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

August 8, 2025

Continued advancement across research and development pipeline, with key program updates expected in 2H 2025

Phase 1/2 Duravelo-4 trial for zelenectide pevedotin in NECTIN4-amplified non-small cell lung cancer open and actively recruiting patients

Strengthened clinical leadership and bolstered roster of scientific advisors with additions to Board of Directors and creation of Research and Innovation Advisory Board

Strategic cost realignment of approximately 30%, primarily through a workforce reduction

Cash and cash equivalents of $721.5 million as of June 30, 2025, with expected financial runway extended into 2028

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Aug. 8, 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 second quarter ended June 30, 2025, and provided recent corporate updates.

"We continue to execute on our strategy, which is grounded in scientific rigor and focused on fulfilling our mission to develop next-generation precision-guided therapeutics that have the potential to help patients live longer and live well," said Bicycle Therapeutics CEO Kevin Lee, Ph.D. "We are energized by the progress we are making across our pipeline, and with this momentum, we are pleased to welcome our new Research and Innovation Advisory Board members, as well as new Board member Charles Swanton, to further our innovation and strategic growth."

Dr. Lee continued: "As we advance our various pipeline programs that hold strong potential for changing the treatment paradigm for patients with cancer and creating value for shareholders, Bicycle remains committed to disciplined capital allocation. Today we announced organizational streamlining efforts that provide us with operational flexibility to deliver potentially value-generating datasets while strengthening our financial position in uncertain market conditions. Saying goodbye to talented team members is very difficult, and we sincerely thank them for their dedication to our company. We believe Bicycle is strongly positioned to realize our strategic priorities and milestones and look forward to providing key program updates over the second half of this year."

Second Quarter 2025 and Recent Events

- **Presented additional human imaging data for an early Bicycle Radioconjugate® (BRC®) molecule targeting MT1-MMP at the American Association for Cancer Research (AACR) Annual Meeting 2025.** A poster presentation included new data from a second patient who underwent MT1-MMP-PET/CT imaging that build on previously announced data. Altogether, the data continue to validate the potential of MT1-MMP as a novel cancer target and demonstrate the positive properties of BRC molecules for radiopharmaceutical imaging. Imaging data from these two patients are representative of the data generated to date in 12 out of 14 patients with various solid tumors.

  Bicycle Therapeutics continues to advance its emerging BRC pipeline, with initial EphA2 human imaging data expected in 2H 2025 and company-sponsored clinical trials planned for 2026.

- **Presented two abstracts highlighting the development of Bicycle® Drug Conjugate (BDC®) zelenectide pevedotin for metastatic urothelial cancer (mUC) at the 2025 American Society for Clinical Oncology (ASCO) Annual Meeting.** The abstracts outlined previously disclosed topline combination data for zelenectide pevedotin plus pembrolizumab in first-line mUC from the Phase 1/2 Duravelo-1 trial and provided an overview of the ongoing Phase 2/3 Duravelo-2 registrational trial for zelenectide pevedotin in mUC.

  Bicycle Therapeutics is on track to provide an update on dose selection from the Duravelo-2 trial and the accelerated approval pathway for zelenectide pevedotin in mUC following a meeting with the U.S. Food and Drug Administration planned for 4Q 2025.

- **Phase 1/2 Duravelo-4 trial for zelenectide pevedotin in NECTIN4-amplified non-small cell lung cancer (NSCLC) open and actively recruiting patients.** Duravelo-4 is Bicycle Therapeutics' second trial to leverage NECTIN4 gene amplification as a biomarker for patient selection and to expand the development of zelenectide pevedotin for additional solid tumors.

  With several trials underway assessing the potential for zelenectide pevedotin to treat mUC, breast cancer and lung cancer, the company has decided to pause the previously announced Phase 1/2 Duravelo-5 trial in multiple tumors.

- **Expanded Board of Directors with the addition of Charles Swanton, M.D., Ph.D., FRS, FMedSci, FRCP,** current chair of Bicycle Therapeutics' Clinical Advisory Board. Dr. Swanton leads the Cancer Evolution and Genome Instability Laboratory at the Francis Crick Institute. His research focuses on how tumors evolve over space and time, developing an understanding of branching evolutionary histories of solid tumors, processes that drive cancer cell-to-cell variation and the impact of cancer diversity on effective immune surveillance and clinical outcomes. Dr. Swanton is a fellow of the Royal Society, a fellow of the Royal College of Physicians and a fellow of the Academy of Medical Sciences. He completed his M.D. and Ph.D. training at the Imperial Cancer Research Fund Laboratories.

