UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

April 11, 2022
Date of Report (Date of earliest event reported)

Bicycle Therapeutics plc
(Exact name of registrant as specified in its charter)

England and Wales	**001-38916**	**Not applicable**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

B900, Babraham Research Campus **Cambridge CB22 3AT** **United Kingdom**	**Not Applicable**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **+44 1223 261503**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, nominal value £0.01 per share	n/a	The Nasdaq Stock Market LLC*
American Depositary Shares, each representing one ordinary share, nominal value £0.01 per share	BCYC	The Nasdaq Stock Market LLC

***** Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market LLC.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On April 11, 2022, Bicycle Therapeutics plc (the "Company") issued a press release announcing interim Phase I results from the Phase I/II trial of BT8009. A copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated into this Item 8.01 by reference.

Also on April 11, 2022, the Company hosted a conference call and webcast to discuss the above-mentioned interim clinical trial results. A copy of the presentation used for the conference call and webcast is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated into this Item 8.01 by reference.

Item 9.01 Financial Statements and Exhibits

(a) Exhibits

99.1	Press Release issued April 11, 2022
99.2	Presentation dated April 11, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: April 12, 2022

BICYCLE THERAPEUTICS PLC

By: /s/ Lee Kalowski
Name: Lee Kalowski
Title: Chief Financial Officer

Bicycle Therapeutics Announces Interim BT8009 Phase I Clinical Trial Results at the 2022 AACR Annual Meeting

- 50% confirmed overall response rate, including one (13%) confirmed complete response in eight urothelial cancer patients dosed at 5.0mg/m^2 weekly

- Median duration of response not yet reached in the 2.5mg/m^2 and 5.0mg/m^2 weekly cohorts; four of five responders in these cohorts still on therapy after at least 24 weeks

- Tolerability profile maintained over time, with low incidence of skin, ocular and neurological toxicities showing potential for differentiation from antibody-based approaches

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- *Company to Host Conference Call Today at 8:30 a.m. ET*

CAMBRIDGE, England, & BOSTON, April 11, 2022 – Bicycle Therapeutics plc (NASDAQ: BCYC), a biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*®) technology, today announced interim Phase I results from the Phase I/II trial of BT8009, a second-generation BTC™ targeting Nectin-4. The results were presented in an oral presentation on Sunday, April 10 at the 2022 American Association for Cancer Research Annual Meeting in New Orleans, LA.

“Since our initial BT8009 Phase I/II trial interim results last year, we are encouraged to see BT8009’s promising profile endure over time. Over the last six months, the preliminary anti-tumor findings have been confirmed, the initial responses have deepened and remained durable, and the tolerability profile remains unchanged,” said Dominic Smethurst, MRCP, Chief Medical Officer of Bicycle Therapeutics. “We believe BT8009 has the potential to offer clinically meaningful differentiation compared to currently available therapies and we look forward to advancing the program once the escalation phase is complete.”

“As previously hypothesized, we believe that the differentiated pharmacokinetic profile of BTCs has the potential to deliver improved outcomes for patients and it is pleasing to see these clinical data mature and with it, the promise for a potentially industry-leading product profile,” said Kevin Lee, Ph.D., Chief Executive Officer. “We look forward to providing additional updates on BT8009 as well as updates from our broad *Bicycle* oncology pipeline this year.”

As of March 7, 2022, thirty-seven patients have been dosed in the Phase I/II trial of BT8009. A total of twelve response evaluable urothelial cancer (UC) patients have been dosed in monotherapy cohorts of 2.5mg/m^2 and 5.0mg/m^2 weekly in the ongoing trial.

- **Four response evaluable UC patients were dosed at 2.5mg/m^2 weekly**. Among these four patients, one patient was observed to have tumor reductions constituting a confirmed partial response (PR) and two patients were observed to have stable disease (SD), reflecting a 25% overall response rate (ORR) and 75% disease control rate (DCR) in patients in this cohort.

- **Eight response evaluable UC patients were dosed at 5.0mg/m^2 weekly**. Among these eight patients, four patients were observed to have a confirmed complete response (CR) or PR, including one patient with a CR and three patients with a PR, and two patients with SD, reflecting a 50% ORR and a 75% DCR in UC patients for this cohort. Prior to enrollment, all patients in this cohort had previously received at least two prior lines of therapy, with a median of three.

