Bicycle Therapeutics Reports Recent Business Progress and First Quarter 2026 Financial Results

April 30, 2026

Presentations at AACR Annual Meeting 2026 underscore significant opportunities for nuzefatide pevedotin in EphA2 expressing cancers, including pancreatic cancer

Human imaging data provides further evidence of the potential of EphA2 as a novel cancer target and the positive properties of Bicycle® radioligand molecules for radiopharmaceutical use

Initial dose selection data from Duravelo-2 trial evaluating zelenectide pevedotin plus pembrolizumab in metastatic urothelial cancer to be presented at 2026 ASCO Annual Meeting

Cash and cash equivalents of $559.5 million as of March 31, 2026, with expected cash runway into 2030

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Apr. 30, 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 reported financial results for the first quarter ended March 31, 2026, and provided recent corporate updates.

"The data we reported in the first quarter continues to provide further validation of the potential of our Bicycle technology to deliver oncology therapeutics with improved benefit/risk profiles compared to existing modalities," said Bicycle CEO Kevin Lee, Ph.D. "We are excited by the emerging profile of our EphA2 drug conjugate, nuzefatide pevedotin, which we have now tested in over 150 patients to date, both as a monotherapy and in combination with a checkpoint inhibitor. Nuzefatide has been shown to be generally well tolerated at clinically active doses, in contrast to previous attempts to drug this target with other modalities. We believe these data, together with those presented at AACR, provide a strong rationale for advancing the development of nuzefatide in pancreatic cancer, and we are pleased to have recently dosed our first patient in our Phase 2 trial. In addition to this, the preliminary data we have reported from our Duravelo-2 program demonstrate zelenectide pevedotin to also be clinically active with a differentiated safety profile, providing convincing evidence that Bicycle drug conjugates may exhibit a fundamentally different tolerability profile to that seen with antibody-based approaches, and support our mission of helping patients not only to live longer but also to live well."

Dr. Lee added: "Following a strategic reprioritization in the first quarter, we are converting the Duravelo-2 trial into a randomized Phase 2 trial, allowing us to focus our internal resources on our emerging pipeline of next-generation therapeutics, including nuzefatide and Bicycle-based radiotherapeutics and imaging agents. We look forward to presenting initial dose selection data from our Duravelo-2 trial at the upcoming 2026 ASCO Annual Meeting and will continue to evaluate the best path for this program as the data continues to mature."

First Quarter 2026 and Recent Events

- **Data presented at the American Association for Cancer Research (AACR) Annual Meeting 2026 demonstrates significant opportunities for nuzefatide pevedotin (nuzefatide), formerly BT5528, a potentially first-in-class EphA2 targeting Bicycle® Drug Conjugate (BDC®), in EphA2 expressing cancers.**
  - Nuzefatide Phase 1/2 data show a differentiated safety profile in combination with nivolumab in metastatic urothelial cancer (mUC) patients as well as promising anti-tumor activity. As of the February 9, 2026 data cutoff, results from the Phase 1/2 trial evaluating nuzefatide 6.5mg/m^2 once every two weeks (Q2W) plus nivolumab 480mg once every four weeks (Q4W) in 14 patients with mUC who had previously progressed on a checkpoint inhibitor (10 while on enfortumab vedotin) showed:
    - 40% confirmed overall response rate (ORR) (4/10) among patients with EphA2+ tumors and 100% confirmed ORR (3/3) among patients with EphA2+ tumors that were monomethyl auristatin E (MMAE)-naïve.
    - Patients who achieved a partial response (PR) or at least 16 weeks of stable disease (SD) were on treatment for a minimum of 56 weeks and most continued on treatment at the time of the data cut-off.
    - Nuzefatide in combination with nivolumab was generally well tolerated with no Grade ≥3 treatment-related adverse events (TRAEs) of clinical interest and no TRAEs of hemorrhage observed. Only one dose-limiting toxicity of Grade 3 fatigue that lasted for five days was reported and improved to Grade 1 without dose reduction.
  - Preclinical assessment of nuzefatide anti-tumor activity in patient-derived xenograft (PDX) models of pancreatic ductal adenocarcinoma (PDAC). Expression of EphA2 was found in all 16 PDAC PDX models. Of the 14 PDAC PDX models assessed for anti-tumor activity, 10 models were sensitive to nuzefatide, six of which showed high sensitivity.
  - Preclinical assessment of nuzefatide anti-tumor activity in cell-line-derived xenograft (CDX) models of head and neck squamous cell carcinoma (HNSCC). Nuzefatide demonstrated potent preclinical anti-tumor activity in EphA2-expressing CDX models of HNSCC.

