Bicycle Therapeutics Announces First Patient Dosed in Expansion Cohorts of Phase I/II Trial of Bicycle® Toxin Conjugate BT5528 in Patients with Advanced Solid Tumors Associated with EphA2 Expression

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Completed Phase I dose escalation; results expected in 3Q22

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Jun. 8, 2022-- Bicycle Therapeutics plc (NASDAQ: BCYC), a biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*®) technology, today announced the first patient has been dosed in the expansion portion of the Phase I/II study of BT5528, Bicycle's second-generation Bicycle Toxin Conjugate (BTC™) targeting EphA2.

"We believe EphA2 is an attractive target for cytotoxin delivery and BT5528 has the potential to overcome the significant safety concerns seen with an antibody drug conjugate (ADC) approach to targeting EphA2," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "We are pleased with the molecule's emerging safety profile and early signs of anti-tumor activity and look forward to providing additional data from the completed Part A portion of the Phase I/II trial next quarter."

The Phase I/II multi-center, open-label trial comprises two parts: Part A, dose escalation and Part B, dose expansion. While Part A of the trial was designed to assess safety, pharmacokinetics and establish a Phase II dose, the dose expansion portion of the trial is primarily designed to assess the clinical activity of BT5528 at the recommended Phase II dose of 6.5mg/m^2 every other week that was established in Part A. Up to 56 patients will be enrolled in the initial expansion cohorts, with the ability to further expand enrollment based on the results of the initial expansion cohorts. Dose expansion in urothelial and ovarian cancers will take place as the Company seeks to build on interim response data previously reported, as well as in a basket cohort of other solid tumors, including non-small cell lung cancer, triple-negative breast cancer, head and neck, and esophageal cancer.

About Bicycle Therapeutics

Bicycle Therapeutics (NASDAQ: BCYC) is a clinical-stage biopharmaceutical company developing a novel class of medicines, referred to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* 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 *Bicycles* attractive candidates for drug development. Bicycle is evaluating BT5528, a second-generation *Bicycle* Toxin Conjugate (BTC™) targeting EphA2; BT8009, a second-generation BTC targeting Nectin-4, a well-validated tumor antigen; and BT7480, a *Bicycle* TICA™ targeting Nectin-4 and agonizing CD137, in company-sponsored Phase I/II trials. In addition, BT1718, a BTC that targets MT1-MMP, is being investigated in an ongoing Phase I/IIa clinical trial sponsored by the Cancer Research UK Centre for Drug Development. Bicycle is headquartered in Cambridge, UK, with many key functions and members of its leadership team located in Lexington, Massachusetts. 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 clinical development of BT5528 or any of Bicycle's other product candidates or programs; the expected design and anticipated progression of and data readouts from Bicycle's clinical trial of BT5528; the safety, tolerability or efficacy of BT5528; and the potential benefits of BT5528 or any of Bicycle's other product candidates. Bicycle 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: risks to site initiation, clinical trial commencement, patient enrollment and follow-up, as well as to Bicycle's abilities to meet other anticipated deadlines and milestones, presented by the ongoing COVID-19 pandemic; uncertainties inherent in the completion of clinical trials and clinical development of Bicycle's product candidates; availability and timing of results from clinical trials; whether initial or interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; the risk that trials and studies may be delayed and may not have satisfactory outcomes; expectations for regulatory approvals to conduct trials or to market product; and other important factors, any of which could cause Bicycle's 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's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 5, 2022, as well as in other filings Bicycle 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 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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