- **The median duration of response has not yet been reached in either the 2.5 mg/m^2 or 5.0mg/m^2 cohort.** Four of the five responders have ongoing Response Evaluation Criteria in Solid Tumors (RECIST) tumor responses. As of the March 7, 2022 data cutoff date, all four of these patients have a treatment duration of at least 24 weeks and all four remain on therapy.

- **Tolerability profile remains consistent with earlier results from this trial.** No dose limiting toxicities have been observed in the 2.5mg/m^2 or the 5.0mg/m^2 cohorts, and with longer-term follow-up, incidence of skin and eye toxicity, neuropathy and hyperglycemia remains low.

- **Phase I dose escalation is ongoing.** Exploration of additional doses and frequencies continues, and Bicycle intends to provide further updates this year.

Conference Call Details

Bicycle Therapeutics will host a conference call and webcast today at 8:30 a.m. ET to review the data being presented. To access the call, please dial (800) 377-9118 (domestic) or (409) 937-8920 (international) and provide the Conference ID 2775710. A live webcast of the presentation will be available on the Investors & Media section of the Bicycle website, bicycletherapeutics.com.

About Bicycle Therapeutics

Bicycle Therapeutics (NASDAQ: BCYC) is a clinical-stage biopharmaceutical company developing a novel class of medicines, referred to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are fully synthetic short peptides constrained with small molecule scaffolds to form two loops that stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making *Bicycles* attractive candidates for drug development. Bicycle is evaluating BT5528, a second-generation *Bicycle* Toxin Conjugate (BTC™) targeting EphA2; BT8009, a second-generation BTC targeting Nectin-4, a well-validated tumor antigen; and BT7480, a *Bicycle* TICA™ targeting Nectin-4 and agonizing CD137, in company-sponsored Phase I/II trials. In addition, BT1718, a BTC that targets MT1-MMP, is being investigated in an ongoing Phase I/IIa clinical trial sponsored by the Cancer Research UK Centre for Drug Development. Bicycle is headquartered in Cambridge, UK, with many key functions and members of its leadership team located in Lexington, Massachusetts. For more information, visit bicycletherapeutics.com.

Forward Looking Statements

This press release 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, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements regarding Bicycle’s anticipated advancement of its product candidates, including BT8009, and participation in the AACR Annual Meeting. Bicycle may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the intentions disclosed in these forward-looking statements as a result of various factors, including: Bicycle’s abilities to meet other anticipated deadlines presented by the ongoing COVID-19 pandemic; uncertainties inherent in the initiation and completion of clinical trials and clinical development of Bicycle’s product candidates; and other important factors, any of which could cause Bicycle’s actual results to differ from those contained in the forward-looking statements, and which are described in greater detail in the section entitled “Risk Factors” in Bicycle’s Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 1, 2022, as well as in other filings Bicycle may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and Bicycle expressly disclaims any obligation to update any forward-looking statements contained herein, whether because of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

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BT8009 clinical trial update

NASDAQ: BCYC
April 2022

Forward-looking statements

This presentation may contain forward-looking statements made pursuant to the safe harbor provisions of the Private S Reform Act of 1995. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "esti "forecasts", "goal," "intends," "may" "plans," "possible," "potential," "seeks," "will," and variations of these words or similar ex intended to identify forward-looking statements. All statements other than statements of historical facts contained in this forward-looking statements, including statements regarding our future financial or business performance, conditions, plans, pr strategies and other financial and business matters; our current and prospective product candidates, planned clinical tri activities, current and prospective collaborations and the timing and success of our development of our anticipated product can

