BT8009-100
Part A1 Monotherapy Escalation

- February 2023

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Agenda

Introduction	**Kevin Lee, Ph.D** Chief Executive Officer
Overview of Nectin-4, escalation trial and trial design	**Dominic Smethurst, MRCP** Chief Medical Officer
Review of BT8009 Phase I clinical data	**Capucine Baldini, MD** Medical Oncologist, Gustave Roussy
Commentary on potential use of BT8009 in current urothelial treatment landscape	**Daniel Petrylak, MD** Professor of Medicine and Urology, Yale University
Expansion trial design, regulatory path and next steps	**Dominic Smethurst**
Question and Answer	**Management team and Drs Baldini and Petrylak**

BT8009-100:
End of Phase I escalation top-line results

- Study design and results

Background to BT8009 and ADC target: Nectin-4

- A cell adhesion molecule and one of four members of the Nectin family
- All Nectins share the same overall structure defined by three extracellular immunoglobulin domains, a single transmembrane helix and an intracellular domain
- Overexpressed in human cancers and correlated with tumor progression
- Solid tumors with high levels of Nectin-4 expression include urothelial, NSCLC, TNBC, and ovarian
- Target for Padcev (enfortumab vedotin), an FDA-approved ADC

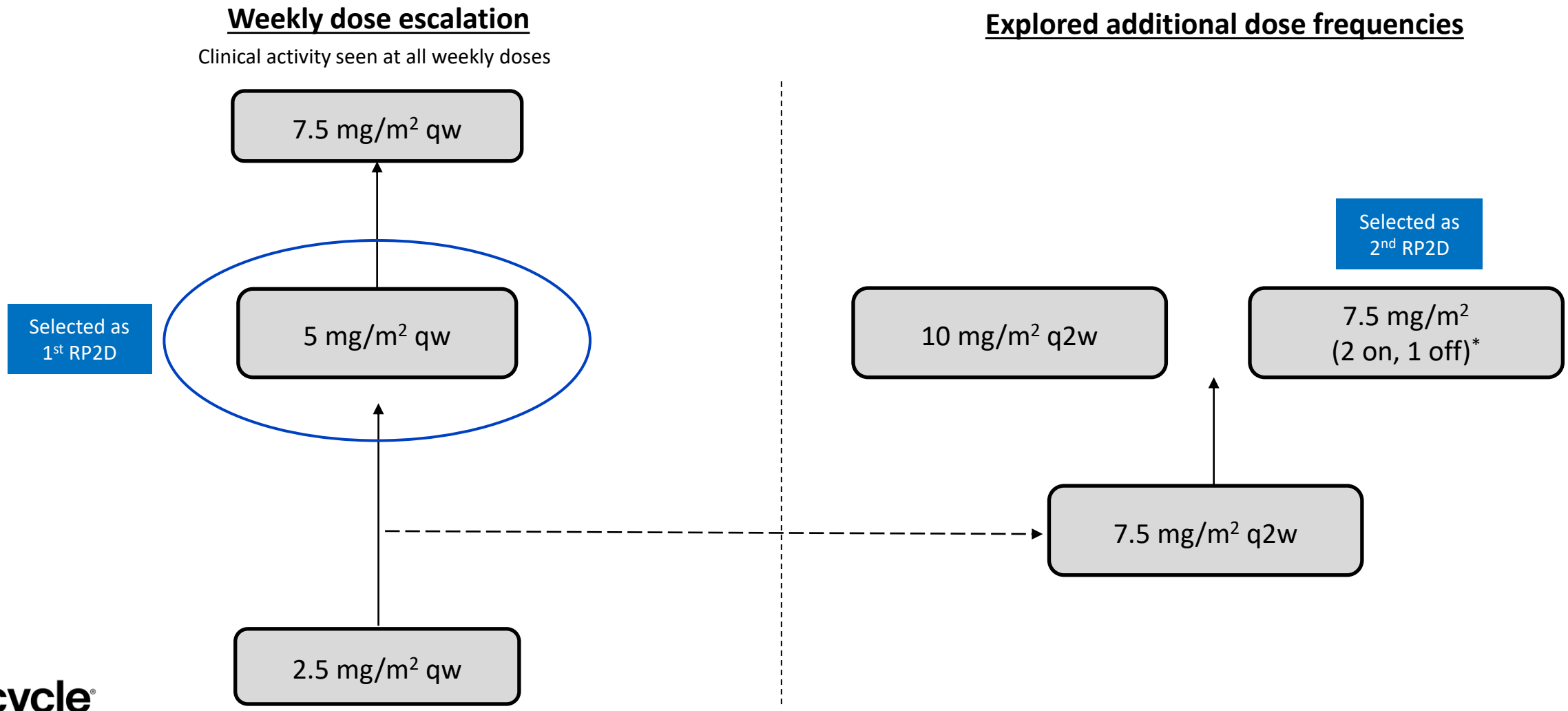
Overview of BT8009 Phase I trial results*

- BT8009 demonstrates preliminary anti-tumor activity in heavily pre-treated urothelial, lung and breast cancer patients with signs of differentiation compared to antibodies and potential for industry-leading product profile
  - 50% ORR and 75% clinical benefit rate, including 1 (13%) complete response in urothelial cancer at 5 mg/m^2 qw dose
  - Breadth of responses at other dose cohorts and other cancer types illustrates drug's potential
  - Durable responses, with tumor reductions maintained over time. Median duration of response (mDOR) still has not been reached among urothelial patients in the 5 mg/m^2 cohort; at least 11 months at data cut off date
    - As of January 2023, mDOR is estimated to be approximately 14 months with 2 out of 4 responders still on therapy
- Emerging efficacy and safety profile potentially distinguishes it from enfortumab vedotin
  - Low incidence of rash and neuropathy with no such ≥ Grade 3 events at or below recommended Phase II doses (RP2Ds), including those on therapy for >12 months
- Announced Fast Track Designation in January

* All data as of 20Sep22 except as otherwise noted and in the case of the breast cancer responder; this response was confirmed in December 2022

Dose escalation progress and strategy

3+3 escalation design: MTD reached for weekly schedule and one go-forward dose identified in April. Investigated alternative dosage regimens as per FDA's Project Optimus guidelines and selected second go-forward dose in November



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Biography of Capucine Baldini, MD

- Dr Capucine Baldini is a medical oncologist working at the Drug Development Department (DITEP), Gustave Roussy, Villejuif, France
- She is involved in early phase trials (including BT8009-100) with a special interest in geriatric oncology, gastro-intestinal cancers, genitourinary cancers, and central nervous system tumors
- Dr Baldini received her medical degree from Lille II University in 2014 and got a MSc from PARIS XI University in 2013. She was an assistant Professor at Lille University Hospital with a specialization in geriatric oncology and at Gustave Roussy in early phase trials at DITEP
- She is a member of ESMO, ASCO, AACR, SIOG, SoFOG and involved in young SIOG and SoFOG interest group leadership. She is working on early phase trials and immunotherapy in older patients.
- She is a sub-investigator of more than 80 clinical trials (phase I trials) and a (co)author of several publications in peer reviewed journals
- Research axes: early clinical trials, geriatric oncology, genitourinary cancers (prostate cancer, bladder cancer), glioma

