Bicycle Therapeutics Reports Recent Business Progress and Fourth Quarter and Full Year 2025 Financial Results

March 17, 2026

Phase 2/3 Duravelo-2 pivotal trial evaluating zelenectide pevedotin (zelenectide) plus pembrolizumab in metastatic urothelial cancer (mUC) successfully identifies 6mg/m^2 zelenectide two weeks on, one week off dose (6mg dose) as optimal, demonstrating response rates comparable to published rates for standards of care with a differentiated tolerability profile

Bicycle to convert Duravelo-2 to a randomized Phase 2 trial while determining appropriate next steps for the program

Strategic reprioritization to focus on BT5528 and next generation Bicycle® conjugates, including Bicycle® Radioconjugates (BRC®); additional EphA2 human imaging data and Phase 1 BT5528 combination data planned for the first half of 2026

Strategic partnerships established to enable an end-to-end isotope agnostic strategy to support the potential discovery, development and commercial supply of a portfolio of BRCs

Cash and cash equivalents of $628 million as of December 31, 2025, with expected cash runway extended into 2030 following a strategic reprioritization, including a proposed workforce reduction of approximately 30%

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Mar. 17, 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 fourth quarter and full year ended December 31, 2025, and provided recent corporate updates.

"We have successfully completed the dose selection portion of the Duravelo-2 trial and received regulatory alignment that the 6mg dose and schedule is optimal for zelenectide in mUC based on strong anti-tumor activity and its differentiated safety profile. We look forward to sharing these data at an upcoming scientific conference. Based on the regulatory feedback we have received, the existing Duravelo-2 trial design is no longer considered acceptable as an approval path for zelenectide in mUC. Preliminary discussions with regulatory agencies have outlined several potential paths for zelenectide's approval in mUC. While we believe the strength of these data and the clear medical need justify continued development of zelenectide, we have reached the difficult decision to deprioritize this program for internal development at this time. We have initiated a process to convert our ongoing Duravelo-2 trial to a randomized Phase 2 study. Once we have these randomized Phase 2 data in hand, we will determine the most appropriate path for zelenectide," said Bicycle Therapeutics CEO Kevin Lee, Ph.D. "We believe these data provide further validation of the ability of our Bicycle technology to deliver oncology therapeutics with a potentially improved benefit/risk profile compared to existing modalities. In view of this, we have decided to conduct a strategic reprioritization, which includes a proposed workforce reduction, to best position the company to focus our resources on our promising pipeline of next-generation therapeutics."

Fourth Quarter 2025 and Recent Events

- **Promising Duravelo-2 data and multiple potential regulatory pathways provide a range of options for a Phase 3 trial and potential commercialization of 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 overall response rate (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%. The 6mg dose demonstrated a differentiated safety profile with only one patient discontinuing therapy due to a treatment-related adverse event (TRAE) at the 27-week cutoff. Bicycle Therapeutics expects to present initial dose selection data from the Duravelo-2 trial at an upcoming scientific conference. 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 plans to convert the ongoing Duravelo-2 trial to a randomized Phase 2 trial and deprioritize this program for internal development at this time. Once available, data from the randomized Phase 2 trial will be shared with the scientific and medical community.
- **Strategic reprioritization focuses on promising pipeline of next-generation therapeutics.** Bicycle Therapeutics has initiated a strategic reprioritization in order to focus its resources on its promising pipeline of next-generation therapeutics, including BT5528, a potentially first-in-class EphA2 targeting Bicycle® Drug Conjugate (BDC®), as well as its emerging bicycle conjugate pipeline, including BRCs. As part of the reprioritization, Bicycle Therapeutics will seek 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. Further enrollment for these trials will be closed, and patients already enrolled will complete their course of treatment. In addition, Bicycle Therapeutics is proposing to implement a workforce reduction pursuant to which it would 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.

