Bicycle Therapeutics to Present Initial Duravelo-2 Data at 2026 ASCO Annual Meeting

May 21, 2026

In the dose optimization stage of the randomized Phase 2 trial (Duravelo-2), zelenectide pevedotin at its optimal dose in combination with pembrolizumab demonstrated response rates comparable to published data for standard of care (SOC) in patients with previously untreated metastatic urothelial cancer (mUC)

The optimal dose of zelenectide demonstrated a potentially differentiated safety profile with incidence rates approximately four-fold lower for skin reactions and half that for peripheral neuropathy as published for SOC

Further data from the randomized Phase 2 trial are expected in 2H 2026

In a separate Phase 1 trial (Duravelo-1) in previously untreated, cisplatin-ineligible mUC, zelenectide in combination with pembrolizumab demonstrated a clinically meaningful median progression-free survival comparable to published data for SOC

These data provide further validation of the potential of Bicycle® technology to deliver oncology therapeutics with improved benefit/risk profiles compared to existing modalities

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--May 21, 2026-- Bicycle Therapeutics plc (NASDAQ: BCYC), a pharmaceutical company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (Bicycle®) technology, today announced the presentation of initial data from the randomized Phase 2 trial (Duravelo-2) evaluating zelenectide pevedotin (zelenectide) in previously untreated patients with metastatic urothelial cancer (mUC), demonstrating encouraging response rates and a potentially differentiated safety profile both as a monotherapy and in combination with pembrolizumab. In addition, updated data from the Phase 1 trial (Duravelo-1) in previously untreated, cisplatin-ineligible mUC patients demonstrated encouraging median progression-free survival (PFS) comparable to published data for standard of care (SOC). The data announced today will be presented at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place May 29 - June 2 in Chicago.

“Despite recent advances for the treatment of bladder cancer, there remains an urgent need for more tolerable therapies. For instance, published clinical data for the current SOC for mUC demonstrate a significant number of tolerability-related drug discontinuations, and high rates of neuropathy and skin toxicities. In contrast, the initial Duravelo-2 data shared today demonstrate that zelenectide in combination with pembrolizumab continues to show response rates comparable to published data for SOC for mUC, while potentially offering substantially lower toxicity and improved tolerability for patients. We have now tested zelenectide as a monotherapy or in combination with pembrolizumab in more than 600 patients and have consistently observed lower rates and severity of neuropathy and skin toxicities,” said Bicycle CEO Kevin Lee, Ph.D. “We believe that the extensive data we have generated in patients continue to demonstrate the unique nature of Bicycle molecules as targeting agents that offer a potentially differentiated tolerability profile to antibody-based approaches. We are excited to continue to explore these advantages with novel targets and novel payloads in our mission to help patients not only live longer but live well. Meanwhile, the Duravelo-2 trial has been converted into a randomized Phase 2 trial and we look forward to sharing further results in the second half of 2026.”

Initial Duravelo-2 Data Results

Zelenectide is a Bicycle® Drug Conjugate (BDC®) targeting Nectin-4, a well-validated tumor antigen. The Duravelo-2 trial evaluated two doses of zelenectide – 5mg/m^2 weekly (5mg dose) and 6mg/m^2 (6mg dose) two weeks on, one week off – in combination with 200mg of pembrolizumab once every three weeks in previously untreated patients with mUC (Cohort 1). Bicycle reached regulatory alignment on the zelenectide 6mg dose as optimal both in combination with pembrolizumab and as a monotherapy. Cohort 1 data were extracted for the interim analysis at Week 27, on July 23, 2025. At the time of the data cut, the median PFS was not mature, and the results at the optimal dose showed:

- 65% (17/26) overall response rate (ORR) regardless of confirmation and blinded independent central review (BICR) confirmed ORR of 58% (15/26) at the 27-week cutoff. Subsequent to the 27-week cutoff, an additional confirmed BICR response was observed, which would result in an ORR of 62% (16/26).
- Median duration of treatment (mDOT) was 6.3 months (0.7-10.6).
- 65% of patients remain on treatment.
- Median relative dose intensity in patients receiving the optimal dose was 97%.
- Low rates of zelenectide-related adverse events (AEs) of clinical interest were observed, including peripheral neuropathy, sensory (33%); skin reactions (17%); eye disorders (10%). There were no reported instances of zelenectide-related hyperglycemia.
- No zelenectide-related severe skin reactions of any grade were reported.
- The single Grade 3 zelenectide-related AE of clinical interest, peripheral neuropathy, resolved to Grade ≤1. There were no Grade 4 or Grade 5 zelenectide-related AEs of clinical interest.
- Notably, only one patient at the optimal dose discontinued therapy due to a zelenectide-related AE at the time of the data cut in Cohort 1.