Overview of key demographics for all patients enrolled in Phase I dose escalation trial

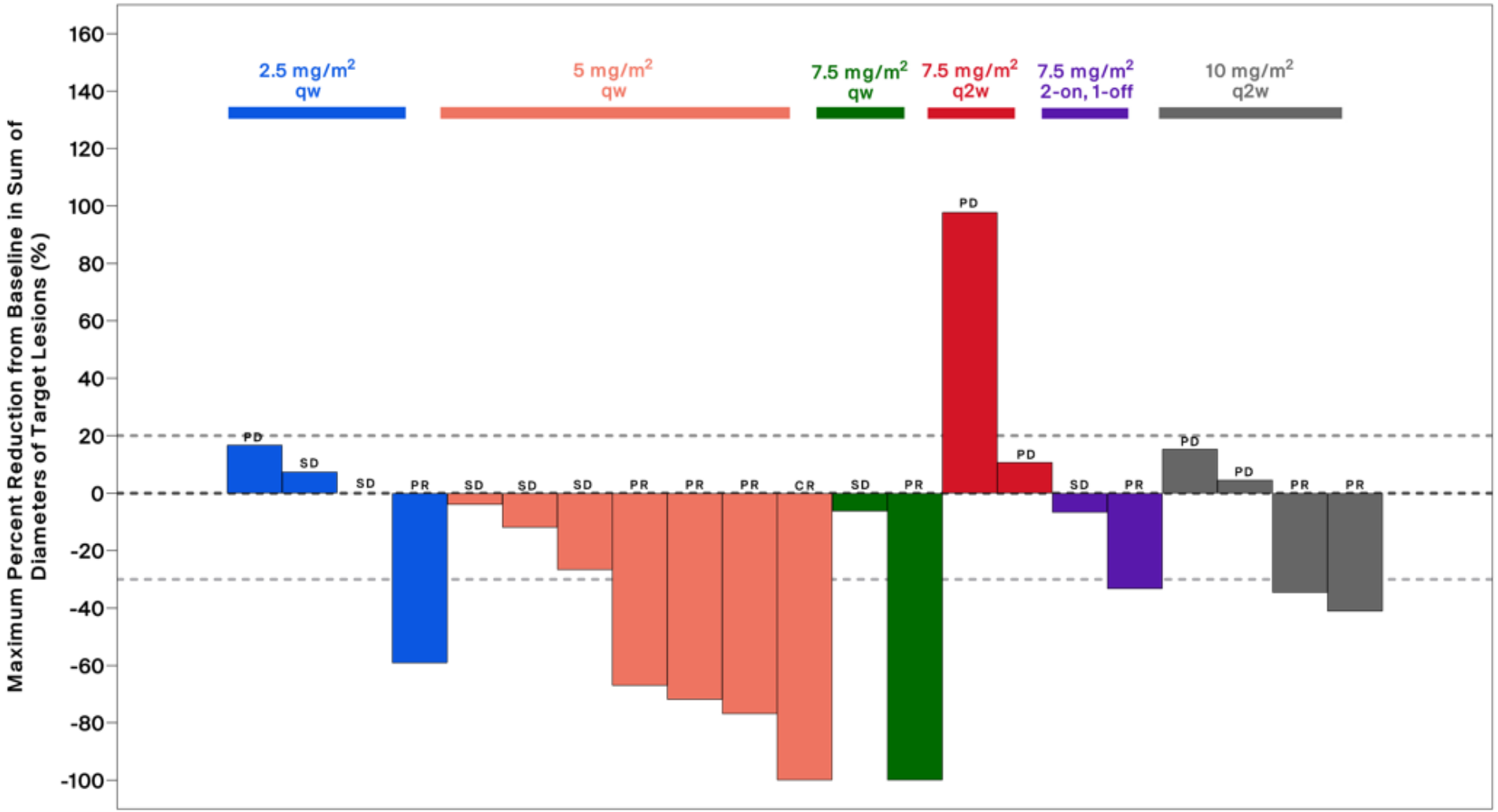
Demographics	
Total	N=49
Age, years, median (range)	66 (35-83)
Sex, n (%)	
Male	29 (59%)
Female	20 (41%)
ECOG, n (%)	
0 (Good performance status)	20 (41%)
1	29 (59%)
Prior lines of therapy, median	3

Overview of disease history for all patients enrolled in Phase I dose escalation trial

Disease history, n (%)*	
Total	N=49
Tumor type	
Breast	7 (14)
Esophageal	1 (2)
Head & Neck	3 (6)
Lung	6 (12)
Ovarian	1 (2)
Pancreatic	6 (12)
Renal	1 (2)
Urothelial	**24 (49)**