- **Formed Research and Innovation Advisory Board (RAB) to support scientific advancement and strategic growth across preclinical programs**. The RAB replaces Bicycle's Scientific Advisory Board. Inaugural RAB members include:

    - **Jose-Carlos Gutierrez-Ramos, Ph.D.,** is a director on the Bicycle Therapeutics Board of Directors. He also serves as the chief science officer at Danaher Corporation, leading the Danaher Innovation Centers and the Danaher Scientific Advisory Board. Previously, Dr. Gutierrez-Ramos was head of global drug discovery at AbbVie Inc., group senior vice president of biotherapeutics research and development (R&D) at Pfizer Inc., and senior vice president and CEDD head of immuno-inflammation at GlaxoSmithKline plc. He was also the founding CEO and president of Repertoire Immune Medicine, where he built and led a team focused on decoding the human immunome. Prior to that, he served as president and CEO of Synlogic, Inc. Dr. Gutierrez-Ramos earned a Ph.D. from the immunology department of the Center for Molecular Biology at the Universidad Autonoma de Madrid, and a B.S., *summa cum laude*, in chemistry with a minor in biochemistry from the Universidad Complutense de Madrid.
    - **Jason Lewis, Ph.D.,** is the Emily Tow Chair at Memorial Sloan Kettering Cancer Center (MSKCC) and currently serves as the deputy director at the Sloan Kettering Institute, overseeing the Office of Scientific Education and Training. He is also the scientific director of the Radiochemistry and Molecular Imaging Probe Core Facility at MSKCC. Dr. Lewis is a laboratory head in Sloan-Kettering Institute's molecular pharmacology program and serves as a professor at the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences and at Weill-Cornell Medical College. He earned a Ph.D. in biochemistry from the University of Kent and an M.S. and B.S. in chemistry from the University of Essex.
    - **Robert Lutz, Ph.D.,** is a consultant/advisor to biotech and pharma with more than 30 years of experience with a significant focus on the development of antibody-drug conjugates (ADCs). He currently serves as chief scientific officer of Iksuda Therapeutics and is a board member and chief development officer of Synthis Therapeutics. Prior to his consulting practice, Dr. Lutz was vice president of translational research and development at ImmunoGen, where he was responsible for the advancement of multiple ADC programs, including KADCYLA® (ado-trastuzumab emtansine), the first ADC to be approved for solid tumor indications, and ELAHERE® (mirvetuximab soravtansine). He earned a Ph.D. in biochemistry from Brandeis University and a B.S. in biochemistry from the University of New Hampshire.
    - **Michael Hofman, MBBS, FRACP, FAANMS, FICIS, GAICD,** is a nuclear medicine physician and professor at the Sir Peter MacCallum Department of Oncology at the University of Melbourne in Australia. His research has been instrumental in advancing PSMA PET imaging and PSMA radioligand therapy, helping to revolutionize the diagnosis and treatment of prostate cancer. He was named Australia's top researcher in nuclear medicine, radiotherapy and molecular imaging in both 2024 and 2025. Professor Hofman leads the PET/CT program and the Prostate Cancer Theranostics and Imaging Centre of Excellence at Peter MacCallum Cancer Centre. He earned a degree in medicine and surgery from Monash University in Australia and undertook a PET/CT fellowship at St. Thomas' Hospital in London.

- **Welcomed Michael Method, M.D., as senior vice president of clinical development.** Dr. Method is an academic and clinical gynecologic oncologist with extensive drug development experience. He most recently served as a senior vice president of clinical development at Karyopharm Therapeutics, Inc., after his time as an executive medical director at ImmunoGen, Inc. where he led global clinical development for gynecologic and female malignancies. Previously, Dr. Method was a senior medical advisor for global medical affairs at Eli Lilly, focused on breast cancer. He earned his M.D. and MPH from Northwestern University, and his B.S. in biochemistry and MBA from the University of Notre Dame.