The Duravelo-2 trial also evaluated the 5mg dose and 6mg dose regimens of zelenectide as a monotherapy in mUC patients with one or more prior lines of systemic therapy (Cohort 2). Cohort 2 data were extracted for the interim analysis at Week 27, on June 14, 2025. At the time of the data cut, the median PFS was not mature, and the results at the optimal dose showed:

- 37% (10/27) ORR regardless of confirmation and 30% confirmed ORR (8/27) was achieved among efficacy-evaluable patients. Of the confirmed responses, 3 (11%) were complete responses (CRs) and 5 (19%) were partial responses (PRs).
- mDOT was 4.8 months (1.3-10.1).
- 31% of patients remain on treatment.
- Median relative dose intensity in patients receiving the optimal dose was 86%.
- Low rates of zelenectide-related AEs of clinical interest were observed, including peripheral neuropathy (38%); skin reactions (28%); eye disorders (10%); and hyperglycemia (3%).
- There were no Grade 4 or Grade 5 zelenectide-related AEs of clinical interest.
- Notably, no zelenectide-related severe skin reactions of any grade were reported, and no treatment discontinuations occurred at the optimal dose.

The company plans to share additional Duravelo-2 data from the randomized Phase 2 trial in the second half of 2026.

Updated Duravelo-1 Data Results

The company also announced the presentation of updated Phase 1 Duravelo-1 data evaluating zelenectide in mUC, including monotherapy data in enfortumab vedotin (EV)-naïve patients and in combination with 200mg of pembrolizumab once every three weeks in previously untreated cisplatin-ineligible patients. Both cohorts evaluated zelenectide at the 5mg dose.

Updated results as of the August 1, 2025 data cutoff evaluating zelenectide in combination with pembrolizumab in previously untreated cisplatin-ineligible patients, 45% of whom were classified as Eastern Cooperative Oncology Group (ECOG) performance status of 2, showed:

- 59% (13/22) ORR regardless of confirmation, 50% confirmed ORR (11/22), and a disease control rate (DCR) of 82%. Of the confirmed responses, 5 (23%) were CRs and 6 (27%) were PRs.
- Median PFS was 13.0 months and median duration of response (mDOR) was not mature at the time of the data cutoff.

Updated results as of the August 1, 2025 data cutoff evaluating zelenectide as a monotherapy in EV-naïve recurrent, unresectable mUC patients who had prior anti-programmed death-1/programmed death ligand-1 (PD-1/PD-L1), had disease progression after or were ineligible for platinum-based chemotherapy showed:

- 38% (20/53) ORR regardless of confirmation, 32% confirmed ORR (17/53) and a DCR of 66%. Of the confirmed responses, 2 (4%) were CRs and 15 (28%) were PRs.
- Median PFS was 5.4 months and mDOR was 10.0 months (5.3-16.6) among patients with confirmed responses.

Across all patients, the safety and tolerability profile was consistent with other zelenectide data to date. No new safety signals were observed and there were no Grade 4 or Grade 5 zelenectide-related AEs of clinical interest reported.

The presentations will be made available in the Publications sections of the Bicycle Therapeutics website following each presentation.

About Bicycle Therapeutics

Bicycle Therapeutics is a clinical-stage pharmaceutical company developing a novel class of medicines, referred to as Bicycle® molecules, for diseases that are underserved by existing therapeutics. Bicycle molecules 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 Bicycle molecules attractive candidates for drug development. The company is evaluating nuzefatide pevedotin, formerly BT5528, a Bicycle® Drug Conjugate (BDC®) targeting EphA2, a historically undruggable target; a pipeline of other bicycle-based conjugate molecules, including Bicycle® Radioconjugates (BRC®) for radiopharmaceutical use; zelenectide pevedotin (formerly BT8009), a BDC® targeting Nectin-4, a well-validated tumor antigen; BT7480, a Bicycle Tumor-Targeted Immune Cell Agonist® (Bicycle TICA®) targeting Nectin-4 and agonizing CD137; and, through various partnerships, is exploring the use of Bicycle® technology to develop therapies for diseases in additional therapeutic areas.

Bicycle Therapeutics is headquartered in Cambridge, UK, with many key functions and members of its leadership team located in Lexington, Mass. 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 Therapeutics’ ability to explore the advantages of Bicycle molecules, and develop Bicycle molecules, with novel targets and novel payloads; the timeline for Bicycle Therapeutics’ clinical trials, including for zelenectide pevedotin, and the release of data therefrom. Bicycle Therapeutics 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 plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties inherent in research and development and in the initiation, progress and completion of clinical trials and clinical development of Bicycle Therapeutics’ product candidates; the risk that Bicycle Therapeutics may not achieve any of its clinical development strategies; timing of results from clinical trials; whether the outcomes of

preclinical studies and prior clinical trials will be predictive of future clinical trial results; the risk that trials may have unsatisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle Therapeutics' product candidates; and other important factors, any of which could cause Bicycle Therapeutics' actual results to differ from those contained in the forward-looking statements, are described in greater detail in the section entitled "Risk Factors" in Bicycle Therapeutics' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on April 30, 2026, as well as in other filings Bicycle Therapeutics 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 Therapeutics 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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