* Sum of percentages does not add to 100 due to rounding

Waterfall plot for response-evaluable urothelial patients



On response evaluable basis…

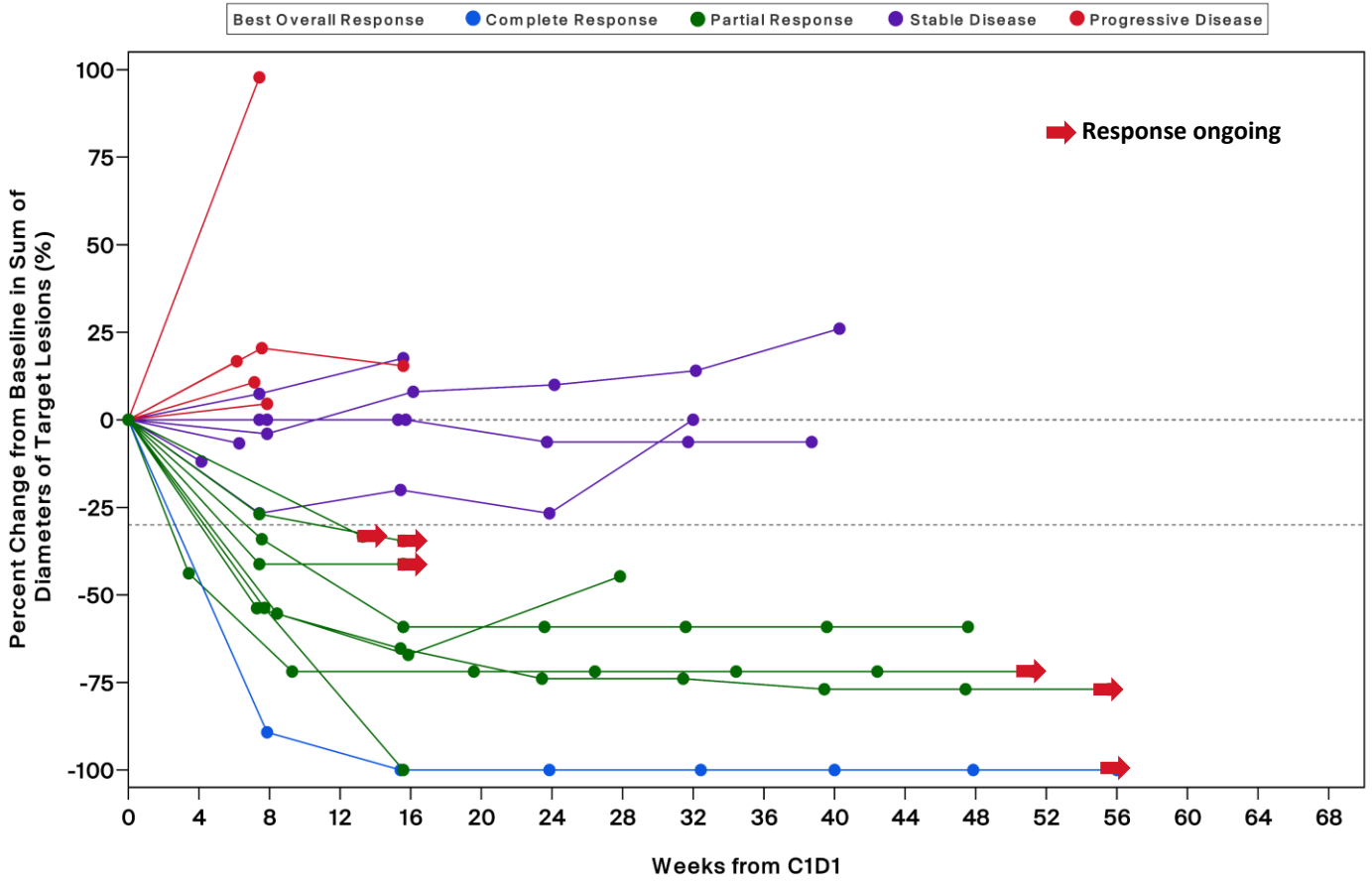
- 57% at 5 mg/m^2 qw
  - Tumor shrinkage in all 5 mg/m^2 qw patients
- 50% at 7.5 mg/m^2 2-on, 1-off
- 50% at 10 mg/m^2 q2w

PRs in 5 of 6 dose cohorts

1. CR = Complete Response; PR = Partial Response; SD = Stable Disease; PD = Progressive Disease
2. Sum of target lesions (TLs) was calculated only if all measurement were recorded for all TLs identified at baseline. Patients with no baseline TLs were not included
3. Confirmation of objective tumor response is not required for this summary presentation
4. PR at 7.5 mg/m^2 qw was a target lesion with 100% reduction but patient developed a new non-target lesion

Responses[1] observed in Phase I dose escalation in response-evaluable urothelial patients

- Median DOR not reached[2]
  - 6 responses ongoing[2]
    - 3 at 5 mg/m^2 qw
      - All 3 responders cited at AACR (data as of 7Mar22) still on trial and responding as of 20Sep22
    - 1 at 7.5 mg/m^2 2-on, 1-off
    - 2 at 10 mg/m^2 q2w



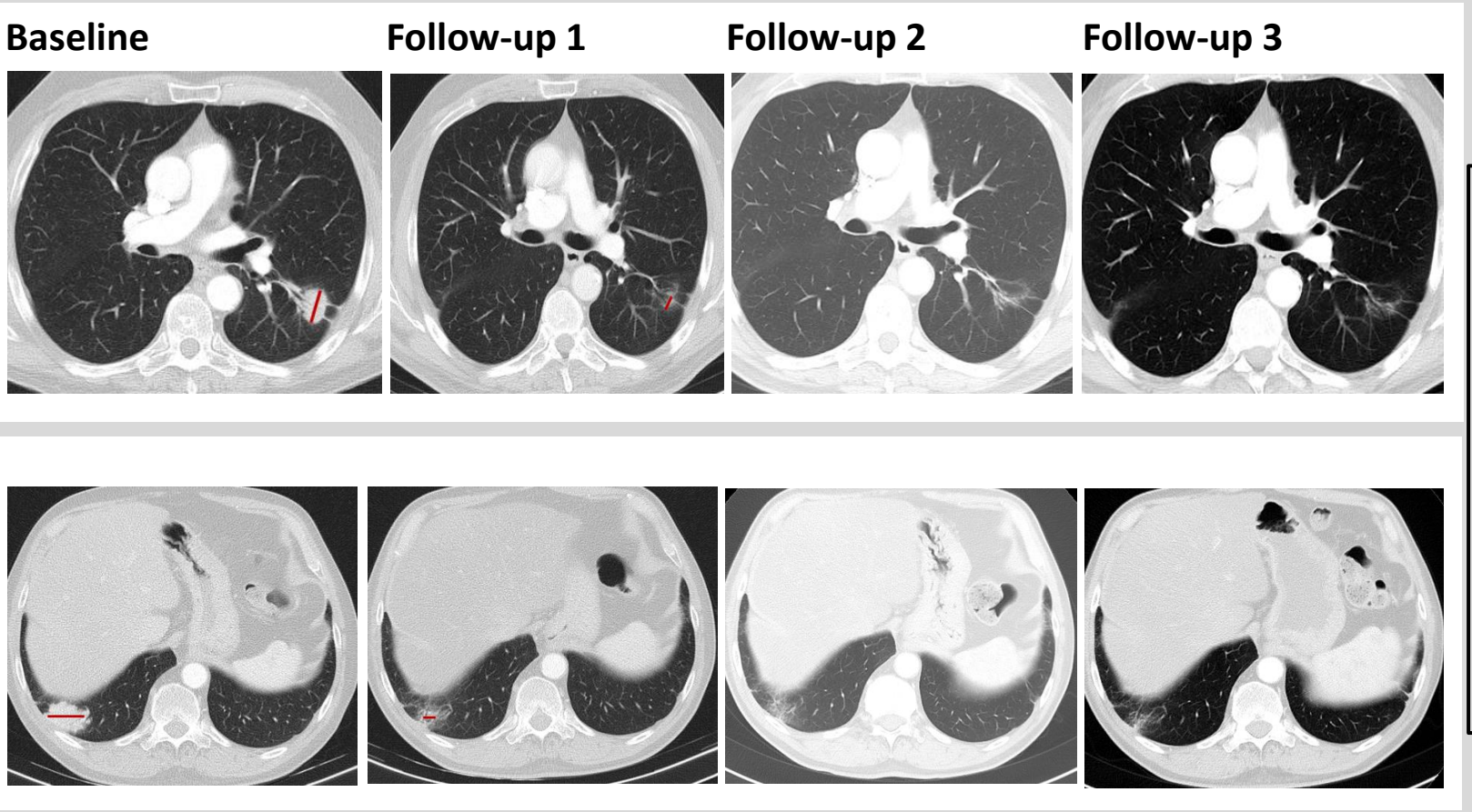
1. Responses under response evaluation criteria in solid tumors (RECIST) version 1.1
2. As of 20Sep22