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on o expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, c clinical results, our plans to initiate clinical trials and the designs of the planned trials and other future conditions, and are subj risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied looking statements. These risks and uncertainties include, but are not limited to, risks related to the ongoing COVID-19 pand any one or more of our product candidates will not be successfully developed or commercialized, the risk of cessation or delay planned clinical trials, the risk that we may not realize the intended benefits of our technology, including that we may not id additional product candidates for our pipeline, the risk that we may not maintain our current collaborations or enter into ne the future, or that we may not realize the intended benefits of these collaborations, the risk that our product candidates connection with the administration thereof will not have the safety or efficacy profile that we anticipate, the risk that prior replicated or will not continue in ongoing or future studies or trials, the risk that we will be unable to obtain and maintain regu our product candidates, the risk that the size and potential of the market for our product candidates will not materialize associated with our dependence on third-parties, risks regarding the accuracy of our estimates of expenses, risks relat requirements and needs for additional financing, and risks relating to our ability to obtain and maintain intellectual property product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which coul results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our Annual R K, filed with the Securities and Exchange Commission on March 1, 2022, as well as in other filings we may make with the SE well as discussions of potential risks, uncertainties and other important factors in our subsequent filings with the Securit Commission. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncer required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whe any new information, future events, changed circumstances or otherwise.

Agenda

Introduction	**Kevin Lee** Chief Executive Officer
Technology overview	**Nick Keen** Chief Scientific Officer
BT8009 clinical experience to date	**Dominic Smethurst** Chief Medical Officer
Q&A	**Executive Management Team**

Clinical stage biopharma company pioneering *Bic*
a new differentiated class of innovative medicine

Unique Platform

Generating Bicycles – a novel synthetic peptide modality that enables complex previously undruggable targets to be drugged.

Bicycle® modular format platform based on Nobel Prize science.

Strong intellectual property portfolio.

Internal Programs

Focused on oncology and immuno-oncology with multiple Phase I/II clinical assets (BT5528, BT8009 and BT7480).

BT5528 and BT8009 have shown preliminary signs of anti-tumor activity.

Trial updates for BT5528 and BT8009 in 2022.

Validating Partnerships

Extending the clinical utility of Bicycle® platform into diverse range of therapeutic areas.

Genentech
A Member of the Roche Group

AstraZeneca

OXURION

Innovate UK

Dementia Discovery Fund

CANCER RESEARCH UK

IONIS

Ambitiou Company

Deeply exper

Located Cam Lexington, M

~119 Employ

NASDAQ: BC

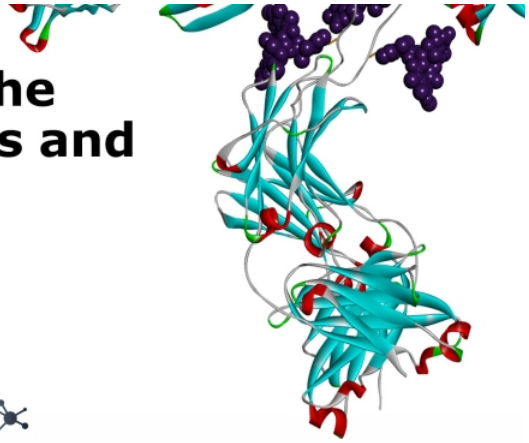
Cash balance (expected ca 2024)

* as of December 3

Robust proprietary and partnered pipeline

Target / Product	Partner / Sponsor	Indication	Modality	Pre-clinical	IND-enabling	Phase I	Phas
Internal programs							
BT5528 (EphA2)		Oncology	Bicycle® Toxin Conjugate				
BT8009 (Nectin-4)		Oncology	Bicycle® Toxin Conjugate				
BT7480 (Nectin-4/CD137)		Immuno-oncology	Bicycle TICA™				
BT7455 (EphA2/CD137)		Immuno-oncology	Bicycle TICA™				
Partnered programs							
THR-149 (Kallikrein inhibitor Bicycle)	OXURION	Ophthalmology					
BT1718 (MT1-MMP)	CANCER RESEARCH UK	Oncology	Bicycle® Toxin Conjugate				
BT7401 (multivalent CD137 systemic agonist)	CANCER RESEARCH UK	Immuno-oncology					
Undisclosed	Genentech A Member of the Roche Group	Immuno-oncology					
Inhaled Bicycles	AstraZeneca	Respiratory					
Novel anti-infectives	Innovate UK	Anti-infectives					
Novel CNS targets	Dementia Discovery Fund IONIS	CNS					
Novel neuromuscular targets	IONIS	Neuromuscular					

Bicycles are designed to combine the advantages of both small molecules and antibodies