- **Established multiple strategic partnerships to create end-to-end supply chain to support wholly owned radiopharmaceutical pipeline.** Bicycle Therapeutics entered into a 15-year contract including an option to renew with the UK Nuclear Decommissioning Authority (NDA) for access to up to 400 tonnes of reprocessed uranium (RepU). RepU continually regenerates providing a potentially sustainable supply of ^{212}Pb. In addition, Bicycle Therapeutics announced a collaboration with United Kingdom National Nuclear Laboratory (UKNNL), pursuant to which it plans to extract ^{228}Th from the RepU obtained from NDA. The extracted ^{228}Th will then be further processed into ^{224}Ra and loaded into bespoke ^{212}Pb generators being developed exclusively for Bicycle Therapeutics by SpectronRx. Collectively, this bespoke set of arrangements is designed to support the potential discovery, development, and commercial supply of a portfolio of BRCs containing ^{212}Pb. These arrangements build on a previously announced agreement with Eckert & Ziegler to supply a range of radioisotopes for the manufacture and development of BRCs and Bicycle Imaging Agents (BIA), enabling an isotope agnostic strategy.
- **Data for an early BIA targeting MT1-MMP presented at European Association of Nuclear Medicine (EANM) 2025 Congress.** An e-poster presentation outlined the first clinical experience with an early BIA targeting MT1-MMP. An additional e-poster presented by the German Cancer Consortium (DKTK), part of a cooperative network with the German Cancer Research Center (DKFZ), highlighted preclinical BRC data demonstrating the potential of this approach for radiotheranostic use. Altogether, these data build on preclinical and first human imaging data previously disclosed at the American Association for Cancer Research (AACR) Annual Meeting 2025 and EANM 2024 Congress. Bicycle Therapeutics believes these data further support the potential of MT1-MMP as a novel target in the treatment of cancer, demonstrate the translatability of BRC preclinical data and highlight the potential of Bicycle® molecules for targeted radionuclide therapies and radiopharmaceutical imaging.

Bicycle Therapeutics continues to advance its emerging radioligand pipeline, with additional EphA2 human imaging data expected in the first half of 2026 and the initiation of the first company-sponsored radioligand clinical trial, for BT1702, an MT1-MMP targeting BRC, expected in 2027.

- **BT5528, a potential first-in-class EphA2 targeting BDC molecule.** Bicycle Therapeutics announced nuzefatide pevedotin (nuzefatide) as the International Nonproprietary Name for BT5528. Phase 1 nuzefatide combination data with nivolumab in mUC patients will be presented at a scientific conference in the first half of 2026.

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 pancreatic ductal adenocarcinoma (PDAC). Additional information regarding this indication will be presented at a scientific conference in the first half of 2026.

- **BT7480, a Bicycle tumor-targeted immune cell agonist® (Bicycle TICA®), is a Nectin-4 targeted CD137 agonist designed to overcome immune agonist toxicities and activate the immune system in Nectin-4 expressing tumors.** Phase 1 BT7480 combination data with nivolumab will be presented at a scientific conference in the first half of 2026. After reporting combination data, Bicycle Therapeutics will no longer develop BT7480 internally and intends to seek a potential partner for future development.

- **Evolving leadership team strengthens transition to next phase of innovation across oncology pipeline.** Bicycle Therapeutics has appointed Jennifer Perry, Pharm.D. as chief operating officer (COO), and Alistair Milnes as chief corporate development officer (CCDO). In her role as COO, Jennifer will oversee portfolio and new product strategy, business development, commercial and medical affairs, while in his role as CCDO, Alistair will oversee government affairs, human resources and information technology. Bicycle Therapeutics also recently promoted Travis Thompson as chief financial officer, overseeing the finance, accounting and investor relations functions and Michael Method, M.D., MPH, MBA, to chief medical officer, overseeing all clinical development and the relationship with Bicycle Therapeutics' Clinical Advisory Board. In addition, Michael Skynner, Ph.D., now serves as chief scientific officer, overseeing scientific discovery, early-stage pipeline development and the relationship with Bicycle Therapeutics' Research and Innovation Advisory Board.

Fourth Quarter and Year End 2025 Financial Results

- Cash and cash equivalents were $628.1 million as of December 31, 2025, compared to $879.5 million as of December 31, 2024. The decrease in cash and cash equivalents is primarily due to cash used in operations, including increased cash payments for clinical program activities.

- Collaboration revenue was $48.0 million for the three months ended December 31, 2025 and $72.6 million for the year ended December 31, 2025, compared to $3.7 million for the three months ended December 31, 2024 and $35.3 million for the year ended December 31, 2024. The increases in collaboration revenue of $44.3 million and $37.3 million for the three months and year ended December 31, 2025, respectively, were primarily due to the recognition of all remaining revenue under Bicycle Therapeutics' collaboration with Novartis Pharma AG upon a notice of termination of the collaboration

agreement, as well as the recognition of revenue under Bicycle Therapeutics' collaboration with Bayer Consumer Care AG upon a notice of termination of one of the target programs under the collaboration agreement.