Response[1] rates in urothelial cancer

Best overall response, n (%)	2.5 mg/m^2 qw (N=4)	5 mg/m^2 qw (N=8)[2]	7.5 mg/m^2 qw (N=4)[3]	7.5 mg/m^2 q2w (N=2)	7.5 mg/m^2 2-on, 1-off (N=2)	10 mg/m^2 q2w (N=4)	Total (N=24)
Complete Response (CR)	0	1 (13)	0	0	0	0	1 (4)
Partial Response (PR)[4]	1 (25)	3 (38)	1 (25)	0	1 (50)	2 (50)	8 (33)
Stable Disease (SD)[5]	2 (50)	3 (38)	1 (25)	0	1 (50)	0	7 (29)
Progressive Disease	1 (25)	0	0	2 (100)	0	2 (50)	5 (21)
Not Evaluable	0	1 (13)	2 (50)	0	0	0	3 (13)
ORR (CR+PR)	**1 (25)**	**4 (50)**	**1 (25)**	**0**	**1 (50)**	**2 (50)**	**9 (38)**
CBR[6] (CR+PR+SD≥16 wks)	**2 (50)**	**6 (75)**	**2 (50)**	**0**	**1 (50)**	**2 (50)**	**13 (54)**

1. Responses under response evaluation criteria in solid tumors (RECIST) version 1.1
2. One patient deemed non-evaluable due to missed end of trial RECIST assessment
3. Two patients deemed non-evaluable due to coming off trial before their first scans
4. Includes 1 unconfirmed PR (7.5 mg/m^2 qw) and 2 that were confirmed post the 20Sep22 data cut off: 7.5 mg/m^2 2-on, 1-off and 10 mg/m^2 q2w
5. The following patients had SD<16 wks: 1 patient at 2.5 mg/m^2, 1 at 5 mg/m^2 and 1 at 7.5 mg/m^2 2-on, 1-off
6. Clinical Benefit Rate

BT8009: Comparison of complete responder* pre-dose tumor images with tumor images after six months treatment (5 mg/m² qw)



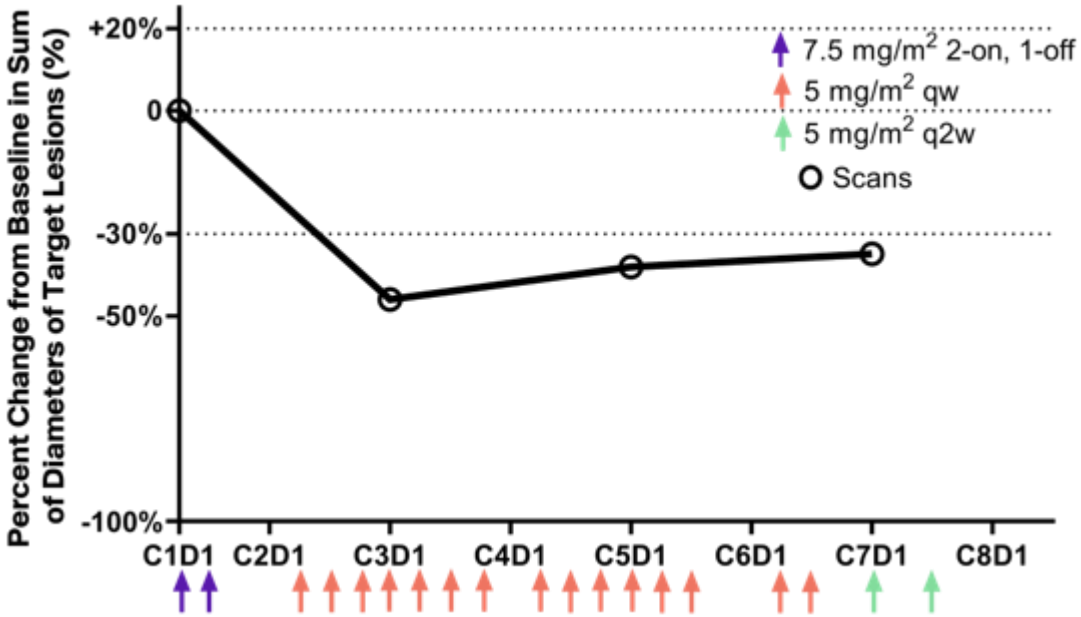
- Target lesions were reduced by 100% after four months of BT8009 treatment
- Patient still on therapy and responding after more than 18 months as of Jan 23

* Response under response evaluation criteria in solid tumors (RECIST) version 1.1

Activity outside of urothelial: Lung and breast cancer responders

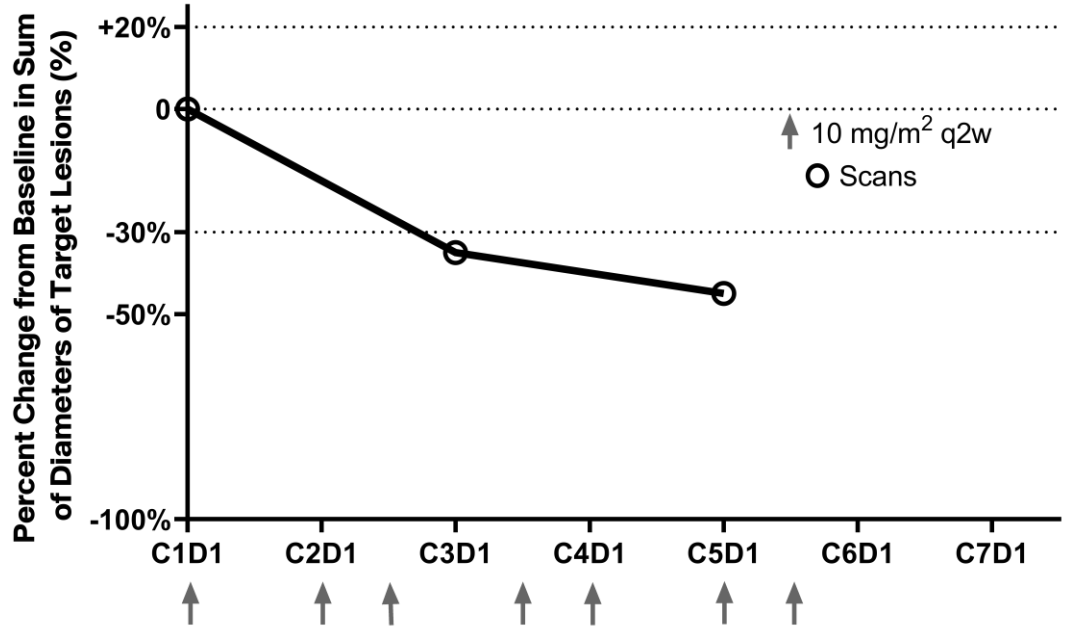
Lung cancer

- Patient: Male, 76
- 4 prior lines of therapy, including pembrolizumab
- Nectin-4 score: 100
- Response confirmed as of data cut off: 20Sep22



