Bicycle Therapeutics Reports Recent Business Progress and Third Quarter 2025 Financial Results

October 30, 2025

Dose selection from Phase 2/3 Duravelo-2 trial and update on potential approval pathway expected in 1Q 2026 as company seeks feedback from multiple regulatory agencies

Enhanced clinical leadership team with appointments to Board of Directors and Research and Innovation Advisory Board

Cash and cash equivalents of $648.3 million as of September 30, 2025, excluding $38.2 million U.K. R&D tax credit received in October 2025; expected financial runway into 2028

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Oct. 30, 2025-- 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 third quarter ended September 30, 2025, and provided recent corporate updates.

"We are currently seeking broad regulatory feedback to make an informed decision on our path forward with zelenectide pevedotin in metastatic urothelial cancer. We look forward to providing updates in the first quarter of 2026," said Bicycle Therapeutics CEO Kevin Lee, Ph.D. "We have also been executing across the rest of our pipeline with the goal of helping patients live longer and live well. The development of zelenectide pevedotin for multiple Nectin-4 associated cancers is ongoing, with the Phase 1/2 Duravelo-3 trial for NECTIN4-amplified breast cancer and the Phase 1/2 Duravelo-4 trial for NECTIN4-amplified non-small cell lung cancer open and actively enrolling. Additionally, we were pleased to welcome additional esteemed global oncology leaders to the Bicycle Board of Directors and to our Research and Innovation Advisory Board to further strengthen our innovation and strategic growth."

Third Quarter 2025 and Recent Events

- **Phase 2/3 Duravelo-2 pivotal trial evaluating zelenectide pevedotin in combination with pembrolizumab in patients with metastatic urothelial cancer (mUC).** Bicycle Therapeutics is currently seeking regulatory feedback on zelenectide pevedotin, a Bicycle® Drug Conjugate (BDC®). The company now expects to provide an update on dose selection for Duravelo-2 and zelenectide pevedotin's potential approval pathway in mUC following meetings with multiple regulatory agencies in the first quarter of 2026.

- **Data for an early Bicycle® Radioconjugate (BRC®) molecule 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 Bicycle Imaging Agent (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, the 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. The company believes this data further supports the potential of MT1-MMP as a novel target in the treatment of cancer, demonstrates the translatability of BRC preclinical data and highlights the potential of Bicycle® molecules for targeted radionuclide therapies and radiopharmaceutical imaging.

  The company continues to advance its emerging BRC pipeline, with initial EphA2 human imaging data expected in the first half of 2026 and the initiation of the first company-sponsored clinical trial expected in 2026.

- **Trial in Progress data for Phase 1/2 Duravelo-3 trial for zelenectide pevedotin in NECTIN4-amplified breast cancer and tissue sample data in patients with NECTIN4-amplified non-small cell lung cancer (NSCLC) presented at the European Society for Medical Oncology (ESMO) Congress 2025.** The Phase 1/2 Duravelo-3 trial for zelenectide pevedotin in NECTIN4-amplified breast cancer and the Phase 1/2 Duravelo-4 trial for zelenectide pevedotin in NECTIN4-amplified NSCLC are open and actively enrolling. Data from post-hoc analyses of late-line breast cancer and lung cancer patients enrolled in Duravelo-1 showed enhanced anti-tumor activity of zelenectide pevedotin in patients with NECTIN4 amplification and/or polysomy. Based on these data, the U.S. Food and Drug Administration (FDA) previously granted Fast Track designation to zelenectide pevedotin for the treatment of adult patients with previously treated, NECTIN4-amplified, advanced or metastatic triple-negative breast cancer and NSCLC.

- **BT5528, a potential first-in-class EphA2 targeting BDC molecule.** Phase 1 BT5528 combination data with nivolumab in mUC patients will now 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 now be presented at scientific conference in the first half of 2026.

- **Strengthened Board of Directors with the addition of Charles Swanton, M.D., Ph.D., FRS, FMedSci, FRCP, Roger Dansey, M.D. and Hervé Hoppenot.** Dr. Swanton leads the Cancer Evolution and Genome Instability Laboratory at the Francis Crick Institute. Dr. Dansey currently serves on the Boards of Directors of Inovio Inc. and Ottimo Pharma. Mr. Hoppenot is an advisor to the CEO and serves on the Board of Directors of Incyte, after serving 11 years as its chairman and CEO. He is also Chairman of the Board of Directors of Maze Therapeutics.