- R&D expenses were $51.8 million for the three months ended December 31, 2025, and $240.3 million for the year ended December 31, 2025, compared to $49.8 million for the three months ended December 31, 2024, and $173.0 million for the year ended December 31, 2024. The increase in expense of $2.0 million for the three months ended December 31, 2025 was primarily due to increased discovery, platform and other expenses and lower U.K. R&D tax credits period over period, offset by decreased clinical program expenses for zelenectide development and Bicycle TICA® molecules. The increase in expense of $67.3 million for the year ended December 31, 2025 was primarily due to increased clinical program expenses for zelenectide development, discovery, platform and other expenses, higher personnel-related costs, including severance-related expenses of the workforce reduction completed in August 2025, and lower U.K. R&D tax credits period over period, offset by decreased clinical program expenses for Bicycle TICA® molecules.

- General and administrative expenses were $20.9 million for the three months ended December 31, 2025, and $79.4 million for the year ended December 31, 2025, compared to $21.6 million for the three months ended December 31, 2024, and $72.2 million for the year ended December 31, 2024. The decrease in expense of $0.7 million for the three months ended December 31, 2025 was primarily due to decreased professional and consulting fees. The increase in expense of $7.2 million for the year ended December 31, 2025 was primarily due to increased personnel-related costs including share-based payments, offset by a favorable impact of foreign exchange rates.

- Net loss was $20.2 million, or $(0.29) basic and diluted net loss per share, for the three months ended December 31, 2025, and net loss was $219.0 million, or $(3.16) basic and diluted net loss per share, for the year ended December 31, 2025, compared to net loss of $51.9 million, or $(0.75) basic and diluted net loss per share, for the three months ended December 31, 2024, and net loss was $169.0 million, or $(2.90) basic and diluted net loss per share, for the year ended December 31, 2024.

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' efforts to identify partners to help advance its product candidates, such as BT7480; the potential benefits of Bicycle Therapeutics' strategic reprioritization, including the potential extension of financial runway; the proposed workforce reduction and its impact on Bicycle Therapeutics' expenditures; Bicycle Therapeutics' expectations with respect to the benefits of its agreements and collaborations with the NDA, UKNNL and SpectronRx, respectively; Bicycle Therapeutics' ability to leverage its agreements with NDA and SpectronRx and collaboration with UKNNL to support the potential discovery, development and commercial supply of a portfolio of BRCs containing ^{212}Pb; the initiation of new clinical trials, including for BT1702, an MT1-MMP targeting BRC, the progress of Bicycle Therapeutics' clinical trials, reporting data from Bicycle Therapeutics' clinical trials, including for BT5528 and BT7480, the timing of EphA2 human imaging data and updates on future clinical development plans for BT5528 and approval pathway; the development of the Bicycle® radioligands pipeline, including BRCs and BIAs; the validation of MT1-MMP as a cancer target and BRC molecules having positive properties for radiopharmaceutical imaging; 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 proposed 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 proposed 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' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on October 30, 2025, 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 December 31,		Year Ended December 31,	
	2025	2024	2025	2024
Collaboration revenue	$ 47,955	$ 3,708	$ 72,586	$ 35,275
Operating expenses:				
Research and development	51,770	49,778	240,283	172,966
General and administrative	20,893	21,593	79,368	72,181
Total operating expenses	72,663	71,371	319,651	245,147
Loss from operations	(24,708)	(67,663)	(247,065)	(209,872)
Other income (expense):				
Interest and other income	5,876	10,303	28,463	34,284
Interest expense	(57)	(52)	(206)	(1,730)
Loss on extinguishment of debt	—	—	—	(954)
Gain on extinguishment of research and development funding liability	—	4,476	—	4,476
Total other income, net	5,819	14,727	28,257	36,076
Net loss before income tax provision	(18,889)	(52,936)	(218,808)	(173,796)
Provision for (benefit from) income taxes	1,265	(1,082)	152	(4,765)
Net loss	$ (20,154)	$ (51,854)	$ (218,960)	$ (169,031)
Net loss per share, basic and diluted	$ (0.29)	$ (0.75)	$ (3.16)	$ (2.90)
Weighted average ordinary shares outstanding, basic and diluted	69,364,546	69,051,745	69,279,838	58,207,593

Balance Sheets Data
(In thousands)
(Unaudited)

	December 31, 2025	December 31, 2024
Cash and cash equivalents	$ 628,110	$ 879,520
Working capital	625,901	861,375
Total assets	717,597	956,868
Total shareholders' equity	609,977	793,060

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