Breast cancer

- Patient: Female, 79
- 1 prior line of therapy
- Nectin-4 score: 160
- Response confirmed December 2022



1 cycle is equivalent to 28 days

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Anti-tumor activity outside of urothelial*

Lung cancer

Cohort (dose)	H-Score	Outcome
2.5 mg/m^2 qw	0	Progressive disease
2.5 mg/m^2 qw	240	Unconfirmed stable disease
2.5 mg/m^2 qw	180	Stable disease: >9 mos on therapy
5 mg/m^2 qw	120	Not evaluable
7.5 mg/m^2 2-on, 1-off	100	Partial response: >6 mos on therapy
7.5 mg/m^2 qw	120	Stable disease: >6 mos on therapy

Breast cancer

Cohort (dose)	H-Score	Outcome
5 mg/m^2 qw	N/A	Not evaluable
5 mg/m^2 qw	135	Progressive disease
5 mg/m^2 qw	120	Unconfirmed stable disease
7.5 mg/m^2 q2w	165	Progressive disease
7.5 mg/m^2 2-on, 1-off	145	Unconfirmed stable disease
10 mg/m^2 q2w	100	Progressive disease
10 mg/m^2 q2w	160	Partial response: >4 mos on therapy (confirmed December 2022)

*Best response data

Overview of adverse events

Number of patients with at least one, n (%)	All Cohorts[4] N=49	5 mg/m^2 qw N=20	7.5 mg/m^2 2-on, 1-off N=5
Any TEAEs[1]	49 (100)	20 (100)	5 (100)
Any TEAE, ≥ Grade 3	33 (67)	13 (65)	4 (80)
BT8009 Related TEAE	46 (94)	17 (85)	5 (100)
BT8009 Related TEAE, ≥ Grade 3	18 (37)	4 (20)	3 (60)
Any TESAE[2]	12 (24)	4 (20)	2 (40)
Any TESAE, ≥ Grade 3	9 (18)	3 (15)	2 (40)
BT8009 Related TESAE[3]	5 (10)	1 (5)	1 (20)
BT8009 Related TESAE, ≥ Grade 3	3 (6)	0	1 (20)

1. Treatment-emergent adverse event
2. Treatment-emergent serious adverse event
3. Treatment-related SAEs occurred in 5 patients. 2 were at the RP2Ds: vomiting (1) at 5 mg/m^2 qw; and nausea and neutropenia (1) at 7.5 mg/m^2 2-on, 1-off. 3 were at doses greater than the RP2Ds: pyrexia (1), sepsis (1); and febrile neutropenia and vomiting (1) at 10 mg/m^2 q2w
4. 2 DLTs occurred in 2 patients: 1 Gr3 asthenia at 7.5 mg/m^2 qw and 1 Gr4 sepsis at 10 mg/m^2 q2w

Most frequent treatment-related adverse events (≥15%) – well tolerated at RP2Ds

Treatment-Related Adverse Event, n (%)	All Cohorts N=49 All Grades	All Cohorts N=49 Grade ≥3	5 mg/m^2 qw N=20 All Grades	5 mg/m^2 qw N=20 Grade ≥3	7.5 mg/m^2 2-on, 1-off N=5 All Grades	7.5 mg/m^2 2-on, 1-off N=5 Grade ≥3
Nausea	23 (47)	1 (2)	7 (35)	0	4 (80)	1 (20)
Fatigue	18 (37)	3 (6)	5 (25)	1 (5)	3 (60)	0
Diarrhea	13 (27)	1 (2)	3 (15)	0	2 (40)	0
Decreased appetite	12 (24)	1 (2)	5 (25)	0	2 (40)	0
Asthenia	11 (22)	2 (4)	3 (15)	1 (5)	0	0
Pyrexia	11 (22)	0	4 (20)	0	2 (40)	0
Neutrophil count decreased	11 (22)	3 (6)	4 (20)	1 (5)	0	0
Alopecia	11 (22)	0	5 (25)	0	2 (40)	0
Neutropenia	8 (16)	7 (14)	1 (5)	1 (5)	3 (60)	2 (40)

Treatment-related adverse events of specific monitoring

Treatment-Related Adverse Event, n (%)	All Cohorts N=49 All Grades	All Cohorts N=49 Grade ≥3	5 mg/m^2 qw N=20 All Grades	5 mg/m^2 qw N=20 Grade ≥3	7.5 mg/m^2 2-on, 1-off N=5 All Grades	7.5 mg/m^2 2-on, 1-off N=5 Grade ≥3
Skin rash	6 (12)	0	2 (10)	0	0	0
Eye disorders	4 (8)	1 (2)	1 (5)	0	2 (40)	1 (20)
Neuropathy	13 (27)	1 (2)	6 (30)	0	2 (40)	0
Pneumonitis	0	0	0	0	0	0

Search for rash events included the following preferred terms: Eczema, photosensitivity reaction, rash, rash maculo-papular, application site rash, urticaria, blister, blood blister, conjunctivitis, dermatitis, dermatitis bullous, drug eruption, erythema, erythema multiforme, exfoliative rash, intertrigo, palmar-plantar erythrodysesthesia syndrome, rash erythematous, rash macular, rash papular, rash pruritic, rash vesicular, skin irritation, skin exfoliation, and stomatitis. Other terms represent Eye Disorders System Organ Class, Peripheral Neuropathy MedDRA SMQ (Broad), and the preferred term of 'Pneumonitis.'

Rash by dose cohort; low incidence and severity

Rash TRAEs, n (%)	2.5 mg/m^2 qw (N=7)	5 mg/m^2 qw (N=20)	7.5 mg/m^2 q2w (N=5)	7.5 mg/m^2 qw (N=5)	7.5 mg/m^2 2-on, 1-off (N=5)	10 mg/m^2 q2w (N=7)	Total (N=49)	≤ RP2Ds* (N=37)
Grade 1	2 (29)	1 (5)	0	1 (20)	0	1 (14)	5 (10)	3 (8)
Grade 2	0	1 (5)	0	0	0	0	1 (2)	1 (3)
≥Grade 3	0	0	0	0	0	0	0	0
Total	2 (29)	2 (10)	0	1 (20)	0	1 (14)	6 (12)	4 (11)

* Excludes patients in 7.5 mg/m^2 qw and 10 mg/m^2 q2w cohorts

Neuropathy by dose cohort; low incidence and severity

Neuropathy TRAEs, n (%)	2.5 mg/m² qw (N=7)	5 mg/m² qw (N=20)	7.5 mg/m² q2w (N=5)	7.5 mg/m² qw (N=5)	7.5 mg/m² 2 on, 1 off (N=5)	10 mg/m² q2w (N=7)	Total (N=49)	≤ RP2Ds (N=37)
Gr1	1 (14)	5 (25)	0	0	1 (20)	0	7 (14)	7 (19%)
Gr2	1 (14)	1 (5)	0	2 (40)	1 (20)	0	5 (10)	3 (8%)
≥Gr3	0	0	0	1 (20)	0	0	1 (2)	0
Total	2 (29)	6 (30)	0	3 (60)	2 (40)	0	13 (27)	10 (27)