- **Expanded Research and Innovation Advisory Board (RAB) with the appointment of additional esteemed global leaders in oncology to further support scientific advancement and strategic growth across the company's discovery research programs.** The new RAB members are as follows:

    - **Steve Davidsen, Ph.D.,** is a biotech executive with over 35 years of experience in drug discovery and development. Dr. Davidsen currently serves as the founder and president of Predawn Discovery Advisors LLC, providing technical and strategic input to organizations engaged in therapeutic drug discovery. He also serves on the Scientific Advisory Boards of Nitrase Therapeutics and BioLoomics. Previously, Dr. Davidsen served as vice president, oncology discovery research at AbbVie, where he was responsible for discovery efforts across all of AbbVie's oncology programs and sites. He held various positions of increasing responsibility at Abbott prior to the separation of AbbVie. Dr. Davidsen has directed research teams and partnerships leading to more than 40 first-in-human clinical trials across a broad range of platforms and biology targeting both hematologic and solid tumor indications. He has more than 70 scientific publications across a diverse range of topics including metalloproteinase inhibitors, kinase inhibitors and the discovery of histone deacetylase inhibitors. Dr. Davidsen earned a Ph.D. in organic chemistry from the University of Texas at Austin and a B.S. in chemistry from the University of Maryland.

    - **Gilles Gallant, B.Pharm, Ph.D., FOPQ,** is an advisor and a consultant to biotechnology and pharmaceutical companies developing oncology drugs. He recently served as chief development officer at Mythic Therapeutics, responsible for the strategy, direction and execution of the company's clinical development program. He also serves as a scientific advisor for Iteru Systems and is the founder and principal consultant of GG Biotech Consulting LLC. Previously, Dr. Gallant was senior vice president, global head of oncology clinical development at Daiichi Sankyo, leading the development of the company's global oncology portfolio. At Daiichi, he led the clinical development and global approval of the antibody-drug conjugate (ADC) Enhertu® (fam-trastuzumab deruxtecan-nxki) for the treatment of advanced breast cancer, gastric cancer and non-small cell lung cancer. Dr. Gallant also held leadership roles of increasing responsibility at Bristol-Myers-Squibb, Human Genome Sciences and BioMarin. Dr. Gallant earned a Ph.D. in medicinal chemistry and a B.Pharm from the Université de Montréal and is a Fellow of the Order of Pharmacists of Québec.

    - **Ken Herrmann, M.D., MBA,** is a well-known leader in oncologic nuclear medicine with more than a decade of experience in clinical investigation. He currently serves on the Board of Directors of Aktis Oncology and as the chair of Aktis' Scientific Advisory Board. Dr. Herrmann also serves as chair of the Department of Nuclear Medicine at the Universitätsklinikum Essen in Germany, member of Pentixapharm Holding AG's Supervisory Board and associate editor of the Journal of Nuclear Medicine. Previously, he served as chair of the European Associates of Nuclear Medicine Oncology & Theranostics Committee, vice chair of the Department of Nuclear Medicine at the Universitätsklinikum Würzburg and associate professor in the Ahmanson Translational Imaging Division at the University of California, Los Angeles. To date, he has authored more than 700 peer-reviewed publications. Dr. Herrmann earned his M.D. from Humboldt Universität Berlin and his MBA from the Universität Zurich.

    - **John Lambert, Ph.D.,** is a recognized global leader in ADC discovery and development, currently serving as a consultant/advisor to biopharma and pharma on ADC technologies. He serves on the Avipep Therapeutics Board of Directors and is a scientific advisor to Cureteq AG, Synaffix BV, CytomX Therapeutics and Mythic Therapeutics, among other companies. Previously, Dr. Lambert was chief scientific officer and executive vice president of research at ImmunoGen. During his tenure in leadership roles there, ImmunoGen invented the ADC technology that resulted in Kadcyla® (ado-trastuzumab emtansine) and Elahere® (mirvetuximab soravtansine-gynx) for the treatment of HER2+ breast cancer and platinum-resistant ovarian cancers, respectively. He is a fellow of the American Institute for Medical and Biological Engineering and an honorary professor at Queen's University Belfast. Dr. Lambert earned a Ph.D. in biochemistry from the University of Cambridge.