	Bicycle®	Small molecule	Antibody
Small size	**Yes – 1.5-2kDa**	Yes – <0.8kDa	No – >150kDa
Specificity	**High**	Low	Multiple
Chemical synthesis (NCEs)	**Yes**	Yes	No
Rapid tissue penetration	**Yes**	Yes	No
Complex protein targets druggable	**Yes**	Limited	Yes
Route of elimination	**Renal**	Liver	Liver

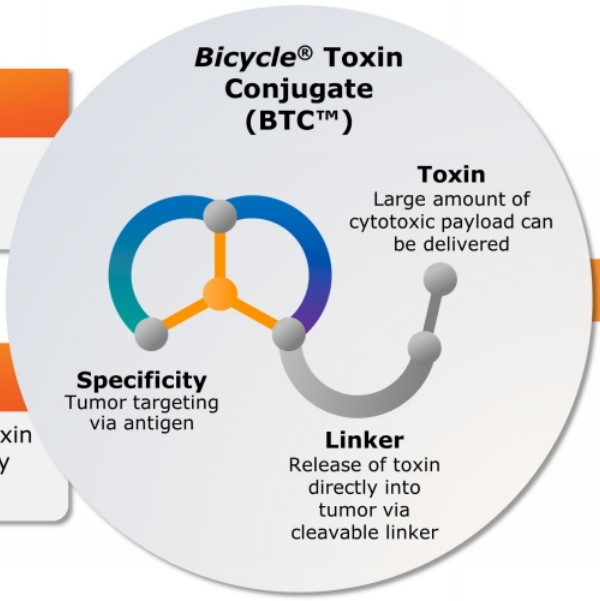
BTCs – preclinical data indicates higher potency and specificity with fewer side effects than ADCs

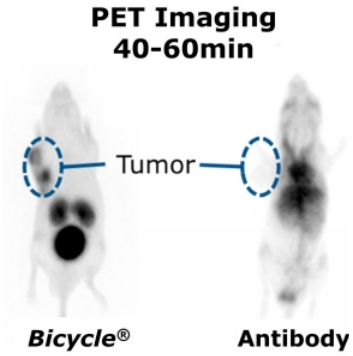
MWt of 1.5-2kDa

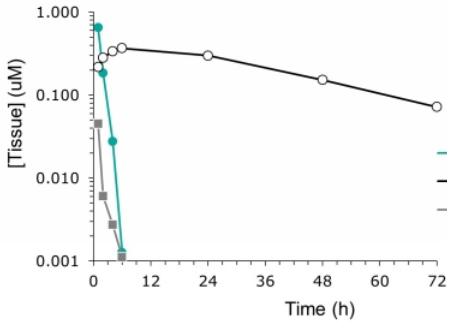
50-100x smaller than antibodies

High selectivity

Allows more potent toxin to be delivered directly to tumor







BT8009 Monotherapy

Key takeaways from phase I dose escalation trial to dat

Promising clinical activity seen at 5mg/m² weekly; dose tolerated, with potential for differentiated and industry-leading product profile

- 50% ORR and 75% disease control, including 1 (13%) complete response
- Durable responses, with tumor reductions maintained over time
- No DLTs, low incidence of skin toxicity, ocular toxicity and neuropathy

7.5mg/m² weekly cohort identified as a non-tolerated dose, with GI and fatigue relat DLTs' being observed