Participation in Upcoming Investor Conferences

Bicycle Therapeutics management will participate in the following investor conferences in September:

- Cantor Global Healthcare Conference on Thursday, Sept. 4; fireside chat at 3:55 p.m. ET
- Morgan Stanley 23rd Annual Global Healthcare Conference on Tuesday, Sept. 9; fireside chat at 7:45 a.m. ET

Live webcasts of the fireside chats will be accessible in the Investor section of the company's website at www.bicycletherapeutics.com. Archived replays of the webcasts will be available following the fireside chat dates.

Second Quarter 2025 Financial Results

- Cash and cash equivalents were $721.5 million as of June 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.
- R&D expenses were $71.0 million for the three months ended June 30, 2025, compared to $40.1 million for the three months ended June 30, 2024. The increase in expense of $30.9 million was primarily due to increased clinical program expenses for zelenectide pevedotin development, increased discovery, platform and other expenses, and increased personnel-related costs, offset by decreased clinical program expenses for Bicycle Tumor-Targeted Immune Cell Agonist® (Bicycle TICA®) molecules as well as higher U.K. R&D tax credits period over period.
- General and administrative expenses were $18.5 million for the three months ended June 30, 2025, compared to $15.9 million for the three months ended June 30, 2024. The increase in expense of $2.6 million was primarily due to increased personnel-related costs, as well as increased professional and consulting fees.
- Net loss was $79.0 million, or $(1.14) basic and diluted net loss per share, for the three months ended June 30, 2025, compared to net loss of $39.8 million, or $(0.77) basic and diluted net loss per share, for three months ended June 30, 2024.

In recognition of the evolving macroeconomic environment and the importance of preserving capital, Bicycle Therapeutics is implementing a workforce reduction and taking other steps to optimize its operations and extend the company's expected financial runway. These strategic cost realignment efforts are being implemented to prioritize potentially high-impact, value-generating programs, which include the advancement of zelenectide pevedotin, BT5528, next-generation Bicycle® Drug Conjugates and the company's wholly owned pipeline of Bicycle ® Radioconjugates. Bicycle Therapeutics anticipates total operational savings of approximately 30% over the course of the financial runway period. These actions are expected to extend the financial runway into 2028 and strengthen the company's ability to weather continued market uncertainty as it advances clinical programs through key milestones.

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 validation of MT1-MMP as a cancer target and BRC molecules having positive properties for radiopharmaceutical imaging; the initiation of new clinical trials, the progress of Bicycle's ongoing clinical trials and the timing of EphA2 human imaging data and updates on dose selection in the Duravelo-2 clinical trial and accelerated approval pathway; the outcome of Bicycle's strategic cost realignment efforts and 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 May 1, 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 June 30,	Six Months Ended June 30,

	2025	2024	2025	2024
Collaboration revenue	$ 2,920	$ 9,361	$ 12,897	$ 28,891
Operating expenses:				
Research and development	71,029	40,059	130,087	74,923
General and administrative	18,493	15,949	39,616	32,331
Total operating expenses	89,522	56,008	169,703	107,254
Loss from operations	(86,602)	(46,647)	(156,806)	(78,363)
Other income (expense):				
Interest and other income	7,473	7,774	15,887	13,398
Interest expense	(54)	(824)	(105)	(1,645)
Total other income, net	7,419	6,950	15,782	11,753
Net loss before income tax provision	(79,183)	(39,697)	(141,024)	(66,610)
(Benefit from) provision for income taxes	(231)	115	(1,318)	(235)
Net loss	$ (78,952)	$ (39,812)	$ (139,706)	$ (66,375)
Net loss per share, basic and diluted	$ (1.14)	$ (0.77)	$ (2.02)	$ (1.40)
Weighted average ordinary shares outstanding, basic and diluted	69,252,009	51,992,034	69,224,629	47,276,062

Balance Sheets Data
(In thousands)
(Unaudited)

	June 30, 2025	December 31, 2024
Cash and cash equivalents	$ 721,451	$ 879,520
Working capital	726,840	861,375
Total assets	832,184	956,868
Total shareholders' equity	668,915	793,060

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