Participation in Upcoming Investor Conference

Bicycle Therapeutics management will participate in the following investor conference in November:

- Jefferies Global Healthcare Conference in London on Tuesday, Nov. 18; fireside chat at 10:30 a.m. GMT

A live webcast of the fireside chat will be accessible in the Investor section of the company's website at www.bicycletherapeutics.com. An archived replay of the webcast will be available following the event.

Third Quarter 2025 Financial Results

- Cash and cash equivalents were $648.3 million as of September 30, 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. In October 2025, we received $38.2 million related to our U.K. research and development (R&D) tax credit claim for the year ended December 31, 2024.

- R&D expenses were $58.4 million for the three months ended September 30, 2025, compared to $48.3 million for the three months ended September 30, 2024. The increase in expense of $10.1 million was primarily due to increased clinical program expenses for zelenectide pevedotin development, discovery, platform and other expenses, and higher personnel-related costs, including severance-related expenses of our workforce reduction in August 2025, offset by decreased clinical program expenses for Bicycle TICA® molecules.

- General and administrative expenses were $18.9 million for the three months ended September 30, 2025, compared to $18.3 million for the three months ended September 30, 2024. The increase in expense of $0.6 million was primarily due to increased personnel-related costs, offset by decreased professional and consulting fees.

- Net loss was $59.1 million, or $(0.85) basic and diluted net loss per share, for the three months ended September 30, 2025, compared to net loss of $50.8 million, or $(0.74) basic and diluted net loss per share, for three months ended September 30, 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 zelenectide pevedotin (formerly BT8009), a Bicycle® Drug Conjugate (BDC®) targeting Nectin-4, a well-validated tumor antigen; BT5528, a BDC molecule targeting EphA2, a historically undruggable target; and BT7480, a Bicycle Tumor-Targeted Immune Cell Agonist® (Bicycle TICA®) targeting Nectin-4 and agonizing CD137, in company-sponsored clinical trials. Additionally, the company is developing Bicycle® Radioconjugates (BRC®) for radiopharmaceutical use and, through various partnerships, is exploring the use of Bicycle® technology to develop therapies for diseases beyond oncology.

Bicycle Therapeutics is headquartered in Cambridge, UK, with many key functions and members of its leadership team located in Cambridge, 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 initiation of new clinical trials, the progress of Bicycle's clinical trials, reporting data from Bicycle's clinical trials, including for BT5528 and BT7480, the timing of EphA2 human imaging data and updates on dose selection in the Duravelo-2 clinical trial and accelerated approval pathway; 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; Bicycle's expected financial runway; and the use of Bicycle Therapeutics' technology through various partnerships to develop therapies for diseases beyond oncology. 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 realize the intended benefits of its cost realignment efforts; the risk that Bicycle's 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-Q filed with the Securities and Exchange Commission (SEC) on August 8, 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 September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Collaboration revenue	$ 11,734	$ 2,676	$ 24,631	$ 31,567
Operating expenses:				
Research and development	58,426	48,265	188,513	123,188
General and administrative	18,859	18,257	58,475	50,588
Total operating expenses	77,285	66,522	246,988	173,776
Loss from operations	(65,551)	(63,846)	(222,357)	(142,209)
Other income (expense):				
Interest and other income	6,700	10,583	22,587	23,981
Interest expense	(44)	(33)	(149)	(1,678)
Loss on extinguishment of debt	—	(954)	—	(954)
Total other income, net	6,656	9,596	22,438	21,349
Net loss before income tax provision	(58,895)	(54,250)	(199,919)	(120,860)
Provision for (benefit from) income taxes	205	(3,448)	(1,113)	(3,683)
Net loss	$ (59,100)	$ (50,802)	$ (198,806)	$ (117,177)
Net loss per share, basic and diluted	$ (0.85)	$ (0.74)	$ (2.87)	$ (2.15)
Weighted average ordinary shares outstanding, basic and diluted	69,303,746	68,988,858	69,251,291	54,566,490

Balance Sheets Data
(In thousands)
(Unaudited)

	September 30, 2025	December 31, 2024
Cash and cash equivalents	$ 648,325	$ 879,520
Working capital	669,537	861,375
Total assets	763,954	956,868
Total shareholders' equity	618,479	793,060

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