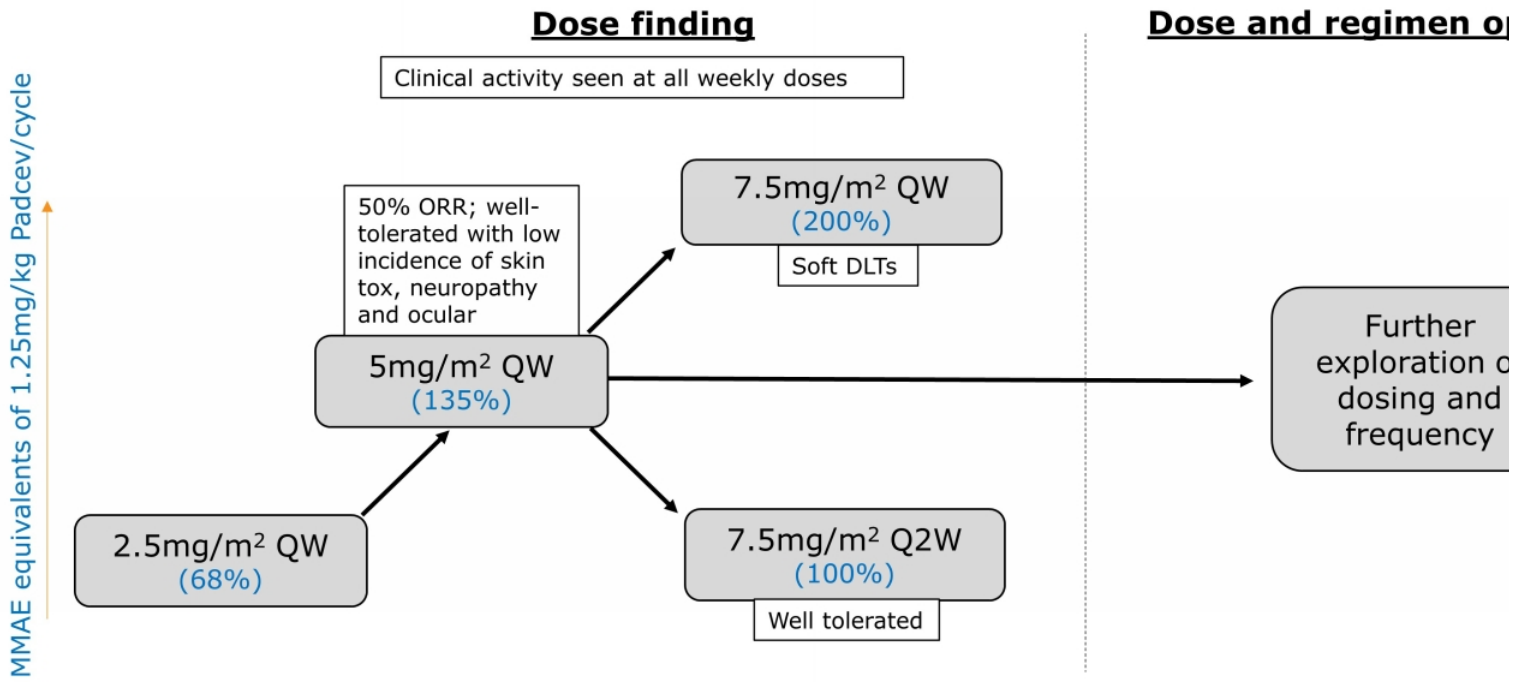
As predicted from preclinical data, BT8009 demonstrates linear pharmacokinetics. In ADCs, it also demonstrates a short terminal half-life.

Alternative dosing frequencies being explored while nearing a recommended Phase 2

Expect to provide further updates on clinical progress later in 2022

* All BT8009 data as of 7Mar22

Dose escalation progress and strategy



Overview of key demographics for all patients en in BT8009 phase I dose escalation trial

Demographics	
Total	N=37
Age, years, median (range)	66 (44-83)
Sex, n (%)	
Male	22 (59%)
Female	15 (41%)
ECOG, n (%)	
0 (Good performance status)	15 (41%)
1	22 (59%)
Prior therapies, median	3

Overview of disease history for all patients enroll
BT8009 phase I dose escalation trial

Demographics	
Total	N=37
Tumor type	
Breast	4 (11%)
Esophageal	1 (3%)
Head/Neck	2 (5%)
Lung	5 (14%)
Ovarian	1 (3%)
Pancreatic	6 (16%)
Urothelial	**18 (49%)**

Responses* observed in 2.5, 5 and 7.5mg/m² phase I dos escalation in response evaluable urothelial cancer patien

Update of First Two Cohorts

2.5mg/m² QW (N=4)
- 1 of 4 responses (25% ORR)
  - 59% tumor reduction
  - Deepened from 37% at 30Sept21
  - Remains on therapy; approaching 11 months
- 2 of 4 stable disease
- 75% disease control

5mg/m² QW (N=8)
- 4 of 8 responses (50% ORR)
  - 1 complete response
  - 3 partial responses
- 2 of 8 stable disease
- 75% disease control
- Greater detail on next slide