Breakdown of UC at 5 mg/m² qw (unchanged from AACR 2022)

Neuropathy TRAEs in UC, n (%)	5 mg/m² qw (N=8)
Gr1	3 (38)
Gr2	1 (13)
≥Gr3	0
Total	4 (50)

Treatment-related neutrophil count decreased and neutropenia

Neutrophil count decreased TRAEs, n (%)	2.5 mg/m² qw (N=7)	5 mg/m² qw (N=20)	7.5 mg/m² q2w (N=5)	7.5 mg/m² qw (N=5)	7.5 mg/m² 2-on, 1-off (N=5)	10 mg/m² q2w (N=7)	Total (N=49)	≤ RP2Ds (N=37)
Grades 2-4	1 (14)	3 (15)	1 (20)	1 (20)	0	2 (29)	8 (16)	5 (14)
Grades 3-4	0	1 (5)	0	2 (40)	0	0	3 (6)	1 (3)

Neutropenia TRAEs, n (%)	2.5 mg/m² qw (N=7)	5 mg/m² qw (N=20)	7.5 mg/m² q2w (N=5)	7.5 mg/m² qw (N=5)	7.5 mg/m² 2-on, 1-off (N=5)	10 mg/m² q2w (N=7)	Total (N=49)	≤ RP2Ds (N=37)
Grades 2-4	0	0	0	0	1 (20)	0	1 (2)	1 (3)
Grades 3-4	0	1 (5)	0	1 (20)	2 (40)	3 (43)	7 (14)	3 (8)

Limited number of treatment-related dose modifications at doses ≤ RP2Ds

Treatment-related modifications, n (%)	(N=37)
Discontinuations	0
Interruptions	9 (24)
Reductions	6 (16)

Exposure to BT8009 for patients enrolled; very high relative dose intensity

All Patients	2.5 mg/m^2 qw (N=7)	5 mg/m^2 qw (N=20)	7.5 mg/m^2 q2w (N=5)	7.5 mg/m^2 qw (N=5)	7.5 mg/m^2 2-on, 1-off (N=5)	10 mg/m^2 q2w (N=7)	Total (N=49)
Median Treatment Duration (weeks)	15.1 (5.1-54.1)	7.1 (1.1-62.0)	6.1 (2.1-10.1)	13.1 (1.1-37.1)	21.4 (12.1-26.1)	10.0 (0.1-18.0)	12.1 (0.1-62.0)
Median % Relative Dose Intensity	100.0	97.6	100.0	93.7	96.8	100.0	98.8

Urothelial Cancer	2.5 mg/m^2 qw (N=4)	5 mg/m^2 qw (N=8)	7.5 mg/m^2 q2w (N=2)	7.5 mg/m^2 qw (N=4)	7.5 mg/m^2 2-on, 1-off (N=2)	10 mg/m^2 q2w (N=4)	Total (N=24)
Median Treatment Duration (weeks)	15.3 (5.1-54.1)	36.7 (1.1-62.0)	5.1 (4.1-6.1)	7.7 (1.1-37.1)	17.4 (13.4-21.4)	15.2 (10.0-18.0)	15.3 (1.1-62.0)
Median % Relative Dose Intensity	100.0	98.4	81.4	90.2	97.8	100.0	98.8

Review of BT8009 Phase I trial results

- BT8009 demonstrates preliminary anti-tumor activity in heavily pre-treated urothelial, lung and breast cancer patients with signs of differentiation compared to antibodies and potential for industry-leading product profile
  - 50% ORR and 75% clinical benefit rate, including 1 (13%) complete response in urothelial cancer at 5 mg/m^2 qw dose
  - Breadth of responses at other dose cohorts and other cancer types illustrates drug's potential
  - Durable responses, with tumor reductions maintained over time. Median duration of response still has not been reached among urothelial patients in the 5 mg/m^2 cohort; at least 11 months at data cut off of 20 Sept 22
    - As of January 2023, mDOR is estimated to be approximately 14 months with 2 out of 4 responders still on therapy
- Emerging efficacy and safety profile potentially distinguishes it from enfortumab vedotin
- Current focus on 5 mg/m^2 qw dose in expansion phase of trial

BT8009-100:
End of Phase I escalation top-line results

- Looking forward:
  - Perspective on where BT8009 would fit in US treatment landscape
  - Phase II trial dose expansion trial design
  - Next steps
  - Conclusion

