECTIN4 gene amplified tumors, in addition to establishing its best-in-class potential in mUC



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CDx: companion diagnostic; mUC: metastatic urothelial cancer.

Zelenectide pevedotin represents a significant opportunity to potentially address multiple Nectin-4 associated cancers

Study	Indication	Phase	Status
		I II III	
Duravelo-1 Open label, all comers	mUC		Ongoing
	Breast		Enrolling
	Lung		Enrolling
Duravelo-2 Randomized pivotal trial, combination with pembrolizumab	1L mUC		Enrolling
	2L+ mUC		Enrolling
Duravelo-3 Open label, *NECTIN4* gene-amplified breast cancer	2L+ HR+/HER2- Breast		Plan to initiate in 1H25
	2L+ TNBC		
Duravelo-4 Open label, *NECTIN4* gene-amplified lung cancer	2L+ squamous NSCLC		Plan to initiate in 2H25
	2L+ non-squamous NSCLC		
Duravelo-5 Open label, *NECTIN4* gene-amplified multi-tumor*	2L+ Head and Neck		Plan to initiate in 2H25
	2L+ Esophageal		
	2L+ Pancreatic		
	2L+ Ovarian		

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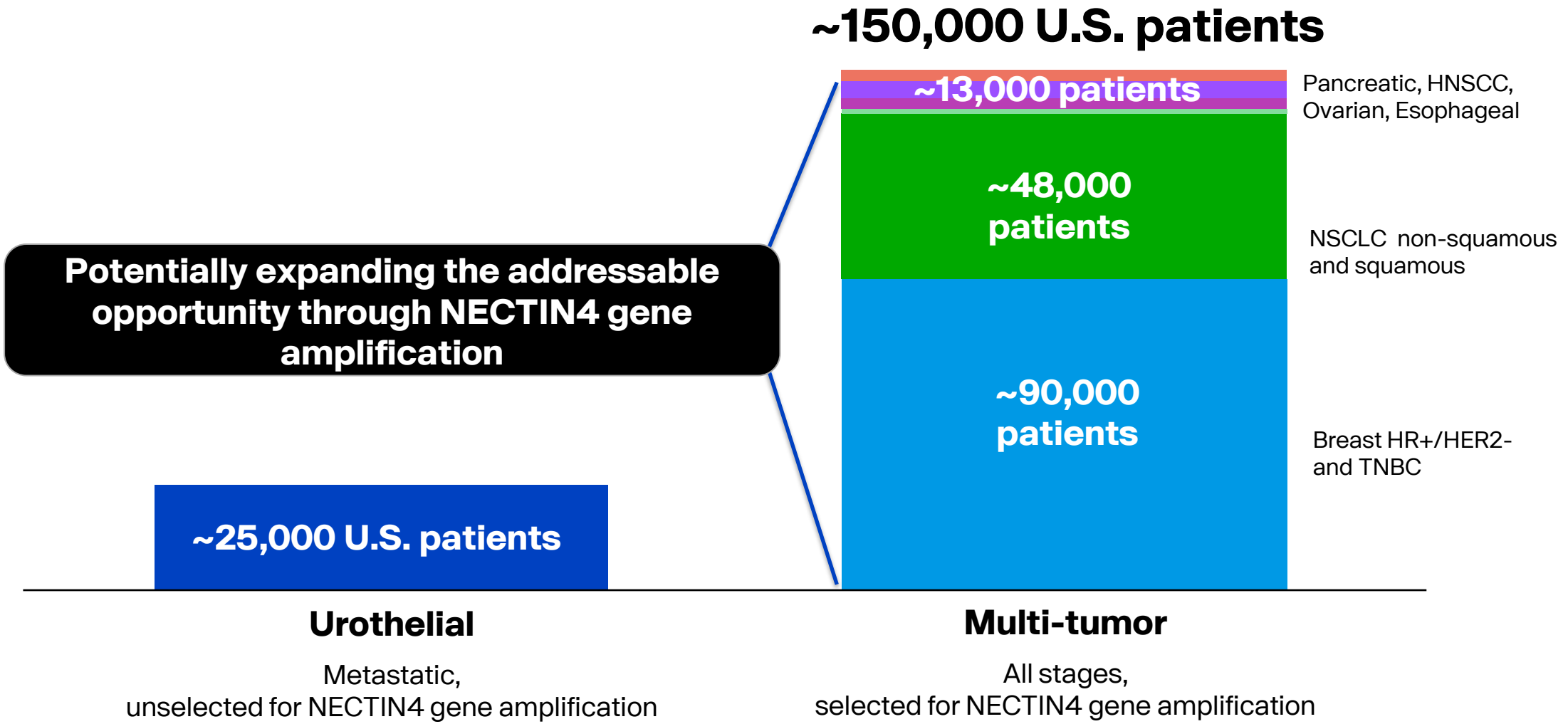
*Exact indications to be finalized
1L: 1st line; 2L+: 2nd line or later; HR+: hormone receptor-positive; HER2-: human epidermal growth factor receptor 2-negative; mUC: metastatic urothelial cancer; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer.