Newer Two Cohor

7.5mg/m² Q2W (N
- Well tolerated

7.5mg/m² QW (N=
- 1 PR prior to dose
- 1 stable disease

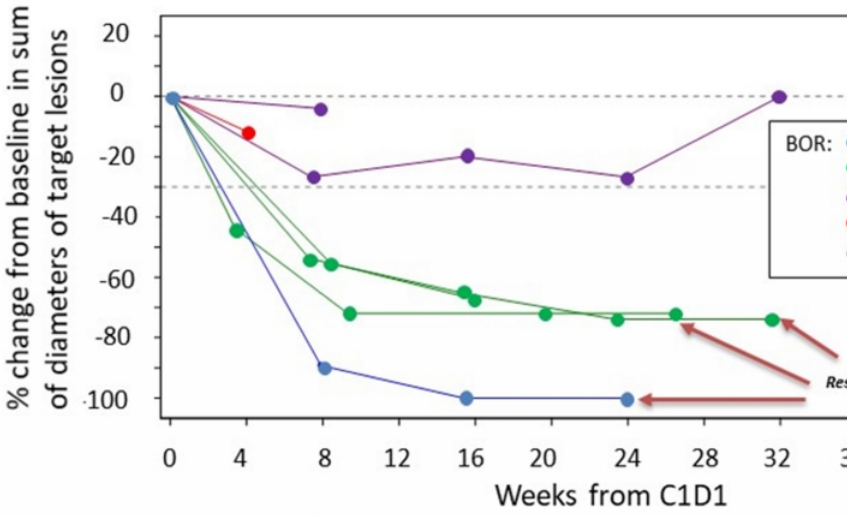
* Responses under response evaluation criteria in solid tumors (RECIST) version 1.1

Responses* observed in 5mg/m² QW cohort phase I dose escalation in response-evaluable urothelial patients

Urothelial Responses

- 4 responses in 8 patients
  - 1 Complete Response
  - 3 Partial Responses
    - 71% tumor reduction

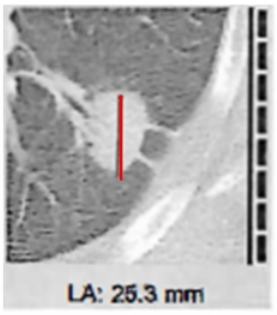
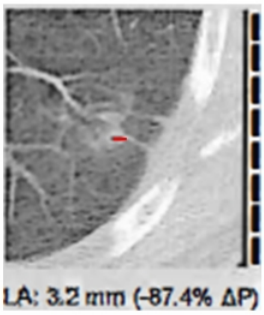
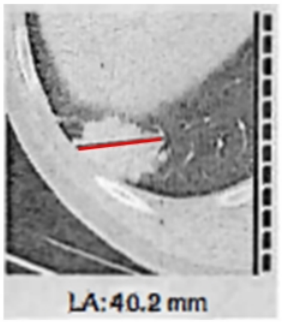
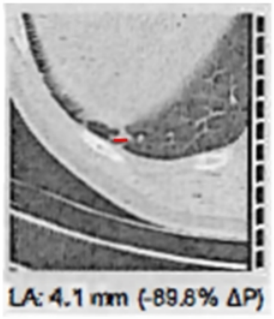
      (100% reduction in target lesion)
    - 65% tumor reduction
    - 54% tumor reduction
- Median DoR not reached
  - 3 responses ongoing
  - 1 progression at ~3 months



One subject who had clinical progression did not have post-baseline RECIST assessment data and

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

Comparison of complete responder pre-dose tumor image tumor images after six months treatment (5mg/m² QW)

	Baseline	Follow-up 1	Follow-up 2	Follow-up 3
Lung lower lobe left			**Disappeared**	**Disappeared**
Lung lower lobe right			**Disappeared**	**Disappeared**

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Phase I interim results from enfortumab vedotin (Padcev

Annals of Oncology 27 (Supplement 6): vi266–vi295, 2016
doi:10.1093/annonc/mdw373.16

genitourinary tumours, non-prostate

788P **Interim analysis of a phase I dose escalation trial of ASG-22CE (ASG-22ME; enfortumab vedotin), an antibody drug conjugate (ADC), in patients (Pts) with metastatic urothelial cancer (mUC)**