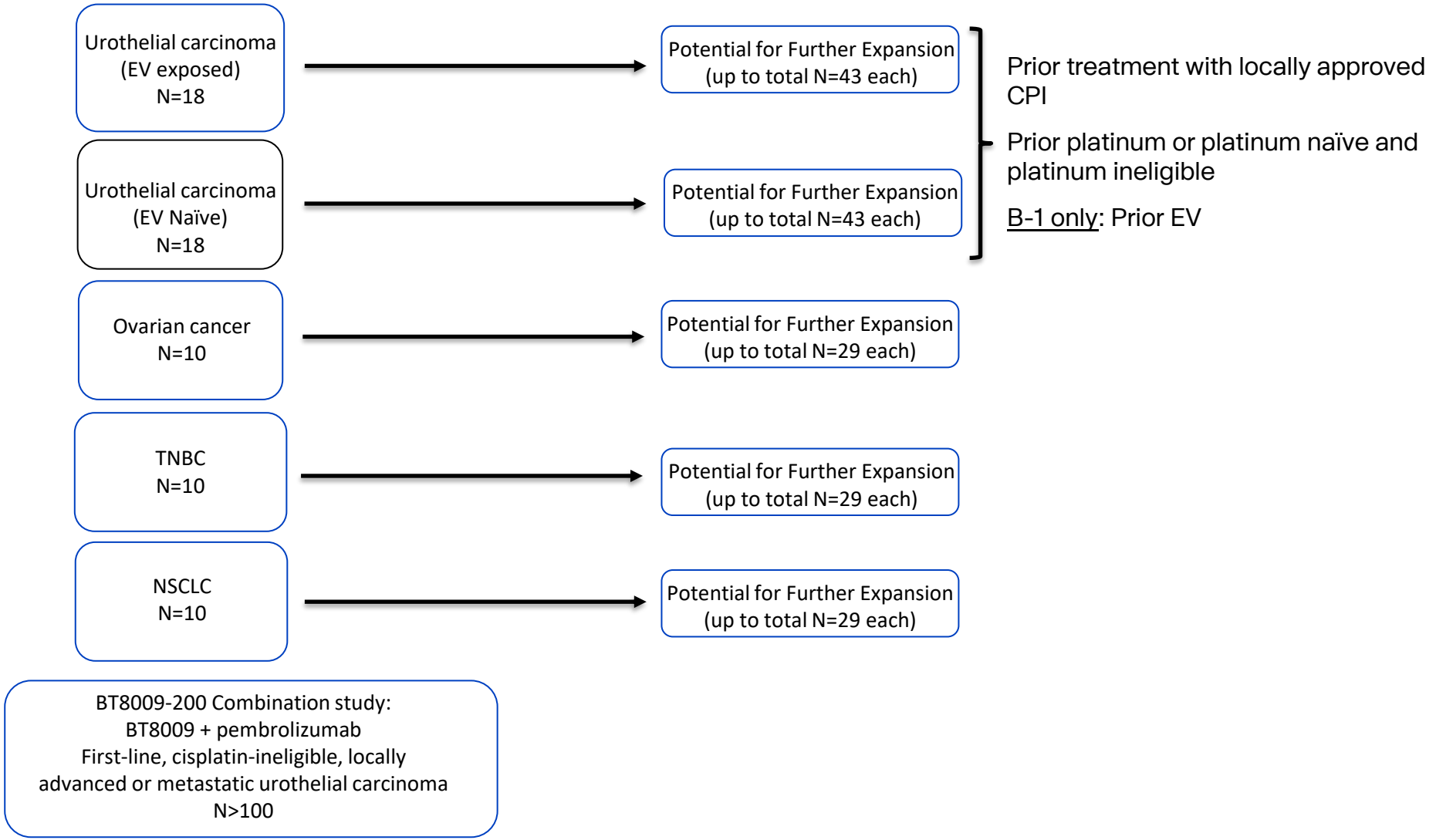
Biography of Daniel P. Petrylak, MD

- Professor of Medicine and Urology, Yale University
- Co-director of the Cancer Signaling Networks Research Program at Yale Cancer Center which studies how cancer stem cells are regulated in the body and communicate with surrounding tissue
- Director of the genitourinary cancer research group, Smilow Cancer Hospital
- Formerly he was Professor of Medicine at the Herbert Irving Cancer Center at Columbia University Medical Center with New York-Presbyterian Hospital
- Dr Petrylak received his undergraduate degree from Columbia College and his MD from Case Western Reserve University School of Medicine and joined the Yale faculty in 2012
- He currently serves as principal investigator or co-principal investigator on seven Southwest Oncology Group clinical trials for genitourinary cancers. To date, he has authored more than 200 peer-reviewed articles and book articles on prostate and bladder cancer research outcomes

Putting BT8009 in perspective

- Promising BT8009 Phase I results
- Anti-tumor activity and tolerability profile differentiated from other urothelial cancer agents
- Duration of response is a function of emerging efficacy and tolerability profile, enabling patients to stay on therapy
- Tolerability profile suggests BT8009 would be a good candidate to be utilized in combination with a checkpoint inhibitor (CPI)
- BT8009 advancing into further clinical trials as a monotherapy and in combination with a CPI for the treatment of mUC
- Has the potential to become an important new drug for the treatment of mUC

BT8009 Ongoing clinical development



Prescreening for Nectin-4 will not be required in expansion cohorts

Path to urothelial cancer commercialization includes key activities for BT8009 in 2023

Accelerate clinical studies with current and future urothelial cancer investigators

- 21 current BT8009 clinical sites
- Actively recruiting more sites; aim to more than double number of sites by year end

Partner with expert study leaders and key advisors to build a best-in-class clinical development program

- Lead investigator Yohann Loriot – Gustave Roussy
- Senior investigator Daniel Petrylak – Yale Cancer Center
- Approach top Urothelial Cancer Centers to form a Strategic Council*

Engage regulatory agencies to guide clinical development and support an expedited path to market

- Utilize opportunities to continue clinical development in late-line urothelial cancer, following receipt of Fast Track designation from FDA
- Capitalize on regulatory discussions to support clinical development in first-line cisplatin ineligible urothelial cancer (in combination with pembrolizumab)

*Advisory and consulting engagements are to gain insights and understanding on Bicycle's products and programs

In conclusion...

- BT8009 demonstrates anti-tumor activity in heavily pre-treated urothelial, lung and breast cancer patients
- Duration of response clearly distinguishes it from other Nectin-4 approaches
- Dosing at recommended Phase II dose of 5 mg/m^2 qw in expansion cohorts is ongoing
- Announced Fast Track Designation in January. Continue to have dialogue with regulators
- Will provide update on program later in 2023

BT8009-100:
End of Phase I escalation top-line results

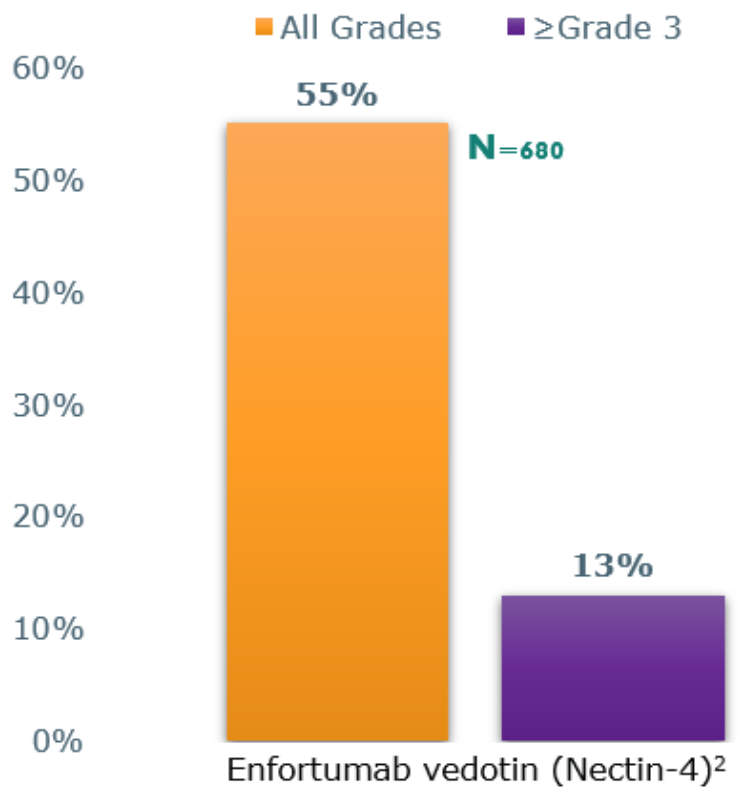
- Appendix

Enfortumab vedotin: Rash incidence in Phase I and label

Table S2. Treatment-Emergent Adverse Events of Special Interest[1]

	Metastatic Urothelial Carcinoma (N=155)	
	All Grades	Grade ≥3
Any Rash	**70 (45)**	**10 (6)**
Maculopapular rash	39 (25)	5 (3)
Rash	11 (7)	0
Blister	7 (5)	0
Bullous dermatitis†	5 (3)	1 (1)
Erythema	5 (3)	0
Erythematous rash	5 (3)	2 (1)
Palmar-plantar erythrodysaesthesia	4 (3)	1 (1)
Papular rash	4 (3)	0
Vesicular rash	4 (3)	0
Eczema	3 (2)	1 (1)
Macular rash	3 (2)	0
Dermatitis	2 (1)	0
Generalised rash	2 (1)	0
Maculovesicular rash	2 (1)	0
Skin irritation	2 (1)	0
Allergic dermatitis	1 (1)	0
Erythema multiforme	1 (1)	0
Pemphigoid	1 (1)	0