Altogether, Bicycle Therapeutics believes that these data highlight significant opportunities for nuzefatide in EphA2 expressing cancers, including pancreatic cancer.

In March 2026, Bicycle Therapeutics began enrolling a Phase 2 clinical trial to evaluate efficacy, safety, and pharmacokinetics of nuzefatide in adult patients with recurrent PDAC, and the first patient was successfully dosed in April 2026. Bicycle Therapeutics has determined 8mg/m^2 Q2W as the preferred dose for the trial.

- **Additional human imaging data of a Bicycle® Imaging Agent (BIA) targeting EphA2 in patients with PDAC presented at AACR Annual Meeting 2026.** The German Cancer Consortium (DKTK), part of a cooperative network with the German Cancer Research Center (DKFZ), presented human imaging data conducted with a Bicycle molecule targeting EphA2 labelled with gallium-68 (EphA2 BIA). Seven patients with histologically confirmed PDAC underwent PET/CT imaging up to three hours post injection of the EphA2 BIA. Data demonstrated rapid tumor uptake in six out of seven patients with excretion primarily via the kidneys. EphA2 BIA PET imaging successfully detected multiple liver, bone, lymph node, and peritoneal metastases.

These data are representative of the results seen in 15 out of 18 patients with PDAC who have undergone EphA2 BIA imaging to date. Bicycle Therapeutics believes these data validate the potential of EphA2 as a novel target in the treatment of cancer, demonstrate the translatability of preclinical data and highlight the potential of Bicycle® molecules for targeted radioligand therapies and radiopharmaceutical imaging.

- **Promising Duravelo-2 data and multiple potential regulatory pathways provide a range of options for a Phase 3 trial and potential commercialization of zelenectide pevedotin (zelenectide) in mUC.** Initial dose selection data from the Duravelo-2 trial demonstrate response rates comparable to those published for existing standards of care, with physician assessed ORR of 65%, blinded independent central review (BICR) confirmed ORR of 58% at the 27-week cutoff and a differentiated safety profile. Subsequent to the 27-week cutoff, an additional confirmed BICR response was observed, which would result in an ORR of 62%. Zelenectide at 6mg/m^2 two weeks on, one week off demonstrated a differentiated safety profile with only one patient discontinuing therapy due to a TRAE at the 27-week cutoff.

While Bicycle Therapeutics evaluates preliminary regulatory feedback from the European Medicines Agency, U.S. Food and Drug Administration (FDA), and Medicines and Healthcare products Regulatory Agency, and the potential paths for this program, the company is converting the ongoing Duravelo-2 trial to a randomized Phase 2 trial and deprioritized the program for internal development.

Bicycle Therapeutics will present initial Duravelo-2 dose selection data at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place May 29-June 2 in Chicago.

- **Strategic reprioritization focuses on promising pipeline of next-generation therapeutics.** In March 2026, Bicycle Therapeutics initiated a strategic reprioritization in order to focus its resources on its promising pipeline of next-generation therapeutics, including nuzefatide, as well as its emerging Bicycle conjugate pipeline, including BRCs. As part of the reprioritization, Bicycle Therapeutics seeks to discontinue the Phase 1/2 Duravelo-3 trial for zelenectide in NECTIN4-amplified breast cancer and the Phase 1/2 Duravelo-4 trial for zelenectide in NECTIN4-amplified non-small cell lung cancer. Enrollment for these trials is closed, and patients currently enrolled will complete their course of treatment. In addition, Bicycle Therapeutics announced a workforce reduction pursuant to which it expects to reduce its workforce by approximately 30%. Anticipated annual operational savings related to the workforce reduction and strategic reprioritization are expected to reduce annual operating expenses by approximately 50% based on the company's current plans. These actions are expected to extend Bicycle Therapeutics' cash runway by approximately two years, into 2030.