J.E. Rosenberg[1], E. Heath[2], R. Perez[3], J. Merchan[4], J. Lang[5], D. Ruether[6], D. Petrylak[7], R. Sangha[8], D.C. Smith[9], S. Sridhar[10], E. Gartner[11], M. Vincent[12], R. Chu[13], B. Anand[13], F. Donate[14], A. Melhem-Bertrandt[15], J. Zhang[16]

[1]*Genitourinary Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA,* [2]*Medical Oncology, Karmanos Cancer Institute, Detroit, MI, USA,* [3]*Medical Oncology, University of Kansas Cancer Center, Fairway, KS, USA,* [4]*Medical Oncology, University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA,* [5]*Genitourinary Oncology, UW Carbone Cancer Center, Madison, WI, USA,* [6]*Medical Oncology, Tom Baker Cancer Centre, Calgary, AB, Canada,* [7]*Medical Oncology, Smilow Cancer Hospital at Yale-New Haven, New Haven, CT, USA,* [8]*Oncology, University of Alberta Cross Cancer Institute, Edmonton, AB, Canada,* [9]*Internal Medicine and Urology, University of Michigan, Ann Arbor, MI, USA,* [10]*Oncology, Princess Margaret Hospital, Toronto, ON, Canada,* [11]*Development, Seattle Genetics, Inc., Seattle, WA, USA,* [12]*Clinical Research and Development, Agensys, Inc., Santa Monica, CA, USA,* [13]*Development, Agensys Inc., Santa Monica, CA, USA,* [14]*Translational Research, Agensys Inc., Santa Monica, CA, USA,* [15]*Clinical Research, Astellas Pharma, Northbrook, IL, USA,* [16]*Medical Oncology, H. Lee Moffitt Cancer Center University of South Florida, Tampa, FL, USA*

Background: Nectin-4 is a protein expressed on several tumors, including mUC. Enfortumab vedotin is an ADC that delivers a small molecule microtubule-disrupting agent, monomethyl auristatin E (MMAE), to tumors expressing Nectin-4.

Methods: Pts with solid tumors, including mUC, treated with ≥ 1 prior chemo were enrolled using a modified continual reassessment method design. Pts were prescreened for Nectin-4 expression (IHC assay) and enrolled if H-score ≥150. Disease assessments were performed every 8 weeks (wks) using RECIST v 1.1. Enfortumab vedotin was administered IV wkly for 3 out of every 4 wks. 4 dose levels were studied: 0.5, 0.75, 1, or 1.25 mg/kg.

Results: As of 4/29/16, 49 solid tumor pts were enrolled; 42 with mUC reported here. Of analyzed tumor tissues, 98% were Nectin-4 positive (93% had H-score ≥ 150). Median age 67 y; 100% ECOG PS ≤ 1; 25 mUC pts (60%) had ≥ 2 prior therapies (tx). Of 33 response evaluable pts, 10 had a partial response (PR) (ORR =30%), including 4/10 pts (40%) with liver metastasis and 3/12 (25%) who failed checkpoint inhibitor tx. Antitumor activity is seen at all dose levels. Median duration on treatment is 12 wks. Both median progression free survival and duration of response are 16 wks. 38 pts (91%) had adverse events (AEs). The most common tx related AE was fatigue (38%). 23 pts (55%) had Grade (G) 3/4 AEs, 10 pts (24%) considered related. 9 pts (21%) had ocular AEs (G1/2). 2 pts had protocol defined dose limiting toxicities. There were 2 deaths, unrelated to tx. Serum concentration of enfortumab vedotin decreased multi-exponentially with half-life ~1.6 days. Exposure was dose proportional. Expansion cohorts are open at 1.25 mg/kg: updated results will be presented.

Table: 788P mUC Pts Only

Dose (mg/kg)	0.5	0.75	1	1.25
Evaluable pts* (n = 33)	2	12	12	7
ORR (CR + PR) n (%)	1 (50)	4 (33)	1 (8)	4 (57)

* ≥ 1 dose of drug and ≥ 1 post-baseline DA.

Conclusions: This novel Nectin-4 targeted ADC, enfortumab vedotin, is well tolerated in mUC pts with encouraging antitumor activity. These results warrant further studies in mUC.

Clinical trial identification: ASG-22CE-13-2

Legal entity responsible for the study: Agensys Inc.

Funding: Agensys Inc. and Seattle Genetics Inc.