†Grade 4



1. Rosenberg, *et al.*, "EV-101: A Phase I Study of Single-Agent Enfortumab Vedotin in Patients With Nectin-4–Positive Solid Tumors, Including Metastatic Urothelial Carcinoma" Journal of Clinical Oncology, 2020 Apr 1; 38(10): 1041–1049
2. Padcev FDA Label, July 2021

Bicycle®

In enfortumab vedotin Phase I trial: "Peripheral neuropathy (of any form)…occurred in 76 patients (49%)"[1]

"Peripheral sensory neuropathy was the most common reason for discontinuation as a result of an AE (5 of 16 patients)"[1]

TABLE 2. Incidence of TRAEs That Occurred in ≥ 20% of Patients With mUC Treated With 1.25 mg/kg EV (N = 112)

	Grade, No. (%)							
	EV 0.50 mg/kg (n = 2)		EV 0.75 mg/kg (n = 14)		EV 1.0 mg/kg (n = 27)		EV 1.25 mg/kg (n = 112)	
TRAE	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3
Fatigue	0	0	3 (21)	0	9 (33)	1 (4)	59 (53)	2 (2)
Alopecia	0	0	2 (14)	0	7 (26)	0	52 (46)	0
Decreased appetite	0	0	1 (7)	0	8 (30)	0	47 (42)	1 (1)
Dysgeusia	0	0	2 (14)	0	7 (26)	0	43 (38)	0
Nausea	0	0	4 (29)	0	12 (44)	0	42 (38)	1 (1)
Peripheral sensory neuropathy[2]	0	0	2 (14)	0	5 (19)	0	42 (38)	1 (1)
Pruritus	0	0	1 (7)	0	11 (41)	0	39 (35)	1 (1)
Diarrhea	1 (50)	0	3 (21)	0	7 (26)	0	37 (33)	1 (1)
Maculopapular rash	0	0	0	0	3 (11)	2 (7)	30 (27)	3 (3)
AST increased	0	0	0	0	5 (19)	0	25 (22)	1 (1)
Dry skin	0	0	1 (7)	0	1 (4)	0	24 (21)	0

49% incidence of Any Peripheral Neuropathy, across all cohorts. Supplemental Appendix, Table S2[1]

1. Rosenberg, *et al.*, "EV-101: A Phase I Study of Single-Agent Enfortumab Vedotin in Patients With Nectin-4–Positive Solid Tumors, Including Metastatic Urothelial Carcinoma" Journal of Clinical Oncology, 2020 Apr 1; 38(10): 1041–1049
2. This definition excludes other forms of peripheral neuropathy (PN) that are included in BT8009's definition of PN: paresthesia, hypoesthesia, neuropathy peripheral, neurotoxicity, and hemiparesis

Enfortumab vedotin: Neutrophil count decreased, incidence and severity*

Neutrophil count decreased TRAEs, N (%)	EV-201 C1 (125)	EV-201 C2 (89)	EV-301 C1 (296)
Grades 2-4	14%	34%	27%
Grades 3-4	5%	5%	12%

*Padcev FDA Label, July 2021

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Relative dose intensity for enfortumab vedotin*

Table 78 Study drug exposure (Safety Analysis Set)

Parameter Category/Statistic	Study EV-301		Study EV-201		
	Enfortumab Vedotin (n = 296)	Chemotherapy (n = 291)	Cohort 1 Enfortumab Vedotin (n = 125)	Cohort 2 Enfortumab Vedotin (n = 89)	Enfortumab Vedotin† 1.25 mg/kg (n =680)
Duration of exposure (months) ‡					
N	296	291	125	89	680
Mean (SD)	5.36 (3.72)	3.96 (2.95)	6.00 (5.73)	6.38 (4.62)	5.77 (5.06)
Min, max	0.5, 19.4	0.2, 15.0	0.5, 29.4	0.3, 24.6	0.3, 34.8
Median	4.99	3.45	4.60	5.98	4.67
Duration of exposure (months), n (%)					
< 1	43 (14.5)	38 (13.1)	14 (11.2)	13 (14.6)	99 (14.6)
≥ 1 and < 6	143 (48.3)	189 (64.9)	71 (56.8)	32 (36.0)	333 (49.0)
≥ 6 and < 12	92 (31.1)	59 (20.3)	27 (21.6)	32 (36.0)	184 (27.1)
≥ 12	18 (6.1)	5 (1.7)	13 (10.4)	12 (13.5)	64 (9.4)
Planned dose intensity ¶					
N	296	N/A*	125	89	680
Mean (SD)	3.750 (0)	N/A	3.750 (0)	3.750 (0)	3.750 (0)
Min, max	3.75, 3.75	N/A	3.75, 3.75	3.75, 3.75	3.75, 3.75
Median	3.750	N/A	3.750	3.750	3.750
Dose intensity ††					
N	296	N/A*	125	89	680
Mean (SD)	2.98 (0.66)	N/A	2.92 (0.66)	2.90 (0.67)	2.94 (0.70)
Min, max	1.1, 3.9	N/A	1.0, 3.8	1.3, 3.8	1.0, 4.5
Median	3.03	N/A	2.95	2.96	3.02
Relative dose intensity (%) ‡‡					
n	296	290	125	89	680
Mean (SD)	79.35 (17.52)	91.76 (11.61)	77.81 (17.60)	77.24 (18.00)	78.46 (18.55)
Min, max	30.6, 104.9	32.5, 114.2	26.2, 101.8	33.3, 102.2	26.2, 120.0
Median	80.73	97.36	78.67	78.95	80.40

ISS: integrated summary of safety; Max: maximum; Min: minimum; RDI: relative dose intensity; SD: standard deviation

† Enfortumab vedotin 1.25 mg/kg column includes all subjects in the following studies who received a 1.25 mg/kg dose of enfortumab vedotin: EV-101, EV-102, EV-201, and EV-301.

‡ Duration of exposure = (min (initial dose date of the last cycle + 27, cutoff date, death date) - first dose date + 1) / 30.4375 for enfortumab vedotin and duration of exposure = (min (initial dose date of the last cycle + 20, cutoff date, death date)- first dose date + 1) / 30.4375 for chemotherapy.

¶ Initial dose multiplied by planned number of dosing days per cycle. Unit for enfortumab vedotin is mg/kg/cycle.

†† Actual weight adjusted total dose per cycle. For derivation details see [SAP Section 5.3]. Unit for enfortumab vedotin is mg/kg/cycle.

‡‡ (Dose intensity/Planned dose intensity) x 100%. RDI calculation uses subject weight capped at 100 kg for enfortumab vedotin. At dose administration, some enfortumab vedotin subjects were not weight capped at 100 kg and as a result, their RDI may be greater than 100%.

* EMA CHMP Assessment Report on Padcev, 24 February 2022, Table 78, p. 133