First Quarter 2026 Financial Results

- Cash and cash equivalents were $559.5 million as of March 31, 2026, compared to $628.1 million as of December 31, 2025. The decrease in cash and cash equivalents is primarily due to cash used in operations, including cash payments for clinical program activities.
- Collaboration revenue was $0.9 million for the three months ended March 31, 2026, compared to $10.0 million for the three months ended March 31, 2025. The decrease in collaboration revenue of $9.1 million was primarily due to the termination of our collaboration programs with Genentech and Novartis.
- Research and development (R&D) expenses were $48.9 million for the three months ended March 31, 2026, compared to $59.1 million for the three months ended March 31, 2025. The decrease in expense of $10.2 million was primarily due to decreased clinical program expenses for zelenectide and share-based compensation due to our workforce reduction, offset by lower U.K. R&D tax credits period over period.
- General and administrative (G&A) expenses were $17.5 million for the three months ended March 31, 2026, compared to $21.1 million for the three months ended March 31, 2025. The decrease in expense of $3.6 million was primarily due to decreased professional and consulting fees and decreased share-based compensation due to our workforce reduction.
- Net loss was $60.8 million, or $(0.87) basic and diluted net loss per share, for the three months ended March 31, 2026, compared to net loss of $60.8 million, or $(0.88) basic and diluted net loss per share, for the three months ended March 31, 2025.

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: the potential therapeutic benefit of nuzefatide pevedotin, including the reproducibility and durability of any favorable results initially seen in patients dosed to date in clinical trials, and the potential development of nuzefatide pevedotin in a number of cancers, including pancreatic cancer; the progress of Bicycle Therapeutics’ clinical trials, reporting data from Bicycle Therapeutics’ clinical trials, including for nuzefatide pevedotin, the timing of EphA2 human imaging data and updates on future clinical development plans for nuzefatide pevedotin; the potential of EphA2 as a novel cancer target and the positive properties of Bicycle® radioligand molecules for radiopharmaceutical use; the development of the Bicycle® radioligands pipeline, including BRCs and BIAs; the potential benefits of Bicycle Therapeutics’ strategic reprioritization, including the potential extension of financial runway; the workforce reduction and its impact on Bicycle Therapeutics’ expenditures; communications with and feedback from the FDA and other regulatory agencies including the potential for multiple regulatory pathways for zelenectide pevedotin in mUC; the existence of a range of options for a Phase 3 trial and potential commercialization of zelenectide pevedotin in mUC; Bicycle Therapeutics’ expected financial runway; and the use of Bicycle Therapeutics’ technology through various partnerships to develop therapies for diseases in additional therapeutic areas. 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: the workforce reduction may take longer or result in more significant charges or cash expenditures than anticipated or otherwise negatively impact Bicycle Therapeutics’ and its business plans during and after the period during which the workforce reduction is being executed; uncertainties related to the benefits of the strategic reprioritization; 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 realize the intended benefits of its technology or partnerships; 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; the risk that Bicycle Therapeutics’ projections regarding its expected cash runway are inaccurate or that its conduct of its business requires more cash than anticipated; 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’ Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 17, 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.

Bicycle Therapeutics plc
Condensed Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended March 31,	
	2026	**2025**
Collaboration revenue	$ 887	$ 9,977
Operating expenses:		
Research and development	48,901	59,058
General and administrative	17,468	21,123
Total operating expenses	66,369	80,181
Loss from operations	(65,482)	(70,204)
Other income (expense):		
Interest and other income	4,877	8,414
Interest expense	(48)	(51)
Total other income, net	4,829	8,363

Net loss before income tax provision	(60,653)	(61,841)
Provision for (benefit from) income taxes	172	(1,087)
Net loss	$ (60,825)	$ (60,764)
Net loss per share, basic and diluted	$ (0.87)	$ (0.88)
Weighted average ordinary shares outstanding, basic and diluted	69,683,471	69,196,945

Balance Sheets Data
(In thousands)
(Unaudited)

	March 31, 2026	December 31, 2025
Cash and cash equivalents	$ 559,474	$ 628,110
Working capital	570,246	625,901
Total assets	652,396	717,597
Total shareholders' equity	554,320	609,977

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