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100% patients pre-screened

60% patients ≥2 prior therapies

Data from BT8009 interim phase I dose escalation trial to in response-evaluable urothelial cancer patients

	2.5mg/m²	5mg/m²
No of patients	4	8
Median age	75	67
≥2 prior lines (%)	4 (100%)	8 (100%)
IHC pre-screen (%)	0	0
Partial or Complete Response (ORR %)	1 (25%)	4 (50%)
Stable Disease or better (DCR %)	3 (75%)	6 (75%)
Median duration of response (weeks)	Not reached	Not reached

Overview of adverse events observed in BT8009 phase I escalation trial across all patients

Preferred Term	Incidence (≥15%)
Fatigue	40.5%
Nausea	37.8%
Diarrhea	32.4%
Pyrexia	32.4%
Anemia	32.4%
Decreased appetite	32.4%
Constipation	29.7%
Urinary tract infection	27.0%
Neutrophil count decreased	24.3%
Asthenia	24.3%
Abdominal pain	21.6%
Pruritus	18.9%
Alopecia	18.9%
Back pain	16.2%
Hypokalemia	16.2%
Hypomagnesmia	16.2%

Summary of adverse event information from Padcev® FDA

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PADCEV safely and effectively. See full prescribing information for PADCEV.

PADCEV® (enfortumab vedotin-ejfv) for injection, for intravenous use
Initial U.S. Approval: 2019

WARNING: SERIOUS SKIN REACTIONS
See full prescribing information for complete boxed warning.

- **PADCEV can cause severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN).**
- **Immediately withhold PADCEV and consider referral for specialized care for suspected SJS or TEN or severe skin reactions.**
- **Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions. (2.2), (5.1) (6.1)**

Adverse Event	Median time to onset (months)*	Padcev incidence*	Padcev severity (Gr≥3)*	Which tria
Skin tox	0.6	55%	13%	All
Neuropathy	4.6	52%	4%	All
Ocular disorders	1.6	40%	N/A	EV-201, EV-EV-102
Hyperglycemia	0.6	14%	7%	All
Pneumonitis	2.9	3%	1%	All

*Data from Padcev FDA approved product label

Overview of key adverse events observed in BT8009 phase I d escalation trial across all cohorts

Adverse Event	Incidence	Severity (Gr≥3)	Related
Skin tox	19%	0%	14%
Neuropathy	24%	3%	19%
Ocular disorders	3%	0%	3%
Hyperglycemia	8%	0%	5%
Febrile neutropenia	0%	0%	0%
Pneumonitis	0%	0%	0%

Other adverse events of interest in BT8009 phase I dose escalation trial across all cohorts

Adverse Events	Incidence	Severity (Gr≥3)	Related
Neutropenia	30%	14%	30%
Gastrointestinal Disorders:			
Nausea	38%	3%	36%
Diarrhea	32%	5%	24%
Vomiting	11%	3%	11%

Potential efficacy in other tumor types will be explored m thoroughly in Phase II expansion trial

Demographics	
Total	N=37
Tumor type	
Breast	4 (11%)
Esophageal	1 (3%)
Head/Neck	**2 (5%)**
Lung	**5 (14%)**
Ovarian	1 (3%)
Pancreatic	6 (16%)
Urothelial	18 (49%)

- 1 SD at 7.5mg Q2W. Disappearance of non-

- 1 SD at 2.5mg. 9+ months on therapy
- 1 SD at 7.5mg QW. 6+ months on therapy

Key takeaways from phase I dose escalation trial to dat

Promising clinical activity seen at 5mg/m² weekly; dose tolerated, with potential for differentiated and industry-leading product profile

- 50% ORR and 75% disease control, including 1 (13%) complete response
- Durable responses, with tumor reductions maintained over time
- No DLTs, low incidence of skin toxicity, ocular toxicity and neuropathy

7.5mg/m² weekly cohort identified as a non-tolerated dose, with GI and fatigue relat DLTs' being observed

As predicted from preclinical data, BT8009 demonstrates linear pharmacokinetics. In ADCs, it also demonstrates a short terminal half-life.

Alternative dosing frequencies being explored while nearing a recommended Phase 2

Expect to provide further updates on clinical progress later in 2022