We believe Bicycle is uniquely positioned to potentially transform patient treatment across multiple Nectin-4 associated cancers



NOTE: The bladder cancer population represents potentially addressable patients in the US in the metastatic or advanced stage. The selected multi-tumor population represents potentially addressable patients in the US for all stages annually and adjusted to reflect Nectin-4 gene amplification occurrence. TNBC: triple negative breast cancer, Breast: hormone receptor positive, HER2 negative. Patient estimates for other tumors include head and neck squamous cell carcinoma, ovarian, esophageal and pancreatic cancer. Patient metrics source: Global Data, Global Drug Forecast and Market Analysis. Global Data, Global Drug Forecast and Market Analysis: Bladder Cancer: Epidemiology Forecast to 2033, published Oct'24. HER2-Positive Breast Cancer: Epidemiology Forecast to 2033, published May'24 (including TNBC). Non-Small Cell Lung Cancer [NSCLC]: Epidemiology Forecast to 2032, published Feb'24. Head and Neck Squamous Cell Carcinoma: Epidemiology Forecast to 2030, published Aug'21. Ovarian Cancer: Opportunity Assessment and Forecast, Feb '24. Pancreatic Cancer: Opportunity Analysis and Forecasts to 2029, published Dec '20. Esophageal Cancer: Competitive Landscape, Oct'24. Pharma-Intelligence: HNSCC: Apr'23, TNBC: Sept'23. Ovarian: Sept'21. SEER US Incidence Data: Surveillance, Epidemiology, and End Results Program, National Cancer Institute, Nov2022 Submission.

Zelenectide pevedotin, a first-in-class BTC® molecule, has significant potential to treat Nectin-4 associated cancers

SUMMARY

- Demonstrated potentially differentiated safety and robust efficacy profile in combination with pembrolizumab in 1L mUC cis-ineligible patients
- Demonstrated NECTIN4 gene amplification as a potential patient selection strategy in breast and lung cancer
- Established an ambitious development strategy that we believe could position Bicycle as the leader in addressing Nectin-4 associated cancers, potentially bringing benefit to ~175,000 U.S. cancer patients

ACHIEVEMENTS AND NEXT STEPS

- ✓ **1Q 2024: Initiated Ph2/3 Duravelo-2 trial**
- ✓ **2H 2024: Data from ongoing open-label expansion cohorts**
  - ✓ zele monotherapy in 2L+ mUC
  - ✓ zele + pembrolizumab in 1L mUC
  - ✓ zele monotherapy in TNBC and NSCLC
- **2025: Plan to initiate Ph1/2 trials in NECTIN4 gene-amplified breast cancer, lung cancer and multi-tumor**
- **2H 2025: Expect phase 2/3 Duravelo-2 trial dose selection and topline data**

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1L: 1st line; 2L+: 2nd line or later; mUC: metastatic urothelial cancer; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer.

Q&A

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Thank you

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